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ABSTRACTS

Acute Lymphoblastic Leukemia

Poster No: 001 Abstract:0086

EVALUATION OF FEBRILE NEUTROPENIC EPISODES IN ACUTE MYELOID LEUKEMIA PATIENTS (SINGLE CENTER)

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Introduction: The most important cause of mortality in febrile neutropenic episodes (FNEs) which mature after chemotherapy is infections. Therefore fewer in neutropenic patients must be accepted as an infection until the contrary is proved and broad-spectrum empric antibiotherapy must be started immediately as a standard approach.

Patients and Methods**:** Two hundred and thirty-six febrile neutropenic episodes of 87 patients who have been treated because of acute myeloid leukemia in İnönü University Turgut Özal Medicine Center Adult Hematology Clinic between 2002 and 2010 was evaluated. The infection categories, isolated pathogen microorganisms, mortality ratios and antibiotherapy regimens in 236 febril neutropenic episodes which mature after chemotherapy were examined retrospectively in this study.

Results: Fifty-three (61.0%) of the patients were males and 34 (39.0%) were females. The median age of the patients was 52.4. The median follow-up period was 9.5 months. In FNEs, fewer was evaluated as microbiologic defined infection (MDI) in 73 (30.9%) episodes, as clinical defined infection (CDI) in 95 (40.3%) episodes and as fewer of unknown origin (FUO) in 68 (28.8%) episodes. In forty-seven (19.9%) episodes efficient pathogen microorganism was isolated from blood cultures. 91.5% of the pathogens which isolated from blood cultures were bacteries and 8.5% was fungal agents. 55.8% of the pathogen bacteries were gram-positive and 44.2% were gram-negative. The predominant isolated gram-positive bacteria was KNS, gram-negative bacteria was E. coli. Pneumonia was the most clinical infection seen in CDI. The mean neutropenia duration was 13.3 days in all episodes, 16.7 days in MDI, 13.1 days in CDI and 10.0 days in FUO. The mortality rate was 8.5% in all episodes, 9.6% in MDI, 11.6% in CDI and 2.9% in FUO. The mean neutropenia duration in exitus patients were 21.6 days and 12.6 days in living patients. This difference was statistically significant.

Conclusion**:** Prolonged fever and neutropenia was more often accompanied with MDI and the lenght of the duration of neutropenia was found to be a risk factor for mortality in this study. For a better febrile neutropenia management process, medical centers must follow their infection agents closely and modify their empiric antibiotic treatment policies.

Keyword: Acute meyeloid leukemia, febrile neutropenia

Poster No: 002 Abstract:0110

MRD-VALUES IN PEDIATRIC B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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Studies of minimal residual disease (MRD) have a powerful clinical application in the management of acute leukemia patients. Detection of MRD with flow cytometric methods (FCM) is faster and cheaper when compared to molecular methods and it is the main reason for utilization in many centers. According to AIEOP-BFM (Associazione Italiana Ematologia Oncologia Pediatrica - AIEOP and Berlin-Frankfurt-Münster - BFM) protocol, evaluation of MRD with FCM is related to comparison of expression levels of major antigens at different time points of remission induction therapy of B cell precursor Acute Lymphoblastic Leukemia (ALL). Leukemic cells were identified using an immunological gate based on CD19 expression associated with a physical parameter (SSC) and they were discriminated from normal B lymphocytes on the basis of leukemia associated immunophenotypes (i.e. over expression of antigens such as CD10, CD34, CD58 and/or under expression of CD45 and CD11a).

We investigated paired samples from diagnosis and early follow up (day 15) from 139 consecutive B-cell precursor ALL cases for the expression levels of seven antigens, highly relevant for MRD studies, on leukemic cells. Nucleated cell counts were determined by Syto16 staining and blast counts among nucleated CD19+ B cells lower than 0.1% was determined as low risk (FLR), between 0.1% - 10% was termed as medium risk (FMR) and over 10% was determined as high risk (FHR). Of the 139 cases (54 female, 85 male, mean age: 6.67 ± 4.67 years), 19 cases were diagnosed as MRD negative (13.71%) whereas 120 cases were diagnosed as MRD positive (86.3%). According to MRD risks, diagnosis of 47 cases were FLR (33.8%), 73 cases were FMR (52.5%) and 19 cases were FHR (13.7%). When groups were compared, there was no statistical significance between ages of male (6.97 ± 4.52 years) and female (6.20 ± 4.90 years) cases (p=0.153); between FLR (7.04 ± 4.77 years), FMR (6.61 ± 4.64 years) and FHR (6.62 ± 4.76 years) cases (p=0.883); between FLR negative (6.29 ± 5.42 years) and positive (6.85 ± 4.34 years) cases (p=0.340); and between MRD negative (6.29 ± 5.42 years) and positive (6.73 ± 4.56 years) cases (p=0.369).

These are the findings of the first center in Turkey who received certificate of proficiency from AIEOP-BFM partner in August, 2011 and can evaluate its own cases. Further studies, to investigate relationship between prognosis and survival or correlation of PCR and MRD findings in more detailed studies with contribution of clinics will be more helpful to apply sensitive and accuracy therapy in B-ALL patients.

Keyword: MRD, flow cytometry

Poster No: 003 Abstract:0118

OVEREXPRESSION OF LYN CONTRIBUTES TO PROLIFERATION IN ALL

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The Src family kinases (SFKs) are important intracellular tyrosine kinase signaling mediators that transmit signals from cell surface receptors and are involved in diverse physiological processes as well as many human malignancies. The SFK, Lyn, Blk and Fyn are known to play a critical role in B-cell development upon B-cell receptor (BCR) crosslinking by inducing phosphorylation of many different downstream targets thereby promoting cell growth and differentiation (Fig. 1).

Objective: Quantification and analysis of the protein tyrosine kinase (PTKs) expression in childhood acute lymphoblastic leukemia (ALL) and ALL cell lines and functional assessment of their potential role in leukemogenesis.

Method: Whole cellular lysate from bone marrow (BM) or peripheral blood (PBL) from primary ALL patients and ALL cell lines were analyzed. Detection of the expression and phosphorylation state of PTKs at the protein level was performed by Western Blot. Modulation of the BCR signalling network by using shRNA mediated repression of the predominant PTK Lyn, in the Nalm6 cell line was carried out. Analysis of cell proliferation and apoptosis was monitored by MTT assay and Anexin V/PI staining, respectively.

Results: TK expression in ALL patient samples is characterized by a high degree of heterogeneity and does not correlate with the immunophenotype of ALL. However, unsupervised hierarchical cluster analyses led to the identification of a subgroup of patients showing a relatively high Lyn expression. The Nalm6 cell line was chosen as a model which mirrors Lyn expression status in ALL patients. Tyrosine phosphorylation pattern was greatly diminished in Nalm6 upon Lyn depletion, furthermore the Lyn-depleted cells showed a substantially reduced cell proliferation and preliminary increased apoptosis.

Conclusion: Our findings indicate that aberrant expression of Lyn in ALL may contribute to cell proliferation. Although we have highlighted substantial contribution of Lyn in cell proliferation in leukemic cells, the impact of combining drugs targeting Lyn with conventional chemotherapeutics agents remains to be determined.

Keyword: Src family kinase, ALL

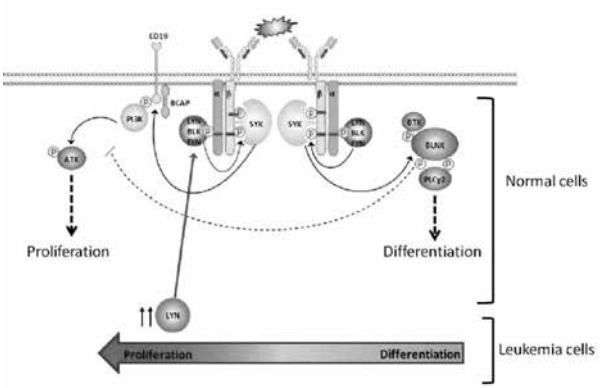

Figure 1. Activation of the pre-BCR signalling leads to a single tyrosine phosphorylation at the immuno-receptor tyrosine-based activation motif (ITAM) (red dash) in the cytoplasmatic portion of Igβ, followed by the recruitment of SFK members like Lyn, Blk, Fyn. Subsequently, the Igβ-ITAMs are double phosphorylated in a SFK dependent manner, then Syk is recruited to the ITAM, where it plays an essential role in proliferation and differentiation1. Contrary, leukemic cells have shown an impaired differentiation2 accompanied by an increased proliferation3. The observed high expression levels of Lyn in ALL cells may substantially increase cell growth suggesting a potential advantage of using Lyn inhibitors in addition to anti ALL chemotherapy-drugs.

Poster No:004 Abstract:0123

PANCREATIC INFILTRATION IN AN ADULT PATIENT WITH COMMON B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute lymphoblastic leukemia (ALL) might involve different extramedullary sites either at diagnosis or during disease course. The most frequently involved organ is the central nervous system. Pancreatic infiltration in ALL is quite rare, being limited to a few pediatric case reports.

Case**:** A 52-year-old male patient was hospitalized in our hospital with the complaints of abdominal pain, nausea and vomiting. Laboratory data were as follows: hemoglobin, 11.6 g/dl; hematocrit, 35.1%; leucocytes, 18000/mm^3; platelets, 64000/mm^3; glucose, 170 mg/dl; ALT, 117 U/L; AST, 172 U/L; ALP, 474 U/L; GGT, 404 U/L; total protein, 4.9 g/dl; albumin, 1.8 g/dl; LDH, 2617 U/L (N<192); ESR, 119 mm/hr; and CRP, 7.9 mg/dl (N<0.8). Serum amylase was 262 U/L (N: 25-125); and lipase was 796 U/L (N: 8-78). Abdominal tomography demonstrated splenomegaly; there was also diffuse pancreatic enlargement and the pancreas had a heterogenous appearance with some small anechoic cysts (Figure 1). There were 80% lymphoblasts on peripheral blood smear, the bone marrow aspiration showed 92% lymphoblasts. Malignant cells were positive for CD45, HLADR, cytoplasmic CD79a, CD19, CD22, CD10 and TdT; and they were negative for

CD2, CD3, CD4, CD7, CD13, CD14, CD33, CD34, and CD56. BCR-ABL and MLL fusion genes were negative with FISH. the patient was administered GMALL (05/93) chemotherapy which included intrathecal prophylaxis. He obtained complete hematologic remission and his control abdominopelvic tomography revealed regression of the pancreatic enlargement. Seven weeks after diagnosis, the patient complained of headache, nausea and vomiting. He had right abducens nerve paralysis; and, a cranial MR revealed an extraaxial tumoral mass of diploe origin in the neurocranium. He was started to be administered GMALL (05/93) chemotherapy for high-risk ALL. Five months after diagnosis, he developed febrile neutropenia and had a pneumonic consolidation on chest X-ray. There were elevations in bilirubin, ALP, GGT levels. Abdominal ultrasonography revealed multiple masses in the liver. He died 6 months after diagnosis.

Conclusion: Pancreatic infiltration causing acute pancreatitis has not been reported in an adult ALL patient until now. Patients with multiple extramedullary organ involvement, including that of the pancreas, might need to be treated with more aggressive chemotherapy protocols.

Keyword: Acute lymphoblastic leukemia; pancreatic infiltration; acute pancreatitis; central nervous system relapse

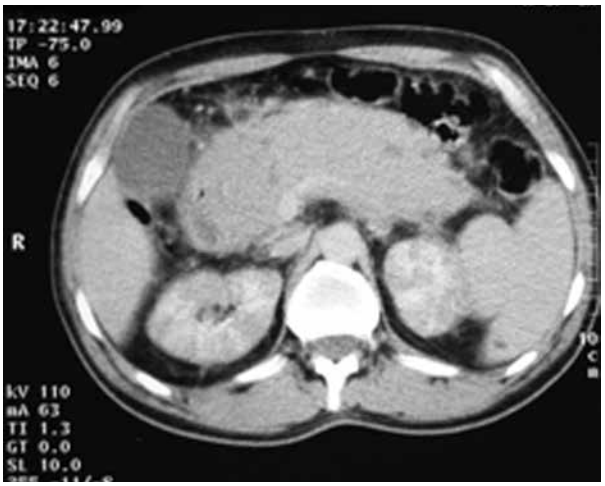

Figure 1. Abdominal tomography showing diffuse pancreatic enlargement

Poster No: 005 Abstract:0129

ACUTE LYMPHOID LEUKEMIA IN A PATIENT WITH ANKYLOSING SPONDYLITIS AFTER ANTI-TNF-ALPHA TREATMENT: CASE REPORT

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Introduction: Tumor necrosis factor alpha (TNF-α) inhibitors are used worldwide in the treatment of several inflammatory diseases, including ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis and inflammatory bowel diseases. We report here a 40–year-old man with ankylosing spondylitis who developed Philedalphia chromosome-positive (Ph+) ALL after treatment with TNF-α inhibitors (etanercept and adalimumab).

Casereport**:** A 40-year-old man was referred to our hematology department for evaluation of leukocytosis, anemia and thrombocytopenia. The patient's history has revealed that, in 2002, he presented with inflammatory back pain, weakness and weight loss and he was diagnosed with ankylosing spondylitis by the rheumatologist. The patient was given an individual treatment including salazopyrine 2g/day and indomethasine 100/mg/day and he followed all scheduled visits during 9 years with a full patient compliance. In his previous visit performed in April 2011, Etanercept therapy (50 mg/every week) was started because of active disease and unresponsiveness to existing drugs. In January 2012, treatment with Etanercept was switch to Adalimumab (40mg/every 2.week), because of failure to improve disease. In November 2012, the patient was reffered to our hematology clinic with the complaints of progressive fatique, joint pain and asthenia. Physical examination showed significant pallor and spleen were palpable 5 cm below the costal margin palpable Laboratory test was performed; leukocyte count was 315.000 $x10^3/L$ with 88 % blasts in peripheral blood smear, hemoglobin level was 6,8 g/dl, platelet count was 92 $X10^9$ /. He was admitted to the hospital subsequently and bone marrow aspiration biopsy was done. Bone marrow biopsy showed marked (75%) infiltration with small-sized blast. According to clinical and laboratory results the patient was diagnosed with Philadelphia chromosome-positive acute lymphoid leukemia (Ph+ ALL). He was given an treatment including Glivec (a tyrosine-kinase inhibitor) 400 mg/day and induction of adult ALL regimen (including glucocorticoid, vincristine, anthracycline and asparaginase). During the induction chemotherapy the patient developed fungal pneumonia. Although to treatment with broad-spectrum antibiotics the patient was died because of sepsis and respiratoty failure.

Discussion: We report this patient to add to the growing literature of patients who develop hematologic malignancies after TNF alfa inhibitor treatment. The majority of cases were non-Hodgkin's lymphomas whereas there is only two reports with Ph+ ALL. The mechanism by which TNF-a protects against cancer and thereby how its inhibition may promote cancer, is not well understood. According to present case and literature knowledge blood counts should be done prior to initiating therapy and during follow up.

Keyword: Acute lymphocytic leukemia, Anti-tnf-alfa therapy

Poster No: 006 Abstract:0157

PRIMARY GRANULOCYTIC SARCOMA CASES: SINGLE INSTITUSION EXPERINCE

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Objective: Granulocytic sarcoma is tumor consists of proliferation of immature myeloid cells at extramedullary sites. Although they accompany mostly acute myeloid

leukemia, myelodisplastic syndrome, chronic myeloproliferative diseases, they might be detected as a isolated infiltrations without systemic disease in a rare cases. In this study, we aimed to document the cases with granulocytic sarcoma without systemic involvement and followed-up in our center.

Method**:** We documented 25 cases with granulocytic sarcoma between the years of 2000 and 2012. Five of 25 were diagnosed as primary disease without systemic infiltration. At this study we present the primary granulocyctic sarcoma cases wihout bone marrow involvement.

Results: The charateristics of the patients were summarized at table 1.

Conclusion**:** Granulocytic sarcomas can be loacalized at any system and organ. They can progress to acute leukemia. They should be considered during differantitial diagnosis of solitary tumors since they can infiltarte especially solid organs and lymph nodes. Since their prognosis become worsened after they progress to acute leukemia, they should be treated with systemic chemotherapies after the diagnoses either as a single modality or in combination with surgery/radiotherapy.

Keyword: granulocytic sarcomes, primary

Table 1: Characteristics of the patients

patients	age	sex	localization	bone marrow involvement	treatment	follow up
1	49	male	pancreas	no	radiothearapy	Proggression to acute myeloid leukami after 4 months of the diagnosis. Remission wa sobtained with chemoterapy followed by allo-tx
2	24	male	conjuctiva	no	radiothearapy	Progression to AML after 2 years. Treated with chemotherapy and allo-tx but died during transplantation due to infection and sepsis
3	34	male	small intestine	no	operation	He is at remission for 10 months
4	31	male	axillary region	no	radiothearapy	He is followed-up at remssion
5	52	female	inguinal region	no	radiothearapy	At 16th month after the diagnosis she relaped with new lesions at inguinal region and breast. She was treated wtih chemotherapy. Followed up at remission for 14 months

Poster No: 007 Abstract:0165

LOW PLATELET COUNTS AS A PROGNOSTIC MARKER IN ALL TREATMENT IN PLACE OF MRD IN COUNTRIES WITH LIMITED FINANCIAL RESOURCES

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Aim: The aim of this study was to estimate prognostic and early response criteria for the patients treated by BFM ALL regimens.

Patients**:** There were 242 newly diagnosed non B-ALL patients enrolled into this retrospective study, who were admitted to Cerrahpasa Pediatric Hematology Department during January 1995 to January 2012.

Results: The median age was 6,18y ±3,75years (8 month-17 years). The %59,4'ü of the group were boys. (boys/girls 1,46). CNS involvement was positive in %7,7. T-cell immunophenotype was shown in11, 8%. Genotypically t(12;21), t(9;22) and t(1,19) were positive in %8, %3 and %3 of patients, respectively. The overall survival of the B-ALL patients was %81±3,1, while that of the T-ALL patients was %62,2±12,4 (p:0.007). The EFS of the patients who had CNS involvement was %47,6±12,1, lower than the ones who had not(p:0,0001).
The OS and EFS of the whole group was 74,8%±3,9 and 74%±3,1 respectively, while EFS ratios for boys 72% and girls 80.5% (p:0.728).The OS and EFS were lower as the age increase (>10 years OS and EFS were 59,9%±8,4 and 57,4%±8,4(p:0,001)) except <1 year (OS and EFS 37,5%±28,6). Being a high risk patient was significantly associated with X3 relaps and X7 exitus (OS 22,7%±9,1 and EFS 27,6%±8 (p:0,0001). Having splenomegaly, hepatomegaly, t (9,22), CNS involvement (CNS leukemia increased exitus risk X4 times), higher Hb and WBC counts at diagnosis were related with poorer treatment results. (WBC >100.000 /mm^3 OS %53,7±12,8 (p:0.028);. Hb >8g/dl and T-ALL patients' OS 44,4%±13,5 (p.0,01).
Although the platelet counts at diagnosis had no prognostic value, platelet count at 15 and 33th days were <50.000/mm^3 had higher risk for exitus (respectively X3 and X7), and had lower OS p:0,008, p:0,0001). Thrombocytopenia usually goes parallel with neutropenia and monocytopenia. Monocytopenia <100/mm^3 at day 33 had EFS 67,3%±5. Lymphopenia at this period is strikely corralated with neurological adverse events.
The blast count at 15 and 33 day were a reliable prognostic marker as if the blasts were >%5 OS 35,8 %±15,9 and 0 % while patients with blasts <%5 had 89,7%±2,6 and 80,2±4,1% respectively (p:0.0001).The 13.3 % of the group relapsed, generally in 3.5 years period after diagnosis, and 72% of the relapsed patients were succumbed in 5 months.
As a conclusion, childhood ALL treatment results have reached great improvements in the MRD era. The potential benefit of simple methods such as full blood count and clinical findings, can predict us the outcome. The most striking and important finding of our study is probably the strong association of platelet counts with the prognosis. Having a platelet count less than 50.000/mm^3 at the 15 and 33th day of treatment, was associated with high mortality(p:0,0001)and this count would be easily used just for a marker in countries with limited financial resources where MRD is not avaliable.

Keyword: ALL, prognostic markers

Poster No:008 Abstract:0184

OCCURRENCE OF L-ASPARAGINASE-ASSOCIATED FULMINANT HEPATITIS IN A CASE DIAGNOSED WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND TREATMENT BY PLASMAPHERESIS

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Introduction: Acute lymphoblastic leukemia (ALL) is a heterogeneous disease with different subtypes exhibiting

typical clinical, biological and prognostic characteristics. Most of the complications are attributed to the synergistic effect of the corticosteroids and asparaginase.Here we report the occurrence of L asparaginase-associated fulminant hepatitis and treatment by plasmapheresis in a case with ALL.

Case: A 48 year old female patient presented to the internal diseases outpatient clinic with the complaints of fatigue and fever; upon detection of a leukocyte count of 42.000 (89% lymphocyte dominant), anemia and thrombocytopenia. Bone marrow was detected to be normocellular with more than 90% of blastic cells. Upon detection of CD79a 92%9,CD19:98%,CD22:53%,CD34:97%, the case was diagnosed with Pro-B ALL and hoelzer phase 1 treatment initiated. On the 18th day (4 days after the L-asparaginase treatment was over), total bilirubin level started increasing progressively. No pathologic findings were detected on abdominal ultrasonography or MRCP. The repeated hepatitis A, B, C, CMV, EBV tests revealed negative results.

On the 26th day of chemotherapy, the following values were detected: 16.9 and direct bilirubin 14.2. Upon detection of hepatic encephalopathy findings in the patient, therapeutic plasmapheresis was planned. A total of 4 sessions of plasma exchange was performed with 15 units of fresh frozen plasma (FFP); 56 units of FFP were used in total. Following the plasma exchange, the total bilirubin level was reduced to 1.5 mg/dl with hepatic encephalopathy showing improvement.

Discussion: Acute lymphoblastic leukemia (ALL) is a malign disease characterized by clonal proliferation of the leukemic cells in the lymph nodes, timus and the spleen. In cases of ALL, the treatment regimens used for remission induction include steroids, vincristine, L-asparaginase and antracyclines. L-asparaginase is a bacterial enzyme. The most significant side effects include hypersensitivity, pancreatitis, coagulation in the large veins, reduction of the coagulation factors together with hemorrhage, hyperglycemia and neuropathy. While it is not common, elevation in the liver enzymes may also occur however fulminant hepatitis is not expected. Our case was a patient who experienced elevation of liver enzymes and developed fulminant hepatitis during treatment. Excluding all the causes for fulminant hepatitis, the occurrence of hepatitis was potentially attributed to L-asparaginase. The patient's overall status was corrected by discontinuation of the drug and plasmapheresis. Based on Pubmed, there is only a single case in Japan, in which the patient died despite the application of plasmapheresis. We wanted to present this case since it was not a common situation reported in the literature and the patient responded treatment with plasmapheresis.

Keyword: l-asparaginase, toxic hepatitis

Poster No: 009 Abstract:0187

QUERCETIN AND EMODIN SYNERGISTICALLY ENHANCED CHEMOTHERAPY ACTIVITY IN HUMAN LYMPHOID AND MYELOID LEUKAEMIA CELL LINES, *IN VITRO*

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Objective: The mortality of leukaemia is still high despite the considerable improvements in chemotherapeutic agents. Our previous work has shown that polyphenols and polyacetylenes have potential in the treatment of leukaemia (Dahlawi et al 2012; Zaini et al 2011). Furthermore, in a comparative study of the effect eight polyphenols in eight leukaemia and one non-tumour control cell lines, quercetin and emodin were shown to be the most effective at induction of apoptosis, causing cell cycle arrest and inhibiting ATP levels (as a marker of proliferation), in leukaemia compared to non-tumour cells. Using IC25 and IC10 treatment doses (the concentration which inhibits 25% and 10% of cell ATP levels respectively) an investigation was made of the effects of the quercetin and emodin on five standard chemotherapy treatments (doxorubicin, etoposide, cisplatin, cyclophosphamide and chlorambucil), on cell proliferation, cell cycle and apoptosis at 24hrs-post-treatment in two human myeloid (KG1a and THP-1) and two human lymphoid (JURKAT and CCRF-CEM) leukaemia cell lines.

Methods: The combination effects of polyphenols and chemotherapies on cell ATP levels was measured by CellTiter-Glo® luminescent assay, cell cycle was assessed using propidium iodide (PI) staining and flow cytometry and induction of apoptosis was investigated by caspase-3 activity assay using flow cytometry and by morphological assessment following Hoechst 33342 staining.

Results: Quercetin synergistically inhibited ATP levels, and induced apoptosis and cell cycle accumulation when combined with eptoside, cisplatin and cyclophosphamide in both lymphoid cell lines, whilst having an additive effect in the myeloid cell lines. Quercetin also had an additive effect when used in combined with doxorubicin and chlorambucil, in all cell lines. Similarly emodin produces a synergistic effect when combined with etoposide and doxorubicin, and an additive affect with cisplatin, cyclophosphamide and chlorambucil in both lymphoid cell lines.

Conclusion: This study show that quercetin and emodin have a potential role at enhancing the action of chemotherapy in the treatment of leukaemia, however the levels of action depend on the polyphenol and cell lineage. This suggests that there is a different mechanism of action of these polyphenol-chemotherapy combinations in the treatment in lymphoid and myeloid leukaemia.

Keyword: Leukemia, Quercetin and Emodin

Poster No: 0010 Abstract:0190

ANTI-PROLIFERATIVE AND PRO-APOPTOTIC EFFECTS OF POLYPHENOLS ON HUMAN MYELOID AND LYMPHOID LEUKAEMIA

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Objective: The mortality of leukaemia is still high despite the considerable improvements in chemotherapeutic agents. For this reason, our study aimed to investigate the polyphenols as alternative agents for leukaemia treatment in which the most recent studies have been focused only on solid tumours. Here, we specifically selected eight compounds from the major classes of polyphenols (quercetin, chrysin, apigenin, emodin, aloeemodin, rhein, cis-stilbene and trans-stilbene) and their effects were investigated on cell proliferation, cell cycle and apoptosis on a panel of human myeloid (KG1a, HL60 THP-1,and K562) and lymphoid (JURKAT, CCRF-CEM, MOLT-3, and U937) leukaemia cell lines.

Methods: The effect of polyphenols on cell proliferation was measured by CellTiter-Glo® Luminescent Assay and cell cycle was assessed using propidium iodide (PI) staining and flow cytometry. Induction of apoptosis was investigated by caspase 3 activity assay using flow cytometry and Hoescht stain using fluorescence microscopy.

Results**:** our study showed that emodin, quercetin, and cis-stilbene were the most effective polyphenols at inhibiting cell proliferation (with IC50 values ranged between 5-22µM, 8-33µM, 30-85µM, respectively) and inducing the apoptosis (with AP50 values ranged between 2-27µM, 19-50µM, 8-50µM, respectively), following 24hr for all the leukemic types. All myeloid cell lines have been more sensitive to apigenin comparing to other compounds in inducing apoptosis while at higher concentrations between 84-235µM. Meanwhile, all lymphoid cell lines showed greatest sensitivity to the all polyphenols comparing to the myeloid cell line.

Conclusions: Our data showed that all eight polyphenols where significantly found to inhibit cell proliferation and arrest the cell cycle for all leukemic cell lines with varied responses in inducing the early and late apoptosis, this variety of action between cell lines suggesting that there is a different mechanism of the action of each of these molecules. In conclusion, our findings suggest that polyphenols could be used as new chemotherapeutic agents in the treatment of leukaemia.

Keyword: Leukemia, Polyphenols

Poster No: 0011 Abstract:0204

SUCCESSFUL TREATMENT OF A CANDIDIASIS CASE THAT SIMULATES MUCORMYCOSIS

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Case: Blood tests performed because of abdominal pain complaints of a 55 years old female patient revealed leukocytosis, anemia and thrombocytopenia and she was directed to the hematology clinic. After further analysis, she was diagnosed with ALL L2. HOELZER chemotherapy (L-asparaginase, doxorubicin, vinkristin, prednisolone) was initiated to the patient and during the neutropenic phase, the patient experienced wide spread, ulcerated lesions inside her mouth and on her pharyrnx and exanthematous, bleeding, necrotic sores on her lips (Figure1). As fungal elements were detected in the specimens obtained from the lesions, treatment with caspofungin was initiated. Under the treatment, lesions of the patient progressed and necrotic tissues increased like mucormycosis. Candida Albicans grew in the samples and the susceptibility test performed showed susceptibility to Amphotericin B and itraconazole, however susceptibility to caspofungin was not studied. The antifungal agent was not switched as there was a febril response in the neutropenic patient. With GCSF injection support, leukocyte count of the patient increased. Although the lesions of the patient suggested mucormycosis they showed dramatic improvement with caspofungin treatment. After 28 days of therapy with caspofungin, inner mouth and labial lesions resided totally (Figure2).

Discussion: Invasive fungal infections (IFI) are one of the main reasons of mortality and morbidity especially in patients having haematological malignancies. Prolonged neutropenia is the most important risk factor for IFI. The most common causative agents are Aspergillus and Candida species (1). On the other hand, mucormycosis is the leading less common agent and it is a fungi infection which has very high mortality rates (2,3). Mucormycosis cause necrotic lesions and prefers upper respiratory tract. Patients who have undergone ASCT (Allogeneik Stem Cell Transplantation) and who are receiving high doses of chemotherapy for AML, ALL are at high risk for IFI (4). Fast diagnostic approaches and early treatment decreases the mortality considerably in this group of patients (5). We presented a successful treatment (cure) of a patient who had candidiasis, and who developed mucormycosis-like necrotic lesions.

Keyword: Mucormycosis, Candidiasis

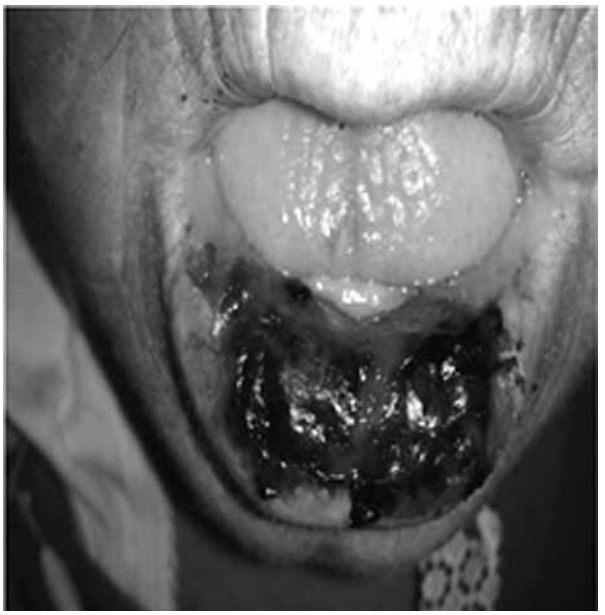

Figure 1

Poster No: 0012 Abstract:0205

ARE HYPOMETHYLATING AGENTS TO BE GIVEN PREFERENCE IN CMML 1?

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Case: 72 year old male patient was examined two years ago at another center and was diagnosed with Myelodysplastic Syndrom (MDS) and then he was monitored without any treatment given. The patient who required intermittant eritrocyte and platelet replacement therapy was receiving iron chelation therapy for the last year. After the blood marrow tests that were performed in September 2012 due to an increase in white blood cells and deepening thrombocytopenia, which revealed dysgranulopoiesis, dyserythropoiesis findings and 1-2% blast cells azacitidine chemotherapy was initiated to the patient on 27.11.2012 for Chronic Myelomonocytic Leukemia (CMML). On the 7th day of chemotherapy the patient was admitted to the emergency care clinic of our hospital due to signs of confusion. Thrombocytopenia and intracranial bleeding was detected and subsequently the patient was operated. After the surgery the patient had been monitored by the Hematology Department and his thrombocytopenia could not be resolved inspite of the replacement therapies given. Although corticostreoids, IVIG (intravenous immunoglobuline) and multiple platelet replacements were administered to the patient the bleeding could not be taken under control and the patient died.

Discussion: Chronic myelomonocytic leukemia (CMML) is a heterogen clonal disorder, which is characterized by monocytosis, less than 20% blast cells in the bone marrow, one or more dysplasia and negativity for philadephia (Ph) chromosome. World Health Organization (WHO) classified CMML as a 'mixed Myelodysplastic/ Myeloproliferative disease' and subgrouped the disease according to the blast cell counts in the peripheral blood and bone marrow. CMML1, <5% blast cells in peripheral blood,<10% blast cells in bone marrow CMML 2; <5-19% blast cells in peripheral blood, <10-19% blast cells in bone marrow. In a trial, average life expentancy is found to be 12-24 months in CMML.

There is no standart approach in treating CMML. Appropriate treatment options are effected by patient related (patients choice, performance status of the patient, age and comorbidities) and disease related (cytogenetic condition, number of cytopenies, bone marrow blast count and transfusion requirements) factors.

When using hypomethylating agents and adjuvant therapy are compared for the treatment of CMML, delay in transformation to acute leukemia and increase in overall survival is found with hypomethylating agents but the improvement in overall survival is still not statistically significant and prospective studies are required. Cytopenies (thrombocytopenia, anemia) and complications occurring after usage of azaticidine and decitabine which inhibit the metillation of the DNA should be treated in the centers who are experienced in this field. We believe that using hypomethylating drugs in CMML patients with low blast counts can lead to shorter life expectancy and life losses therefore should be carefully considered.

Keyword: Hypometylating Agents, Thrombocytopenia

Poster No: 0013 Abstract:0207

EVALUATION OF PEDIATRIC T-ALL MRD VALUES BY FLOW CYTOMETRY

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Assessment of minimal residual disease (MRD) during the first months of therapy gives information on the timely response to treatment, and proves to be a powerful and independent indicator of treatment outcome in patients with acute lymphoblastic leukemia (ALL). Different study groups indicated that detecting submicroscopic levels of leukemia cells in bone marrow on 15th day of treatment is associated with prognosis. Flow cytometry (FCM) is faster and cheaper than molecular methods, and is performed for leukemia immunophenotyping in many centers today. There are early T cell precursors in bone marrow of T-ALL patients, and these precursors constitute thymocyte subgroups migrate to thymus and it is considered that they are derived from hematopoietic stem cells because of their multilineage differentiation potential. They have a distinctive immunophenotype with CD1a-CD8-CD5dim stem cell or myeloid markers. T-ALL MRD results have importance due to patient follow up and chemotherapy dose adjustment. In Turkey, MRD is started to apply as pioneer in our institute, and MRD levels in T-ALL samples were determined by FCM according to Associazione Italiana Ematologia Oncologia Pediatrica -Berlin-Franklin-Munster (AIEOP-BFM) protocol.

In this study, blasts were detected in bone marrow samples from T-ALL patients (n=14) on the 15th day of treatment and the MRD ratio and relapse risk were evaluated. CD45, CD3, CD4, CD5, CD7, CD8, CD99, cytoplasmic CD3 and cytoplasmic TdT antigen expressions in bone marrow samples were detected by FACSAria and data were analyzed using DiVa software. After determining the number of nucleated cells by Syto41 staining, leukemic cell ratio (blast or MRD%) detected in nucleated

CD7+ T cell population was scored as; lower than 0.1% was flow low risk (FLR), between 0.1-10% is medium risk (FMR) and higher from 10% is high risk (FHR).

Three of 14 cases (1 female, 13 male, 9.01 ± 5.16 years) were MRD negative (18.75%), 11 were positive. According to MRD risk, cases were grouped as 5 FLR (35.71%), 6 FMR (42.86%) and 3 FHR (21.43%). All of the measurements were confirmed by AIEOP-BFM partner (100%). There were no significant differences between male (9.39 ± 4.69 years) and female (7.37 ± 7.92 years) cases, FLR (10.69 ± 5.13 years), FMR (6.83 ± 3.81 years) and FHR (11.51 ± 4.80 years) groups and FLR negative (10.92 ± 6.42 years) and positive (10.24 ± 4.72 years) groups, according to their ages.

In this study, flow cytometric T-ALL MRD results on the 15th day of the treatment were discussed.

Keyword: MRD, T-ALL

Poster No: 0014 Abstract:0209

STUDY OF ACUTE LYMPHOBLASTIC LEUKEMIA AT TABRIZ ASADABADI CHILDREN HOSPITAL

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Background: Acute lymphoblastic leulemia (ALL) is the most common leukemia in children under 10 years of age.The clinical manifestations of ALL are extremely variable and nonspecific are those due to leukemic cell proliferation, and usually appear 2 to 6 weeks before the diagnosis.

In this study which lastet ten years, 67 cases ALL was seen that include: ALL-L1, ALL-2, ALL-3. In the WHO classification these cases are categorized as lymphoma rather than as acute leulemia,this more accurately refrects the nature of the disease. In L1 ALL the blast cells small to medium in size and are fairly uniform in appearance. Larger cells have diffuse chromatin and sometimes small nucleoli whereas the small blasts have no visible nucleolus and show some chromatin condensation. Cytoplasm is scanty. In L2 ALL the blasts are larger more pleomorphic with irregular nuclei, more prominent nucleoli more abundant cytoplasm. L3 ALL is characterzed by moderately intense cytoplasmic basophilia and variable but usually heavy cytoplasmic vacuolation.

ALL is a curable disease for most children. The majority (55%) of cases of this heterogeneous disease are standard-risk ALL of B-cell lineage, and the best prognosis for an overall survival rate for this group of patients is about 90 percent.Complete remission(CR) in children with ALL is one of the greatest achievement of modern oncology.

Keyword: Leukemia, Lymphoblast

Poster No: 0015 Abstract:0221

INTRAABDOMINAL GRANULOCYTIC SARCOMA AS AN ISOLATED EXTRAMEDULLARY RELAPSE OF ACUTE MYELOID LEUKEMIA

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Extramedullary relapse also know as granulocytic sarcoma is a relaps of leukemia in sites other than bone marrow. It may be associated with or without bone marrow disease. The most common sites of granulocytic sarcoma are the central nervous system, subcutaneous tissue and genitourinary system Here we report a case of intraabdominal isolated extramedullary relapse after three years of remission in an AML patiA 68-year-old man diagnosed with acute monoblastic leukemia in 2007, and treated with idarubicin and cytosine arabinosid induction.chemotherapy regime.Bone marrow aspiration was revealed remision with 1% marrow blast. Patient was in remision, after one cycle of consolidation theapy with high dose cytosin arabinosid. There is no information about cytogenetic analayses at the time of diagnosis. After that time there in no followup due to patient incompliance.

Jaudice was developed 4 months ago. Abdominal MR imaging revealed intrahepatic bile duct dilatation and 4cm pancreatic mass. Biopsy was performed by upper endoscopy.from pancreatic mass.Histopathological examination of the pancreatic biopsy specimen from showed diffuse blast cell infiltration,which were CD34 and MPO positive on immunohistochemical staining. Bone marrow examination showed no evidence of leukemia. After diagnosis of the extramedullary relaps systemic chemoterapy was started.. Then patient become pancytopenic. and died because of systemic infection

Keyword: AML, extramedullary relaps

Poster No: 0016 Abstract:0228

SUCCESSFULL TREATMENT OF ISOLATED CUTANEOUS RELAPSE AML WITH ELECTRON BEAM THERAPY IN A CHILD

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Background: Primary myelosarcomas, also called leukemia cutis, granulocytic sarcomas or chloromas, are rare extramedullary manifestations of acute myeloid leukemia (AML) which precede bone marrow involvement. Skin infiltration was the most frequent localization associated with a myelomonocytic differentiation.

Case: A 9 year old girl diagnosed with AML M4 without any extramedullary involvement and was treated according to AML BFM 2004 protocol. After.completion of treatment she was planned to be transplanted from her matched brother. However she developed several skin lesions and biopsy showed myeloblastic cells in these lesions. Bone marrow aspiration and biopsy revealed hematological remission and no additional extramedullary

involvement was detected. She was accepted as isolated cutaneous AML relapse. She was given chemotherapy including idarubicin and fludarabine. Although she developed very severe pancytopenia, skin lesions did not improve, and some of them showed enlargement. Repeated skin biopsy showed persistent leukemic cells infiltration. Electron beam therapy was applied to the skin lesions for 15 days.

The whole skin electron radyotherapy acording to Stanford technique was used. She was treated in 6 different position with a distance of 310 cm SSD. A total of 18 Gy, 1.2 daily dose was reached with electron energy of 6 MeV. Since there was no central involvement cranium was protected. After treatment degree 2-3 radiodermitis was seen in hands and feet.

After resolution of the skin findings, biopsy was again taken and showed no blastic cells. Then she underwent bone marrow transplantation from her matched brother. Six months after transplantation she is fine without any event.

Conclusion: According to our experience and review of the literature, an early diagnostic workup is needed in AML patients with unusual skin lesions, considering leukemia cutis as first manifestation of relapse AML. Electron beam therapy seems an effective and safe approach for treatment treatment is recommended soon after diagnosis.

Keyword: AML, cutaneous

Poster No: 0017 Abstract:0229

SEVERE INVASIVE FUNGAL INFECTIONS IN CHILDREN RECEIVING EMPIRICAL CASPOFUNGIN TREATMENT FOR FEBRILE NEUTROPENIA

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Invasive fungal infections have significant impact on leukemia patients' survival. Antifungal drugs are empirically given most of the patients. However breakthrough fungal infections under some antifungal drugs are not uncommon.

Four patients, 3 girls and one boy, aged between 2.5 and 16 (median 4) years old developed rare mycotic breakthrough infections while they were receiving caspofungin treatment. The primary diagnosis of the patients were PreB Cell ALL (n=3) and very severe acquired aplastic anemia (n=1). The median time of severe neutropenia before detection of mycotic agent was 33 (range, 16-55) days. The median time of febrile neutropenia period before detection of the agent was 16 (range, 14-19) days. All patients were given broad spectrum antibiotic initially. Since the fecver persisted empirical changes in antibiotic combinations were made despite any agent was isolated from the cultures. At the median of 5th (range, 4-12 days) day of febrile neutropenia caspofungin was started as empirical antifungal therapy. They all had fever and hepatosplenomegaly. Cutaneous maculopapular rash was seen in 2 of the patients. One had status epilepticus and multipl cerebral abcess at presentation of mycotic infection. Three of these patients required entubation and mechanically ventilation, and entered into pediatric Intensive Care Unit. Trichosporon ashaii was detected in 2 patients' blood culture and Geotrichum capitatum in the others (one also had positive CSF culture).

Median time between initiation of caspofungin and first time for detection of mycotic agent was 14 (11-19) days. Because the patients' clinical situation worsened, in two patients voriconazole was added to antifungal therapy empirically 3 and 5 days before the agent was detected.

The first sterile blood culture was obtained 3-10 days after the day of first detection of fungal agent, and 3-7th days of voriconazole treatment

All patients reached clear cultures but one patient died. One patient with central infection with T. asahii had severe neurological sequele.

According to our experience and literature very severe fungal infections could occur during empirical caspofungin treatment. We must evaluate this observaton very carefully. Randomized, controlled studies should be planned.

Keyword: caspofungin, breakthrough fungal infectiion

Poster No: 0018 Abstract:0242

INVASIVE FUNGAL INFECTIONS IN PEDIATRIC ACUTE LEUKEMIA: WHEN TO RESTART CHEMOTHERAPY?

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Aim: Invasive fungal infection (IFI) is a life-threatening problem that is seen in patients with acute leukemia (AL) despite advances in antifungal treatment. We aimed to describe variations regarding site of infection, clinical features, treatment modalities, time of restarting chemotherapy (CT), and outcome.

Methods: The charts of all patients who were treated as AL in our hematology unit between April 2001 and July 2011 were retrospectively reviewed and data of patients with IFI were analysed.

Results: IFI was defined in 15 (12.4%) children (9 ALL and 6 AML). The median age was 10 years (range 9 months -17 years). Ten of them were male. Seven patients were treated in the high risk treatment group according to the ALL BFM and AML BFM protocols. The phase of CT at the time of IFI diagnosis was induction in 4 (26.7%) and consolidation in 9 (60%) patients. In each one (6.7%) patient IFI was diagnosed during maintenance and after the cessation of CT. The time between the leukemia diagnosis and the definition of IFI was median 105 days (range 15-305 days). Twelve patients (80%) were in remission at the time of IFI. Absolute neutrophil count at the time of the IFI diagnosis was $<500/mm^3$ in 80%. The duration of neutropenia was mean 13.9 days (range 0-47 days). Steroids were given to 10 (66.7%) patients. All patients were febrile at the time of IFI diagnosis. Fourteen patients had isolated pulmonary IFI and 1 patient with Mucor + Aspergillosis had orbitocerebral and pulmonary IFI. Nine patients had abnormal findings on chest x-ray. The most frequent finding on computerized thorax tomography was

typical parenchymal nodules. In 3 patients, a fungus was detected in the blood culture (Candida kefyr, Aspergillus flavus, and Mucor). Galactomannan antigenemia was positive in 3 patients (20%). The episodes were defined as proven in 1 (6.7%) patient, probable in 3 (20%), and possible in 11 (73.3%) cases. The lenght of CT discontinuation was mean 30.6 days (range 0-57 days). In 3 patients diagnosed in the induction phase of CT, the discontinuation duration of CT was mean 22.6 days (range 18-30 days). IFI was treated with voriconazole, amphotericin deoxycholate, liposomal amphotericin B, caspofungin, or posocanazole alone or in combination. Granulocyte colony stimulating factor was used in 93,3% of episodes. Secondary antifungal prophylaxis was given to all patients and the most used antifungal was vorikonazole (66.7%). Three (20%) patients had a relapse of IFI. Six patients died because of leukemia relapse or resistant disease. There was no death because of IFI itself.

Conclusion: Our data shows that IFI is an important problem in children with AL and effective antifungal therapy with different treatment modalities may decrease the incidence of death. Although the optimal time of restarting CT in patients with AL is not clear, 2 to 4 weeks seems to be safe.

Keyword: Invasive fungal infections, acute leukemia

Poster No: 0019 Abstract:0261

HEPATOSPLENIC HYALOHYPHOMYCOSIS: A CASE REPORT

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Invasive aspergillosis has an increasing incidence worldwide especially in immune compromised patients (1). Extrapulmonary aspergillosis cases reported as a considerable morbidity and mortality cause latterly (2). We have mentioned an invasive pulmonary aspergillosis case which progress to fungus ball in liver and spleen.

A 65-year-old woman with B-acute lymphoblastic leukemia who was under remission for 6 months took medication of low-dose cytosine arabinoside therapy for relapse. On the 13th day of the therapy the patient complained of fever, cough and sputum. Laboratory findings were as follows: hemoglobin 9gr/dl, neutrophil 200/mm^3, eosinophil 5/mm^3, blasts 400/mm^3, platelet count 28000/mm^3, sedimentation rate 71 mm/h and C-reactive protein 161 mg/l. Other laboratory values were normal. Broad-spectrum antibiotic therapy and antifungal therapy including liposomal amphotericin B was initiated. The patient persisted febrile and symptoms and radiological findings progressed. Liposomal amphotericin B replaced with itraconazole. On day 26, nausea, vomiting and abdominal pain occurred. Abdominal ultrasonography and computerized tomography showed multiple fungus balls in liver and spleen (Figure 1).

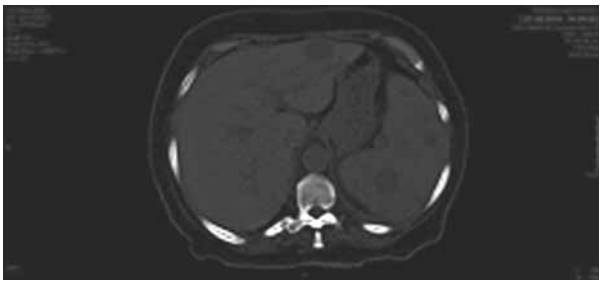

Figure 1. Multiple fungus ball seen in the spleen. Hyper dens central zone and hypo dens peripheral halo clearly viewed. Also hepatic fungus ball seen in the left lobe of the liver.

Surgical therapy recommended but the patient refused operation. Although itraconazole therapy, the disease progressed. The patient is under follow-up with voriconazole therapy. Extra-pulmonary involvement, especially cerebral or sinonasal, is frequently found in immune compromised patients with pulmonary invasive aspergillosis, occurring as a dissemination from the primary lesions to a variety of organs, via hematogenous spread. Although retrospective autopsy-based studies reported splenic involvement in about 16% of patients with invasive aspergillosis, with pathological findings consistent with either infarction or abscess, splenic invasive aspergillosis is rarely reported and may be underestimated in clinical practice when presenting without symptoms especially (3). In another study, it was shown that 55 of 107 patient with invasive aspergillosis had extrapulmonary involvement in autopsy series (2). In conclusion, extrapulmonary involvement must be thought in drug-resistant invasive fungus infections and surgical therapy should be considered.

Keyword: B-acute lymphoblastic leukemia, Hepatosplenic Hyalohyphomycosis

Poster No: 0020 Abstract:0264

MANAGEMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING AS SPONTANEOUS SEVERE TUMOR LYSIS SYNDROME: A CASE REPORT

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Hyperuricemia, mostly seen in tumor lysis syndrome (TLS), is a well-recognized complication of various cancers, especially in patients with hematologic malignancies, such as acute lymphoblastic leukemia (ALL) and Burkitt's lymphoma mostly (1). Tumor lysis syndrome frequently seen after treatment of hematologic malignancies but may also be seen before treatment (2,3). We here report management of a patient diagnosed as B-ALL with spontaneous tumor lysis syndrome and severe hyperuricemia.

A 48-year-old male presented to our clinic with dyspnea. His physical examination was normal and laboratory

results showed white blood cell count of 44.000/mm^3 being %54 lymphoid blasts, 16% neutrophil, 22% lymphocyte, 5% monocyte, 3% eosinophil, hemoglobin 13.8 gr/dl, thrombocyte 26.000/mm^3, serum creatinine 4.6 mg/dl, BUN 46 mg/dl, Na 138 mmol/L, K 5.9 mmol/L, Ca 10.8 mg/dl, lactic dehidrogenase (LDH) 2861 u/l, and uric acid 60 mg/dl. Bone marrow biopsy detected 44% B cell origin lymphoblasts. Cytogenetic examination revealed t(8:14) abnormality and diagnosed as B-ALL. Because of decreased urine output, very high uric acid levels and nephrotoxic side effects of chemotherapeutic agents chemotherapy was delayed. Allopurinol 75 mg/day and hydration were started. New generation xanthine oxidase inhibitors couldn't be given due to social security problems and within the first 24 hours two leukopheresis and one hemodialysis were performed. One leukopheresis and one dialysis were applied in following 24 hours also. Leucocyte and creatinine values decreased to 25000/mm^3 and 2.2 mg/dl, respectively. Uric acid level was 20 mg/dl. HyperCVAD protocol with dose reduction was started after increased urine output.. Hemodialysis was performed six times on alternate days and quitted after having normal uric acid level of 5 mg/dl, normal renal function tests and electrolyte levels. Results of bone marrow biopsy and flow cytometry applied on the 23th day of the treatment revealed remission and his renal function tests, LDH and uric acid results were all normal.

TLS sometimes occurs spontaneously before starting cancer chemotherapy. However, presumably due to the limited number of patients experiencing spontaneous TLS, there have been no large-scale cohort studies of spontaneous TLS to date. Hyperuricemia is apparently one of the cardinal manifestations of TLS (1). Four independent risk factors defined for TLS including age>10, splenomegaly, mediastinal mass and initial WBC>20000/mm^3. Also our patient classified as grade 3 which means high morbidity and mortality risk according to Cairo and Bishop grading classification of TLS (2). Therefore in this case because of nephrotoxic effects of chemotherapy and worsening risk of TLS, we chose white blood cell reduction by leukopheresis as the first line treatment. Also allopurinol utilization for decreasing uric acid levels and hemodialysis sessions for improving hemodynamic stability have a positive influence on overall survival.

Keyword: acute lymphoblastic leukemia, tumor lysis syndrome

Poster No: 0021 Abstract:0276

INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH ACUTE LEUKEMIA

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Invasive fungal infection (IFI) is an important cause of morbidity and mortality in children with leukemia.

The medical records of the patients with acute lymphoblastic (n=112) and acute myeloblastic leukemia (n=26) who were treated at Ege University Medical School, Pediatric Hematology Department between 2005 and 2012 were retropectively reviewed to determine the rate, causative agents, and the outcome of IFI.

All pateients received nystatin oral solution since the diagnosis. None of the patients were given prophylactic antifungal treatment. A total of 53 IFI episodes were recorded in 51 (Male/ Female= 25/26) patients. The rate of IFI among the patients with acute leukemia was 36.9%. The median age of the patients was 8.2 (range 1.5-16) years.

IFI was classified as proven in 17 (32%), probable in 8 (15.1%) and possible in 28 (52.8%) episodes. Ten of the episodes (18.9%) were disseminated fungal infection, 37 (69.8%) were lower respiratory tract infection and 6 (11.3%) were sinonasal infections. The causative fungus was microbiologically documented in 21 episodes (39.6%). In 9 IFI episodes (42.9%) Candida spp. (2 albicans, 2 parapsilosis, 2 krusei, 1 kefyr, 1 gullimanti, 1 tropicalis), in 5 IFI episodes (23.8%) Aspergillus spp. (3 fumigatus, 2 flavus) and in four IFI episodes (19.1%) Geotrichum capitatum were isolated. Acremonium spp., Mucor and Trichosporon asahii, each were documented in one episode.

Three month survival of these patients after the diagnosis of IFI was (84.3%). IFI was the main cause of death in 4 patients (7.8%).

Keyword: invasive fungal infection, children

Poster No: 0022 Abstract:0281

METHYLENE TETRAHYDROFOLATE REDUCTASE GENE POLYMORPHISM AND RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction and Objectives: Childhood acute lymphoblastic leukemia (ALL) is the most common malignancy affecting children, constituting about 30% of all cancers among children. It constitutes about 75% of pediatric acute leukemia with peak incidence between ages 3 and 4. Genetic factors may predispose children to develop leukemia. Recently, genetic variants of the Methylene tetrahydrofolate reductase (MTHFR) gene have been subject to increasing attention in the etiology of leukemia. Gene polymorphism at the nucleotide 677 in MTHFR gene (C677T) (Ala→Val) results in a less stable version of the enzyme. This study aimed at determination of the relationship between MTHFR gene polymorphism (C677T) and increasing susceptibility of childhood ALL among Egyptian children.

Methods: DNA was isolated from 60 pediatric ALL patients (cases) and from 40 healthy donors (controls). We detected the MTHFR C677T genotype in ALL patients and compared it with the genotype of controls by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) using Hinf I restriction endonuclease.

Results: T-allele carriers were significantly lower in ALL cases (43.3%) than healthy controls (55%). Reduction in ALL risk was observed for heterozygous (CT) or homozygous (TT) carriers of the MTHFR 677T allele (OR 0.7; 95% CI, 0.5-1.0; P < 0.05).

Conclusion: our data suggest that the MTHFR gene variants are associated with decreased ALL rate and risk. the reduced risk associated with the MTHFR C677T polymorphisms may be the result of changed intracellular folate redistribution.

Keyword: ALL, MTHFR

Poster No: 0023 Abstract:0284

ASSESSMENT OF NEUROPSYCOLOGICAL LATE EFFECTS IN SURVIVORS OF CHILDHOOD LEUKEMIA

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The neurologic dysfunctions caused by treatment may affect health and quality of life in survivors of childhood leukemia. The objective of this study was to identify the neuropsychological late effects of leukemia treatment to provide an assessment about the degree and incidence of these late effects. Neurological and ophtalmological examination, cranial magnetic resonance imaging (MRI), auditory and neurocognitive tests, and questionnaires of quality of life were performed to 44 acute leukemia survivors at least 5 years after diagnosis. Median time since completion of chemotherapy was 7.5 years (2-18) and median age at the time of the study was 16.4 years (8-31). At least one or more late effects detected by physical examination, neurological tests or neurocognitive tests encountered in 80% of the patients, and 64% of the patients specified at least one complaint in the quality of life questionnaire. MRI revealed pathological findings in 18% and EEG abnormalities were present in 9% of the patients. Evaluation of total intelligence scores revealed that 30% of patients' IQ scores were <80 and 70% of the patients' scores demonstrated neurocognitive dysfunctions. The patients >6 years at the time of diagnosis were found to have more psychological problems and higher rates of smoking and alcohol consumption. The most frequent complaint was headache and the most common problem in school was denoted as difficulty in concentration. Our study demonstrated that most of the survivors of childhood leukemia are at risk of developing neuropsycological late effects.

Keyword: Acute leukemia, late effect

Poster No: 0024 Abstract:0287

SERUM CYTOKINE AND ADHESION MOLECULE LEVELS IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND IN HEALTHY SUBJECTS

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Background: Cytokines and adhesion molecules have been studied as markers of immune system activation in various diseases including hematological malignancies. Alterations in this network may have direct effect on the malignant cells or have indirect effect on leukemogenesis through altered functions of bone marrow stromal elements. The knowledge gained from multiple cytokine and adhesion molecule analysis should allow better diagnosis and disease management.

Objectives: The aim of our study was to evaluate serum cytokine and adhesion molecule levels by biochip array technology in patients with acute lymphoblastic leukemia (ALL) and in healthy subjects.

Methods: Serum samples of 15 newly diagnosed ALL patients (median age 46, range 24 - 63 years, 11 males) and 15 healthy subjects (median age 41, range 25 - 58 years, 11 males) were analyzed. We evaluated serum levels of the following 22 cytokines and adhesion molecules: interleukins (IL-1 alpha, IL-1 beta, IL-2, IL-3, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-23), vascular endothelial growth factor (VEGF), tumor necrosis factor-alpha (TNF-alpha), interferon-gamma (IFN-gamma), epidermal growth factor (EGF), monocyte chemotactic protein-1 (MCP-1), E-selectin, L-selectin, P-selectin, intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1). All biomarkers were measured by biochip array technology on Evidence Investigator analyzer (Randox). Probability values (p) < 0.01 were considered statistically significant.

Results: In newly diagnosed ALL patients, we found significant increase in serum VCAM-1 (1078.54 ± 456.96 mcg/L vs. 328.31 ± 88.66 mcg/L; p < 0.000001), ICAM-1 (499.57 ± 237.53 mcg/L vs. 196.69 ± 36.06 mcg/L; p < 0.0001), L-selectin (2366.33 ± 1035.37 mcg/L vs. 1104.54 ± 243.45 mcg/L; p < 0.0001), IL-8 (34.07 ± 28.52 ng/L vs. 4.87 ± 3.09 ng/L; p < 0.001), MCP-1 (433.99 ± 328.59 ng/L vs. 153.25 ± 53.60 ng/L; p < 0.01). On the other hand, we found significant decrease in serum IL-3 (7.34 ± 3.41 ng/L vs. 11.53 ± 4.66 ng/L; p < 0.01), IL-4 (1.10 ± 1.08 ng/L vs. 3.27 ± 2.21 ng/L; p < 0.01). Serum levels of other evaluated cytokines and adhesion molecules were without significant differences.

Conclusions: Our results indicate that serum levels of some cytokines and adhesion molecules (VCAM-1, ICAM-1, L-selectin, IL-8, IL-3, IL-4, MCP-1) are significantly altered in patients with newly diagnosed ALL, reflecting activity of the disease. Whether these alterations could have a prognostic meaning for ALL is not known. Further studies in a larger number of patients and comparing cytokine and adhesion molecule levels with established prognostic markers will be essential to assess the potential role of these and additional markers in the risk stratification of ALL patients.

The work was supported by a long-term organization development plan 1011 (FMHS).

Keyword: cytokines, acute lymphoblastic leukemia

Poster No: 0025 Abstract:0296

DETECTION OF *MYC* GENE REARRANGEMENTS BY FLUORESCENT IN SITU HYBRIDIZATION IN ACUTE LYMPHOBLASTIC LEUKEMIA CASES

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Objective: The aim of this study, to investigate changes at the region of MYC gene by interphase FISH in patients with acute lymphoblastic leukemia that analized by conventional cytogenetic methods.

Material-Methods: The study was carried out on 33 bone marrow specimens of 25 ALL patients were referred to our laboratory between 2007 and 2009. Fourteen childhood ALL and 11 adult ALL cases were examined. For conventional cytogenetic analysis, overnight colcemid incubation and 24 hour culture methods were performed and GTL banding technique was applied. To investigate changes at the region of MYC gene Fluorescent In Situ Hybridization technique with MYC breakapart probe (Cytocell) was used.

Results: FISH analysis was applied successfully in all 33 samples from 25 cases, while in 29 samples out of 33 (88%) cytogenetic results were obtained. We observed MYC rearrangements in one or more samples of 21 cases (84%) by FISH. Abnormal karyotypes were found in 16 out of 29 (55%) samples which cytogenetic examination was performed. In 9 cases, these abnormalities were simple, and complex in 7 cases. The only cytogenetic abnormality that contain MYC region was t(8;14)(q24;q32) which observed in one case.

Conclusion: The rate of MYC rearrangements found by FISH in this study (84%) was higher than literature (47-52%). Findings of t(8;14)(q24;q32), t(9;22)(q34;22), 6q deletions and 11q23 rearrangements that we observed by karyotyping are reported in literature as common chromosomal abnormalities in ALL. FISH method is more suitable for investigating MYC rearrangements as being easy, fast and sensitive to the submicroscobic rearrangements than karyotyping. Nevertheless, conventional karyotyping has still great value as being informative for the entire genome and enabling to detect the changes other than known target sites.

Keyword: Acute Lymphoblastic Leukemia, MYC

Poster No: 0026 Abstract:0297

THE OUTCOMES OF TURKISH CHILDREN WITH ACUTE MYELOID LEUKEMIA TREATED ON AML- BERLIN-MUNSTER-FRANKFURT (AML-BFM) PROTOCOL: TURKISH AML-BFM STUDY GROUP

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Aim: Acute myeloid leukemia (AML) is a heterogenous disease in which leukemic blasts proliferate and invade healthy bone marrow. It makes 15 to 20 % of childhood acute leukemias. Recent developments in both the chemotherapeutic regimens and supportive result in a better survival in children with AML. We evaluated the 192 Turkish children with AML treated in 23 different centers, and received AML-Berlin-Munster-Frankfurt (BFM) protocol.

Patients and Methods: We retrospectively evaluated the medical records of the children with AML, who received AML-BFM regimen, and analysed the data gathered from different centers.

Results: Mean age of the patients were 8.7±7.9 months (10 days–17 year), and male/female ratio was 1.4. The most common French-American-British subgroup among the patients with a known subgroup was M2 with a frequency of 31.3%. Complete remission rate was 98.4%. Eleven percent received hematopoetic stem cell transplantation. Overall survival and event free survivals were 58.8 and 58.4 % respectively. Among them 29.2% died. Infection (57.7%) was the most common cause of death, followed by relapse, resistant disease, and hemorrhagy.

Conclusion: Although our patients have a high rate of complete remission, overall and event free survivals were similar to previously reported results. Since the most common cause of death was infection, a standardized and good supportive care plan may improve survival or the patients.

Keyword: AML, treatment

Poster No: 0027 Abstract:0305

USEFULNESS OF FLOW CYTOMETRY IN DISTINCTION BETWEEN ACUTE PROMIELOCYTIC LEUKEMIA AND ACUTE MYELOID LEUKEMIA- SINGLE CENTER EXPERIENCE

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Acute promyelocitic leukemia (APL) is unique clinicobiologic entity. Loss of HLA-DR and CD34 is characteristic of malignant promyelocytes. But some cases of acute myeloid leukemia(AML) have an immunophenotype that is similar to APL(HLA-DR- CD34-).The objective of the study was to investigate antigenic features in a group of APL with presence of PML-RAR alfa fusion gene and non-APL patients in order that differences to allow more clearly define criteria to separate APL from non-APL.

Methods: We analyzed a series of 30 APL and 32 of non-APL patients who were diagnosed in the last three years at the University Clinic for Hematology in Skopje, Macedonia. The diagnosis of acute leukemia was made by standard morphological examination and cyto-chemical analyses of bone marrow smears according to the criteria established by FAB Cooperative Study Group and confirmed by immunophenotyping of bone marrow aspirates and/or peripheral blood samples following the criteria of the European group for the immunological Classification of acute leukemias (EGIL). Flow cytometry analyses were performed by using the FAXS Canto II BD flow cytometer analyzer. Acquired data were analyzed with the software FACSDiva version 6.1.2 by using CD45 gating strategy Slightly modified panel of monoclonal antibodies (McAb) against myeloid- and lymphoid-associated antigens as suggested by the EGIL was utilized.

Results: Our results showed significant differences between APL and non-APL patients in CD2, CD13, CD33 reactivity. Aberrant CD2 expression was absent in every patient with non- APL, also we found absent CD15 expression in whole non-APL group. Mean florescence intensity of CD33, CD13 showed differences between the two groups. Also we noticed increased leukocyte and platelets counts in HLA-DR- CD34- non- APL patients.

Conclusion: CD2, CD13, CD33 may be useful to distinguish APL from non-APL patients with HLA-DR-CD34-.But cytogenetic and molecular characterization is necessary to establish the diagnose of AML.

Keyword: APL, immunophenotype

Poster No: 0028 Abstract:0317

BLASTIC PLASMOCYTOID DENDRITIC CELL NEOPLASM (BPDCN): SINGLE CENTER EXPERIENCE OF A RARE MALIGNANCY

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Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, highly aggressive hematopoietic malignancy that is characterized by cutaneous infiltration with or without bone marrow involvement and further leukemic spread. Its overall incidence is very low, accounting for 0.44% of all hematologic malignancies. The leukemic form of the disease is an extremely rare situation, representing <1% of all cases of acute leukemia. BPDCN predominantly affects males, with a sex ratio of 3:1, and generally occurs in the elderly. Aim: The aim of this presentation was to evaluate symptoms, signs and outcome of one case of BPDCN in our center. Method: We identified 1 patient with BPDCN presenting with skin lesions. Data regarding clinical presentation, diagnosis, staging, treatment and outcome was collected. Results: The patient was male, 75 years-old. At diagnosis he had asymptomatic skin lesions. He had a generalized purplish dermal rash arising from the head to the lower extremities that presented one week before and progressed very rapidly. Laboratory data revealed anemia (hemoglobin: 10, 9 g/dl), thrombocytopenia (100×109/L), WBC: 8.30*103/μL with 42% of morphologically immature atypical cells. Bone marrow aspiration showed 88% infiltration of immature blastic cells with the following immunophenotype: CD45 (+) low, CD43 (+), CD123 (+), CD56 (+), CD4(+), CD34 (-). Cytogenetic analysis showed deletion of the long arm of chromosome 12 - deletion of ETV6 gene and deletion of the long arm of chromosome 17- deletion of P53 gene. Computed tomography scans did not disclosed any pathologic lymphadenopathy. Histopathology of skin lesions showed infiltration of blastic cells. Immunohistochemical analysis confirmed the presence of cells with the same immunophenotypic features. He started chemotherapy with Zavedos and Aracytin (3+7) and he is now in CR after this induction.

Conclusion: We present a case of a rare clinical entity with cutaneous and bone marrow infiltration with blastic plasmocytoid dendritic cells. The diagnosis relied on the immunophenotypic features of the malignant cells, particularly with the presence of CD4 (+) and CD 56(+). Several treatment options have been used so far, all with poor results. The ALL-type treatment regimen seems to result to a better outcome, according to recent publication. Unfortunately, our patient couldn't proceed to bone marrow transplantation which is a better therapeutic option for younger patients with good performance status.

Keyword: dendritic cell, leukemia

Chronic Lymphocytic Leukemia

Poster No: 0029 Abstract:0124

THE SIMULTANEOUS DIAGNOSIS OF CHRONIC LYMPHOCYTIC LEUKEMIA AND MEGALOBLASTIC ANEMIA SECONDARY TO VITAMIN B12 DEFICIENCY

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Introduction: Cytopenias in chronic lymphocytic leukemia (CLL) might have various causes like bone marrow infiltration, autoimmunity, hypersplenism and drugs. Pernicious anemia is an autoimmune disease which might result in cytopenias; and pernicious anemia as an autoimmune phenomenon has not been described in CLL.

Case: A 71-year-old man was hospitalized with the complaints of fatigue, tiredness. On physical examination, he had conjunctival pallor and there was atrophy of tongue papillae. There was no peripheral lymphadenopathy, hepatomegaly or splenomegaly. His whole blood count was as follows: hemoglobin, 6.4 g/dl; hematocrit, 19%; MCV, 136.5 fL; leucocytes, 30900/mm^3; platelets, 35000/mm^3. Blood biochemistries were normal, except for a LDH of 729 U/L (N<192). On peripheral blood smear, there were macroovalocytes and hypersegmentation of neutrophil nuclei, with 5% neutrophils and 95% small-appearing lymphocytes. Serum folic acid level was 7.3 ng/ml (N:3-17), and vitamin B12 level was 100 pg/ml (N:140-950). Haptoglobin was <5.83 mg/dl (N:36-195). The corrected reticulocyte count was 3%. Both direct and indirect Coombs tests were negative. Flow cytometric analysis of peripheral blood showed a monoclonal B-cell population which was positive for CD5, CD19, CD20, and CD23 with a dim surface k light chain restriction. Bone marrow aspiration revealed 48% lymphocytes; there were megaloblastic changes of erythroid and myeloid cells, with giant metamyelocytes and stabs (Figure 1). Thorax and abdominopelvic CT scans demonstrated no lymph nodes or hepatosplenomegaly. Being diagnosed simultaneously with Rai stage 0 CLL and megaloblastic anemia secondary to vitamin B12 deficiency, the patient was administered replacement therapy with intramuscular vitamin B12. The cause for his megaloblastic anemia was assumed to be pernicious anemia because there was no other cause which could explain the vitamin B12 deficiency. On his last follow-up, his hemoglobin was 14.8 g/dl; hematocrit, 44.8%; MCV, 86.7 fL; leucocytes, 29800/mm^3; platelets, 342000/mm^3.

Conclusion: Our case was interesting in that there was a co-incidence of CLL and vitamin B12 deficiency. We reported this case to draw attention to the fact that cytopenias in CLL might have rare causes which might even be missed if a bone marrow examination is not performed. We suggest that even if the diagnosis of CLL is straightforward, the bone marrow aspiration should be examined in every patient with CLL.

Keyword: Chronic lymhocytic leukemia, megaloblastic anemia

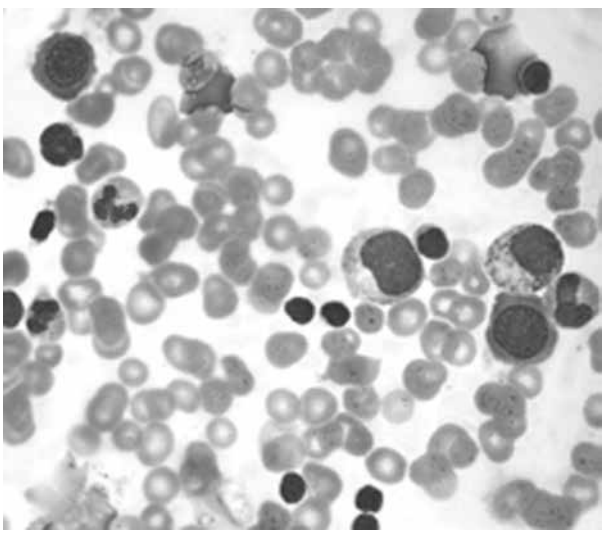

Figure 1.Bone marrow aspiration showing many small, mature lymphocytes, two megaloblastic erythroblasts, and some myeloid cells.

Poster No: 0030 Abstract:0143

GROWTH ARRREST SPECIFIC (GAS6) LEVEL IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

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Background: Gas6 (growth arrest-specific gene 6) is from the family of plasma vitamin K-dependent proteins. Gas6 was similar to the plasma anticoagulant protein S. Whereas protein S is as a negative regulator of procoagulant pathways, no such a role has been found for Gas6. Gas6 binds to Tyro3, Axl and Mer tyrosine kinase receptors (TAM receptors). Increased plasma concentration of Gas6 has been found in patients with sepsis and chronic inflammatory neuropathy, whereas decreased in acute coronary syndrome. This contradiction may suggest that Axl/Gas6 pathway varies depending on the type of patient's illness. The objective of this study was to investigate the total plasma level of Gas6 in patients with B-Cell chronic lymphocytic leukemia (B-Cell-CLL).

Material-Methods: B-Cell-CLL patients (grade 0-1, according to the classification of RAI), who were not on a drug treatment, were recruited in this study (n= 24, 11 female, 13 male). Their ages were 39 to 79 years (mean= 60.7), and the control group consisted of 24 healthy volunteers (8 female, 16 male), whose age range was 51-78 years (mean= 63.5). EDTA-plasma (platelet poor) was isolated by centrifugation (3100 x g) and then human Gas6 ELISA Kit (R&D, Minneapolis, MN, US) was used to assay Gas concentration.

Results: The quantitative of total plasma Gas6 range in patient group is 4.11-26.44 ng/ml (mean= 14.85 ± 5.77). In the control group, range of total plasma Gas6 was between 9.57-31,28 ng/ml (mean= 16.8±6.18). The concentration of plasma Gas6 in the B-Cell-CLL group was not significantly different than those of the control group (p=0.265).

Conclusion: This is a preliminary study with a small group, future studies will show us that whether plasma Gas6 concentrations in patients with CLL are different from control group or not. Further studies focusing on molecular mechanism are required to elucidate the actual role of Gas6/TAM signaling in B-Cell-CLL.

Keyword: ELISA, growth arrest-specific gene 6(Gas6)

Poster No: 0031 Abstract:0152

CHRONIC LYMPHOCYTIC LEUKEMIA AND CD11C EXPRESSION

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Objective: CD11c belongs to the integrin family which is a group of cell adhesion molecules. There is a clinical significance of CD 11c positivity is in hairy cell leukemia. CD11c has been evaluated in the patients with chronic lymphocytic leukemia (CLL) in a few studies. CD11c positivity has been detected in 13-78% of patients with

CLL. The present study aims to evaluate the relationship between CLL and CD11c.

Material-Methods: In 81 patients (44 male and 37 female with mean age of 64±16 years) with CLL studied, CD11c values were retrospectively evaluated with flow cytometry using with EPICS XL-MCL instrument. The positivity of CD11c was accepted when values were more 20%. The relationship between CD positivity and stage and life expectancy was investigated with Kaplan-Maier survival analysis and ANOVA tests. 53 of the patients were Binet stage A, 26 patients were Binet stage C.

Results: The mean level of CD11c expression was 24%±19%. There was no difference for CD11c expression between Binet stage A and C. CD11c positivity was detected in 39 (48%) of the patients with CLL positive. Median survival could not be reached in both CD11c positive and negative patients. There is no statistically significant difference for mean overall survival between both CD11c positive and negative with Binet A and C ($p>0.05$). The durations of mean overall survival were 122 months for CD11c negative patients with Binet A and 70 months CD11c positive patients with Binet A. These durations are 113 months for CD11c negative patients with Binet C and 31 months CD11c positive patients with Binet C.

Conclusion: The significance of CD11c expression is not clear in CLL. Although CD11c expression did not affect survival duration in CLL according to Binet stages, new studies with more patients can be benefit.

Keyword: CD 11c expression, Chronic Lymphocytic Leukemia

Poster No: 0032 Abstract:0177

DETECTION OF T(14;18)(Q32;Q21) AND TRISOMY 12 IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA

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Summary: Chromosomal abnormalities are observed in most hematologic malignancies. t (14.18) positivity which is diagnosed in 80-90% follicular lymphoma is seen rarely in Chronic Lymhocytic Leukemıa (CLL) patients. For this reason, we found this case suitable for presantation.

Case: 53-years-old male patient was admitted to hospital with weight loss, had multiple lymphadenopathy at neck, axilla and hapatosplenomegaly. The patient had leukocytosis and thrombocytopenia. Mature lymphocytosis, basket cells and prolymphocyte 15% respectively was determined in the patient's peripheral blood smear. The flow cytometric analysis of bone marrow aspiration was considered as CLL with the bone marrow biopsy. Trisomy 12; 85.5% positive, t(11.14); negative, t (14.18) were positive in patients. t (14.18) was repeated twice and positivity was confirmed. Oral fludarabine, cyclophosphamide therapy was started due to weight loss and thrombocytopenia. After 6 cycles of treatment, complete haematological remission was achieved.

Discussion: t(14,18) translocation is seen in 80-90% of follicular lymphomas. It is often associated with low-grade lymphoma. Bcl2 gene regulates programmed cell death and a small number of patients with CLL (5-10%) t(14,18) positivity is determined. Bcl2 inhibits apoptotic cell death. Course of patients with BCL2-expressing in high-titer can seen poor outcome in CLL patients ($p<0.02$). t (14.18) positivity is thought to be a poor prognostic indicator in CLL patients. Only one of 300 patients who were followed in our clinic with the diagnosis of CLL had t (14.18) positivity. Conventional cytogenetic analysis were made to 2215 patients with CLL in M.D. Anderson cancer center, t (14.18) and the trisomy 12 positive found in only two of them. After 8 years of the diagnosis, the patient died due to secondary infection of treatment. t (14.18) were positive at only 3 patients in 640 CLL patients of an international working group.

Chemotherapy was started due to weight loss, and thrombocytopenia. Treatment response was very good. Considering the literature, donor were searched for allogeneic stem cell transplantation because of the possibilty of t (14.18) translocation with poor clinical outcome in CLL. Our patient remains in remission after treatment for 2 years.

Keyword: Chronıc lymhocytıc leukemia, bcl2

Poster No: 0033 Abstract:0188

CHRONIC LYMPHOCYTIC LEUKEMIA-ASSOCIATED IMMUNE THROMBOCYTOPENIA SUCCESSFULLY TREATED WITH RITUXIMAB: A CASE REPORT

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Introduction: The clinical course of chronic lymphocytic leukemia (CLL) may be complicated by hematologic autoimmune disorders. The most common of them being autoimmune hemolytic anemia. Immune thrombocytopenia (IT), and pure red cell aplasia is may also be observed despite less commonly. It has been estimated that IT can complicate the course off CLL in approximately 2% of patients. However, its occurrence appears to be associated with a poor prognosis of CLL. In addition, platelet count < 100 x 10^9/L at diagnosis recognizes more advanced patients with CLL according to Rai and Binet clinical staging systems independent of the etiology of thrombocytopenia. Rituximab chimeric monoclonal antibody targeting CD20 antigen on B-lymphocytes. It has become therapeutic regimens of non-Hodgkin's lymphomas and CLL because of its efficacy on lymphoid B-cells. Rituximab is also successfully used to treat hematologic autoimmune disorders both related to or not to CLL and is now increasingly used for non-hemic autoimmune disorders such as rheumatoid arthritis. It has been used in the treatment of fludarabine-induced İT.

Case presentation: Forty-eight-year-old male patient was diagnosed with stage I CLL in Rai staging system In December 2012. In the first diagnosis, leucocyte 56000/mm^3, lymphocyte 46000/mm^3, hemoglobin 11.7g/dl, platelet count 4810/mm^3, respectively. In peripheral blood smear, 85% mature lymphocytes and many smudge cells were observed. On physical examination the patient had 2 cm cervical lymphadenopathy. He had no B symptoms. Deletion 13q and 17p were negative. Autoimmune work up for coombs tests and anti-platelet antibodies were negative. The patients was given steroids at a dose of 1mg/kg/gün as first-line treatment. There was no answer. The two-day high-dose intravenöz immunglobuline (1g/kg/gün) treatment was applied. Again, no response. Helicobacter pylori was positive with urea breath test. Eradication therapy was given. The single cycles of CHOP (cyclophosphamide, vincristine, doxorubicin, prednisolone) chemotherapy to patients was received as cytotoxic therapy. At the end of treatments

remained below 25,000 platelets. İn recent studies, response to first-line treatments was 50% to %60; about 20% was refractory. We think that this refractory group of our patients. Later, the patient was scheduled to receive rituximab at a dosage of 375mg/m^2/weekly for four consecutive weeks. Maximum platelet count at the end of treatment reached to 95000/mm^3, but remained stable in 52900/mm^3. Partial response was accepted as. An Italian study; in 21 patients with CLL-associated İT, complete response to treatment with rituximab.was observed in 57% of cases, partial response in 29% of cases. In the same study 14% of patients were no response. The mean duration of response was observed for 21 months (ranging from 4 months-49 months). We believe that in our case that rituximab is an effective and well-tolerated alternative treatment for CLL-associated İT.

Keyword: CLL, rituximab

Poster No: 0034 Abstract:0203

THE CLINICAL SIGNIFICANCE OF ZAP-70 AND OTHER CELL SURFACE-ANTIGEN EXPRESSION (CD38-CD138-CD56-CD16) PROFILING OF CHRONIC LYMPHOCYTIC LEUKAEMIA

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Objective: Chronic Lymphocytic Leukemia (CLL) is characterized by increased number of mature non-proliferative lymphocytes in blood stream, bone marrow, lymph node and spleen with different clinical course. Family history is an important risk factor for CLL. It is suggested that the malignant transformation of B cells play an important role for CLL development while less than 1 % is caused by T lymphocytes. Although most CLL patients are elderly, 10% of them are younger than 50.

In CLL patients, Rai and Binet classification systems are established for determination of the necessity of treatment and prediction of survival. However, the prognostic value of these classifications is limited in early staged patients. The presence IgVH somatic mutation in the heavy chain variable region of immunoglobulin has been found a valuable prognostic factor. Patients with IgVH mutation shows a better clinical course than those without. After determination of the relationship between expression of zeta-associated protein (ZAP70) and IgVH mutation in CLL cells, a lot of research has been made for the usage of expression of ZAP70 rather than IgVH mutation of an expensive technique.

Finally, CD38 and CD138 are suggested to be important prognostic markers in some studies.

Methods: In this study, ZAP70, CD38, CD138, CD56, CD16 expression levels were measured from bone marrow aspirations of patients with CLL by flow cytometry of an inexpensive and easy method. Expression levels over 20% were considered as positive.

Results: ZAP70 expression was positive in 5 of 35 investigated patients. There was no significant correlation between ZAP 70 expression and patients' age, sex, hemoglobin and LDH levels, leukocyte, lymphocyte and platelet counts.

CD38 expression was positive in 3 of 35 investigated patients. There was no significant correlation between CD38 expression and patients' age, sex, hemoglobin and LDH levels, leukocyte, lymphocyte and platelet counts. In only one patient, both ZAP70 and CD38 expressions were positive. There was no significant correlation between ZAP70 with CD38 positivity.

CD138, CD56, CD16 was expressed at low levels in all patients.For demonstrating the relation between the expression of ZAP70 and CD38 over 20% and the prognosis of CLL patients, long-term observational studies are needed.

Conclusion: Long-term clinical observational studies with control groups should be made for understanding the effects of surface antigens in staging and prognosis of CLL.

Keyword: CLL, surface-antigen expression

Poster No: 0035 Abstract:0243

CEREBRAL INVOLVEMENT AS THE INITIAL MANIFESTATION OF CHRONIC LYMPHOCYTIC LEUKAEMIA

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Introduction: Chronic Lymphocytic Leukemia (CLL) is the most common type of leukemia in adults, which is around 24%. Its rate is 6.7% in all non-Hodgkin lymphoma. CLL is a disease caused by monoclonal mature lymphocytes accumulation. The roots of more than 95% of the cases consist of B lymphocytes. The prevalence increases with the age. CLL is more common in men. The median age of the patients is 60 - 65. The cerebral involvement in CLL is very rare. However, it may occur in early stages of CLL.

Case: A male patient with the age of 40 applied to the neurosurgery with the complaints of headache lasting around 20 days, paresthaesia and weakness in the right side of the body, sight impairment in the right eye and seizures, and a cerebral mass has been detected after the examination, and then stereotactic needle biopsy has been performed. As the result of biopsy has been atypical lymphoid cells infiltration, the patient has been sent to the hematology out-patient clinic. When the patient applied to our clinic, there has been symptoms of fever, perspiration, weight loss and B symptoms. The leukocyte count in CBC has been 24.800/µL, and lymphocyte count has been 13.000/µL. Haemoglobin and platelet values have been normal. There has been mature lymphocytosis and smudge cells in peripheral blood smear. Multiple cervical and axillary lymphadenopathy in 20 mm size in maximum has been detected at neck, thorax and abdominal computarized tomography, and splenic size has been 15 cm. Basal ganglia has been detected in left periventricular area and hypodens areas in corona radiata at cranial tomography. CLL has been diagnosed in the patient with flowcytometric examination, bone marrow aspiration and biopsy evaluation. Rai Stage II CLL has been accepted. Even though the patient has been at the early stages, systemic chemotherapy, intrathecal treatment, and cranial radiotherapy has been applied due to B symptoms and symptomatic cerebral mass.

Discussion: The cerebral involvement in CLL is extremely rare. Central nervous system involvement can be observed particularly during the transformation process into agresive lymphoma, called Richter syndrome. However, it can be rarely observed in early stages of CLL.

There is not any standardized treatment protocol for CLL patients with cerebral involvement. If there is cranial radiotherapy and spinal liquid involvement, the treatment protocol should include intrathecal chemotherapy with methotrexate. In this way, long term remissions can be achieved. This case has been presented because cerebral involvement is very rare in early stages of CLL and so as to review the treatment for CLL cases with cerebral involvement.

Keyword: Chronic Lymphocytic Leukemia, cerebral involvement

Poster No: 0036 Abstract:0247

EVALUATION OF CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS FOLLOWED BY HEMATOLOGY DEPARTMENT OF BASKENT UNIVERSITY: SINGLE CENTER EXPERIENCE

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Objective: Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults(1). It is unclear what aberrations are associated with the disease onset and its strikingly heterogeneous clinical course (2). Multiple factors, measured in standard clinical laboratory tests, affect the clinical course of CLL. Currently, the most important traditional prognostic factor include clinical staging (3); and the most important novel markers include karyotypic aberrations. The 13q14 deletion is the most common genetic abnormality in CLL (4). Patients have a minimum 1 year follow-up. We divided the patients into two groups: the patients who survived at least until the end of follow-up and the patients who died during the follow-up. In this study, we evaluated the demografic and prognostic factors of patients such as age, gender, lymphocyte doubling time (LDT), CD38 and ZAP-70 expression, type of bone marrow infiltration pattern within these two groups in 52 CLL patients who were observed from 2005 to 2012 in hematology department of Baskent University Faculty of Medicine.

Methods: Demographics of 52 patients who admitted to the hematology department between 2005 and 2012 were investigated retrospectively.

Results: 34 patients were male (% 65,4), 18 patients were female (%34,6). The age range at the onset of chronic lymphocytic leukemia is from 46 to 93. The median age was 69. While 26 patients were being observed without treatment, 26 patients were treated with oral or iv multidrug chemotherapy. At the time of diagnosis, 17 (33%) patients were at Binet stage A, 29 (56%) were at stage B, 6 (11%) were at stage C. After the first line Chemotherapy (iv or oral chemotherapy agents); partial remission for 12 (%46), complete remission for 7 (%27), progression for 7 (%27) patients were observed. 13 (%25) patients died during the follow-up. Cytogenetic analysis was performed in 45 patients. Of these patients, 30 (58 %) have no cytogenetic abnormality, 9 have (17%) del(13q14), 3 have (6%) trisomy 12, 2 have (4%) del(11q22) and 1 patient (2%) has del(17p13) respectively. There was no relationship between the expression of zeta-associated protein (ZAP-70) (p=0,295) and the β2 microglobulin (β2 MG)(p=0,099) with survival but the serum LDH level (p=0,008), the absolute lymphocyte count more than 50000/µl (p=0,035), the expression of CD38 (p=0,011), the stage of disease (p<0.0001), diffuse infiltration pattern of bone marrow (p=0,033) was inversely related with the survival. Survival in male patients was significantly less than female patients (p=0.018)

Conclusion: Multiple factors affect the clinical course and survival of CLL. Some of these; absolute lymphocyte count, bone marrow infiltration pattern, elevated LDH, lymphocyte doubling time; ß2-microglobulin; genetic markers of tumor cells, gene abnormalities, the expression of CD38 and ZAP70. We founded same results mentioned before in literature in our CLL patient group.

Keyword: chronic lymphocytic leukemia, prognostic factors

Poster No: 0037 Abstract:0265

UNUSUAL CLINICAL SITUATION AND COURSE OF BLASTOID VARIANT T-CELL PROLYMPHOCYTIC LEUKEMIA

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Introduction: T-cell prolymphocytic leukemia (T-PLL) is a rare, aggressive lymphoid malignancy composed of mature T-cells that usually presents in older people. Prognosis for these patients remains poor, with short survival times and no curative therapy.

Case: Seventy-seven years old male was presented to Internal Medicine with weakness in December 2012. Physical examination was revealed bilateral basillar decreased breath sounds. There was no hepatomegaly, splenomegaly or lymphadenopathy. Laboratory tests were revealed WBC 692,06 x 103/mm^3, Hb 8.9 g/dL, Htc 27.6 %, Plt 77 x 103/mm^3 and LDH 1907 U\L. Leukocytosis, smudge cells, 98 % small to medium sized some of them with single nucleolus blastoid variant lymphocytes was detected in peripheral blood smear examination. He interned to intensive care unit with initial diagnosis of acute leukemia. Immunophenotyping of the peripheral blood revealed positivity for CD45, CD2, CD3, CD5, CD7. TDT and the B-cell markers were negative. Bone marrow aspiration was hypercellular and revealed increased number of prolymphocytes. Based on the morphologic features and the immunophenotypic profile, a diagnosis of T-cell prolymphocytic leukemia (T-PLL) was offered. Leukopheresis was performed for 7 days after the diagnosis but sufficient reduction in leukocyte count did not provided. The patient was treated with cyclophosphamide (200 mg/m^2, 5 days) and prednisone (60 mg/m^2, 5 days) regimen in addition to leukopheresis but did not respond to treatment. Bone marrow biopsy was reported as TDT negative T-cell lymphoblastic leukemia/lymphoma. After this report the patient was treated with Hoelzer-1 chemotherapy regimen but an adequate response was not achieved. WBC count was still 500 x 10^3/mm^3. The patient was treated with FC (fludarabin [25 mg/m^2, 4 days] and cyclophosphamide [200 mg/m^2, 3 days] as the second line therapy. WBC count was decreased to 21 x 10^3/mm^3. The patient without any sort of compliant was

discharged to receive fludarabine treatment every for four weeks.

Conclusion: Common clinical features of T-PLL are marked lymphocytosis, generalized lymphadenopathy, and hepatosplenomegaly. The patient was presented with an unusual clinical situation of PLL with blastoid variant hyperleukocytosis which was resistant to initial chemotherapy and also he was asymptomatic except weakness despite of large amount of WBC. Dramatic response was observed with fludarabin treatment similar with classic PLL. Blastoid variant PLL can be described with hyperleukocytosis, blastoid morphology and negative TDT. Fludarabin treatment can be used in blastoid variant PLL.

Keyword: Prolymphocytic Leukemia, Blastoid variant

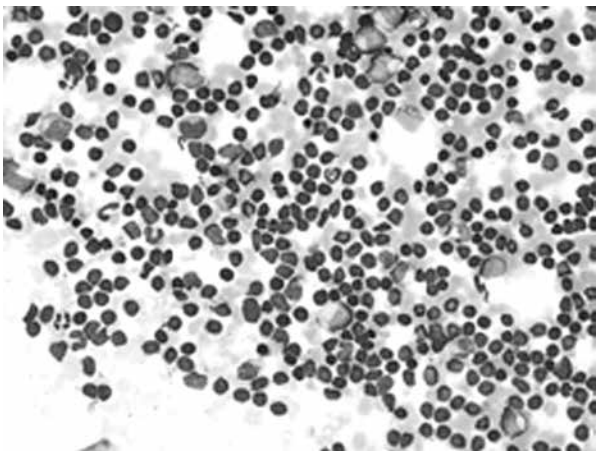

Figure 1. Aspiration Biopsy, Giemsa

Poster No: 0038 Abstract:0269

HEMATHEMESIS DUE THE PEPTIC ULCER AS THE FIRST CLINICAL MANIFESTATION OF RICHER'S SYNDROME CAUSED HYPERCALCEMIA

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Background: Richter's syndrome (RS) is defined as a high grade lymphoma occurring during the course of a low grade lymphoproliferative neoplasms. Its frequency is estimated to be between 3–6% of chronic lymphocytic leukemia (CLL) patients. In patients with RS hypercalcemia has rarely been seen and is considered to be associated with increased bone resorption. Hypercalcemia is reported to result in an increase of gastric acid secretion via the activation of stomach calcium sensing receptor (SCAR) on the basolateral membrane of gastric parietal cells by Ca2+

Case: A 60-year-old male patient presented to the Emergency Department (ED) of Clinical Hospital Center Zemun with acute mid-epigastric abdominal pain accompanied by nausea and hemathemesis. He also complained of progressive muscular weakness, lethargy and impaired concentration. Urgent upper gastrointestinal endoscopy revealed peptic ulcer on gastric lesser curvature with an adherent clot and endoscopic haemostasis was performed. Patient was admitted to the Department of gastroenterology for further intravenous proton pump inhibitors treatment and fluid resuscitation. Despite of given therapy his mental status deteriorated to coma shortly after admission. In laboratory analyses mild normocytic anemia (Hb 105 g/L, MCV 89 fL) and leucocytosis (WBC:13700/mL; neutrophils 60% and lymphocytes 21%), hypercalcemia (4.5 mmol/L) with high urinary calcium excretion (5.48 mmol/L), elevated serum creatinine (337 μmoL/l), and blood urea nitrogen (20.1 mmol/L) vere present. Serum intact PTH, calcitriol and gastrin levels were within normal values as well as other laboratory analyses. Treatment comprised of intensive rehydration and loop diuretics was immediately intitiated but with no clinical and laboratory improvement. Then, his previous medical record was obtained which documented that the diagnosis of Coombs negative B chronic lymphocytic leukemia was established five years ago when patient underwent splenectomy because of massive splenomegaly. He refused any further treatment. According to given history, intravenous pamidronate corrected for creatinine level was given and the bone marrow biopsy was performed. Histological analysis revealed diffuse large B cell infiltration of bone marrow consistent with a diagnosis of RS and 5% of eroded surface. Serum calcium level returned to normal within 72h after pamidoronate infusion, and his mental status was completely normalized after one week. Two weeks later, after the complete resolution of peptic ulcer chemotherapy with cyclophosphamide-vincristine-adriamycin-prednison was initiated in 21day cycles. The patient died after receiving five cycles of chemotherapy because of septicemia occurring during profound neutropenia. On the day of death, his serum calcium level was normal.

Conclusion: Hypercalcemia in RS is very rare, and we have found no similar documented reports of a patient developing peptic ulcer as a first clinical sign of RS.

Keyword: Richer's sundrome, peptic ulcer

Poster No: 0039 Abstract:0304

DISTINGUISHING HAIRY CELL LEUKEMIA FROM B-CELL LYMPHOPROLIFERATIVE DISORDERS WITH HAIRY LYMPHOCYTES: VALIDATION OF DIAGNOSTIC APPROACH

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Introduction: Hairy cell leukemia (HCL) and hairy cell leukemia-variant (HCL-v) are rare B-cell lymphoproliferative disorders (BC-LPD) with overlapping clinico-pathological features. However, certain morphological features of HCL, such as villous cytoplasmic projections or characteristic tissue specific infiltrative patterns, including red pulp expansion with pseudosinuses, may be seen in other B-cell lymphoproliferative disorders. A methodical and thorough approach evaluating immunophenotypic features will aid in rendering the appropriate diagnosis. CD123 is an antibody that identifies the Alfa chain of the human interleukin – 3 receptor. It is expressed in hairy cells, also in normal hematopoietic cells The aim of the study was to determinate the diagnostic value of CD123 expression in HCL and other B-cell lymphoproliferative disorder cases with hairy lymphocytes.

Design and Methods: We investigated the diagnostic value of CD123 expression in neoplastic cells from 50

patients with B – cell disorder with circulating hairy lymphocytes We performed flow cytometry analysis (FCM) of 50 cases (30 HCL, 5 HCL-v, 15 splenic marginal zone lymphoma (SMZL)), correlating results with available corresponding clinical and morphological data.. Immmunophenotype analyses were performed by using the FAXS Canto II BD flow cytometer analyzer on 50 samples, from peripheral blood (23) and bone marrow (27). Acquired data were analyzed with the software FACS Diva version 6.1.2 by using CD19 gating strategy using panel for immmunophenotype diagnosis of lymphoproliferative disorders according to BSCH (CD11c, CD25, CD103, CD123) combined with B-cell markers (CD19, CD20, CD22).

Results: Our findings show that cells from 100% of typical HCL expressed CD123 with strong intensity, while cells from other other B – cell disorder with hairy lymphocytes did not expressed CD123. HCL expressed bright CD20, bright CD22, bright CD11c, bright CD25, CD103, and bright homogeneous CD123(100%). HCL-v expressed bright CD20, bright CD22, CD11c(20%) and uniformly lacked CD103(100%), CD123(100%),CD25(100%). SMZL cases were CD103(-) and CD123(-).Detection of BRAFV600E mutation was examined in a subset of cases to further validate FCM diagnostic criteria. HCL-v was negative for BRAFV600E mutation (100%), in contrast to HCL (50% positive for BRAFV600E mutation).

Conclusion: We conclude that CD123is a useful marker for distinguishing B cell disorder with villous lymphocytes from HCL with high sensitivity and specificity.

Keyword: HCL, CD123

Poster No: 0040 Abstract:0306

DETERMINATION OF TIME TO FIRST TREATMENT IN CLL PATIENTS WITH PROGNOSTIC NOMOGRAM, INDEX AND BIOLOGICAL MARKERS: PRELIMINARY RESULTS FROM SINGLE CENTER EXPERIENCE

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Introduction: The clinical course for patients with chronic lymphocytic leukemia is extremely heterogeneous, one of the most important challenges in the clinical management of those patients is the decision of initiating their treatment, but there is no available prognostic system that will resolve this issue. Usually, criteria for active disease are used to initiate therapy. Recently, some authors proposed prognostic models, scoring systems involving a set of clinical and biological risk factors and estimates individual patient survivals. Here, we report our initial results from a study designed to evaluate the statistical association of the distinct clinical and biological parameters with the prognosis and time to initiating treatment for patients with CLL.

Material-Methods: Our study incorporated 100 consecutive, treatment naïve CLL patients. In each patient all traditional laboratory, clinical and biological prognostic factors were evaluated at their first visit to our Institution. Than we combined the following independent characteristics: age, β-2 microglobulin, absolute lymphocyte count, sex, Rai stage, and number of involved lymph node groups, which are included in some of the already published CLL prognostics index, in association with the CD38 expression and mutational status of the IGVH gene regions. Further, we correlate those factors by multivariable analysis with time to first treatment. This multivariable model was used to develop a nomogram-a weighted tool to calculate 5- and 10-year survival probability and estimate median time to first treatment.

Results: According to prognostic index a classification tree was built that identified three subsets of patients who scores were 1-3 (low risk- 32pts- 32%), 4-7 (intermediate risk-48pts- 48%) and >8 (high risk-20pts- 20%). Estimated median survival at low risk subset of patients is 14,1years, 10,7 and 4,6 years respectively at intermediate and high risk subsets of patients. Projected survival in respectively low, intermediate and high-risk groups are 100%, 100%, 25%, and 34%, 43%, 25% at 5-year and10-year, respectively. Also, statistical analyses showed that three involved lymph node sites, increased size of cervical lymph nodes, increased serum lactate dehydrogenase,CD38 expression and unmutated IGHV mutation status are associated with shorter time to first treatment.

Conclusion: Our prognostic model that combines and correlates the distinct clinical and biological markers of CLL patients enables identification of the patients that are at high risk for progression. This prognostic model may facilitate clinical decision for initiating treatment.

Keyword: CLL, prognostic model

Poster No: 0041 Abstract:0316

RESTORATION OF THE MIR-181A/B AND THE MIR-130A EXPRESSION IN B CLL CELLS BY ACTIVATED CD4+ T CELLS

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To date one of the major challenges in Chronic lymphocytic leukemia (CLL) is to identify genes responsible for the progression of the disease and functionally characterize them. We previously found that the miR-181b significantly decreases during the progression of CLL as specific effect and its expression inversely correlated with protein levels of the anti-apoptotic target genes MCL1 and BCL21.

Based on our data, we aim at identifying the stimuli that regulate the expression of miR-181b and other miRNAs involved in the progression of the disease, such as the miR-181a and the miR-130a. Progression of CLL is characterized by gradual reduction of the ratio T/B cells, along with immune cell dysfunction due in part to the T cell defects, such as decreased expression of CD40L and reduced signaling via the TCR CD3. This compromise the ability of T cells to eliminate leukemic cell from CLL patients. Since enhanced activation of either the allogenic or autologous T cells can drive the death of CLL cells in vitro and in few human subjects2-3, we speculate that

this death is due, at least in part, to increased expression of the 3 miRs in B cells.

To investigate the effect of T cells on the expression of the candidate microRNAs, we co-cultured allogenic pure CLL-B cells with either activated (CD2, CD3 and CD28 antibodies, used to mimic antigen-presenting cells) or not activated CD4+ T cells from healthy donors. We observed a significant increase of mir-181b/a and miR-130a expression in CLL B-cells after co-culture with activated CD4+ T cells in 8 out of 11 cases. A significant increase of these miRs was also determined in purified CLL B-cells after 4 days activation of peripheral blood mononuclear cells (PBMCs) from CLL patients, even if in minor rate. By the use of specific antibodies, co-culture with Hela CD40 expressing cells and transwell experiments, we established that this effect is a T/B contact-dependent signal mediated through CD40L-CD40 interaction.

In conclusion, our preliminary data show that an efficient activation of CD4+ T cells through CD3-complex pathway and a right CD40L-CD40 interaction lead to a significant increase of the candidate miRs, which are extremely down-regulated in the disease.

These findings open up the possibility of intervening in the management of CLL patients through the restoration of the activity of the miR-181b and consequently the decrease of the protein levels of the anti-apoptotic MCL1 and BCL2 genes, thereby reestablishing, at least in part, a proper apoptosis rate of the CLL B-cells.

Keyword: CLL, microRNA

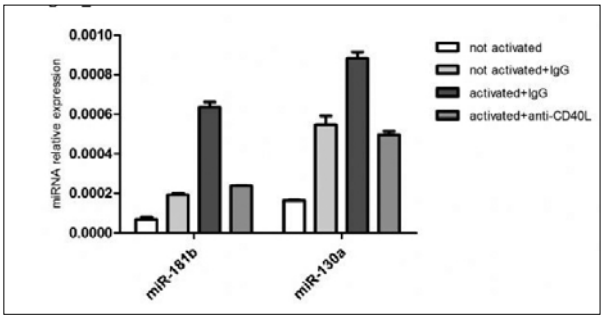

Figure 1.Activation of T cells from healthy donors increase the expression of the miR-181b and miR-130a in B-CLL. MiR-181b and miR-130a expression in purified B-CLL cells after 24hrs of co-culture with either activated or not activated T cells from healthy donors in presence of either the blocking ab-CD40L or the control IgG. Ratio was 1:1 for T:B cells. The expression has been determined by stem-loop real-time qPCR. Each sample of data was normalized to the endogenous reference RNU44 with the use of the 2-Δct method.

Hodgkin's Lymphoma

Poster No: 0042 Abstract:0108

BRENTUXIMAB BEFORE THE ALLOGRAFTING FOR RELAPSED/ REFRACTORY HODGKIN LYMPHOMA

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Brentuximab vedotin may be useful in relapsed/ refractory Hodgkin lymphoma (HL) in relation to hematopoietic cell transplantation (HSCT). Graft versus lymphoma devoid of GVHD with chimerism-mediated immunotherapy (CMI) is the goal of allogeneic HSCT in HL.4 Brentuximab vedotin (anti-CD30) seems to be a promising agent in this context. In our institution, we have performed allo-HSCT for a 19-year-old male patient with nodular sclerosing Hodgkin lymphoma (HL) relapsed after auto-HSCT. Before transplantation, he had received multiple chemotherapy regimens (ABVD, ICE, DHAP and BEACOPP). After the auto-HSCT, his disease recurred within 5 months. Since he relapsed quickly, the disease was considered as relapsed/refractory HL. Brentuximab vedotin was administrated intravenously twice prior to allografting; one month had elapsed between the last dose of brentuximab vedotin and allo-HCT. He went into complete remission after anti-CD30 treatment just prior to allo-HCT. He had achieved engraftment successfully. The median time to neutrophil recovery was 9 days (range, 0-21 days) as defined by absolute neutrophil count 500 cells/L. The median time to platelet recovery was 11 days (range, 0-21 days) as defined by platelet count >20 000 cells/L without transfusion support. Brentuximab vedotin treatment seemed to have no adverse impact on engraftment. He is currently in good health and in complete remission 7 months following transplant. We have observed that allo-HCT with reduced intensity conditioning after brentuximab vedotin was safe in our heavily pretreated relapsed HL patient. Brentuximab vedotin was generally well tolerated in our patient. We did not observe any delays in the engraftment time, severe transplant toxicity, or signs of acute GVHD. Several clinical trials have evaluated monoclonal antibodies or receptor antagonist therapy for steroid-resistant acute GVHD, with different outcomes in a variety of settings. Anti-CD30 seems to be a great candidate based on both its anti-neoplastic efficacy and its possible modulation of GVHD in HL.

Keyword: Brentuximab, Hodgkin Disease

Poster No: 0043 Abstract:0138

LONG-TERM SURVIVAL ANALYSES OF AN ONGOING PHASE 2 STUDY OF BRENTUXIMAB VEDOTIN IN PATIENTS WITH RELAPSED OR REFRACTORY HODGKIN LYMPHOMA

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Objectives: Hodgkin lymphoma (HL) is characterized by CD30-positive Hodgkin Reed-Sternberg cells. The standard of care for pts with relapsed/refractory (RR) HL is salvage chemotherapy followed by autologous stem cell transplant (ASCT). However, around 50% of pts relapse

after ASCT. Brentuximab Vedotin (ADCETRIS®), an anti-CD30 antibody conjugated by a protease cleavable linker to a microtubule disrupting agent, monomethyl auristatin E (MMAE), induces apoptotic death of CD30-expressing cells by binding, internalizing and releasing MMAE. A pivotal phase 2 study was conducted to determine the efficacy and safety of Brentuximab Vedotin in 102 pts with RR HL following ASCT (NCT00848926). Long-term survival data from this ongoing trial are described.

Methods: Pts received 1.8 mg/kg Brentuximab Vedotin Q3wk as a 30-min IV infusion for <=16 cycles. Primary endpoint: objective response rate (ORR) per independent review. Long-term follow-up assessments to determine survival and disease status: every 3 mos for 2 years, every 6 mos during years 3 to 5, then annually.

Results: Median time to relapse after ASCT was 6.7 mos (range, 0–131). Pts received a median 9 cycles of Brentuximab Vedotin. The ORR was 75% (76/102 pts), with complete remissions (CRs) in 34 pts (33%). At time of analysis (July 2012), the median time from first dose was 29.5 mos (range, 1.8–36.9). 60/102 pts (59%) were alive at the time of last follow up and median overall survival (OS) has not been reached. The estimated 24-mo OS was 65% (95% CI: 55, 74). The median OS by best clinical response was 31.6 mos for pts with partial remission (PR, n=42), 20.6 mos for pts with stable disease (SD, n=22), and 10.2 mos for pts with progressive disease (PD, n=3); median OS for pts with CR (n=34) has not been reached. Evaluation of demographic and baseline characteristics found that pts with a baseline ECOG score of 0 were the only subgroup with a significantly more favorable OS following Brentuximab Vedotin treatment (24-mo OS: 81% vs. 47% for ECOG scores of 0 vs 1, respectively). There was no significant difference in OS fo pts who had relapsed within a year of ASCT compared with pts relapsing >1 year after ASCT. The most common (>=15%) Brentuximab Vedotin-related AE of any grade: peripheral sensory neuropathy, nausea, fatigue, neutropenia and diarrhea. AE Grade >=3 occurring in >=5% of pts: neutropenia, peripheral sensory neuropathy, thrombocytopenia and anemia.

Conclusions: After a median observation time of approximately 2.5 years, 60 of 102 pts (59%) were alive at the time of last follow up and the median OS has not been reached. The estimated 24-mo OS was 65%. Baseline ECOG score of 0 was the only pretreatment factor associated with a higher 24-mo OS. Treatment with Brentuximab Vedotin in pts with RR HL following ASCT is associated with prolonged OS compared with historical control pts.[1] Brentuximab Vedotin is under evaluation as front line therapy for adult pts with advanced classic HL.

Keyword: Hodgkin lymphoma, brentuximab vedotin

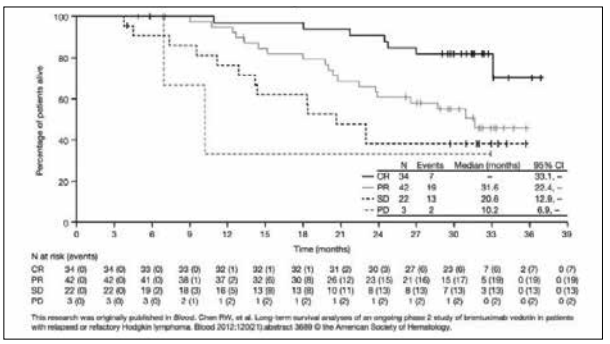

Figure 1. Overall Survival by Best Clinical Response

Poster No: 0044 Abstract:0153

MONOCYTE COUNT IN HODGKIN'S LYMPHOMA

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There is only one study about monocyte count and clinical stage in patients with lymphomas in literature (EHA, 2012 P0318). In this study, monocyte count less than 800/mm³ was associated with a poor prognosis in non-Hodgkin's lymphoma. So monocyte count can be accepted as cheap and available prognostic marker and used for clinical follow-up of the lymphomas. We evaluated monocyte counts at diagnosis in this retrospective study in the patients with Hodgkin's lymphoma (HL). 70 patients (40 male and 30 female with mean age of 47±16. years) were included to the study. 31 of the patients were at early stage (According to Ann Arbor stage I and II). Stage III and IV were accepted as late stage. Monocyte counts were compared between early and late stages. We did not find any difference for monocyte counts between early and late stages (p>0.05). (Table 1). To detect the prognostic importance of monocyte count in HL, new studies with more patients may be benefit.

Keyword: Monocyte count, Hodgkin's Lymphoma

Table 1

	Clinical stage	*Monocyte count (/mm³)*	*p value*
HL (n=70)	Early stage (n=31)	590±74	>0.05
HL (n=70)	Late stage (n=39)	679±449	>0.05

Poster No: 0045 Abstract:0154

MEAN PLATELET VOLUME IN NON-HODGKIN'S LYMPHOMA

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Mean platelet volume (MPV) indicates platelet activation. Especially in inflammatory conditions such as connective tissue diseases, myocardial infarction, there are studies showing increase in MPV. There is no study evaluating MPV in lymphomas. In lymphomas, inexpensive and easy prognostic markers are needed to evaluate prognosis. In this retrospective study, we investigate the relationship between MPV and non-Hodgkin's lymphoma (NHL) stage. 89 patients (51 male and 38 female with mean age of 62±14.years) were included to the study. 63 of the patients were diffuse large B-cell lymphoma. 26 of the patients were at early stage (According to Ann Arbor stage I and II). Stage III and IV were accepted as late stage. MPV was compared between early and late stages. We did not find any difference for MPV between early and late stages (p>0.05). (Table 1). To detect the prognostic importance of MPV in NHL, new studies with more patients may be benefit.

Keyword: Mean platelet volume, Non-Hodgkin's lymphoma

Table 1

	Clinical stage	*MPV (fl)*	*P value*
NHL (n=89)	Early stage (n=26)	7,9± 1.1	>0.05
NHL (n=89)	Late stage (n=63)	8.3±1.2	>0.05

Poster No: 0046 Abstract:0170

IGA NEPHROPATHY ASSOCIATED WITH HODGKIN'S DISEASE: A CASE REPORT

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IgA nephropathy (IgAN) is the most common cause of glomerulonephritis, and is characterized by mesangial proliferation and deposition of IgA. Secondary IgAN is associated with several diseases, including immunological disorders, infections and cancers. Malignancies that have been reported to be associated with IgAN include renal cell carcinoma, cancers of the lung, larynx and esophagus, cutaneous T-cell lymphoma, Hodgkin's disease and non-Hodgkin lymphoma. Secondary IgAN in patients with Hodgkin's lymphoma is very rare and its pathogenic mechanisms remain unclear. We aimed to report a patient with secondary IgAN associated with Hodgkin's disease.

32 years old man was admitted to our hospital weakness and signs of anemia. On physical examination multiple lymphadenopathies were found both side of the neck. CT showed multiple lymphadenopathies in both mediastinum and the abdomen. Splenic and hepatic involment was suspected. Lymph node excision from the neck was diagnosed with lymphocyte depletion type hodgkin lymphoma. Chemotherapy was performed with an ABVD (adriamycin, blomycin, vinblastin, dacarbazine) regiman two cycles. Then he had abdominal pain, arthralgia, purpura and edama of both legs. The patient had proteinuria 13 g/day and increased serum creatinin level. Skin biopsy showed leukocytoclastic vasculitis and renal biopsy diagnosed IgA nephropathy. The patient received pulse methylprednisolone for 3 days, cyclophosphamide 1 day. After this therapy, chemotherapy was performed with EPOCH (etoposide, vincristin, adriamycin, cyclophosphamide, prednisone) regiman two cycles. His therapy has been continued.

The association between Hodgkin's lymphoma, particularly the mixed-cellularity type and glomerular diseases is well recognized. In Hodgkin's disease, the most common paraneoplastic glomerular abnormality is minimal change nephropathy, although other glomerular diseases occasionally have been described. A case report of extracapillary immunoglobulin A glomerulonephritis presenting as acute renal failure in a woman with newly diagnosed Hodgkin's disease. Treatment with the bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone regimen resulted in complete hematologic and renal remission for more than 1 year after diagnosis. The possible explainations could be either T cell dysfunction that causes local damage to the glomerulus by formations by immun complexes or impairment of the basement membrane by the lymphokines by tumor cells. Several case reports have shown complete recovery of renal function after chemotherapy and this strengthens the pathogenetic relationship between Hodgkin's lymphoma IgAN.

Studies have low evidence-based value. There is no widely accepted experimental model of the association of glomerulopathy and cancer. Thus, epidemiologic and mechanistic studies are needed to determine the true prevalence of paraneoplastic glomerulopathies and investigate new pathophysiologic approaches.

Keyword: IgA nephropathy, Hodgkin's disease

Poster No: 0047 Abstract:0213

A STORY OF HODGKIN LYMPHOMA IN A CHILD

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Introduction: Hodgkin lymphoma (HL) is a malignant B cell neoplasm which usually originates from a centriaxially located lymph node and disseminates to the adjacent lymph node groups or organs via direct and/or hematogen dissemination. Response to treatment is usually satisfactory especially when the disease is not resistant to therapy and diagnosed at an early stage.

Case presentation: A nine-year-old male patient came to our clinic with the complaints of abdominal swelling, fatigue and night sweats. Physical examination revealed 5 cm splenomegaly and axillary lymphadenopathy (LAP). Complete blood count and basic metabolic profile were all within normal limits except high erythrocyte sedimentation rate (117mm/h). PPD test for tuberculosis was negative and bone marrow aspiration was normal. Abdominal ultrasonography showed paraaortic and splenic hilar LAP with nodular hypoechoic areas in the spleen. Thoracic and abdominopelvic computerized tomography (CT) revealed supraclavicular, subcarinal and paraesophageal LAPs in mediastinum, and celiac, retrocaval, interaortocaval, left paraaortic LAPs in the abdomen. Since the peripheral LAPs are too small to allow for a biopsy, surgical exploration of the abdomen was performed in order to take biopsies from liver and spleen. Liver biopsy was compatible with the infiltration of mixed type HL. Although six cycles of ABVD regimen were given to the patient as an initial treatment, he had no significant response and splenectomy was performed. Diffuse infiltration of mixed type HL was evident. After 4 cycles of COPP and 3 cycles of IEP regimens, the patient was lost to follow-up for five years. When he came back to the hospital with persistent intraabdominal LAPs, there was no bone marrow infiltration or lung metastasis. Since the patient was not a reliable candidate for bone marrow transplantation due to severe scoliosis, limited lung capacity and active hepatitis B, 3 cycles of ICE regimen and 6 cycles of BECOP were given, but the patient did not respond well. 8 cycles of gemcitabin and vineralbine, 4 cycles of lomustine, vinblastine, bleomycin, dexamethasone and intermittent radiotherapies also failed and relapses occured. Although the patient was under control for 13 years, repeated bone marrow aspirations and thoracic imaging did not reveal any infiltration of HL, but the last positron emission tomography showed a vertebral involvement very recently.

Discussion: It is different from the usual natural history of Hodgkin lymphoma that during the 13 year follow-up of the patient, he had no bone marrow or lung

involvement although he did not respond well to any therapy regimens.

Keyword: Hodgkin Lymphoma, child

Molecular Hematology–Cytogenetics

Poster No: 0048 Abstract:0162

CD56 ANTIGEN EXPRESSION AS THE MOST IMPORTANT PROGNOSTIC FACTOR IN NORMAL KARYOTYPE ACUTE MYELOID LEUKEMIA

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Objectives: Patients with normal karyotype acute myeloid leukemia (NK-AML) without the FLT3 internal tandem duplication (FLT3-ITD) mutation account for approximately 30% of all AML cases and exhibit a heterogeneous clinical outcome. The prognostic factors in this subgroup of AML patients are still unknown. The aims of this study were to estimate the prognostic factors for complete remission (CR) rate, overall survival (OS) and disease-free survival (DFS) in patients with NK-AML in the absence of the FLT3-ITD mutation as well as to determine the relevance of CD56 antigen expression, an immunophenotypic marker, on outcome in this cohort of patients.

Methods: The study involved 143 subjects with NK-AML without the FLT3-ITD mutation during a follow-up period of 54 months. As risk factors for rate of CR, OS and DFS in months in this cohort of patients the following were evaluated: age, ECOG performance status (PS), leukocytosis (<30x10^9/L vs >=30$10^9$/L), lactate dehydrogenase (LDH) more than 1.5 x upper limit of normal, and CD34 expression (<10% vs >=10%). For CD56 antigen expression, detected by flow-cytometry, the cut-off value >=20% was taken as positive (CD56+). Patients were treated by the Medical Research Council (MRC) 12 regimen. Risk factors were identified using univariate and multivariate analysis.

Results: The mean age of the patients was 53 years (range 18-79). Univariate analysis showed that the following risk factors were significant for CR rate: age >=55 years (p = 0.014), leukocytosis (p = 0.050), and CD56+ (p = 0.003). Multivariate analysis indicated CD56+ as the most important risk factor for CR rate: p = 0.001, HR 2.114 (95%CI 1.376-3.249). Significant factors for OS in univariate analysis were: age >=55 years (p = 0.001), leukocytosis (p <0.001), LDH (p = 0.050) and CD56+ (p < 0.001). Multivariate analysis indicated CD56+ as the most important risk factor for OS: p = 0.001, HR 1.948 (95%CI 1.306-2.905). Significant factors for DFS in univariate analysis were: leukocytosis (p = 0.034), LDH (p = 0.050) and CD56+ (p = 0.001). Multivariate analysis indicated CD56+ as the most important risk factor for DFS: p = 0.005, HR 3.857 (95%CI 1.495-9.952).

Conclusions: This study showed that CD56 antigen expression on leukemic cells in patients with NK-AML without the FLT3-ITD mutation predicts shorter OS and DFS as well as a lower rate of CR in comparison with patients from the same subgroup without CD56 positivity. Therefore, more intensive therapeutic regimens should be considered in such cases.

Keyword: CD56 antigen, NK-AML

Poster No: 0049 Abstract:0164

PROGNOSTIC IMPACT OF LEUKOCYTOSIS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA AND MUTATED NPM1 AND FLT3-ITD

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Objectives: Mutation in nucleophosmin (NPM1) is the most frequently observed molecular abnormality, present in about 50% of acute myeloid leukemia (AML) cases, and is associated with a favorable outcome. Internal tandem duplication of the fms-related tyrosine kinase 3 gene (FLT3-ITD) is another frequent molecular abnormality and can be observed in about 25% of patients with AML. The presence of FLT3-ITD is generally considered as an unfavorable prognostic factor. The aim of this study was to investigate the prognostic impact of white blood cell (WBC) count at diagnosis on outcome within specific AML subgroups of patients with mutated NPM1 (as a favorable risk factor) and FLT3-ITD (as a poor risk factor).

Methods: This single-center study involved 32 AML patients with mutated NPM1 and FLT3-ITD. The follow up period was 3 years. Patients with all other cytogenetic abnormalities and AML patients without cytogenetic abnormalities were excluded from this investigation. Patients were divided into three groups according to their WBC count: 1) a WBC count <20x10^9/L; 2) a WBC count 20-100x10^9/L and 3) a WBC count >100x10^9/L. Cox regression analysis was applied to determine the association of WBC and overall survival (OS) in months.

Results: The mean age of the patients was 51 years (range 21-71). There was a strong correlation between the NPM1 mutation and a high WBC count, p = 0.004. Also, differences in OS between the three groups of patients divided according to WBC count (<20x10^9/L vs 20-100x10^9/L vs >100x10^9/L) were statistically significant, p = 0.003.

Conclusions: This study demonstrated that leukocytosis is an important unfavorable risk factor for OS in the subgroup of patients with AML and mutated NPM1 and FLT3-IDT.

Keyword: mutated NPM1 and FLT3, AML

Poster No: 0050 Abstract:0178

SCREENING OF C/EBPA VARIATIONS BY NEXT GENERATION DNA SEQUENCING (NGS) IN COMPARISON WITH OTHER PROGNOSTIC MARKERS IN CHILDREN WITH ACUTE MYELOBLASTIC LEUKEMIA

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Objectives: CCAAT/enhancer binding protein alpha (C/EBPα) is a transcription factor involved in the regulation of myelopoiesis. C/EBPα expression occurs predominantly in myelomonocytic cells and is specifically upregulated during granulocyte differentiation. It is an intronless gene located on chromosome 19q13.1.The importance of CEBPα in hematopoiesis can be attributed to its crucial role during the development of granulocytes and its deregulation associated with myeloid transformation. Mutations in CEBPA are found in 5-14% of AML patients. Most CEBPα mutant AML patients simultaneously exhibit 2 mutations.These mutations largely fall into two major categories: one comprises those mutations that prevent C/EBPα DNA binding via alteration of its COOH-terminal bZIP, and the other comprises those that disrupt translation of the C/EBPα NH2 terminus, leading to reinitiation of translation at an alternative internal ATG codon located 351 nucleotides downstream of the main AUG initiation codon, and as a result, formation of a 30-kDa C/EBPα 30 isoform. This isoform has the capacity to further reduce wild-type C/EBPα activity by inhibiting its DNA binding and transactivation of the target genes in a dominant-negative effect.Our study group consisted of children with acute leukemia.

We aimed at screening the whole C/EBPα gene by NGS analysis, in order to find clinical and prognostic genetic markers for acute leukemia.

Methods: Study population consisted of 4 patients aged between 1 and 15 years who were admitted to our hospital with the diagnosis of acute leukemia. Blood samples were drawn into EDTA-containing tubes and DNAs were extracted from peripheral blood leukocytes with MagNA Pure automatic DNA isolation instrument. Amplification of gene was performed by PCR (amplicon preparation- sequencing techniques) and amplified fragments were sequenced by NGS analysis (GS Junior Sequencing) and the results were analyzed using AVA software. For DNTM3A gene variations, perfect well-matched primers were used to amplify the target exon 23. region and variation detections were performed by DNA sequencing (Beckman Coulter) analysis. FLT3-ITD variations were screened with real time PCR using fluorescence high resolution melting analysis.

Conclusion: Identified variants in the C/EBPα gene could disturb function and regulation of transcription factor that lead to development of leukemia. Identified variants in the 5' UTR and exon regions of the gene are responsible for gene m-RNA stability and formation of protein. FLT3 gene mutations are strongly associated with leukocytosis and poor prognosis in AML patients. DNMT3A mutations are recurrent in patients with AML and are associated with poor event-free and overall survival, independently of age and the presence of FLT3 or NPM1 mutations and regardless of the type of mutation or genetic location.These variations (C/EBPα,FLT3/ITD,DNMT3A) probably are relevant to the pathogenesis of AML. Further studies are on the way.

Keyword: Pediatrik AML, C/EBPα-DNMT3A-FLT3 genes

Table 1. Distribution, classification and characterization of the gene variants in C /EBPα gene in our study

No	Statue	Variant	Coverage	Rs Number	Detection in Patients	Localization
1	CTAC/-, frameshift	226 CTAC/-	68 coverage	rs137852731	1	5'UTR
2	novel	273 G/-	37 coverage	novel	2	ekzonik
3	novel	69–71/ GCC	74 coverage	novel	1	ekzonik
4	G/T, sinonim	195 T/-	1105/ 443 Coverage	rs34529039	2	ekzonik

Table 2. Clinical and molecular characteristics of 4 pediatric patients with AML in our study

Patients No	Age/Sex	Diagnosis	Karyotype	C /EBPAα Variations	DNMT3A 23. Exon R882	FLT3-ITD Variations
1	E/15	AML-M2	Normal Karyotype (46, XY)	273 G/- 195 T/-	negative	positive
2	K/15	AML-MDS	Normal Karyotype (46,XX)	-	negative	negative
3	E/15	(Ly+) AML-M1	Relapse/ Normal Karyotype (46, XY)	226 CTAC/-	negative	positive
4	E/4	Mixed Leukemia	Relapse/ Normal Karyotype (46, XY)	226 G/- 195 T/-	negative	positive

Poster No: 0051 Abstract:0193

SYNERGESTIC INTRACTION WITH FALCARINOL ON HUMAN LYMPHOID LEUKAEMIA CELL LINES AND INCREASE THE EXPRESSION OF CYTOCHROME C, BAX AND SMAC/ DIABLO

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Objective: Leukaemia is the most common childhood blood malignancy and its treatments are associated with serious side effects. Thus, new therapies are urgently needed to improve leukaemia patient's health and survival. This study investigated the effects on apoptotic induction and cellular proliferation inhibition on lymphoid leukaemia cell lines following 24 h treatment with Falcarinol- a polyacetylene from carrots (Daucus carota) alone and in combination with chemotherapy and apoptotic inducer agents to investigate their additive, synergistic or inhibitory effects. Moreover, expressions of some pro-apoptotic proteins, which play crucial roles in intrinsic apoptotic pathway, were investigated.

Methods: Three Leukaemia cell lines (Jurkat, MOLT-3 and CCRF-CEM) were investigated following treatment with Falcarinol alone or in combination with apoptosis inducers or chemotherapy agents. Flow cytometric analysis was used to detect active caspase 3 following 24 h treatment and apoptotic morphology was confirmed using Hoechst stain. Inhibition of cellular proliferation was assessed by cell titre glo, which measures the ATP level within viable cells, and cell cycle analysis using propidum iodide staining of DNA content using flow cytometry. Caspase Glo 8 and 9 was used to investigate activation of caspases, and cytochrome C, Bax and SMAC/Diablo antibodies were used to detect any activated proteins

during the cascade of events associated with apoptosis induced by Falcarinol.

Results: Jurkat cells showed a significant synergistic response following combination treatment with Falcarinol and DR5 agonist after 24 h. The percentage of caspase 3 activity was increased with 13% and 30% after 24 h treatment with Falcarinol and DR5 respectively, whereas the combination treatment showed 58% apoptotic cells. These were confirmed by morphological examination. However, CCRF-CEM showed only an additive response after 24 h treatment with Falcarinol combined with DR5, Bortezomib, Leptomycin B or Sulforaphane. MOLT-3 cells demonstrated a significant synergistic response indicated by a significant decrease in cellular viability and significant increase in caspase 3 activity with Falcarinol combined with 2.5 nM Bortezomib or 25 μM Sulforaphane. In addtion, treatment with 10 μM 6-MP alone and combined with Falcarinol arrested the cells at G0/G1 phase. The activities of both caspase 8 and 9 were significantly increased after 6 h post treatment with 12 and 25 μM Falcarinol. The expression of active Bax was increased in Jurkat cells 3 h after treatment with 12 μM Falcarinol followed by significant increase in cytochrome C and SMAC/Diablo after 6 h.

Conclusion: For the first time, we have shown that Falcarinol acts in a synergistic, additive or inhibitory manner with different agents in human leukaemia cell lines. The apoptosis was induced through both intrinsic and extrinsic pathways and the pro-apoptotic proteins Bax, cytochrome C and SMAC/Diablo were involved.

Keyword: Falcarinol, Synergistic

Poster No: 0052 Abstract:0198

SCREENING OF FLT3 GENE MUTATIONS (FLT3-ITD AND D835) IN CHILDHOOD ACUTE LEUKEMIA PATIENTS

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Objective: AML is a clonal disorder characterized by various genetic abnormalities and variable response to treatment. The discovery of an internal tandem duplication (ITD) in the FLT3 gene was a significant step in the process of understanding the genetic background of AML. The FLT3 gene encodes the tyrosine kinase receptor critical for normal hematopoiesis. The FLT3 gene is located on chromosome 13.There are two types of FLT3 mutations an ITD and a point mutation (D835), which both have constitutively active tyrosine kinase, thereby promoting proliferation and inhibiting apoptosis in leukemic cells. FLT3 is aberrantly expressed in the most of AML patients. Approximately 20 to 30% of AML cases carry an ITD mutation and 8 to 12% an D835 mutation. AML patients with an ITD mutation appear to have poorer clinical outcome. In our study we aimed to investigate the status of FLT3 (ITD and D835 mutations) in 15 pediatric AML patients, a patient' family member and 183 ALL patients were categorized into karyotype and identified for FLT3 mutation status.

Methods: For screening FLT3-ITD mutation: The study population consisted of 16 children with AML aged between 1 and 15 years of age who were admitted to our hospital with the diagnosis of AML and a patient's their immediate healthy parents (2). Blood samples were collected and DNA were extracted from MagNA Pure automatic DNA isolation instrument (Roche). FLT3-ITD variation was screened with real time PCR (Roche) using fluorescence HRM (High Resolution Melting) analysis.

For screening FLT3-D835 mutation: The study population consisted of 183 children with ALL aged between 1 and 15 years of age who were admitted to our hospital with the diagnosis of ALL. Amplifications of gene were performed by PCR and amplified fragments were digested with appropriate restriction endonucleases (EcoRV) and sequencing of different band profiles were performed by sequencer (Beckman Coulter, USA). Sequencing of the gene revealed a heterozygous " C/A" variation at c.32705 resulted with a transition of Serin to Serin.

Results: We worked in 17 children 8 (50%) of them were defined FLT3-ITD mutation. ALL were diagnosed in 183 children 14 (7,6%) of them were carried heterozygote genotype. One (5,8%) of the 17 patients carried both mutations. Sequencing of the gene revealed a heterozygous " C/A" variation at c.32705 resulted with a transition of Serin to Serin.

Comment**:** FLT3 mutations are poor prognostic markers of AML. Ozbek et al (TJH 2012) reported that their patients (4 %) had FLT3-ITD mutation and FLT3-D835 point mutation heterozygosity was observed in only 1 patient (2%). Cytogenetic prognostic factors are more precise and in wide clinical use. But there is a need to improve molecular factors (the mutation status of genes such as FLT3, MLL, NPM1, CEBPA), especially in cases with normal karyotype. FLT3/ITD, which is known to be a poor prognostic factor, is present in 20–30% of AML patients with different karyotype status.

Keyword: Childhood AML, FLT3 gene mutations(ITD/ D835 mutations)

Table.1. Classification and characterization of the FLT3 gene mutations

Poster No: 0053 Abstract:0210

EFFECT OF POMEGRANATE ANTHOCYANIDINS (DELPHINIDIN, CYANIDIN AND PELARGONIDIN) ON INHIBITION OF PROLIFERATION AND INDUCTION OF APOPTOSIS IN HUMAN LEUKAEMIA CELL LINES

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Methodology: The anti-cancerous effect of three different anthocyanidins was investigated on four leukaemia cell lines (CCRF-CEM, MOLT-3, HL-60 and THP-1). Cells were treated with 0μM to 100μM of each anthocyanidins

for 24hours. Cell proliferation was assessed using CellTiter-Glo® Luminescent Cell Viability Assay. The pro-apoptotic actions of anthocyanidins were assessed by two assays: Annxien V/Propidium iodide staining and staining for caspase3-activity using flow cytometry. Cell cycle arrest was investigated using flow cytometry. The caspase-Glo® 8 and 9 assays were used to measure the effect of delphinidn on Caspase-8 and caspase-9 activity. The effect of Delphinidn on expression on some apoptotic proteins (Cytochrome C, SMAC/Diablo and Bax) were investigated using immunocytochemistry.

Results: Delphinidin was found to have the greatest inhibitory effect on cell proliferation which was found to be significantly greater than that shown by cyanidin and pelargonidin (Figure2). Delphinidin also significantly induced apoptosis in all four cell lines. Cyanidin induced apoptosis only in CCRF-CEM and pelargonidin failed to induce apoptosis in any cell lines. Delphinidin increased both caspase 8 and 9 activity following 6 hr. treatment. Expression of Bax, cytochrome C and SMAC/Diablo were also activated following treatment with delphinidin.

Conclusion: Taken together, our data suggest that delphinidin could be developed as an agent against leukaemia.

Keyword: anthocyanins, apoptosis

Poster No: 0054 Abstract:0223

SEX, ABO BLOOD GROUPS, AND SECRETOR STATUS FREQUENCY IN HEMATOLOGICAL MALIGNANCIES

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Background: Associations of sex, ABO blood groups with some diseases including leukemia have been described earlier and their role in influencing the etiology, pathogenesis and prognosis of these diseases have been speculated. Despite the profound differences in the incidence of hematological malignancies in both sexes, the pathogophysiology of these relations are often overlooked. The aim of this study was to examine such associations and the possibility of explaining it.

Subjects: In Nanakaly Hematology hospital, Erbil, Iraq, during 2010-2012; (566) patients were studied; (174) patients with myeloid malignancies; AML, CML, and (392) patients with lymphoid malignancies; ALL, CLL, HL, NHL, and MM. Compared to (196) blood donors as controls.

Methods: Standard conventional techniques were used for ABO, Rh and Lewis blood grouping and haem-agglutination inhibition test for secretor status.

Results: (table 1 and 2): A significant lower incidence of females was found in lymphoid malignancies (M:F= 1.42:1) (P<0.0002), while no sex difference in myeloid malignancies (M:F=0.93:1) (P:0.203)and even a significant higher female incidence in CML (0.7:1) (P:0.047).).

ABO & Rh blood groups and secretor status results showed no significant difference from controls, except in CML patients; blood group A incidence was significantly (P: 0.006) higher (54.3%) and O blood group was significantly (P: 0.036) lower (22.9%).Regarding the secretor status there was no significant difference between different diseases and between males and females patients.

Lymphoid malignancies have higher O blood group incidence (P: 0.067) than myeloid malignancies.

Discussion: The secret of women's resistance to lymphoid malignancies and stronger immunity lies in having (a) two X-chromosomes, which might provide women with extra protection against cancer, as X chromosomes carry micro-RNA molecules which are very important for cell growth and cancer control through regulating proteins which are also major regulators of the immune system,(b) the gene encoding for sex steroid is located on chromosome 9 near the ABO locus which could protect O blood group women against acute leukemia, through (17-b estradiol in women) which has anti-proliferative control effect on leukemia cells, and (c) the indoor life-style of women with less exposure to environmental and occupational hazards. The low frequency of O group in CML in this study can possibly be explained partially, by the higher frequency of secretor status in O blood group (from previous study), conferring some protection from myeloid carcinogens and possibly a milder disease.

Conclusion: Larger prospective trials are necessary to evaluate these factors and possibly prevention/treatment could be tailored to clinical profiles and genetic background including gender and blood groups.

Keyword: ABO, Secretors

Poster No: 0055 Abstract:0227

LENALIDOMIDE IN ACUTE MYELOID LEUKEMIA; TWO CASES

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Lenalimide, which is an immunomodulatuar agent, is highly effective in myelodysplastic syndrome with 5q deletion (del). There are some studies purposed that lenalidomide can also be effective in AML with 5q del. We presented two AML patients with 5q del treated with lenalidomide.

Case 1**:** A 72-year-old female who had diagnosed as acute myeloid leukemia with myelodysplasia-related changes was admitted to our clinic for treatment. Before admission the patients had skin lesions and diagnosed as Sweet syndrome and started metil-prednisolon by a dermatologist. Cytogenetic analysis on bone marrow revealed 46XX, t(3;5;3) (q21,q13,p25), inv(9)((p11q13) [2], moreover FISH analyses showed 75% 5q deletion. Induction treatment (high dose cytarabine and mitoxantrene day 1 and day 5) was administrated. In spite of a decrease in blast count, no remission is provided. Considering 5q del positivity, the treatment of lenalidomide (25mg/day) with 5-azacitidin combination was decided. After 2 month treatment any response was provided; blast count was increased under treatment. Patient died after six month from the diagnosis with progression of leukemia.

Case 2: 39 years old woman admitted to our clinic with long-term anemia and concomitant thrombocytopenia and leucocytosis and diagnosed as acute myeloid leukemia with myelodysplasia-related changes. Cytogenetic analysis on bone marrow revealed 45XX,rob(13;15) (q10;q10), moreover FISH analyses showed %14 5q31del. Her disease was resistance to standard induction treatment and also to FLAG-ida as salvage treatment. Another salvage protocol (EMA) was administrated; once again we did not observe any response. Despite to refractoriness, her leukemia was slowly progressive, hence, we administrated to 5 azacytidine but no response was

observed. After that, we tried clofarabine combining with high dose cytarabine, unfortunately no response again was provided. After follow up with palliative treatment for a while, we decided to give lenalidomide because of 5qdel positivity. Lenalidomide 50mg/day was started and continued for 21 days. Peripheral blast count increased under lenalidomide treatment, so the treatment was not continued. The patient still is alive and allogenic stem cell transplantation is being planned.

Discussion: We experienced lenalidomide on two patients; both of them were acute myeloid leukemia with myelodysplasia-related changes and with 5q del. We did not observe any objective response to lenalidomide.

Keyword: acute myeloid leukemia, lenalidomide

Poster No: 0056 Abstract:0234

EVALUATION OF MIR-155 INHIBITION EFFECTS ON JURKAT CELL LIN

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Objectives: MicroRNAs are small non-coding RNA molecules with approximately 22 nt in length and cause inhibition of translation or degradation of mRNA. Mir-155 is a molecule with different functions, such as role in proliferation and immunity. Overexpression of this miRNA has been found in a number of cancers. One of its best known functions is apoptosis that affectsa on caspase-3 activity. The main aim of this study was evaluation of LNA mir-155 inhibitor effect in apoptosis.

Methods: In this study, Jurkat cells were used and for evaluation of sensitivity to varied concentrations (25, 50 and 75 nmol) of mir-155 inhibitor using MTT assay. Mir-155 expression level was analyzed using the quantitative real-time polymerase chain reaction (QRT-PCR). Caspase-3 activity was measured by caspase-3 colorimetric activity assay kit. Unpaired t test were used for analysis of the MTT and apoptosis results. Probability of 5% was assumed as statistically significant.

Results: According to our results, the use of mir-155 inhibitor increased activity of caspase-3 by 2 fold in 75 n mol concentrations. In this research, we found that the proper increase of mir-155 inhibitor concentration can inhibit mir-155 and consequently increase caspase-3 activity and induce apoptosis in the Jurkat cells leading to cell death ultimately.

Conclusions: Apoptosis stimulation by miRNAs is probably will be one of the best and low risk ways of cell death induction in malignancies. Due to role of mir-155 in several cancer cells, it may be used as a therapeutic tool in future.

Keyword: mir-155 inhibitor, Apoptosis

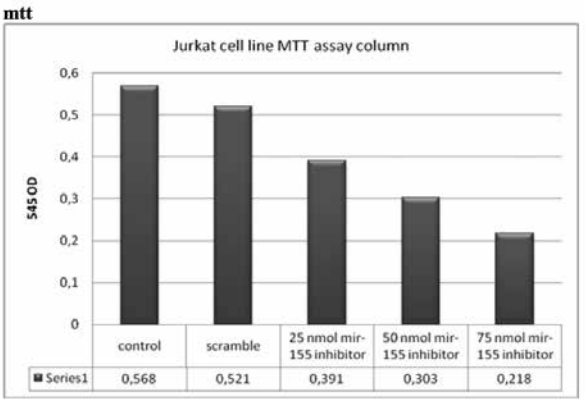

Figure 1. MTT assay on the control, scramble and test groups. OD of the tests is shown in the below row.

Poster No: 0057 Abstract:0249

THE MOLECULAR ANALYSIS OF B-THALASSEMIA MUTATIONS IN NORTHEAST EGYPT

Othman Soliman[1], Sohier Yahia[2], Amany Shouma[3], Hala Shafiek[4], Ashraf Fouda[5], Hanan Azzam[6], Enas Goda[7], Nashwa Abou Samra[8], Rabab Mahfouz[9], Solafa Abd Elraouf Elshrawy[10]

Background: β-Thalassemia (β-thal), the most common genetic disorder in Egypt, is widely distributed particularly in Mediterranean and Middle Eastern countries. β-globin alleles were studied by different molecular methods which are known to be difficult, time consuming and more liable to contamination. The β-Globin StripAssay method is reported to be rapid, simple, reproducible and less expensive.

Aim: Our study aimed to evaluate The β-Globin StripAssay method based on reverse hybridization for detection of β-thal mutations in Egyptian children living in Northeast Egypt, and detect possible genotype/phenotype correlation.

Subjects & Methods: For this purpose forty children with β-thal major (20 males and 20 females) with mean age of 10.33±4.75 years were recruited consecutively from outpatient Hematology Clinic of Mansoura University Children's Hospital. In addition to full history, clinical and routine laboratory evaluation, mutation analysis was performed by the β-Globin StripAssay MED (Vienna Lab, Vienna, Austria).

Results: The most common genotypes encountered were; homozygous IVS 1.110 (6 patients, 15%) and IVS 1.1 (5 patients, 12.5%) while compound heterozygous genotypes were detected in the remainder mainly IVS 1.110/IVS 1.6 (8 patients 20%), IVS 1.110/IVS 1.1 (5 patients, 12.5%). The most frequent mutant alleles detected were; IVS 1.110, IVS 1.1 and IVS 1.6 accounting for 33.75%, 27.5% and 18.75% respectively while the least frequent was Codon 39 that represented 2.5% of recovered alleles. The detection rate of the used method in our population was 90% where 8 alleles out of 80 (10%) remained uncharacterized. No genotype/phenotype correlation was demonstrated in studied patients.

Conclusion: β-Globin StripAssay is a fast, easy-to-perform and reliable method for genetic screening of β-thalassemia patients in Egypt. IVS 1.110, IVS 1.1 and

IVS 1.6 are the most frequent mutant alleles with poor phenotype/ genotype correlation.

Keyword: β-Thalassemia

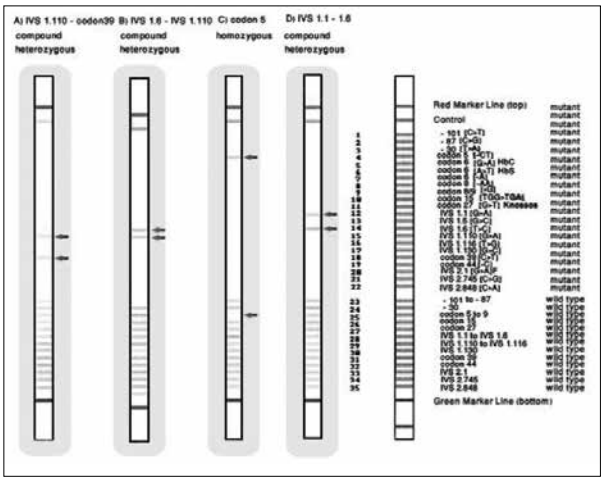

Figure 1 Interpretation of the β-globin Strip Assay results (Vienna Lab, Vienna, Austria).

Poster No: 0058 Abstract:0258

EXPRESSION OF THE AURORA A AND AURKAIP1 GENES IN AML PATIENTS

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Objectives: Acute myeloid leukemia (AML) arises in the precursors of myeloid, erythroid, megakaryocytic, and monocytic cell lineages. Advances in our understanding of the molecular genetics of AML have not yet led to improvements in therapy. Most human cancers display genomic instabilities in forms of chromosome losses, translocations, aberrant chromosomal duplications and segregations. Recent studies indicate that instability occurs early during mitosis. Aurora kinases are one of the most conserved regulatory protein families and defects in the aurora kinase genes may lead to tumorigenesis. The Aurora A protein activates its substrates by phosphorylation and initiates mitosis. It is involved in mitotic entry, separation of the centriole pairs, accurate bipolar spindle assembly, alignment of the metaphase chromosomes and completion of cytokinesis. Recent studies show that Aurora A also plays a role in the degradation of the nuclear membrane. The capacity of a single mitotic kinase in initiating tumor development indicates the importance of this protein. A better understanding of the Aurora kinase family may have important consequences for the control of the cell cycle and the design of new therapeutic cancer drugs. The Aurora-A kinase interacting protein 1 (AURKAIP1), is a negative regulator of Aurora-A, and promotes proteasome-dependent Aurora-A degradation through an ubiquitin-independent mechanism. Studies analyzing Aurora A expression in leukemia are very few and the AURKAIP1 gene has not been analyzed in leukemias at all. In this study we aimed to investigate expression of the Aurora A an AURKAIP1 genes in patients with AML.

Methods: 41 patients with AML and 23 healthy controls were studied. RNA was isolated and complementary cDNA was sythesized. Real time PCR was performed using the ABI7500 system. Expression levels of the Aurora A and AURKAIP1 genes were compared with Zinc finger protein 207 (ZNF207) expression as the reference gene. The results were analyzed by the ΔΔCt method.

Results: In this study Aurora A expression levels were significantly higher in the patients when compared to the control group (2-ΔΔCt =1,95). Likewise, AURKAIP1 expression levels were much lower than the control groups (2-ΔΔCt =0,03).

Conclusion: Overexpression of the Aurora A gene supports the role of Aurora A in leukemia development and progression. The decrease in AURKAIP1 is consistent with lack of Aurora A degradation and stimulation of cell proliferation by increased kinase activity due to high Aurora A expression.

Keyword: Acute myeloid leukemia, Aurora A

Poster No: 0059 Abstract:0309

OPTICAL AND MORPHOMETRIC PARAMETERS OF MONONUCLEAR CELLS IN MORBIDITY INCLUDING LEUKEMIA

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Conventional flow cytometry measures intensity of scattered light at two directions. Some advanced experimental devices, known as scanning (wide-angle) flow cytometers, measure angular dependences of intensity of scattered light ("cell fingerprints") over a wide interval of scattering angles. Such flow-cytometric light-scattering patterns give new opportunities for characterization of normal and pathological cells. Mononuclear cells of fresh peripheral blood were investigated in parallel for healthy donors, hepatitis B/C and acute lymphoblastic leukemia patients aged 26 to 48 y.o. The cells were isolated using Ficoll-PaqueTM PLUS separation solution. The purity of lymphocyte population isolated for analysis was approximately 94%. Computational modeling for single-lymphocyte light scattering was fulfilled. The findings showed that the scattering channels of flow cytometer provide opportunity of express assessment of cell optical pattern and allow one to refer the cell to "normal", "viral" or "malignant" population without use monoclonal CD markers. Modeling data were validated by simultaneous flow-cytometry investigation. Both the experimental and modeling data demonstrated the utility of optical cell pattern ("cell fingerprint") in biomedical applications. To enhance reliability of leukemia cells revelation, we proposed our novel method, based on the differential-interference contrast (DIC) microscopy. DIC-microscopy allows one to investigate morphometric characteristics of living unstained human mononuclears in cells suspension. The live cell suspension makes possible to evaluate a real (true) cells' form and dimensions apart from other approaches, where the cells are undergone the violent impact of staining and fixative agents, etc.

Our results show that the mononuclear size distributions for the patients and healthy individuals are significantly differ from each other. In particular, maxima of the mononuclear size distributions for acute-mieloid

leukemia samples are substantially shifted to larger sizes as compared to healthy ones.

Thus our DIC-microscopy measurements for living blood cells demonstrated that mononuclear size distributions can be used as an additional criterion in leukemia diagnostics. The advantage of the method proposed - there is no need of any staining or other labeling procedures which are potentially toxic or interfere with normal cell functions. Method allows to study the same cells simultaneously with other approaches to cell diagnostics.

In conclusion, optical and morphometric characterization of mononuclear cells may become useful and perspective method in diagnostics of clonal (leukemia) and polyclonal (hepatitis B/C) cell proliferation.

Keyword: leukemia, differential-interference contrast microscopy

Poster No: 0060 Abstract:0315

RECURRENT MONOSOMIES CONFIRMED BY INTERPHASE FISH IN 3 CML CASES

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Objectives: Monosomies were most frequently seen chromosome abnormalities in bone marrow samples of CML cases that we followed for cytogenetic response to imatinib therapy, both in Ph(-)and in Ph(+) cells1,2. In some cases, there were recurrent monosomies in more than one sample. To evaluate the genuineness of these monosomies, we applied FISH to 3 such cases. We selected chromosomes 8, 10, 17, and 20 for FISH experiments, because they were in relatively common monosomies in our series.

Methods: GTL banded metaphases were examined according to the ISCN3,4. 20 metaphases were studied whenever possible. Cytocell Aquarius alpha satellite probes were used according to the manufacturers instructions for FISH. 200 interphase cells were counted by two different researchers. Normal karyotyped blood or marrow samples were used as controls.

Results: Our cytogenetics and FISH results are seen in the Table. *not in the karyotype **under IFN therapy

Conclusion: In the first three sample of Case 1, -8, -10 and -20 were confirmed by FISH. In the fourth sample of this patient, we performed FISH for 10 and 20 in spite of their absence in karyotype to see if there is a hidden monosomy that we could not find with karyotyping. FISH revealed a hidden monosomy for 20, but not for 10. In the first two samples of Case 2, -17 was observed in cytogenetics, and confirmed by FISH too, but in the third sample there was not a -17 in karyotype and not found by FISH, either. In Case 3, -8 was confirmed with FISH, but -20 could not be observed by FISH in spite of its existence in karyotype.

In some instances FISH confirmed the cytogenetic result, but in others, not. These results indicate the necessity to use FISH in concordance with conventional cytogenetics. To evaluate if certain monosomies have an impact on the disease course, it is necessary to follow more cases with recurrent monosomies for longer durations.

Keyword: Cytogenetics, CML

Tablo 1. Cytogenetics and FISH Results

Case No.	Sample No.	Cytogenetic Results	Chromosome numbers analyzed by FISH	Monosomy percentages by FISH	
				Cases	Controls
Case 1	1	38~46,X,-Y[4],t(9;22)(q34;q11) [6],-10[4], -15[4], -16[3] [cp15]/46,XY[8]	10	%30	%7
	2	37~47,XY,-Y[3],-3[3],-7[4],-8[3],-9[3],-10[4],-11[3],-14[3],-15[3],-18[4],-20[4],+mar1[3],+mar2[2][cp16]/46,XY[13]	10 20	%16.5 %40	%7 %14
	3	35~45,XY,-4[3],-8[4],-9[3],-10[5],-13[6],-14[3],-15[5],-16[4],-18[3],-21[3],-22[3][cp12]/46,XY[6]	8 10	%12 %14	%6.4 %7
	4	46,XY,t(9;22)[3]/46,XY[13]	10* 20*	%5,5 %43.5	%7 %14
Case 2	1**	39~46,XX,t(9;22)(q34;q11)[12],-17[3],-21[3][cp12]	17	%46	%15.6
	2	41~46,XX,-9[3],t(9;22)[25],-14[5],-15[4],-17[3],-18[4],-21[3][cp25]	17	%31	%15.6
	3	35~46,XX,-3[5],-7[4],-8[5],t(9;22)[18],-10[3],-12[3],-13[5],-15[4],-19[3],-20[6],-21[4],-22[6][cp18]	8 10 17* 20	%9 %9 %11 %15	%6.4 %7 %15.6 %14
Case 3	1	44~38,XY,-6[3],-8[5],-20[4][cp8]/32,X,+1,+7,+10,+19,+20[cp2]/46,XY[9]	8 20	%12 %8.5	%6.4 %14
	2	40~46,XY,-8[3],-9[4],-13[3],-20[3][cp7]/46,XY[20]	8 20	%13 %9	%6.4 %14

Multiple Myeloma

Poster No: 0061 Abstract:0087

IGA KAPPA MULTIPL MYELOMA CASE PRESENTING WITH MICROSCOPIC HEMATURIA AND PROTEINURIA

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We report a challenging case who was first presented with vasculitic symptoms and microscopic hematuria and underwent renal biopsy revealing ig a and kappa deposition. Despite having no symptoms or signs rather than the renal biopsy findings he was diagnosed with multipl myeloma due to bone marrow aspiration and biopsy. Initial diagnostic workup involving skeletal surveys showed no sign of active disease but PET scan revealed multipl bone lesions attributable to plasma cell dyscrasia.

A 56 years old male patient who was previously well admitted to an outpatient clinic with the complaint of purpuric lesions involving the distal extremities. Skin biopsy was performed and revealed leucocytoclastic vasculitis. Patient was put on to steroid therapy. The etiologic cause of vasculitis was investigated and microscopic hematuria and non nephrotic proteinuria was detected while the glomerular filtration rate was in normal range during diagnostic workup. Patient was referred to our nephrology clinic with the pre-diagnosis of nephritic syndrome. Renal biopsy was performed, and revealed ig a heavy chain and kappa light chain deposition in mesengial matrix. Patient had no symptoms or signs which could be attributable to plasma cell dyscrasia. However, bone marrow aspiration revealed 40% plasma cells with some bizarre shaped cells. Bone marrow biopsy has proved the cells to be monoclonal and staining predominantly with kappa. Serum protein electrophoresis showed monoclonal gammopathy which was identified as ig a kappa in immunofixation. Ig A level was 1262 mg/dl and kappa light chain was 535 mg/dl. His purpuric lesions

resolved and steroid therapy was stopped. Considering the active (symptomatic) myeloma criteria he had no anemia, his creatinine level was under 2 mg/dl and calcium level was under 11,5 mg/dl and skeletal surveys revealed no lesions which may be attributable to multipl myeloma. Instead having heavy and light chain deposition in kidney he had no worsening renal dysfunction. With regard to criteria proposed to initiate myeloma treatment the patient was naive and had to be regularly followed up. But in systemic evaluation the patient complained about bone pain conserning the extremities. PET scan was ordered to search for any undetectable bone lesions under skeletal surveys. PET results revealed multipl lytic sclerotic lesions at costal, vertebral and femoral regions with suv max values changing between 3,5 and 7,5 (figure 1). Because of the documented bone lesions patient was put on to combination chemotherapy.

Sometimes simply "renal insufficiency" defined as having a serum creatinine level of more than 2 mg/dl should not be enough to describe active renal and systemic disorder. In such situations some further investigations should be done in order to better identify end-organ involvement and active (symptomatic) disorder. PET scan could be considered as one of these studies in some circumstances.

Keyword: multipl myeloma, renal disease

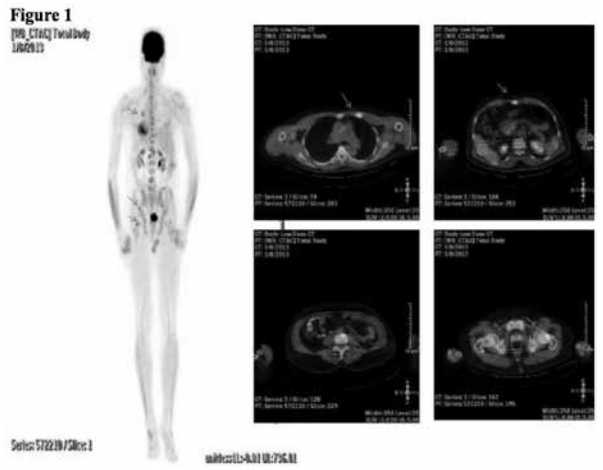

Figure 1. PET Scan with multipl bone lesions

Poster No: 0062 Abstract:0091

CENTRAL NERVOUS SYSTEM RELAPSE AFTER HIGH DOSE CHEMOTHERAPY IN A PATIENT WITH MULTIPL MYELOMA

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We report a case of central nervous system relapse with intraparenchymal, dural and leptomeningeal involvement after high dose chemotherapy and autologous stem cell transplantation. A 51 year old man received two cycles of cyclophosphamide and dexamethasone as an induction treatment for stage IIIA IgG k multipl myeloma with multipl soft tissue plasmocytomas. After additional two cycles of bortezomib with partial response, high dose chemotherapy with autologous stem cell transplantation was performed at the 4th month of diagnosis. Very good partial remission achieved after high dose chemotherapy and patient began to be followed up with only biphosphonate treatment. 11 months after high dose therapy the patient admitted with sudden transient loss of vision, headache and palpable temporomandibular mass. Magnetic resonance and pet imaging revealed mass lesion occupying right infratemporal fossa and another mass lesion occupying left petrous apex, extending through the sphenoid sinus and infiltrating cavernous sinus involving the 6th cranial nerve. Heterogenous dural and leptomeningeal infiltration was detected. In the cerebrospinal fluid analysis monomorphic plasma cells were seen (Figure 1). FISH analysis did not reveal deletion 17p or deletion 13q. Both localized radiotherapy and combined systemic chemotherapy (cyclophosphamide, bortezomib, doxorubicin and dexamethasone) initiated. Intrathecal methotrexate was also applied for 4 times concurrently. After 3 cycles of systemic chemotherapy a reasonable response was achieved and considering the side effects of combination regimen (severe peripheral neuropathy related with bortezomib) patient put on to lenalidomide and dexamethasone therapy. After six cycles of lenalidomide therapy symptoms related with central nervous system involvement and cytopenias related with bone marrow infiltration got worse and patient was lost from multiorgan failure and sepsis.

Considering the initiation of symptoms, patient has survived for 9 months after diagnosed with leptomeningeal infiltration. In the literature there is no standard therapeutic approach regarding the central nervous system relapse after high dose therapy and median survival of patients with cns relapse is 2 to 3 months. Several systemic conventional combination regimens, raidotherapy and intrathecal chemotherapy were tried, but never achieved a long survival. The impact of novel therapeutic drugs like lenalidomide remains unclear. As in our case lenalidomide may prolong the survival of patients with cns relapse.

Keyword: cns, myeloma

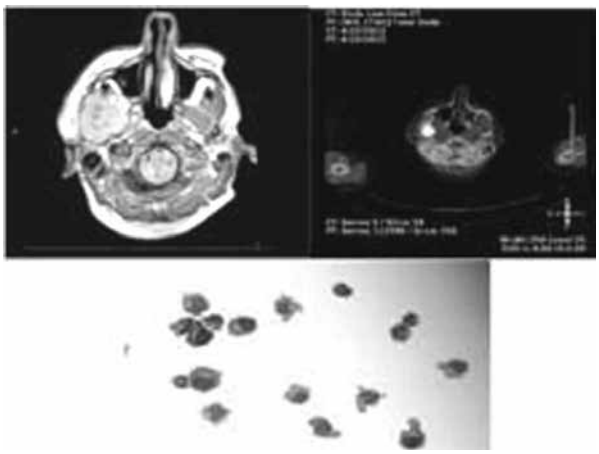

Figure 1. MRI, PET imaging and CSF

Poster No: 0063 Abstract:0102

A RARE ENTITY: IGD LAMBDA MULTIPLE MYELOMA

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Multiple myeloma (MM) is characterized by the neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. MM accounts for approximately 1 percent of all cancers and slightly more than 10 percent of hematologic malignancies in the United States.

Approximately %60 of myeloma patients have detectable monoclonal IgG, %20 monoclonal Ig A and %20 percent have only monoclonal immunglobulin light chains. Myelomas producing monoclonal IgD, IgE, IgM, or more than one immunglobulin class are rare. This case with IgD lambda light chain disease was a rare entity and has expending clinical features that we concerned to share in this report.

A 39 year of man admitted our internal medicine policlinic with the complaint of anorexia, weight loss, severe back pain and immobilization. Routine blood tests revealed hypercalsemia (13.7mmol/dl), hyperurisemia (109.1 mg/dl, kreatinin 2.3mg/dl) and anemia (Hg: 7.0 g/dl). Sedimentation rate was 120 mm/hour. Radiographic examnations showed multiple lytic lesion of ribs and diffuse osteoporosis.

Serum albümin was 4.5 gr/dl and serum globulin was 4.2 gr/dl. Ig A, G and M levels were low. Serum protein electroforesis showed a gamma globulin peak. Urine immunfixation electrophoresis showed no monoclonal bands but detected Lambda light chain.

Bone marrow aspiration specimen revealed an abnormal proliferation of atypical plasma cells (%75) Bone marrow biopsy interpreted IgD/Lambda Multiple Myeloma and grade III-IV reticulin and collagen fibre rise. Peripheral blood FISH analysis remained negative for del [13q], del 17p t(14;16) t(11;14).

We maintain his hydration and diuresis in order to correct hypercalsemia and decrease blood urea and creatinine levels. He also needed packed RBCs transfusion for increasing hemoglobin levels above 8 mg/dl. Dexametasone infusion therapy was given for four days following a pause of four days repeated 4 cycles.

Multiple myeloma is a plasma cell disorder usually seen at 5-6 th decade. Malignant plasma cells synthesize monoclonal immunoglobulins most commonly IgG, IgA or only light chains. About 1 percent of cases are IgD myeloma. Osteolytic lesions or diffuse osteoporosis occurs by the mass effect of plasmacytomas, or by the cytokines that are secreted by malignant plasma cells.

In our case with multiple myeloma secreting IgD lambda light chain, diffuse osteoporotic lesions was seen at X-ray graphies at skull, ribs, vertebra. Pathological bone fractures was demonstrated at multiple levels of vertebra with a CT screening.

The presence of low concentration of serum monoclonal immunoglobulin should alert to the possibility of the IgD myeloma isotype, especially when associated with excess lambda light chains in the serum and light chain proteinuria.

Keyword: Multiple Myeloma, IgD Lambda

Poster No: 0064 Abstract:0107

LOCAL RENIN-ANGIOTENSIN SYSTEM IN NORMAL HEMATOPOIETIC AND MULTIPLE MYELOMA-RELATED PROGENITOR CELLS

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Objective: The prominent functions of local renninangiotensin system (RAS) in primitive hematopoiesis further support the hypothesis that local autocrine BM RAS could also be active in the neoplastic hematopoiesis. The aim of this study is to search critical RAS elements in normal CD34+ hematopoietic stem cells and multiple myeloma (MM)-related progenitor cells.

Patients and Methods: The study group comprised the total bone marrow cells (CBM) of 10 hematologically normal people and the CD34+ stem cell samples (CD34+CBM) of 9 healthy donors for allogeneic peripheral stem cell transplantation, and the CD34+ stem cell samples (CD34+MM) of 9 MM patients undergoing autologous peripheral stem cell transplantation. We searched for the gene expression of the major RAS components in healthy hematopoietic cells and myeloma cells by qRT-PCR.

Results: RENIN, angiotensinogen (ANGTS), and angiotensin converting enzyme-I (ACE I) mRNA expression levels of CBM were significantly higher than those in myeloma patients (p=.03, p=.002, and p=.0008, respectively). Moreover, RENIN and ANGTS mRNA expression levels were significantly higher in CD34+ stem cell samples of healthy allogeneic donors compared to those in myeloma patients (p=.001 and p=.01). However, ACE I expression levels were similar in CD34+CBM and CD34+MM hematopoietic cells (p=.89).

Conclusion: Although it was found to be lower then the CBM and CD34+CBM hematopoietic cells, the local RAS components were also expressed from CD34+MM hematopoietic cells. This point should be kept in mind while focusing on the immunobiology of MM and processing of autologous cells during the formation of the transplantation treatment protocols.

Keyword: Renin-angiotensin system, multiple myeloma

Poster No: 0065 Abstract:0114

SCLEROMYXEDEMA: A RARE VARIANT OF LICHEN MYXEDEMATOSUS ASSOCIATED WITH MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE

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A 54-year-old female presented with a one-year history of papules and erythematous skin induration, initially limited to the head and upper extremities and subsequently spread to the knees and lower extremities over the last three months. On physical examination, characteristically leonine facial changes including deep longitudinal facial furrows and intense erythema of the glabella were noted (Figure 1). In addition, physical examination revealed 2 to 5 mm waxy papules, fusing into plaques on the glabella, dorsum of the nose, perioral region (Figure 1) and erythematous plaques on the knees, dorsal area of her hands and feet. Histopathologic analysis of two skin punch biopsy specimens showed proliferation of fibroblasts and diffuse mucin deposition within the upper reticular dermis. The blood count revealed a hemoglobin of 12 g/dl, a white blood cell count of 6000/mm^3 and a platelet count of 250000/mm^3. A serum monoclonal protein of 0.22 g/dl was detected. Serum immunfixation electrophoresis confirmed the monoclonal gammopathy of IgG-lambda type and on urine electrophoresis monoclonal lambda free light chain was detected. Nodular and interstitial neoplastic plasma cell infiltration (5%) with monotypic CD38 expression was detected in bone marrow biopsy. On skeletal survey, no destructive lesions were present. The patient was diagnosed as scleromyxedema and monoclonal gammopathy of undetermined significance. Oral methylprednisolone was started and after 15 days, oral isotretinoin was added to the therapy. After ten weeks of treatment, skin lesions located on the upper and lower extremities resolved while edema and deep longitudinal furrows improved only slightly. The patient is still under follow-up in our Hematology and Dermatology departments.

Scleromyxedema, a generalized papular and sclerodermoid form of Lichen myxedematosus, is characterized by waxy yellow-red papules on the head, neck, arms, and upper trunk commonly developing over thickened and indurated skin. Specific areas typically involved include the posterior-auricular area, the forehead and glabella, posterior neck, fingers, and forearms. It is a rare fibromucinous connective tissue disorder characterized by mucin deposition, fibroblast proliferation, and fibrosis, monoclonal gammopathy in the absence of thyroid disease. Patients have variable organ involvements (e.g. gastrointestinal, musculoskeletal, cardiac, pulmonary, neurological and renal complications) that mimic scleroderma. A monoclonal gammopathy of undetermined significance predominantly of the IgG lambda light chains is present. It may be associated with multiple myeloma in only 10% of patients. Various therapies (e.g. corticosteroids, melphelan, thalidomide, high dose intravenous immunoglobulin and autologous stem cell transplantation) have been described to treat symptoms of scleromyxedema and reduce the paraprotein. Currently, therapy of patients with scleromyxedema are often a challenge.

Keyword: monoclonal gammopathy of undetermined significance, scleromyxedema

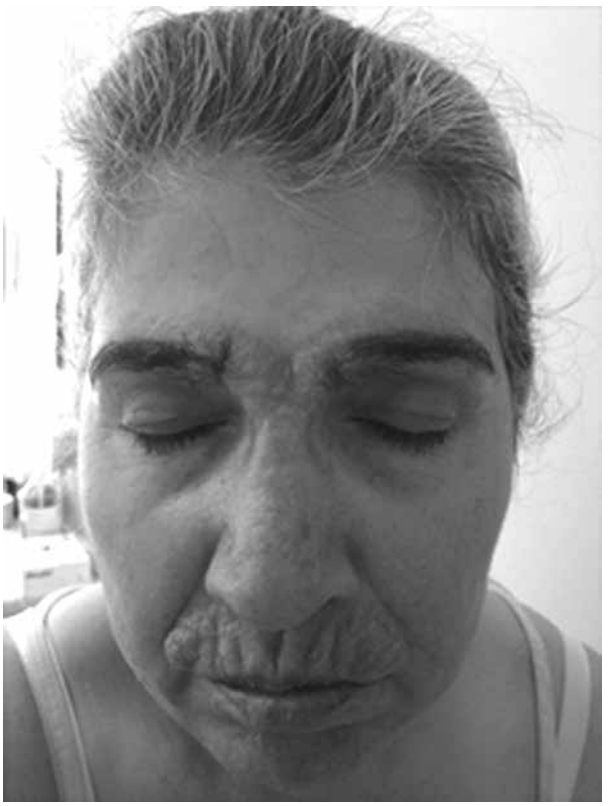

Figure 1. Leonine facial changes accompanied by papules coalescing to into plaques on the glabella, dorsum of the nose and the perioral region.

Poster No: 0066 Abstract:0115

SINGLE CENTER EXPERIENCE OF MYELOMA PATIENTS TREATED WITH LENALIDOMIDE

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We have aimed to evaluate myeloma patients in terms of demographic features and clinical status treated with lenalidomide.

Data of thirty-four patients who have been treated with lenalidomide with diagnosis of multiple myeloma in our center between 2010 and 2012 were evaluated. The relationship between the variables; age, sex, first, second and third line chemotherapy regimens, daily lenalidomide dose, overall survival (OS), mortality were analyzed.

The median age of the patients was 61.3 years (45-78 years), and of 22 (64.7%) males and of 12 (35.2%) females. Eighteen patients were stage 3A, 10 were 3B, 4 were 2A, 1 (2.9%) was 2B and 1 (2.9%) of the patients was stage 1A. Most of the patients were IgG/kapa myeloma. ASCT was performed in 15 patients before the lenalidomide treatment. Median time from diagnosis to use of lenalidomide was found 33.1 months. In all cases, lenadilomide was combined with dexametasone. Lenalidomide treatment was used as a second line therapy in 9 (26.4%), as a third line treatment in 17 (50%) and as a fourth line

therapy in 8 (23.5%) patients. The median lenalidomide dose was 18.3 mg/day (5-25 mg). OS was 44 months. Lenalidomide was ceased in 4 (11.7%) patients because of progression and in 4 (11.7%) patients because of persistent cytopenias. One (2.9%) patient died under lenalidomide. Lenalidomide treatment stil continues in 25 (73.5%) patients.

According to our results, lenalidomide was provided to our patients at least after 2 or 3 prior therapies with lesser efficacy and relatively high side effects

Keyword: Myeloma, lenalidomide

Poster No: 0067 Abstract:0116

MAY HEMOGLOBIN VALUES IN PATIENTS WITH MULTIPLE MYELOMA USING THALIDOMIDE BE AN EARLY PREDICTIVE INDICATOR FOR RESPONSE ?

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Thalidomide is an immunomodulatory drug which provides improvement in overall survival in multiple myeloma In this study, we aimed to evaluate myeloma patients under treatment of thalidomide and investigate the potential predictive value of increase in hemoglobin levels as an indicator for response to thalidomide therapy.

Thirty-four myeloma patients treated with thalidomide between 2001 and 2012 in our center were enrolled to this analyses. The relationship between the variables (age, sex, first and second chemotherapy regimens, daily thalidomide dose, complete blood count with first 3 months after initiation of thalidomide) and overall survival (OS), progression free survival (PFS) and mortality were evaluated. After thalidomid prescrition, the first 3 months hemoglobin levels were extracted for evaluation. Statistical evaluation was performed with the SPSS 17.0 program and the threshold level of significance was accepted as p = 0.05.

Twenty-eight (82.3%) of 34 multiple myeloma patients were stage 3A, 3 (8.8%) of them were stage 3B, 2 (5.8%) of them were stage 2A and 1 (2.9%) of the patients was stage 1A. Fourteen (41.1%) of the patients were Ig G-kappa myeloma, 6 (17.6%) of them were Ig G-lambda, 4 (11.7%) of them were Ig A, 2 (5.8%) of them were Ig A-kappa, 2 (5.8%) of them were Ig A-lambda, 3 (8.8%) of them Ig G, 1 (2.9%) patients was Ig kappa myeloma and two of them were unknown. Autologous hematopoetic stem cell transplantation was performed in 17 (50.0%) patients before the thalidomide treatment. The time from diagnosis to the use of thalidomide was found as 26.1 months. The median thalidomide dose was 285 mg/day and the median duration of thalidomide use was 20 months. The median values of the patients before the use of thalidomide were; Hb: 11.6 g/dl, Htc: 34.8%, WBC: 4587/µl, Plt: 182.000/µl. The median values of the first month after initiation of thalidomide were; Hb: 11.5 g/dl, Htc: 35.2%, WBC: 4430/µl, Plt: 197.000/µl, second month values were; Hb: 11.8 g/dl, Htc: 35.2%, WBC: 4650/µl, Plt: 212.000/µl, 3rd month values were; Hb: 12.0g/dl, Htc: 36.2%, WBC: 4730/µl, Plt: 212.600/µl There were no statistically significant difference in hemoglobin levels, hematocrit and WBC before and after thalidomide OS was 65.5 months, survival after initiation of thalidomide was 39.2 months and PFS was 20.3 months. Thalidomide was stopped in 17 (50.0%) cpatients because of progression and in 2 (5.8%) patients because of neuropathy. Three (8.8%) patients died while using thalidomide. Five (14.7%) patients left the follow-up. Thalidomide treatment stil continues in 7 (20.5%) patients. 18 patients died during the follow-up.

Although there was no difference in patients with stable and progressive disease status under treatment with thalidomide in terms of hemoglobin levels, it is needed to have longer follow-up period. Hemoglobin levels might be good indicator for evaluation of response to thalidomide therapy for patients treated for longer period.

Keyword: Myeloma, Thalidomide

Poster No: 0068 Abstract:0119

ASCITES FORMATION AND RESPONSE TO INTRA-PERITONEAL DEXAMETASONE IN THE COURSE OF REFRACTORY MYELOMA

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Introduction: Ascites is a rare complication of multipl myeloma and generally occurs because of portal hypertension due to the infiltration of liver by plasma cells. Infrequently, ascites is detected as a result of peritoneal infiltration by myeloma cells. We, hereby, present a case with sudden ascites due to peritoneal infiltration by malignant plasma cells and responded to intra-peritoneal dexametasone application.

Case: Forty-eight years old male was diagnosed with stage 2A non-secretory myeloma in December 2008 and treated with four courses of VAD. He relapsed in July 2009 and treated with bortezomib containing VCD regimen After 8 cycles, renal failure has developed and he was undergone regular hemodialysis programme. He was followed-up with stable disease until development of abdominal distantion and ascites was detected in the abdomen at May 2012. Small lymphocytes, polymorphonuclear leukocytes, mesotelial cells and atypical plasma cells were detected in cytological examination of the ascites. Bone marrow biopsy revealed persistant atypical plasma cells Patient was accepted as peritoneal infiltration of multiple myeloma and regular paracentesis was performed every other day for palliation. But ascites was refractory to regular paracenthesis and forty miligrams of dexametasone was given as intraperitoneal injection after each paracentesis for 3 times. Ascites decreased and plasma cells disappeared. But, patient died due to septic shock.

Discussion: Peritoneal involvement by plasma cells is rare but it should be considered in patients with refractory ascites. When peritoneal involvement detected, intraperitoneal dexametasone injection can be used as palliation.

Keyword: Multiple myeloma, Ascites

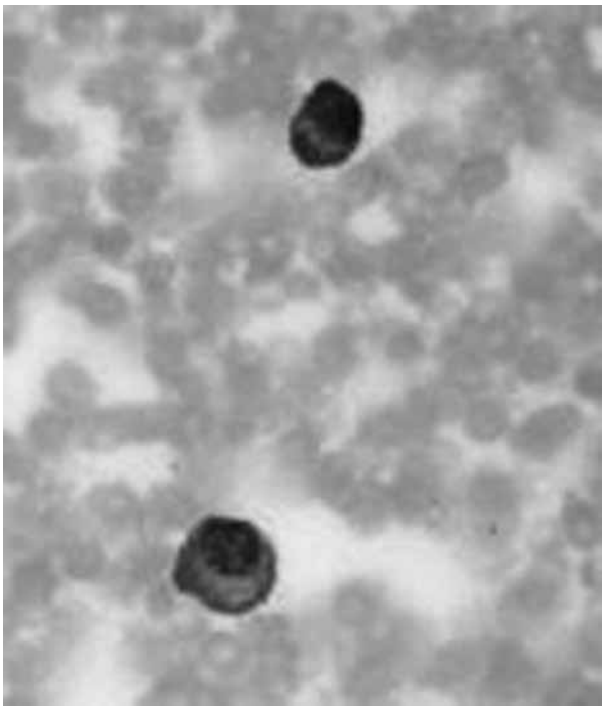

Figure 1. Plasma cells in ascites

Poster No: 0069 Abstract:0121

DENDRITIC CELL VACCINATION LOADED WITH TUMOR CELL ANTIGENS IN MULTIPLE MYELOMA

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Multiple myeloma (MM) is a disease that has not provided a long term complete cure, despite use of new drugs and high response rates with autologous stem cell transplantation (autoSCT). Cancer vaccines eliminate minimal residual disease in MM by stimulating tumor-specific T cells and decreasing tolerance of T cells, it is not sufficiently reflected to result of treatment. In the study, we designed to evaluate the efficacy and safety of dendritic cell (DC) cancer vaccine pulsed with tumor antigen in MM patients.

27 patients diagnosed with MM were enrolled in the study. After appropriate treatment, autoSCT was performed in all patients. Post-transplantation, DC cancer vaccine was administered to 10 patients, thalidomide treatment was provided to 7 patients. 10 patients were followed-up without any treatment. Response to treatment, time to disease progression and treatment-related side effects were evaluated in all patients. At the end of follow-up period of 2 years, progression of disease was observed in approximately 8 months in 3 patients in DC cancer vaccine group while the corresponding time of disease progression in other cases were determined as 7, 9, 11, 14, 15 and 23 months, respectively; no progression of disease was found in 1 patient in 42th week of follow up. On the other hand, progression of disease was found in 3rd month in 2 patients who received thalidomide after autoSCT while the corresponding time of disease progression was detected as 7 and 18th months in other patients; no disease progression was found in 1 patient during a follow-up period of 28 months. Among patients with no additional treatment following autoSCT, progression of disease was found during 2-7 months after autoSCT in 4 patients with PR and within 3-13 months in 6 patients with VGPR. Assessment of time to disease progression after autoSCT showed a duration of 15 months in patients who received DC cancer vaccine, 12 months in patients treated with thalidomide and 6 months in patients followed up without any further treatment. While time to disease progression after autoSCT were longer in DC cancer vaccine and thalidomide groups, in untreated patients was significantly shorter than DC cancer vaccine group ($p<0.05$). Treatment-associated side effects were observed in all patients treated with thalidomide, leading to stop of treatment in 2 patients. Side effects in DC cancer vaccine group were transient and tolerable while no stop of treatment was observed.

In conclusion, DC cancer vaccine was demonstrated to be safe and effective as a maintenance treatment following autoSCT in MM cases and it is suggest that utilization of new cytokines and adjuvants in formulation of cancer vaccine and reduction of T regulatory cells (Treg) will be able to provide more improvement in efficacy.

Keyword: multiple myeloma, cancer vaccine

Poster No: 0070 Abstract:0133

THE COINCIDENCE OF THREE SOLID TUMORS IN A PATIENT WITH MULTIPLE MYELOMA: A RARE CASE

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The incidence of Multiple Primary Cancer (MPC) is very low, and it is even less common than synchronous presentation of a solid tumor with a hematological malignancy. The precise mechanism of MPC has remained unknown. The treatment modality should be determined using the doctor experience and close attention to the characteristics of the patient's illness and performance status. Multiple myeloma is rarely developed, although bone metastasis are commonly seen in many of the solid tumors. In this study, we presented a case diagnosed as multiple myeloma in addition to colon cancer, gastrointestinal stromal tumor and lung adenocarcinoma association; since it doesn't exist in the literature. A 67-years old male presented to Gastroenterology Department with abdominal pain and nausea lasting for 2-3 months. A dynamic liver abdominal CT scan was performed which suggested that solid mass is consistent to liver metastasis. In the colonoscopy, an annular mass was detected at descending colon, where a biopsy was done. Sigmoid resection, metastasectomy and left hemicolectomy were performed in the patient who underwent surgery with a

diagnosis of colon adenocarcinoma with liver metastasis. During operation, a mass seen at gastric wall was resected and reported as gastrointestinal stromal tumor of gastric wall. Patient received 6 cycles of chemotherapy regimen including folinic acid, 5-Flurouracyl, irinotecan and bevacizumab. On the positron emission tomography/computed tomography (PET CT) scan performed 9 months after completion of chemotherapy, a suspected metastasis at upper lobe of right lung, intraabdominal lymph nodes, paratracheal lymph nodes, diffuse bone involvement and involved humeral and femoral diaphysis (bone marrow involvement?) were detected in the patient who had been followed with stable disease. A biopsy was performed to pulmonary lesion, which was reported as adenocarcinoma. In the bone marrow aspiration, plasma cells (50%) were detected; thus, bone marrow biopsy was done. Biopsy result were reported as plasmacytoma. Right upper lobectomy was performed to patient who underwent surgery due to pulmonary mass. Involved-field radiotherapy in conjunction with new chemotherapy for lung cancer and multiple myeloma as well as biphosphonate therapy were scheduled in the follow-up. His survival duration was 18 months from time of diagnosis. In conclusion, to the best of our knowledge, our case was the first multiple myeloma case accompanying to lung, colon and gastric cancer to be reported in the literature.

Keyword: Multiple Myeloma, Multiple Primary Cancer

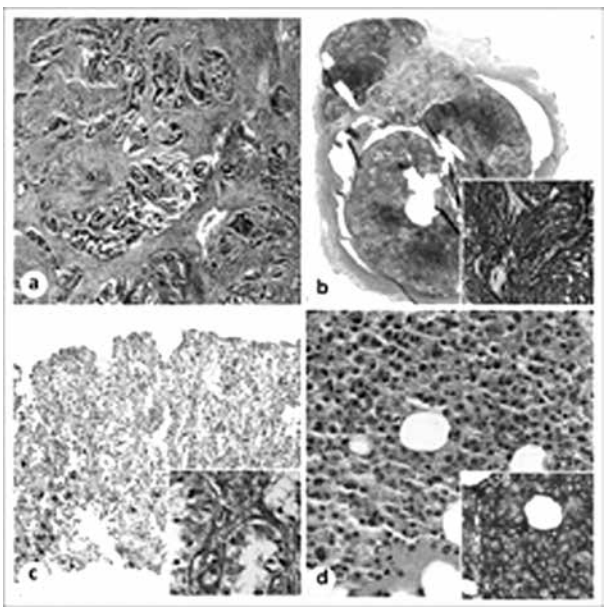

Figure 1. Pathological figures. (a) Neoplastic tissue composed of adenoid structures infiltrating the intestinal wall (H&E staining,x40). (b) Palisanding spindle cells in gastrointestinal stromal tumor (inset showing CD117 pozitivity in neoplastic cells) (H&E staining,x10). (c) Trucut biopsy of the lung showing neoplastic adenoid structures (inset showing TTF1 pozitivity) (H&E staining,x200). (d) Bone marrow biopsy showing neoplastic infiltrating of plasma cells (inset showing CD138 pozitivity) (H&E staining,x400).

Poster No: 0070 Abstract:0155

RECOGNITION OF IMMUNOGLOBULIN D MULTIPLE MYELOMA: CASE REPORT AND SHORT REVIEW

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Objective: Immunoglobulin (Ig)D multiple myeloma (IgD MM) is a rare subtype of myeloma, accounts for less than 2% of all myelomas. An estimate of the prevalence of IgD MM is 0.2%-0.3% of all patients having a monoclonal protein. For the last 7 years 7 cases were diagnosed as IgD MM in our laboratory. The disease is often associated with relatively high frequencies of renal failure, extra osseous disease, hypercalcemia, amyloidosis and Bence-Jones proteinuria. These patients appeared to have significantly worse survival than patients with non-IgD MM.

The IgD MM is mainly type λ, the IgD κ is rare, the predominance of λ light chains could be explained by rearrangements at the immunoglobulin genes. Bence-Jones proteinuria is almost constant in the IgD MM, and mainly type λ, reflecting excess production of light chains by plasma cells. The marrow is invaded by plasma cells in very different proportions of up to 95%. IgD MM is usually misdiagnosed as a light chain types MM by using routine laboratory examination. We present the laboratory examination characteristics of two patients to improve the recognition and reduce the mis-diagnosis of IgD MM.

Case 1: 61 years old female patient presented with expansive bone aches in January 2010. The imaging indicated multiple bone lesions. The bone marrow biopsy revealed 30% lambda monoclonal plasma cells. The serum IgD level was 160 IU/mL (reference <100). The serum immunofixation shows 2 bands on lambda column but no bands on Immunoglobulins G, A and M. On urine immunofixation one of them was found. Further IgD and IgE specific immunofixation test performed and a paraprotein band was found on IgD column.

Case 2: 61 years old female patient presented with abdominal pain, nausea, lumbar ache and fatigue. Laboratory findings were consistent with acute renal failure. Increased lambda light chains in the serum (3390mg/L) and urine (266mg/L) were reported in the serum and urine. Regarding the monoclonal band in the serum protein electrophoresis (SPE) bone marrow biopsy performed and indicated IgD/lambda myeloma, with a 45% of atypical plasma cells.

Conclusion: IgD monoclonal protein is not easy to be detected owing to its low protein level. It is resulting in missed diagnosis particularly when low homogeneous band on electrophoresis goes unnoticed for an inexperienced eye or when immune serum anti-IgD was not used during the immunotyping.

Because of indistinct clinical presentation of IgD Myeloma, its laboratory diagnosis is important. It may not be easy to recognize a faint band on SPE. With immunofixation if a band only appears on light chain columns, a urine immunofixation must be performed to rule out the diseases with monoclonal free light chain. An Immunofixation electrophoresis using Anti-IgD serum which is highly sensitive and specific for diagnosis of IgD MM, enhance accuracy of diagnosis for this rare disease.

Keyword: Immunoglobulin D, Multiple myeloma

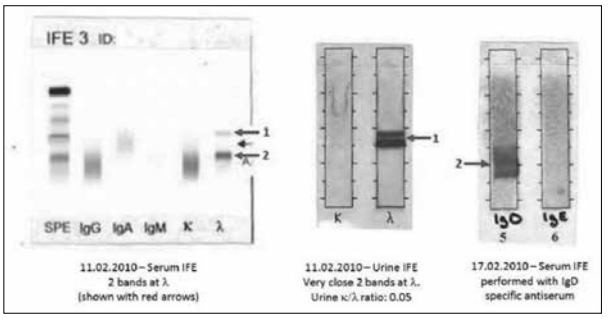

Figure 1. Serum and Urine Immunofixation

Poster No: 0072 Abstract:0172

MULTICENTRIC EXTRAMEDULLARY INVOLVEMENT OF MULTIPL MYELOMA

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Extramedullary disease(EMD) is an uncommon manifestation in multipl myeloma (MM) and either accompany newly diagnosed disease (15-20%) or develop with disease progression or relapse (+15%). The extramedullary disease confers a poorer prognosis. Hereby we will present a patient presented with multicentric extramedullary involvement at the presentation of MM and another one who relapsed with extramedullary disease.

Case1: 59 –year –old man presented with mass after a trauma of the chest. An excisional biopsy which then revealed plasmacytoma had been perfomed. Bone marrow aspirate noted 70% plasma cell. The patient diagnosed with lambda light chain MM, stage 3A. Physical examination showed a 13x8 cm fix mass on the left part of the chest. PET analysis revealed obliteration of left nasal cavity with hypermetabolic massive lesion, another mass infiltrating all adjacent muscles and costas on the left anterior chest wall, infiltration in pancreas tail and corpus and infiltration in manibrium sterni, left iliac wing and right proximal femur. His hematologic parameters, calcium and renal functions were normal. Albumin was 3.8g/d L and beta 2 mikroglobulin 5714. He did not have 13q and 17q deletions. The patient treated with cyclophosphamide 1000mg/m^2 and dexamethasone 40 mg for four days. After 2 cycles of Cyc-Dex, bortesomib, adriablastina, dexamethasone (PAD) regimen initiated. As he had progression while he was on the therapy, the chemotherapy regimen swiched to lenalidomide, bortesomib and dexamethasone (VRD). As no result have obtained the patient referred for autologous transplant. Local radiotherapy applied but after the progression of the lesions and the addition of infection the patient has been died because of sepsis.

Case2: 61-year-old man diagnosed stage 3B lambda light chain MM in 2008 when we was on 3/7 dialysis programme. He was put on 2 cycles of VAD and then switched to PAD. On the 9th month of the therapy he had become dialysis off. We had very good response but the patient refused to be autologous transplanted. Maintenance therapy with thalidomide 100 mgr initiated. But he had relapsed after 10 months. Four cycles of PAD again applied. Very good response again achieved. But on the second year of the disease myeloma relapsed at the occipital part of the skull as a 5x10 cm soft tissue mass infiltrating the skull also and testicular mass. There was no increase in bone marrow plasma cells. The VRD treatment initiated. After the first month of the treatment the lesion regressed. After the 6th month of the treatment his light chain in the urine immunofixation increased. He developed urinary infection and pneumonia and had been lost because of the disease progression and sepsis.

Conclusion: EMD of MM has increased as the avalibility of sensitive imaging techniques. It has poor prognosis. High dose treatment regimens must be applied as a first line therapy for extramedullary disease.

Keyword: multipl myeloma, extramedullary disease

Poster No: 0073 Abstract:0173

CURRENT TREATMENT OF MULTIPLE MYELOMA: SERBIAN MYELOMA GROUP EXPERIENCE

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Introduction: A novel agents as optimal partners to standard/high-dose therapy (HDT) followed by the autologous stem cell transplantation (ASCT), dramatically changed the prognosis of patients (pts) with multiple myeloma (MM). The aim of study was to analyze efficacy of the current treatment modalities.

Patients and treatment: Study analyzed treatment results of 57 newly diagnosed MM pts (32 male/ 25 female, mean age 55 yrs, range 40-65) treated with CTD induction, and 53 MM pts (27 male/ 26 female, mean age 56 yrs, range 38-81) in the first relapse. IgG myeloma existed in 31pts, IgA in 12pts, light chains in 11pts and non-secretory in 3pts. According to the clinical stage (CS), distribution was: II 20pts; III 37pts. Regarding ISS score, the group included: ISS1 10pts; ISS2 25pts; ISS3 22pts. Renal impairment was present in 5pts. CTD induction was applied in all of 57 pts. HDT with Melphalan 200mg/m^2 and ASCT were performed in 35/47pts (74%), followed with Thalidomide maintenance (Thal 100mg/day, median duration 16m, range 6-24m) in patients with CR/VGPR/PR. Routine thromboprophylaxis was applied in all pts. In the first relapse, Thalidomide based regimens (Thal-Dex 13pts; CTD 7pts; TCED 5pts) were applied in the group of 25pts (mean 6 cycles, range 2-8 cycles), while 28 pts were treated with bortezomib based therapy (Vel-Dex 26pts; CVD 1pts; MPV 1pts, mean no.6 cycles, range 2-8 cycles).

Results: CTD induction resulted with CR in 7/57pts (12,3%), and VGPR/PR in 40/57pts (70,2%). Further improvement of the response was obtained after HDT and autoSCT (CR 9/35pts, 25,7%; VGPR/PR 21/35pts, 60%). Median follow-up was 20m (6-36m). The 3-yrs probability of event-free, relapse-free and overall survival of 35/57pts treated with CTD+HDT+Thal was as follows: EFS 48%, RFS 60%, and OS 87%. In the pts group within first relapse, 18/25 pts treated with thalidomide based regimens achieved positive treatment response (CR+VGPR+PR). High-risk pts with ISS3 score had significantly shorter duration of progression-free interval (mean: ISS3 3,38m vs. ISS1+ISS2 26,8m, Mann-Whitney test p=0,021). Median overall survival for this group of

pts was 81m (range 14-100m). In the group of pts treated with bortezomib based therapy, treatment response (CR+VGPR+PR) was achieved in 25/28pts. No difference was found in duration of the progression-free interval between ISS score different groups (mean: ISS3 15,17m vs. ISS1+ISS2 15,38m, Mann-Whitney test p=0,641). Median overall survival for pts treated with bortezomib based therapy was 72m (range 18-120m).

Conclusion: CTD chemotherapy represents highly effective induction in MM patients eligible for the autoSCT. HDT followed by Thalidomide maintenance improves quality and duration of the response, as well as overall survival. The notified influence of thalidomide- and bortezomib-based regimens on the prognosis of relapsed patients indicates these agents as superior constituents of induction and maintenance therapy.

Keyword: multiple myeloma, treatment

Poster No: 0074 Abstract:0179

A CASE OF MULTIPLE MYELOMA DEVELOPING BREAST PLASMOCYTOMA ON TREATMENT

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Introduction: Multiple myeloma is a hematologic malignity characterized by neoplastic proliferation of the plasma cells and monoclonal immunoglobulin synthesis. Extramedullary plasmocytomas are the solitary masses of the monoclonal plasma cells in the bone or the soft tissue. When they are located in the soft tissue, they mostly affect the respiratory tract and the gastrointestinal system. Plasmocytomas of the breast are quite rare. Since our patient developed breast plasmocytoma while she was on treatment and there are no such reports in the literature, we present this case.

Case: A 82-year-old female patient presented to the emergency due to impaired overall status and widespread bone pain on 19.11.2012. Upon detecting a high level of urea-creatinine level and hypercalcemia, she was admitted to the internal disease unit. As a result of the consultation requested from the hematology department, the patient was detected to have anemia, a high sedimentation level, hypercalcemia and renal failure and thus she underwent bone marrow aspiration and biopsy at our unit under the preliminary diagnosis of multiple myeloma. The bone marrow showed normocellular bone marrow, 50% plasma cell infiltration; the biopsy result was consistent with multiple myeloma. Serum and urine immunoelectrophoresis detected a high kappa light chain. Treatment with melph alan+prednisolone+thalidomide was started (MPT) in the patient. Following two courses of MPT, the patient gave a partial response. At the time of the start of the 3rd course, formation of ulcerovegetant mass occurred. Based on the biopsy taken from the mass after consultation with the general surgery, the result was consistent with plasmocytoma. The mass was removed by surgical operation and the patient was administered 7 days of radiotherapy. The treatment for multiple myeloma was replaced by bortezo mib+dexamethasone+cyclophosphamide. The patient died after experiencing deterioration in her overall status while she was on treatment.

Discussion: 15% of the extramedullary plasmocytoma cases occur at the time of multiple myeloma diagnosis and 15% occur during the course of the disease. While extramedullary plasmocytomas are mostly observed in the upper respiratory tract and gastrointestinal tractus, they may also occur in the bladder, central nervous system, testicles, parathyroid, lymph nodes, thyroid, breasts and the skin. While the primary plasmocytomas are generally of good prognosis, plasmocytomas that are secondary to the myeloma progression are aggressive. Breast plasmocytomas are quite rare. The breast biopsy performed while the patient was under treatment for myeloma revealed findings consistent with plasmocytoma. If the patient's pre-treatment peformance status were better, change in treatment or concomitant radiotherapy could have been administered. We presented this patient since the case occurred during the treatment course and is very rarely reported in the literature

Keyword: multiple myeloma, extramedullary plasmocytomas

Poster No: 0075 Abstract:0181

A CASE OF MULTIPLE MYELOMA WITH DECOMPANSATED LIVER CIRRHOSIS

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Introduction: Multiple myeloma is a malignant disease characterized by the neoplastic proliferation of the plasma cell clone producing monoclonal immunoglobulin.

The characteristic finding in cirrhosis include the impaired macroscopic image, histologic structure and the circulation of liver as a result of the incerased fibrosis. Albumin, a parameter showing the liver synthesis functions, is decreased and gamma-globulins produced in the non-hepatic reticuloendothelial system are increased. However this represents an example to polyclonal gammopathy.

Here we present a 81-year-old male patient, who presented to the emergency with decompansated liver cirrhosis and was diagnosed with multiple myeloma.

Case: The 81-year-old male patient has been diagnosed with criptogenic liver cirrhosis 5 years ago. The patient, who presented to the emergency with the complaints of itching, abdominal swelling and confusion on 07.03.2012 was admitted to the internal diseases unit under the diagnosis of decompensated liver cirrhosis. Upon detection of normochromic normocytic anemia, hypercalcemia, high sedimentation, and a reversing of the albumin/ globulin ratio at the hematology consultation requested due to anemia and high sedimentation, an investigation of the immunoglobulins was requested; the following were detected: Ig G: 700, Ig A: 2920, Ig M: 31.2 mg/dl. The bone marrow aspiration and bone marrow biopsy detected approximately 50% plasma cells. For the plasma cells, CD38 lambda and IgA were positive. The patient was diagnosed with stage IIA based on the Durie Salmon staging system, respectively. The patient and his relatives refused treatment for multiple myeloma; his decompansated status for liver cirrhosis was continuing; the patient died during follow-up due to esophageal varicose hemorrhage.

Discussion: The association of multiple myeloma and decompensated liver cirrhosis is reported very rarely in the literature. While ascites is a very rare complication of multiple myeloma, most of the cases are associated with IgA type myeloma. Our patient also had IgA multiple myeloma. Development of ascites through peritoneal infiltration of the myeloma cells is less common. In cases of myeloma-associated liver, liver function test

abnormalities may be more common. While infiltration of the liver by the plasma cells may also occur, the patients are mostly asymptomatic clinically. Myeloma may very rarely manifest with findings of acute liver disease; findings of liver failure may be observed in this period.

Before the consultation, normochromic normocytic anemia, high sedimentation and the reversing of the albumin globulin ratio were attributed potentially to the liver cirrhosis, and the patient was not investigated for multiple myeloma. This case was presented since detection of IgA type multiple myeloma in this patient, who has had cryptogenic decompansated liver cirrhosis for the last 5 years, was very rare

Keyword: multiple myeloma, liver cirrhosis

Poster No: 0076 Abstract:0196

PLEURAL EFFUSION FORMATION IN THE COURSE OF MYELOMA

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Introduction: Pleural effusion is a rare complication of multiple myeloma. The most common type of Immunoglobulin in myelomatous pleural effusion is Ig A. We present a case with sudden onset pleural effusion due to infiltration of pleura by malignant plasma cells.

Case: Sixty-two years old male was diagnosed with stage IA, Ig G-kappa myeloma in June 2010 and was treated with two courses of bortezomibe in another hospital. 13q del was negative in cytogenetic examination. Autologous hematopoietic stem cell transplantation was performed at September 2010. He was treated with 50 mg/day cyclophosphamide as maintenance therapy and applied to our hospital. Multiple bilateral rib fractures, splenomegaly, hepatomegaly and a 3,5x2.5 cm solid mass in liver was occured in August 2012. After 3 courses of revlimide 25 mg/day and dexametasone 40 mg (12 days/cycle), bortezomibe was added to the treatment. After two courses of combination therapy, thorax computerized tomography revealed 68x44 mm irregular shaped soft tissue mass in the apikal of right hemitorax and pleural thickness in left hemitorax at November 2012. Small lymphocytes, polymorphonuclear leukocytes, mesotelial cells and atypical plasma cells were detected in cytological examination of the pleural effusion.

Conclusion: Pleural effusion can be seen almost 10% in myeloma patients. Plasmatic cell involvement is extremely rare but it should be considered in patients with pleural effusion. The extrameduller complications of MM are usually unresponsive to conventional chemotherapy and rapidly fatal with a median survival of 3 months. Thus, more aggressive chemotherapy regimens may be indicated in myeloma with involvement of pleural cavities.

Keyword: Multiple Myeloma, Pleural Effusion

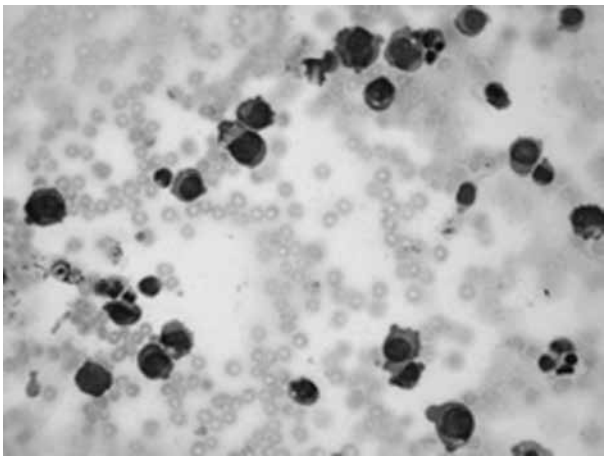

Figure 1. Plasma cells in pleural effusion

Poster No: 0077 Abstract:0206

POSSIBLE LENALIDOMIDE-INDUCED ERYTHEMA MULTIFORME DURING TREATMENT FOR MULTIPLE MYELOMA

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Objective: A case of erythema multiforme (EM) associated with use of lenalidomide for consolidation of multiple myeloma is reported. EM can usually be distinguished on a number of clinical criteria from Steven-Jonhson syndrome (SJS) that has been already reported as a rare adverse reaction to Lenalidomide. The physicians have to stress the awareness of these skin reactions in which the distinction is not always clear.

Methods: A 56 year-old woman with multiple myeloma (IgG, lambda, DSIIA, IPSS:III) who had massive chest wall plasmacytoma, greater than 10cm in diameter, with evidence of overt myeloma, was treated with a combination of VAD followed by bortezomib and dexamethason. After eight courses, bone marrow plasma cell ratio was turned to the normal level but free light chain ratio was still abnormal and mass lesion did not disappear completely though reduced in size significantly. Peripheral blood stem cells were collected after mobilization with cyclophosphamide and G-CSF and storaged. Lenalidomide (25mg/day, 1-21 days/28days) was started with dexamethasone (RD) to get more qualified response. During second course of lenalidomide on 13th day, the patient developed a minor macular erythematous skin reaction around neck region that was diagnosed possible drug-associated allergic skin lesions. Beside of RD she received also lamivudine, esomeprazole, pregabalin, acetylsalicylic acid and calcium. Lenalidomide was not discontinued and antihistaminic drugs were started. In a couple of days the eruption dramatically extended with "target lesion" appearance with a pink-red ring around a pale center. No skin detachment and mucosa involve-

ment were documented nor systemic symptoms, e.g. fever. Skin biopsy was not performed.

Results: EM was suspected. As a possible grade 2 skin reaction lenalidomide was discontinued and methylprednison was started in a dose of 40mg/day. In 5 days the lesions were regressed and steroid was tapered and ceased.

Conclusion: Incorporating lenalidomide as a treatment early in the disease courses of myeloma may prove to be beneficial but may be associated with skin eruptions that are, for the most part, mild. EM and SJS are separate diseases with different etiologies and different treatment requirement. Drugs had higher etiologic fractions for SJS, overlap, or toxic epidermal necrolysis (64%-66%) than for EM (18%). For most skin reactions discontinuation of lenalidomide is not necessitated but for unclassified cases mostly behaving clinically like EM, a reduction in drug dosage and close scrutiny is warranted to prevent to progress to SJS. To our knowledge, no published case reports of EM like lesions to lenalidomide have been reported

Keyword: lenalidomide, skin reaction

Erythema multiforme lesions

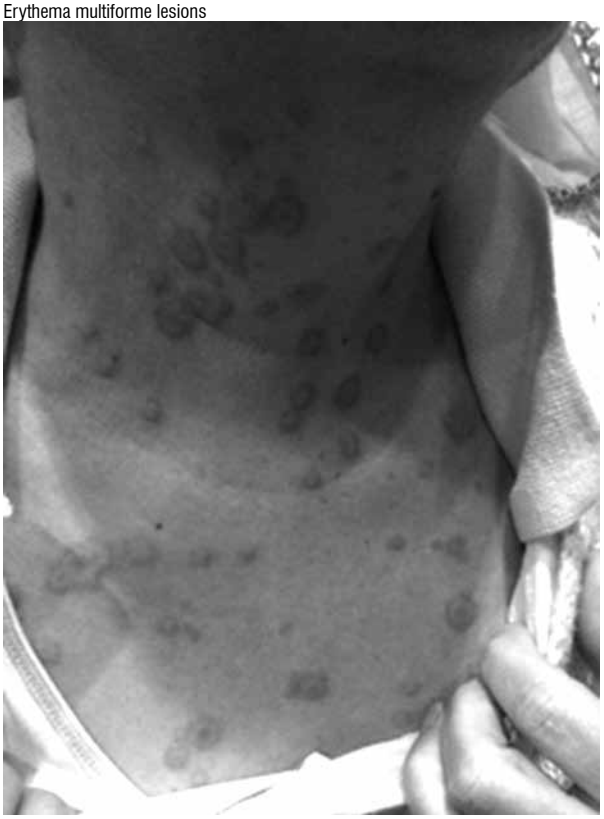

Figure 1. Center of the lesions were typically pale and surrounded with a reddened middle ring

Poster No: 0078 Abstract:0215

Bortezomib related reversible cerebellar ataxia

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Introduction: Bortezomib is a proteasome inhibitor effective in the treatment of multiple myeloma. The drug may induce an axonal neuropathy. We here present a case of standard dose bortezomib-related severe cerebellar ataxia.

Case: In December 2011, this 62-year-old man received a diagnosis of multiple myeloma IgGκ. At the same time, he was diagnosed with the alcoholic cirrhosis, therefore off-label approval bortezomib therapy was administered at the dose of 1.3 mg/m^2/day 1, 4, 8 and 11.days with 40 mg/day dexamethasone on the same and next day of bortezomib. On the 8th day of 2 cycles of bortezomib/dexamethasone (VD) combination therapy, the patient began to complain of difficulty in walking, pain in his legs and gait unsteadiness. In his first neurological examination, a marked dysmetria in four extremities with dysdiadokokinesia and intentional tremor in upper limbs were present. Patient was severly ataxic. Cranial MRI yielded normal findings. Nerve conduction studies and needle EMG have not revealed any pathological data. Based on these findings we concluded that the bortezomib therapy may engender a cerebellar ataxia. Bortezomib was discontinued; 30 days after, a dramatical improvement in neurological findings was detected that the patient was able to walk a short way without crutches.

Discussion: Bortezomib is a proteasome inhibitor beneficial in treatment of multiple myeloma. Bortezomib may cause mainly a sensory, painful, axonal, dose-related neuropathy which worsens through the treatment cycles and is often reversible after drug dose reduction or discontinuation. At best of our knowledge, there is only one report describing a sensory ataxia associated with high dose bortezomib neuropathy. In current case however, we here describe a standard dose bortezomib-induced cerebellar ataxia which is reversible with drug discontinuation.

Keyword: bortezomib, cerebellar ataxia

Poster No: 0079 Abstract:0231

ELEVATED SERUM THYMIDINE KINASE LEVELS (TK1) MAY IDENTIFY PATIENTS AT HIGH RISK OF DISEASE PROGRESSION IN NEWLY DIAGNOSED MULTIPLE MYELOMA

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Objective: Multiple myeloma (MM) shows a remarkably heterogeneous biological and clinical outcome which affect survival ranges from a few years in advanced stages to 10 years. The DS and IPS staging systems distinguish

some prognostic subgroups. More accurately cytogenetic aberration and microRNAs are important factors in anticancer drug activity and resistance and may predict the individual risk of disease progression for newly diagnosed MM. Thymidine kinase (TK) is the enzyme which catalyses deoxythymidine phosphorilation before incorporation in DNA and supports DNA synthesis under conditions of increased cell proliferation. In clinical chemistry it is used as a proliferation marker in the diagnosis, control of treatment and follow-up of malignant disease, mainly of hematological malignancies. Little is known about the prognostic significance of TK1 activity in MM. This study aimed to assess the prognostic value of as a simple test, the serum TK (s-TK) in previously untreated semptomatic MM patients.

Methods: TK1 activity was measured by means of ELISA (Biovica, Sweden). Measurements were performed prospectively at diagnosis in 53 consecutive MM patients. 47 healthy volunteers were also included as a control group.The clinical significance were assessed according to the stage.

Results: The mean TK1 level in the study group was significantly higher than the controls (respectively 85 332,09±22 1099,59 vs. 10143,81±11030,70; p<0.001). TK1 level did not change according to the age. TK1 activity levels in advanced stages were higher. TK levels in patients having 13th chromosom abnormality seemed to be higher compared who did not have the abnormality (22125,50±1307,44 vs 129940,12±299772,67) which was not statistically significant.

Conclusion: The results demonstrate that TK1 may add an independent prognostic information to the definitions of clinical outcome of MM among staging. In addition, evaluation of TK1 levels can be a valuable simple test for monitoring maintanence of response and may identify biologically aggressive disease at early stages.

Keyword: multiple myeloma, thymidine kinase

Poster No: 0080 Abstract:0239

MULTIPLE MYELOMA AND GLIOBLASTOMA MULTIFORME COMMUNITY; A CASE REPORT

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Glioblastoma multiforme (GBM) is the most malignant astrocytic tumour that can be multifocal, is usually supratentorial localized, can intensively infiltrate to peripherial tissues. A case will be presented in which GBM was thought to be available in the right frontal area during chemotherapy treatment owing to multiple myeloma and mass lesion was followed.

A 74 year-old female patient applied to physical therapy polyclinic with low back pain, weakness and fatigue complaints was evaluated due to sedimentation and CRP elevation at Hematology Polyclinic on September 2012. The patient values were as follows: hb.7.2 g/dl, hct 22.1%, MCV.75 FI, leucocyte 4330, thrombocyte 68000, creatinine 0.7 mg/dl, ferritin 580 ng/ml, sedimentation 148 mm-hour, Ca. 11.5 mg/dl, Ig A 6684mg/dl. Ig A kappa monoclonal gammopathies were determined in her serum immunofixation, >%80 plasma cell proliferation was observed in the bone marrow aspiration and biopsy,the case was assessed as Multiple Myeloma. Owing to the imagings carried out, the patient in whom there were lytic areas in all bones and collapse fracture in the L2,L4,L5 vertebrae was evaluated as Durie Salmon stage 3A Multiple myeloma. Radiotherapy was performed in lumbar region on account of low back pain and then MPV treatment was initiated. During the 2nd cure of MPV treatment, a severe headache developed in the patient accompanied by nausea and vomiting. Around the 47 mm area in the right frontoparietal region, mass lesion occupying an environmental contrast was observed in the cranial MR and the patient was evaluated by neurology and neurosurgery. Antiedema treatment was commenced, however, no biopsy could be performed on the tissue by taking into consideration patient's performance and accompanying comorbid cardiovascular disease,cranial radiotherapy was applied to the patient as palliative. MPV chemotheraphy of the patient schema was continued after radiotherapy. The patient for whom VGPR response was obtained following two cure treatments had a generalized tonic-clonic seizure attack in the follow-up. In the cranial MR two months after the radiotherapy, mass progressed to 9 cm and caused a 2 cm shift from midline to left and developed a severe edema around it. Antiedema treatment was initiated again. The patient whose condition was deteriorated and consciusness was lost developed respiratory failure and then cardiac arrest and died.

As a conclusion; GBM is seen as an irregular restricted mass around which is edematous, binding contrast and in the middle of which has necrotic cavity. The localization of tumor in our case was evaluated as GBM when its radiological appearance, its fast progression despite radiotheraphy and the clinical condition of the patient were taken into consideration. In patients with multiple myeloma, plasmocytoma determined within mass lesions in brain and also GBM, the most common malignant brain tumor in adults, should be considered.

Keyword: glioblastoma multiforme, multiple myeloma

Poster No: 0081 Abstract:0241

CYTOGENETIC ANALYSES IN TURKISH PATIENTS WITH MULTIPLE MYELOMA

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Multiple Myeloma is a clonal disorder characterized by accumulation,and proliferation of plasma cells and secretion of monoclonal immunoglobulin. Genetic abnormalities is quite important in multiple myeloma in terms of showing the prognosis such as in hematologic malignancies In recent years, many recurrent genetic abnormalities have been reported by the conventional cytogenetic and molecular cytogenetic studies in MM. In this study we aimed to determine the incidence of chromosomal anomalies by interphase FISH and conventional chromosome analysis in MM patients that are followed and treated in 19 Mayıs University of Hematology Department.

Material-Methods: A total of 53 patients with a diagnosis of multiple myeloma classical cytogenetic and molecular cytogenetic (FISH) analyzes were evaluated. Demographic data and the results of FISH analysis are shown in Table 1and 2..

Results: Conventional cytogenetic analysis of the cases could be performed in 31 of 53 patients and in 24 cases (45.3%) with normal karyotype, 3 cases (5.7%), chromosome aberrations, and in 1 patient hypodiploidy and in 1 case complex anomalies were observed. FISH analysis of the cases, 30 patients (56.6%) had normal results and at least one abnormality was observed in 43.4% of cases(23/53). 30.3% of the cases (16/52) chromosome 13 aberrations have been observed.

Conclusion: Recent studies have shown that the identification of genetic factors, is important in diagnosis, etiopathogenesis, prognosis and the decision of treatment protocols. For this reason, we think that in the use of treatment and prognosis of MM cases conventional cytogenetic and especially FISH are significant methods.

Keyword: Cytogenetic Analyses, Multiple Myeloma

Table 1. Demografic data of patients

Patients	53
Age	62 (35-85)
Sex	
Male	25 (52,8%)
Female	28 (47,2%)
M protein Type	
IgG Kappa	18(34%)
IgA Kappa	11(20,8%)
IgG Lambda	9 (17%)
Kappa or Lambda	15 (28,3%)
Stage	
ISS stage I	6 (11,4%)
ISS stage II	27 (50,9%)
ISS stage III	20 (37,7%)

Table 2. FISH analyses of patients

	Frequency	*Percent*
del13q14-del13q34	10	18,9
del13q14	1	1,9
del13q34-del13q11	1	1,9
del13q34	2	3,8
del14q32	1	1,9
del6q	1	1,9
Hyperdiploidi	1	1,9
Monozomi13	1	1,9
Normal	30	56,6
Tetraploidi	2	3,8
Trizomi11	2	3,8
Trizomi11 del13q	1	1,9
Total	53	100,0

Poster No: 0082 Abstract:0251

A CASE OF MULTIPLE MYELOMA DIAGNOSED BY PLEURAL INVOLVEMENT

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Background: Multiple myeloma is a malign disease characterised by neoplastic proliferation of plasma cells and monoclonal immunoglobulin synthesis. The clinical manifestations are due to the infiltration of bone and bone marrow by plasma cells or renal injury caused by light chains. Extramedullary plasmocytomas can be seen in %7 of patients at the time of diagnosis, however pleural involvement is extremely rare and if present, it is usually together with progressive disease.

Aim: We aimed to present a case of multiple myeloma who presented with myelomatous pleural effussion.

Methods: Case presentation

Results: Sixty-five year-old female patient was admitted due to back pain. Physical examination revealed decreased respiratory sounds on the left side and there was opacity on the chest X-ray compatible with pleural effusion. Thoracentesis resulted in exudative effusion, while cytological examination showed atypical malign cells. Pleural biopsy was performed and neoplastic infiltration of plasma cells were seen on the specimen. Laboratory examination revealed hemoglobin 7.7 gr/dL, hematocrite 22 %, creatinine 0.6 mg/dL, calcium 8.2 mg/dL, albumin: 2.1gr/dL, LDH: 280U/L, IgG:69 g/L, IgM:0.1 g/L, IgA:0.2 g/L and there was monoclonal IgG kappa on serum immunofixation electrophoresis. With the diagnosis of multiple myeloma we performed bone marrow biopsy and found infiltration of plasma cells. Bone X-ray showed compression fracture of the vertebra and paliative radiotherapy was given for back pain. After radiotherapy the patient was hospitalised for chemotherapy including vincristine, adriamycin and dexamethasone. Before chemotherapy because of respiratory distress torax tube was placed. On the third day of treatment, chemotherapy was interrupted due to fever. Cultures resulted in staphylococal infection of lung and antibiotic was prescribed. After antibiotherapy pleurodesis with bleomycin was done. After all, the patient was no more candidate for autologous tranplantation and treatment with bortezomib, melphalan and prednisolone (VMP) was started. After 3 cycles of chemotherapy, M protein was negative and there was no new lesion onthe chest X-ray. This patient is still on therapy with VMP protocole and the follow-up is in the outpatient clinic.

Conclusion: Pleural effusion is a rare complication during the course of myeloma and various conditions may be the cause: nephrotic syndrome, pulmonary emboli, amyloidosis, heart failure, etc. On the other hand, malign effusion because of pleural involvement is very rare (<%1) which is usually together with advanced disesase indicating poor prognosis. There are a few case reports in the literature like our case who is presenting with myelomatous effusion, however our case is unique because the disease has responded to chemotherapy and the patient is still alive.

Keyword: multiple myeloma, pleura

Poster No: 0083 Abstract:0255

MENTAL NERVE NEUROPATHY AS FIRST MANIFESTATION OF PLASMACYTOMA WITH BREAST INVOLVEMENT FOLLOWED BY OVERT RECURRENT MYELOMA

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Objective: A rare case of multiple myeloma (MM) was reported which was diagnosed from an intraoral gingival lesion on the lower mandible following mental nerve neuropathy related neuralgic symptoms characterized by hypoesthesia, paresthesia or anesthesia of the skin of the chin and lower lip, limited to the region served by the mental nerve. Extramedullary disease in MM occurs mostly in advanced disease or relapse. Outcome is poor and prognostic factors predicting the development of extramedullary disease have not been defined. Primary extramedullary plasmacytomas (EP) are generally pursuing an indolent clinical course but may, rarely, convert to overt MM.

Methods: A 34-year-old woman was presented with numbness in the jaw. Panoramic radiography examination revealed a moth-eaten shape, and radiolucent appearance. Biopsy of the lesion revealed plasmacytic infiltration. During evaluation for occult disease, a right breast lesion with axillary lymph node involvement was documented suspecting metastatic breast tumor. Initial workup discovered multiple lytic bone lesions, liver involvement and anemia. Biopsy of the breast mass and bone marrow displayed plasmacytoid/plasmablastic cells, expressing high percentage Ki-67 antigen. Conventional karyogram showed multiple cytogenetic aberrations including 13q deletion. Immunofixation studies showed serum IgG,kappa positivity. As having MM staged DSIIIA, ISSII, bortezomib and dexamethason (VD) with zoledronic acid was started which was complicated by increased paraprotein level and long bone fracture of large lytic lesions. Surgical reconstruction was instituted. Treatment was changed as adding cyclophosphamide (Cy) and radiotherapy to involved bones. She rapidly achieved complete remission with normalization of PET-CT, free light chain ratio and karyogram. After 6 courses of CyVD she underwent autologous peripheral blood stem cell transplantation. Five months after transplantation she developed swelling on multiple sites of scalp. Biopsy of the lesions consisted of monoclonal plasma cells. A bortezomib based combination chemotherapy was used for tumor cell debulking. A rapid response was followed by disease progress as emerging EP on different regions including the presentation site, right breast. She has no donor. Results: Salvage therapy as different type's chemotherapy was always terminated by short duration of response and aggressive progression. She is still alive since 3 years and experienced tumor lysis syndrome after bendamustine which again showed high tumor proliferation rate.

Conclusion: Nearly all body regions can be involved by EP. The prognosis is very poor once the diagnosis of EP is concurrent with MM. Mental nerve neuropathy may be forerunner to malignancy progression and relapse, but it may also precede the diagnosis of cancer. In adults, metastatic breast cancer (64%) and lymphoproliferative disorders (14%) account for most cases can mimic each other as in our case

Keyword: plasmacytoma, oral cavity

Plasmacytoma of the jaws

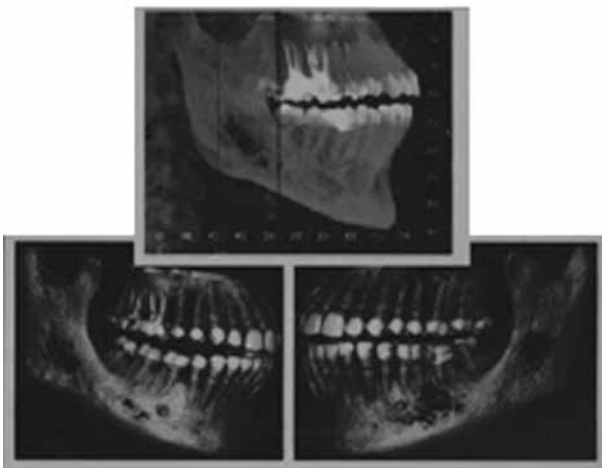

Figure 1.Panoramic radiography examination revealed a moth-eaten shape, and radiolucent appearance.

Poster No: 0084 Abstract:0271

A UNIQUE TRANSFORMATION IN PLASMA CELL MYELOMA FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION, FURTHER TREATED WITH ALLOGENEIC STEM CELL TRANSPLANTATION

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Objective: Herein, we report a unique transformation process of plasma cell myeloma that developed following autologous stem cell transplantation (ASCT). Allogeneic SCT provided donor hematopoiesis but persistence of myeloma with dedifferentiated morphology. This transformation with its unusual clinical, morphologic and immunophenotypic characteristics, may be the result of reemerging aggressive biology. Method: A 46-year-old woman with MM (IgG, kappa, DSIIIB, IPSS:III) achieved nearly complete response after 4 courses of VAD, zoledronic asid and radiotherapy. High dose vepeside and G-CSF were used as mobilization. She underwent ASCT following high dose melphalan.

Results: On 11th month of ASCT, she complained of severe generalized bone pain, skin and mucosal bleeding and rapid onset constitutional symptoms. A gross hepatosplenomegaly with pancytopenia, increased serum beta2microglobulin, IgG, kappa levels, and laboratory data consistent with DIC were documented. PET-CT

confirmed multiple bone lesions and hepatosplenomegaly. Bone marrow examination revealed morphologically very heterogenous infiltrate. The cellular spectrum comprised cells ranging from plasmablasts, to monoblast like cells and more primitive cells reminiscent of myeloblasts. By immunohistochemistry, the cells were uniformly and strongly CD138(+), supporting plasma cell origin. Flow-cytometry showed that the cellular composition widespread expressed myeloid markers (CD117+, CD33+, CD13+, CD15+) also. High dose steroid was started as tumor cell reduction and allogeneic transplantation was decided. Her brother was found to be HLA full-matched. She directly underwent SCT after conditioning with fludarabine and melphalan. Leukocyte engraftment was noted within the first month followed by late developed thrombocyte engraftment. The bone marrow at that point showed persistent neoplastic infiltration on the trephine biopsy while FISH analysis on the hemodilute aspirate proved to be 100% XY. Immunsupressive treatment was tapered. Gradually red blood cell and trombocyte transfusion need was ceased.

Conclusion: It has been known for decades that extended therapy with alkylating chemotherapy agents, such as melphalan, carries an increased risk of therapy-related myelodysplastic syndrome and/or AML. The typical secondary leukemias after MM show aggressive behavior and all patients on follow-up die within a period of one month. For our case, we avoided to call the transformation process as AML since diffuse and strong CD138 positivity namely regarded as a reliable plasma cell marker. In the era of emerging novel drugs with allogeneic SCT provided cellular immunotherapy, the eradication of the clones were planned.

Keyword: plasma cell, undifferentiated Bone marrow morphology

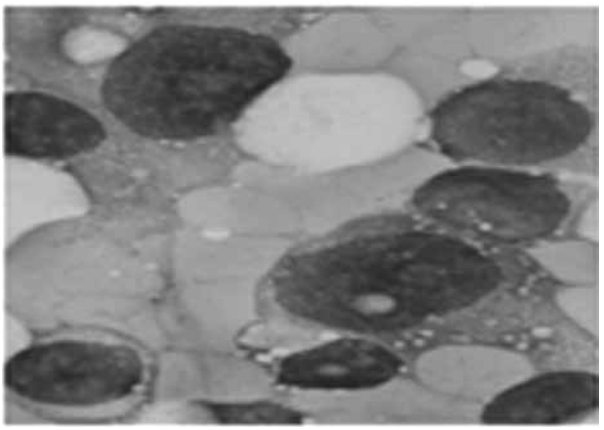

Figure 1. Bone marrow examination revealed morphologically very heterogenous infiltrate; plasmablasts, monoblast like cells and more primitive cells reminiscent of myeloblasts

Poster No: 0085 Abstract:0280

A CASE OF MULTIPLE MYELOMA WITH PLASMOCYTOMA IN THE LIVER AND MYELOMATOUS ASCITES

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Extramedullary infiltration of multiple myeloma (MM) is relatively frequent in the autopsy series (%70), however clinical manifestations before death are rarely seen. Considering liver involvement diffuse hepatic infiltration is common, while the nodular form as liver plasmocytoma is extremely rare. If present, plasmocytoma in the liver is associated with aggressive disease and indicates poor prognosis despite intensive treatment. On the other hand, ascites is an unusual complication of multiple myeloma and myelomatous ascites due to peritoneal infiltration of malign plasma cells is very rare. Most of the reported cases are Ig A type MM and these patients are reported to have Ig A paraproteinemia without bone abnormalities which is a different clinical entity.

Our case is a 51 year-old female patient. She was diagnosed with multiple myeloma 1 year ago and autologous stem cell transplantation was performed after 2 cycles of chemotherapy including vincristine, adriamycin, deksamethasone which was preceding 4 cycles of chemotherapy including bortezomib and dexamethasone. Six months after transplantation she was admitted because of neck swelling and icterus. Biopsy of the mass in the neck revealed plasmocytoma. Concurrently, two masses in the liver was detected by computed tomography and the biliary tract proximal to these masses were found to be dilated. Laboratory examination was as follows: Hgb 10.9, wbc 5900, trombosit 227000, AST 255, ALT 472, ALP 709, GGT 458, total bilirubin 7.9, direct bilirubin 7.1. Serum protein electrophoresis showed M spike and there was Ig A lambda in the immunofixation electrophoresis. After 4 cycles of chemotherapy with bortezomib and dexamethasone partial remission was achieved, however progression developed soon after 5th cycle. Biopsy from the mass in the liver revealed plasmocytoma and radiotherapy was initiated. After a short period of partial regression, abdominal distention due to ascites was evolved. There were atypical plasma cells on the microscobic examination of the ascites. therapy with lenalidomide was started, but patient was lost shortly after.

Amyloid deposition and biliary obstruction by plasmocytoma of the pancreas or biliary tract may result in liver dysfunction in MM. On the other hand, involvement of the liver by diffusely infiltrating malign plasma cells or in the form of plasmocytoma may also rarely occur. Ascites in multiple myeloma may be due to heart failure, renal disease, portal hypertension, infectious peritonitis and rarely because of liver infiltration or peritoneal infiltration by neoplastic plasma cells. In the literature, there are reported MM patients with liver involvement or myelomatous ascites, however there is no reported case having both together. Our case is unique, since liver plasmocytoma is seen together with myelomatous ascites.

Keyword: liver plasmocytoma, myelomatous ascites

Poster No: 0086 Abstract:0320

MACROPHAGES AS AN ABUNDANT COMPONENT OF MYELOMA MICROENVIRONMENT: A CASE REPORT

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Introduction: Multiple myeloma (MM) is a malignant B-cell tumor characterized by proliferation of monoclonal plasma cells in the bone marrow. MM remains an incurable disease. One of the major problems is that myeloma cells develop drug resistance on interaction with bone marrow stromal cells. Tumor associated macrophages are one of these stromal cells. Macrophages found in bone marrow may be preventing MM cell death.

Case: A 56-year-old woman presented with fatique. Physical examination, imaging studies and laboratory investigations revealed anemia, trombocytopenia and splenomegaly. Bone marrow trephine biopsy was performed. Bone marrow was heavily infiltrated with monotypic Kappa expressing neoplastic plasma cells accompanied by benign appearing macrophages partly obscuring the neoplastic component. İmmunohistochemically macrophages expressed CD68 antigen and lacked S-100 and CD1a. The patient was treated with 2 cures of VAD followed by 2 cures of Veldex chemotherapy. After completion of therapy, a control bone marrow trephine biopsy was performed. The time interval between the two marrow trephine biopsies was five months. Bone marrow was still infiltrated by neoplastic plasma cells and accompanying macrophages and the percentage of involvement was not significantly reduced.

Conclusion: We report a myeloma case heavily infiltrated by benign appearing macrophages. Neoplastic infiltration was continuing after the completion of the chemotherapy.Macrophages found in bone marrow may be keeping MM cells from dying. Myeloma-macrophage relationship should be investigated to determine their role in supporting myeloma growth because this information may provide additional potential opportunities for the development of novel approaches to myeloma therapy.

Keyword: myeloma, macrophage

Myeloprofilerative Disorders

Poster No: 0087 Abstract:0109

BLASTIC PHASE CHRONIC MYELOID LEUKEMIA SUCCESSFULLY TREATED WITH RE-ALLOGENEIC STEM CELL TRANSPLANTATION FROM SAME DONOR

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We report a challenging case with blastic phase chronic myeloid leukemia (cml) and treated with re-allogeneic stem cell transplantation with the same donor after 10 years from the previous one.

A 31-years-old male patient was first diagnosed as chronic phase cml in 2002 and treated with allogeneic stem cell transplantation from the full HLA matched brother. After transplantation he was followed up for a period of 5 years with remission. On May 2007 he relapsed with chronic phase cml. He did not respond to donor lymphocyte infusion (DLI) and was put on to imatinib therapy. While receiving imatinib, he achieved complete hematologic, cytogenetic and major molecular response. However, in 2010 he progressed to the accelerated phase and was put on to nilotinib therapy. While receiving nilotinib he could achieved complete hematologic response, complete cytogenetic response but could never achieved major molecular response. The mutational analysis revealed no T315I mutation, and cytogenetic analysis showed no additional chromosomal abnormality. At the 6th month of nilotinib therapy, because of insufficient molecular and cytogenetic response, nilotinib was stopped and he had switched to dasatinib therapy. While receiving dasatinib therapy he achieved partial cytogenetic response at 6 months of therapy. He admitted with increased leukocyte count and peripheral smear revealing blastic cells at the 10th month of dasatinib therapy. Bone marrow aspiration showed 35% blastic cells with myeloid morphology. Immediately he was hospitalized and 7+3 AML induction regimen was initiated. Remission was achieved, unrelated hsct was offered but the patient refused. Finally stem cells from his brother, who was his previous donor, were reinfused. After leukocyte and thrombocyte engraftments achieved he was discharged at the 28th day of reinfusion. After transplantation his BCR-ABL IS values decreased drammatically (Table 1). Full donor chimerism was achieved. He is now on 138th day of reinfusion and is followed up with complete hematologic, complete cytogenetic and significant molecular response.

With imatinib and second line tyrosine kinase inhibitors the need for stem cell transplantation has decreased significantly. But still it is an option in patients who are resistant to tyrosine kinase inhibitors. Our patient is a good candidate for novel TKI inhibitors like ponatinib regarding not yet achieved major molecular response after transplantation. We planned to apply to the ministry of health to access the aforementioned drug.

Keyword: cml, allogeneic stem cell transplantation

Table 1. BCR-ABL IS values before and after transplantation

Time	*BCR-ABL IS (%)*
Prior to stem cell transplantation	399,16
3 weeks after stem cell transplantation	3,89
2 months after stem cell transplantation	0,25
3 months after stem cell transplantation	0,42
4 months after stem cell transplantation	0,37

Poster No: 0088 Abstract:0113

SERUM LEVELS OF MULTIPLE CYTOKINES AND ADHESION MOLECULES IN PATIENTS TREATED FOR ACUTE MYELOID LEUKEMIA

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Background: Cytokines and adhesion molecules have been studied as markers of immune system activation in various diseases including hematological malignancies. Alterations in this network may have direct effect on the malignant cells or have indirect effect on leukemogenesis through altered functions of bone marrow stromal elements. The knowledge gained from multiple cytokine and adhesion molecule analysis should allow better diagnosis and disease management.

Objectives: The aim of our study was to evaluate serum levels of multiple cytokines and adhesion molecules in patients treated for acute myeloid leukemia (AML).

Methods: A total of 15 AML patients (mean age 48.7 ± 12.1 years, median 51, 8 males and 7 females) treated with cyclic chemotherapy (3+7, 2+5, HiDAC) alone or in combination with high-dose chemotherapy (preparative regimen Bu/Cy2 or Cy/TBI) followed by autologous hematopoietic stem cell transplantation were studied. We evaluated serum levels of the following 22 cytokines and adhesion molecules: interleukins (IL-1 alpha, IL-1 beta, IL-2, IL-3, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-23), vascular endothelial growth factor (VEGF), tumor necrosis factor-alpha (TNF-alpha), interferon-gamma (IFN-gamma), epidermal growth factor (EGF), monocyte chemotactic protein-1 (MCP-1), E-selectin, L-selectin, P-selectin, intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1). All biomarkers were measured by biochip array technology on Evidence Investigator analyzer (Randox) at the diagnosis of AML (active leukemia) and in durable complete remission (CR) at circa 6 months after completion of chemotherapy. Probability values (p) < 0.01 were considered statistically significant.

Results: Comparing serum cytokine and adhesion molecule levels in active leukemia and in durable CR, we found significant increase in serum IL-7 (5.34 ± 4.32 ng/L vs. 19.62 ± 12.05 ng/L; p < 0.001), EGF (16.48 ± 33.50 ng/L vs. 64.42 ± 35.33 ng/L; p < 0.001) and VEGF (63.93 ± 67.85 ng/L vs. 114.39 ± 54.90 ng/L; p < 0.01). On the other hand, we found significant decrease in serum E-selectin (30.19 ± 20.46 mcg/L vs. 12.99 ± 8.00 mcg/L; p < 0.01). Plasma levels of other evaluated cytokines and adhesion molecules were without significant differences.

Conclusions: Our results indicate that serum levels of some cytokines and adhesion molecules (IL-7, EGF, VEGF, E-selectin) are significantly altered in patients treated for AML, showing activity of the disease. Whether these alterations could serve as a prognostic marker for AML is not known. Further studies in a larger number of patients and comparing cytokine and adhesion molecule levels with established prognostic markers (cytogenetics, molecular genetics) will be needed to define the potential role of these and additional markers in the risk stratification of AML patients.

The work was supported by a long-term organization development plan 1011 (FMHS).

Keyword: cytokines, acute myeloid leukemia

Poster No: 0089 Abstract:0131

MAST CELL TRYPTASE ACTIVITY AND CD34 POSITIVE CELL EXPRESSION IN CHRONIC MYELOPROLIFERATIVE NEOPLASMS

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Objectives: The aim of this study is to determine the relationship between increased reticulin staining (reticulin fibrosis) in bone marrow biopsies of bcr-abl negative myeloproliferative neoplasm patients and mast cell proliferation and CD34 positive cell expression.

Methods: A total of 77 patients were included in the study. 47 patients with bcr-abl negative myeloproliferative neoplasm and 30 controls were examined. The patients were diagnosed according to WHO diagnostic criteria revised in 2008. Bone marrow biopsy were performed in all patients and specimens were evaluated in the division of pathology. Each specimen was stained with Gomory and graded for reticulin fibrosis. Then they were stained with mast cell tryptase and CD34 immunostain. Specimens were obseved under a light microscobe at 40x magnification. The number of mast cells and CD34+ cells seen in 20 different areas were averaged. The average CD34+ cells and mast cells were correlated with the degree of the reticulin fibrosis by Kruskal Wallis test. P value <0,05 was statistically significant.

Results: Mean age of patients was 54,71 years, whereas mean age of the control group was 52,63 years. There was statistically advanced level of significance between reticulin fiber levels and mean mast cell count in patients with bcr-abl negative chronic myeloproliferative neoplasm (p<0,05). While there was no statistically significant difference between means of CD34+ cell counts of cases according to reticulin fibers levels (p<0,05); mean CD34+ cell count in cases with intense reticulin fibers was lower than those cases without reticulin fibers. Means of mast cells in JAK2 positive cases were significantly higher than those cases with the negative cases (p<0,05).

Discussion and Conclusion: It has been demonstrated that many substances and cytokines produced in mast cells contribute in fibrogenesis. In this present study, we showed that reticulin fiber increase, which was encountered at various rates in myeloproliferative neoplasm subtypes, was correlated with mast cell increase. Moreover, we detected the decrease in CD34+ stained cell number in the bone marrow as the intensity of reticulin fibers was increased. CD34+ cell counts were increased in patients with mildly fibrotic, predominantly hypercellular bone marrows. According to these results, drugs inhibiting mast cells in myeloproliferative neoplasms might modify fibrosis. Possibly, increase in CD34+ cells secreted from fibrotic bone marrow to the circulation can be guiding us for the disease progression.

Keyword: myeloproliferative neoplasm, mast cell

Table 1. Evaluation of CD34 positive cell an mast cell acccording to degree of reticulin fibrosis.

		Mast cell tryptase	*CD34+ cell*
		Average±SD (Median)	Average±SD (Median)
Reticulin fiber	negative	15,22±18,24 (7,8)	2,79±2,14 (2,2)
Reticulin fiber	mild	30,24±15,18 (31,8)	2,04±1,70 (1,4)
Reticulin fiber	moderate	26,76±27,07 (20,4)	2,28±1,60 (1,6)
Reticulin fiber	severe	41,46±25,98 (44,4)	1,17±0,85 (1)
	p value	0,001**	0,080

Poster No: 0090 Abstract:0145

ESSENTIAL THROMBOCYTOSIS DEVELOPING IN A PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN REMISSION: A CASE REPORT

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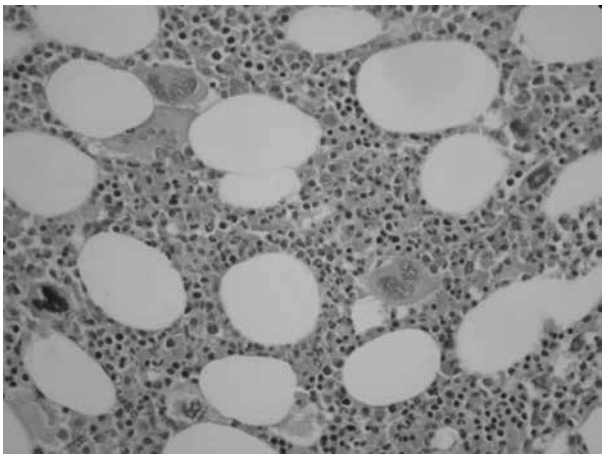
We know that the JAK2-V617F mutation is found in approximately half the cases with essential thromcytosis. Although the mutation is sometimes present in all the myeloid cells in ET and the XCIP pattern is fully clonal (analogous to PV), more often the JAK2-V617F mutation is present in only a subpopulation of neutrophils and platelets, and the XCIP in these mutant-positive patients is frequently nonclonal. In our case essential thrombocytosis developed in a patient with acute lymphoblastic leukemia while he is in complete response and Jak-2 mutation was found to be heterozygous.

Keyword: Jak2 mutation, myeloproliferative disorders bone marrow aspiration

Figure 1. Essential thrombocytosis developing in a patient with acute lymphoblastic leukemia in remission, megacaryocytes are seen in bone marrow aspiration



Poster No: 0091 Abstract:0161

RETROSPECTIVE ANALYSIS OF 114 PATIENTS WITH PH (-) CHRONIC MYELOPROLIFERATIVE NEOPLASMS

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Chronic myeloproliferative neoplasms (CMN) are disorders of heamatopoetic stem cells with uncontrolled proliferation, inability to differantiation and also maturation. This disorders first described by Damashek in 1951. World Health Organisation (WHO) reclassified and renamed

CMN in 2008. By this classification this disorders are considered distinct entities and the name 'disorders' changed as 'neoplasms'. Polycythemia vera, essential thrombocytosis, myelofibrosis, chronic neutrophilic leukemia, chronic eosinophilic leukemia and mastocytosis are included in this group of myeloproliferative neoplasms. The most important common specialites of this neoplasms are; transformation to leukemia, fibrosis of the bone marrow and thrombosis. Altough recent developments leads to treat more than last years there is no cure yet. In our study we investigated 114 patients age, sex, physical examination, laboratry values, thrombosis episodes, with Ph (-) CMN. 56 (49 %) patients were male and 58 (51 %) were female.There were 52 essential thrombosis (ET), 39 polycytemia vera (PV) patients and 23 primer myelofibrosis (MF) patients. In all subtypes of CMN 29 (25,4 %) of patients administered with ischemic events (loss of vision, Budd Chiari Syndrome and cerebrovasculary events). Jak 2 was heterozygote positive for 36,5% for ET patients and homozygote positive for 1,9 % patients,84,6 % of PV patients were positive for heterozygote jak 2 and 2,6 % for homozygote patients the ratios for MF were 61 % for heterozygote, 4,3 % for homozygote and negative for 34,7 %.Many of the thrombotic events occur at diagnosis or in 2 years after the first diagnosis. We report our other results in tables and graphics.

Keyword: Ph negative chronic myeloproliferative neoplasms

Table 1. Splenomegaly Ratios

ET	61 %
PV	66%
MF	73%

Table 2. Thrombosis Ratios

ET	23 %
PV	33%
MF	8 %

Poster No: 0092 Abstract:0169

JAK-2 V617F MUTATION STATUS OF 232 PATIENTS DIAGNOSED AS CMPDS

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JAK-2 V617F mutation has been a key molecular marker of the diagnosis of Philadelphia chromosome negative chronic myeloproliferative diseases (CMPDs). During the twelve years period between November 2000 to November 2012, 233 patients (110 Male, 123 Female, M/F: 0,9/1) diagnosed having CMPDs followed at our center's hematology outpatient clinic. Median age is 63 years (range 18-89). We are presenting here demographics, presence and quantitation of JAK-2 mutation, clinical course, therapy and follow up time, and survival of the patients diagnosed as polycytemia vera (PV) and essential thrombocytemia (ET) according to WHO 2008 criteria, and patients diagnosed as primary myelofibrosis (PMF) according to WHO criteria. One male patient excluded with the chronic myelomonocytic leukemia diagnosis who has JAK-2 mutation with splenomegaly, anemia, absolute monocytosis but no bone marrow fibrosis. All data summarised in Table 1 to 3. One patient who developed post-PV-MF (1.2%) after 52 months, and three patients who developed postET-MF (2.9%) after 44, 66 and 92 months respectively, were diagnosed increased reticular fibrosis with bone marrow biopsy. Estimated survival rates were respectively 75% for 134 months in PV patients and 50% for 62 months in MF patients. Four patients with ET who are 40 years old or younger and have thrombosis or vasomotor complications and heterozygous JAK-2 mutation had additional hereditary thrombofilia.

Keyword: CMPDs, JAK-2 V617F mutation

Table 1. Clinical characteristics of Ph(-) CMPDs patients (n=232)

no	age	gender (M/F)	splenomegaly	thrombosis	bleeding	CVA history	digital ischemia	diabetes mellitus	hypertension
PV (81)	62 (35-86)	30/51	46 (%69)/68	14 (%17,4)	4 (%4, 9)	13 (%16)	7 (%8, 6)	12 (%14, 8)	15 (%18, 5)
ET (129)	63 (18-89)	65/64	57 (%47)/120	25 (%19,4)	10 (%7,6)	8 (%6,2)	8 (%6,2)	16 (%12,4)	25 (%19,4)

Table 2. JAK-2 presence of CMPDs patients(n=232)

JAK-2 V617F no (%)	%78-100	%50-78	Homozygous	%31-50	%12,5-30	%5-12,5	%2-5	Heterozygous
PV: 77 (% 95)	12 (%15)	27 (%33)	39 (%48)	21 (%26)	17 (%21)	0	0	38 (%47)
ET: 85 (%68)	14 (%11)	9 (%7)	23 (%18)	25 (%19)	24 (%19)	14 (%11)	2 (%1,6)	65 (%50)
PMF:17(% 77)	5 (%23)	6 (%27)	11 (%50)	6 (%27)	0	0	0	6 (%27)
179 (%77)	31 (%14)	42 (%18)	73 (%32)	52 (%22)	41 (%18)	14 (%6)	2 (%0,9)	109 (%47)

Poster No: 0093 Abstract:0182

IMPAIRED APOPTOSIS AS A CAUSE OF ACCUMULATION OF MALIGNANT GRANULOCYTES IN MYELOPROLIFERATIVE NEOPLASMS

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Objectives: The apoptotic process was found to be deregulated in several hematopoietic neoplasms, leading to resistance to therapy and progression of disease. Resistance to apoptosis could result from survival signals from hematopoietic cell microenvironment, as well as from inherent deregulation of apoptotic machinery in malignant cells. Our hypothesis was that impaired expression of apoptotic-related genes is linked to myeloaccumulation and contribute to the pathogenesis of myeloproliferative neoplasms (MPN). In support of this notion, in this study we analyzed expression of genes of intrinsic (BAX, BCL2, BCL2L12) and extrinsic apoptotic pathway (FASR, FASL) in granulocytes of MPN patients and healthy controls. BCL2L12 is a novel member of BCL2 family of apoptosis regulators, whose pro- or anti- apoptotic role has not been fully elucidated yet. Nevertheless, its altered expression relative to normal tissue has been reported in several types of cancers.

We also determined JAK2-V617F allele burden and correlated the level of expression of apoptotic genes with the presence of the JAK2-V617F mutation and different level of V617F allele.

Methods: This study enrolled 37 unselected MPN patients and 8 healthy controls. The expression of BAX, BCL2 and BCL2L12 genes was analyzed in peripheral blood granulocytes by RQ-PCR methodology using SYBR Green chemistry, while the expression of FASR and FASL genes was analyzed using TaqMan chemistry. In all RQ-PCR experiments, ABL was used as endogenous control gene. Quantification of target gene expression was made by comparative ddCt method, using HL-60 cell line as the calibrator. Determination of JAK2-V617F alelle burden was performed using alelle specific primers and standard curve was constructed using serial dilution of DNK from HEL and K562 cells.

Results:RQ-PCR expression analysis of BAX, BCL2L12 and FASR genes revealed significantly lower levels of mRNA in MPN samples in comparison to normal blood samples ($p<0.01$). The level of expression of BCL2 and FASL genes did not differ between patient and controls. When JAK2-V617F mutation status was correlated with the expression of apoptotic genes, it was found that the mRNA level of pro-apoptotic BAX gene in ET patients was significantly reduced in patients withouth V617F mutation in comparison to the control group, whereas patients with V617F mutation expressed the same levels of BAX gene in their granulocytes as healthy controls.

Conclusion:Our results demonstrated a significant downregulation of BAX, BCL2L12 and FASR genes in MPN patients in comparison to healthy controls, implying its role in the pathogenesis of the disease. Different levels of expression of BAX gene correlated with the presence of JAK2-V617F mutation, suggesting that mutated JAK2

gene influences its expression. Concerning BCL2L12 gene, results presented in this study support the possible pro- apoptotic role of these gene.

Keyword: Myeloproliferative neoplasms, apoptosis

Poster No: 0094 Abstract:0194

RETROSPECTIVE EVALUATION OF CHRONIC MYELOID LEUKEMIA CASES: SINGLE CENTER EXPERIENCE

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Objective: Chronic myeloid leukemia (KML) is a clonal hematopoietic pluripotent stem cell disorder characterized by the presence of Philadelphia (Ph) chromosome. In this study, 42 CML patients monitored in İzmir Bozyaka Training and Research Hospital, Hematology Clinic were retrospectively evaluated in terms of demographic attributes, treatments and response statuses.

Material-Method: 42 patients monitored with Ph (+) KML diagnosis in Hematology Clinic of Izmir Bozyaka Training and Research Hospital between 2005 and 2012 were retrospectively evaluated in terms of tyrosine kinase inhibitor treatment and response attributes.

Findings: 21 of 42 patients (50%) were females and 21 of patients (50%) were males. Median age was identified as 56.5 (33- 83) during diagnosis. The median leukocyte count of patients at the time of diagnosis was 64.904/mm^3 (4700-309.500), median hemoglobin level was 12.3 mg/dl (8.5- 15.9 mg/dl) and median platelet count was 339.600/mm^3 (113.000-1.910.000). The median spleen identified by ultrasonography at the time of diagnosis was determined as 157 mm (130- 230).

Imatinib of 400 mg/day was administered to all patients at the time of diagnosis. 11 patients received hydroxyurea either prior to imatinib or with imatinib. Following diagnosis, hematologic response was achieved at all patients on month 3.

Once the final treatments of patients and the response statuses of patients were evaluated on median 63 months (3- 144), 29 patients (69%) continued to receive 400 mg/day imatinib. Tyrosine kinase treatment was discontinued for 1 patient with major molecular response planning pregnancy and interferon treatment was initiated. 1 patient that did not give response to tyrosine kinase inhibitors was directed to an external center for allogeneic stem cell. One patient died due to accompanying comorbid diseases. Second generation tyrosine kinase inhibitors were administered in ten patients and 3 of patients (7.1%) received 100 mg/day dasatinib and 7 of patients (16.7%) received 2*400 mg/day nilotinib. The reasons for switching to second generation agents are treatment unresponsiveness in 7 patients (16.7%) and intolerance in 3 patients (7.2%). 2 of 3 patients with intolerance changed drug due to gastrointestinal system findings not responding to the treatment and 1 patient changed drug due to skin manifestations of level 3. 31 patients (73.8%) with major molecular response are still monitored. The responses obtained in 9 patients (21.4%) are full molecular response and 2 patients (4.8%) are irresponsive to the treatment.

Result: Although KML ismore common in males compared to females, the number of males and females is equal in our study. 69% of our patients continue imatinib treatment. Imatinib remains as an effective treatment at first line. The treatments administered to our patients at our center and the response statuses display similarity in literature.

Keyword: chronic myeloid leukemia

Poster No: 0095 Abstract:0222

UNUSUAL PRESENTATION OF A RARE DISEASE; A CASE REPORT OF MYELOID SARCOMA

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Myeloid sarcoma is a tumoral mass consisting of myeloid blasts with or without maturation occuring at an anatomical site other than the bone marrow. Infiltrates of any site of the body by myeloid blasts in leukaemic patients are not classified as myeloid sarcoma unless they present with tumor masses in which the tissue architecture is affaced. The tumos also known as extramedullary myeloid tumor, granulositic sarcoma, chloroma. In this study, we present a 52 years old patient admitiing to gynocology clinic with the complaining of difficulty with urination. In physical examination, a mass located anterior wall of vagina was detected. An incisional biopsy from the mass revealed a monoton infiltaration of small-medium size cells under the squamous epithelium. Immunohistochemical staining was negative for pancytokeratin, CD3, CD20, CD79a, Bcl-2, EMA, S 100, CD30, cytokeratin 7 and 20, desmin, SMA, NSE, HMB-43, kromogranin expression. Immunostaining for MPO, LCA, CD68, CD99, CD117 were positive. Ki-67 (MIB1) proliferation index was over 80%. Bone marrow aspiration biopsy revealed myeloid blasts. White blood cell count was $46x10^3$ /µl. With clinical, laboratory, histopathological and immunohistochemical findings, the patient was diagnosed as acute myeloid leukemia presenting as a myeloid sarcoma.

Keyword: myeloid sarcoma, vagina

Poster No: 0096 Abstract:0232

JAK2 MUTATION PROFILE, JAK2 46/1 HAPLOTYPE AND CLINICAL FEATURES IN MACEDONIAN ESSENTIAL THROMBOCYTHEMIA PATIENTS

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It is predicted that the inherited genetic background in the individual patients with myeloproliferative neoplasm (MPN) influences the disease susceptibility and the phenotype expression of the MPN. Several groups discovered that the germline JAK2 46/1 haplotype, tagged by the "C" allele of single nucleotide polymorphism (SNP) rs12343867 (C/T) is associated with the JAK2V617F positive MPN. Moreover, some recent studies showed equal distribution of this SNP among JAK2V617F negative MPN and questioned his role in MPN patients.

In order to extend further those observations we designed a study to examine the association of the JAK246/1 haplotype with Essential thrombocyhemia (ET) in Macedonian population. We also evaluate the association of 46/1 with the JAK2 mutation profile and the clinical features in the series of patients with ET that were diagnosed and treated at the University Clinic of Hematology-Skopje, Republic of Macedonia.

One hundred and seven consecutive patients diagnosed with ET according to proposed criteria for diagnosis in 2008 by the World Health Organization were included in our study. The 46/1 tag SNP rs12343867 (C/T) was genotyped on a MxPro 3005P real-time PCR system (Stratagene, La Jolla, CA,USA) using the TaqMan SNP genotyping assay (Applied Biosystems, Foster City, CA, USA) according to the manufacturer's instructions. The JAK2 V617F mutation was analyzed by fluorescent allele-specific PCR followed by CE on ABI 310 Genetic analyzer.

JAK2 V617F mutation negative patients were further analyzed by using RNA based direct sequencing protocol for JAK2 that encompass entire JAK2 exons, from 12 through 15 and DNA based protocol for MPL sequencing that encompass only exon 10. Associations with risk of MPN were estimated by odds ratios and their 95% confidence intervals using logistic regression.

The fluorescent allele-specific PCR analyses revealed that JAK2 V617F mutation was present in 58 (54,2 %) of patients with ET. In one (out of 9 already tested) of our ET JAK2V617F negative patient a G571S mutation point was detected at the exon 13 of JAK2 gene. The incidence of 46/1-linked C allele was significantly higher in ET (genotype: CC 13%, CT 60%, TT 27%; C-allele frequency: 43,7) than in population control (C-allele frequency 29%), P<0,01. Genotype distribution were similar among JAK2V617F positive/ JAK2V617F negative patients (genotype: CC 7/14%, CT 22/29%, TT 67/57%; C-allele frequency: 41/43%; P=0,76).The clinical characteristics of 46/1 positive and negative ET were comparable regarding all tested parameters such as blood counts, NAP score, rate of thrombotic and hemorrhagic complications, disease transformation and survival.

Our results confirmed latest observations that the "C" allele of JAK2 rs12343867 designate the genetic basis of ET in Macedonian population independent of the JAK2V617F mutational status and also showed that JAK2 46/1 haplotype does not further affect the clinical course and prognosis of the disease.

Keyword: Essential thrombocyhemia, JAK2 46/1 haplotype

Poster No: 0097 Abstract:0233

EVALUATION OF THE JAK2 MUTATIONAL PROFILE IN THE DIAGNOSIS OF CLASSICAL MYLEOPROLIFERATIVE NEOPLASMS (MPN) IN REPUBLIC OF MACEDONIA: OUR INITIAL EXPERIENCE

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Modern diagnosis of the classical myleoproliferative neoplasms (MPN) is based on a complex appraisal of the clinical and laboratory characteristics of the disorders. Key role in the diagnostic work-up of MPN has screening for JAK2V617F mutation and the presence of the mutation is considered as a major criterion for diagnosis. The mutation is present in more than 95% of cases with Polycythemia Vera (PV) and in 50 to 60% of Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF). Additional JAK2 mutations such as JAK2 exon 12 mutation in 3% of the PV cases and abnormalities affecting MPL of 3% ET and 10% PMF cases have been reported in the JAK2617F negative patients. Further molecular testing for demonstrating their presence additionally facilitates MPN diagnosis. Moreover, recently, other than already described JAK2 mutations, that potentially could be used as clonal markers of the disease were described in MPN patients by using direct sequencing approach.

In order to improve the molecular diagnosis and follow-up of BCR-ABL negative MPN in Republic of Macedonia we designed a RNA based direct sequencing protocol for JAK2 that encompass entire JAK2 exons, from 12 through 15 and DNA based protocol for MPL sequencing that encompass only exon 10. The primer pair designed for JAK2 was: JAK2 ex11F: 5'-TGGAAACTGTTCGCTCAGAC-3' (forward) and JAK2 ex16R: 5'-TGGCACATACATTCCCATGA-3' (reverse). For MPL sequencing we create direct DNA sequencing method and used the following primers: forward primer GAGTAGGGGCTGGCTGGAT and as reverse primer: AGCGAACCAAGAATGCCTGT.

Our initial study group consisted only of 14 JAK2V617F negative adult MPN patients (9 ET and 5 PV) that were diagnosed at the UNIVERSTY Clinic of Hematology-Skopje | according to the 2008 WHO criteria for diagnosis of MPN. The JAK2 V617F mutation and direct RNA and DNA sequencing procedures were performed at the Center of Biomolecular Sciences, Faculty of Pharmacy –Skopje

In one of our ET JAK2V617F negative patient a point mutation was revealed in the exon 13 of JAK2, at glycine at the codon 571 (GGT > AGT). This mutation, although extremely rear is already referred by Ma and al. with frequency of occurrence<0.01%. Furthermore, it is suggested that G571S mutation may cause a conformational change in the JAK2 resulting in a constitutively active kinase.

Our preliminary results support the latest recommendation that molecular testing for JAK2 mutation should be extended to most of the pseudokinase domain coding region, and not to be restricted to the V617F and exon 12 mutations only.

Keyword: myleoproliferative neoplasms, JAK2 Mutational profile

Poster No: 0098 Abstract:0237

COMBINATION LOW-DOSE THALIDOMID AND PREDNISONE FOR THE TREATMENT OF MYELOFIBROSIS WITH MYELOID METAPLASIA

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Single-agent thalidomide (THAL) at "conventional" doses (> 100 mg /d) has been evaluated in myelofibrosis with myeloid metaplasia (MMM) based on its

antiangiogenic properties. THAL monotherapy at such doses produces approximately a 20 % response rate in anemia but is poorly tolerated.

A sixty five year-old female patient with myelodysplastic syndrome who was treated with THAL-PRED (prednizone) after transformation to myelofibrosis was presented. The patient was diagnosed as refractory anemia in 1997. There was no splenomegali in her physical examination and there was not any fibrosis in her bone marrow at the time of the diagnosis. In 2007 she developed 5 cm hapatomegali and 5 cm splenomegali. Re-evaluation of the bone marrow biopsy showed severe increase in collagen fibers and moderate increase in reticulin fibers. Early satiety, weight loss and fatigue were prominent symptoms and her hemoglobin level was 7.9 g/dl. She was treated with mainly transfusions. Her transfusion requirement was 2 units/month. THAL 50 mg/day and PRED, 0.5 mg/kg/day was started in 2009. Grade 3 peripheral neuropathy was observed in the 3rd weeks of therapy. Thalidomide dose was reduced to 50 mg every other day and steroid dose was tapered gradually and lowered to 10 mg/day at 3 rd month of therapy. In the fourth month of therapy liver and spleen were nonpalpabl. Her hemoglobin level increased gradually and reached 9-11 g/dl.

THAL-PRED was well tolerated and an objective clinical response was demonstrated in our patient. She became transfusion independant. The dose of THAL in this patient (50 mg/d) was better tolerated than the higger doses used in previous studies. Adverse events associated with corticosteroid therapy were mild and transient. Low dose THAL-PRED is well tolerated and can be effective in myelofibrosis with myeloid metaplasia.

Keyword: myelofibrosis with myeloid metaplasia, thalidomide and prednisone therapy

Poster No: 0099 Abstract:0248

TETRASOMY 5 SHOWED FOR THE FIRST TIME AS CYTOGENETIC ABNORMALITY IN AN ADULT PATIENT WITH MYELODYSPLASTIC SYNDROMES

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Myelodysplastic syndromes (MDS) comprise a group of heterogeneous clonal hematopoietic cell disorders characterized by cytopenias, bone marrow hypercellularity, and increased risk of transformation to acute leukemia's. Approximately 50% of MDS patients have clonally chromosome abnormalities. The karyotypic differences turned out to be one of the most important prognostic parameters in these patients. 5q-deletions, monosomy 7, trisomy 8 and complex abnormalities are the most common cytogenetic anomalies in MDS. Rare abnormalities occurring in a substantial portion of patients with MDS is still unknown. Here we present a case of 72-year-old women who applied with fatigue and headache. Her leukocyte 5160 /uL, Hg: 10.6 gr/dL, platelet. 336000/Ul. Bone marrow aspiration demonstrated hypocellularity. She was diagnosed as MDS. Her Fluorescence in situ hybridization (FISH) revealed a tetrasomy 5 clone that could not be detected by conventional cytogenetic. In this study, bone marrow and peripheral blood cells were collected analyzed by FISH with DNA probes for chromosomes 5, 7, 8, and 20. FISH analysis revealed tetrasomy 5 frequency of a percentage of %30 in the investigated cells, but not in other chromosomes examined. This is the first reported case of MDS with tetrasomy 5 that is reported till date. Our findings indicate the utility of FISH analysis in cytogenetic monitoring of MDS patients are important to discover new cytogenetic aberrations.

Keyword: Myelodysplastic syndromes, Tetrasomy 5

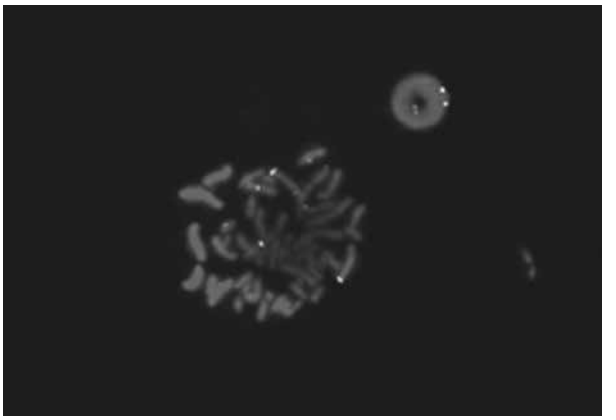

Figure 1. Methaphase FISH analysis of the case with tetrasomy 5

Poster No: 00100 Abstract:0257

ACHIEVEMENT OF MAJOR MOLECULAR RESPONSE WITH IMATINIB THERAPY IN AN ALLO-TRANSPLANTED CHILDHOOD CHRONIC MYELOID LEUKEMIA PATIENT AFTER RELAPSE

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Childhood chronic myelogenous leukemia (CML) is a rare malignancy, accounting for less than %3 of all pediatric leukemias. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) was considered as the only curative treatment before 2000 for CML patients. CML treatment has greatly changed after the introduction of tyrosine kinase inhibitors (TKIs). In the TKI era, only the minority of the patients with advanced phase at diagnosis or resistant toTKIs are candidates for allo-HSCT. A relapse risk as high as 5% to 20% has been reported after allo-HSCT for chronic phase CML. The choice of treatment for CML patients relapsed after allo-HSCT is controversial. Both imatinib mesylate(IM) or donor lymphocyte infusions (DLI) are effective in inducing remissions in patients with relapsed CML following allo-HSCT. Since DLI might induce life-threatening graft versus host disease, it may be reasonable to postpone DLI, when IM therapy failed optimal molecular response in relapsed CML patients

Case: A 26-year-old woman was admitted to hematology department with asymptomatic leukocytosis. She had been diagnosed with Philadelphia chromosome-positive (Ph+) childhood CML, as she was 12 years old in 1998. Because pediatric CML scoring systems hasn't yet been established, adult prognostic scoring system for CML were applied. She was in low risk group (risk score:0.41) according to Sokal risk score. Interferon alpha and

hydroxyurea was used before performing an allo-HSCT from her HLA matched sibling in 1999. She achieved complete chimerism (CC) after the allo-HSCT and didn't lost CC for 5 years during her follow up, which was then interrupted for 7 years.

During her admission clinical examination didn't show any specific features. Her hemogram had been as follows; Hb:11g/dl, Htc:29%, WBC:20700/μL, Plt:274000/μL. Her peripheral blood film revealed leukocytosis with a predominance of myelocytes, metamyelocytes, segmented neutrophils. The bone marrow examination showed myeloid hyperplasia with predominance of myelocytes and metamyelocytes. Cytogenetic analysis for the Ph [46XX, t(9;22)] was 75% positive and real time polymerase chain reaction (PCR) for BCR-ABL/ABL was 243%(IS). She had relapsed 12 years later after the allo-HSCT. Since she lost donor related hematopoesis, which was shown by cytogenetic analysis, we didn't treat her with DLI. IM 400 mg/day was initiated. She achieved complete hematologic response, complete cytogenetic response, major molecular response(MMR) after 1,3 and 6 months, respectively. In the first year of IM treatment follow up MMR was sustained and mixed chimerism (90% donor cells and 10% recipient cells) was detected by FISH. We are planning to repeat her chimerism analysis using short tandem repeats (STR)-PCR and molecular response. Without achieving CC or having complete molecular response, DLI therapy will gain priority.

Here we report a childhood CML patient who relapsed 12 years after allo-HSCT and had MMR with IM treatment.

Keyword: childhood CML, relapse after Allo-HSCT

Poster No: 00101 Abstract:0259

NON-INFERIORITY OF ANAGRELIDE COMPARED TO HYDROXYUREA IN WHO-ESSENTIAL THROMBOCYTHEMIA, A PHASE III TRIAL

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High platelet counts in essential thrombocythemia (ET) can be effectively lowered by treatment with either anagrelide or hydroxyurea. However, the data on this treatment stem from PVSG classified ET and it is still unknown whether these recommendations can be applied to ET patients diagnosed following the World Health Organization (WHO) classification (WHO-ET). The data of the ANAYDRET study provide evidence that anagrelide is non-inferior to hydroxyurea in the treatment of WHO-ET. In 259 previously untreated, high-risk ET patients, diagnosed according to the WHO classification system, efficacy and tolerability of anagrelide compared to hydroxyurea was investigated in a prospective randomized non-inferiority phase III study in an a-priori ordered hypothesis. Confirmatory proof of non-inferiority of anagrelide was achieved after 6 months using the primary endpoint criteria and further confirmed after an observation time of 12 and 36 months for platelet counts, hemoglobin levels, leukocyte counts ($p<0.001$) and ET related events (HR[95%CI]=1.19[0.61-2.30], 1.03[0.57-1.81] and 0.92[0.57-1.46] respectively). During the total observation time of 730 patient-years, there was no significant difference between the anagrelide and hydroxyurea group regarding incidences of major arterial (7 vs. 8) and venous (2 vs.6) thrombosis, severe bleeding events (5 vs. 2), minor arterial (24 vs. 20) and venous (3 vs. 3) thrombosis and minor bleeding events (18 vs. 15), or discontinuation rates (adverse events 12 vs. 15 or lack of response 5 vs. 2). Disease transformation into myelofibrosis or secondary leukemia was not reported. Anagrelide as selective platelet lowering agent is not inferior compared to hydroxyurea in preventing thrombotic complications in patients with WHO-ET. These data provide evidence that anagrelide can be considered as first line therapy for lowering of platelet count in WHO-ET. This trial was registered at www.clinicaltrials.gov as #NCT01065038. Prepublished online, Blood, Jan. 11, 2013

Keyword: Anagrelide, Hydroxyurea

Poster No: 00102 Abstract:0268

USE OF THYROSINE KINASE INHIBITORS IN SETTING OF RELAPSE AND AS MAINTENANCE THERAPY AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HIGH RISK PHILADELPHIA POSITIVE MYELOID NEOPLASMS

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Outcome of HSCT for AP or BP CML is disappointing with a 2-year survival of 47% and 16% for AP and BC CML,respectively. Ph (+) AML, comprising 1–2% of AMLs, has high risk of treatment failure and relapse even after HSCT. 1st and 2nd generation TKIs are suggested as options after transplantation in advanced CML, but algorithms for dosage, intervals from HSCT, duration of application, and combination with DLI are not yet defined.

Two BP CML, 1 Ph+ de novo AML and 1 relapsed/refractory Ph+ AML were included. Case 1 presented with blastic crisis 6 years after diagnosis of CP-CML following loss of molecular and hematological response under imatinib and dasatinib. Minimal residual was present prior to allo-HSCT. On day +38, CHR, CCyR, CMR and complete chimerism were achieved. On day +100, dasatinib 2x70 mg was begun to preserve CMR. Ten months after HSCT, CHR, CCyR and CMR are maintained. Case 3 showed loss of hematologic and molecular response under imatinib, nilotinib and dasatinib and finally presented with blastic crisis 12 years after diagnosis of CP CML. On day +32 after allo-HSCT, CHR, CCyR and MMR were obtained in presence of complete donor chimerism. On day +90, molecular relapse and decrease of molecular chimerism was observed. CsA was tapered; dasatinib 2x50 mg was started and increased to 2x70 mg by day +120. On day +180, MMR and complete molecular chimerism were reestablished. Dasatinib was reduced to 2x50 mg due to pancytopenia. Case 2 diagnosed with de novo Ph+ AML-M0 obtained CHR and CCyR after 7+3 and imatinib 600 mg/day and CMR after 2 courses of HD-ARA-C. 6 months after diagnosis, consolidation treatment was completed by autologous HSCT. By day +100 after auto-HSCT, imatinib 400 mg/day was reinitiated. One year after HSCT, imatinib was cessated in presence of CHR, CCyR and CMR. On month +15 after auto-HSCT, molecular relapse was detected and imatinib 400 mg/day was started. Search for unrelated donor is underway. Case 4 diagnosed as

relapsed/refractory Ph+ AML showed 10% blasts in bone marrow on day +35 after allo-HSCT. CSa was tapered and dasatinib 140 mg/day was started. Because of oral intolerance due to grade II GI tract acute GVHD, dasatinib was suspended until day +58 and started at 70 mg/day due to cytopenias in presence of CMV infection. CHR, CCyR and CMR was achieved on day +75. By day +300, CHR, CCyR and CMR are maintaned.

Optimal strategy for advanced CML needs to be defined. In advanced CML, CMR appears to be crucial in providing long term control yet for relapse after HSCT, there is limited data on association between CMR and survival. Our cases indicate TKİ with chemotherapy followed by autologous or allogeneic HSCT and TKİ maintenance is associated with favorable outcome for Ph+ AML. Experience with 2nd generation TKIs in relapsed Ph+ AML is limited; studies with larger number of patients and longer follow-up should be considered.

Keyword: Ph chromosome, thyrosine kinase inhibitors

Table 1. Patients characteristics

Patients characteristics (n=4)	
Age, median (range), years	48,5 (29-58)
Gender (female/male)	2/2
Diagnosis	
CML in blastic crisis	2 (50%)
Ph-positive de novo AML	1 (25%)
Relapsed/refractory Ph-positive AML	1 (25%)
Type of stem cell transplantation	
Allogeneic (myeloablative)	3 (75%)
Autologous	1 (25%)
Diagnosis to transplant, median (range), months	63 (6-144)
Graft, median (range) CD34 cell count	3,98 (2,31-6,78)x106/kg
Conditioning regimen	
Bu/Cy	4 (100%)
Source of stem cells	
Peripheral blood	4 (100%)
Follow-up, median (range), months	10(5-15)

Table 2. Pre- and post-transplant TKIs for high-risk Ph(+) myeloid malignancies

Case no.	Diagnosis	IM pre-transplant (months/ response)	Other treatment pre-transplant/ status	Response one month after transplant	TKI post-transplant months, response	Relapse after	Therapy for relapse	Disease status at last follow up
1	CML in BC	45/disease progress/ BC	Dasatinib+ Chemo/CP	CCyR/ CMoR	dasatinib, 6-9 m CMoR	-	-	CMoR
2	Ph-positive de novo AML	6/CHR/CCR/ CMoR	Chemo/CHR/ CCR/CMoR	CCyR/ CMoR	Imatinib, 3-15 m CMoR	Molecular relapse (15 m)	Imatinib	CHR, CCR, CMoR
3	CML in BC	72/disease progress/ BC	Dasa/ nilo+chemo/ BP	CHR/CCR/ CMoR	dasatinib, 3-6 m CMoR	Molecular relapse (3 m)	Dasatinib	CMoR
4	Relaps/refr Ph-positive AML	6/no response	Chemotherapy/ NR	No response	dasatinib, 1-10 m CMoR	Mixed chimerism (1 m)	Dasarinib	CMoR

Poster No: 00103 Abstract:0274

ACUTE MYELOID LEUKEMIA SUBSEQUENT TO AUTOIMMUNE HEMOLYTIC ANEMIA: A REPORT OF THREE CASES

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Autoimmune conditions are associated with an increased risk of acute myelocytic leukemia (AML) and myelodysplastic syndrome (MDS). Autoimmune hemolytic anemia (AIHA) is considered to be a complication of several lymphoproliferative disorders, such as chronic lymphocytic leukemia (CLL) and B-cell non-Hodgkin lymphoma (NHL). AIHA has rarely been reported in patients with B-cell acute lymphoblastic leukemia (ALL).As MDS and myeloproliferative disorders (MPDs) are indolent and may be present years before diagnosis, it is possible that AIHA arose as a result of these conditions. Herein, we report three cases of AML developed subsequent to AIHA. A 58-year-old man, a 70-year-old woman, a 43-year-old woman are first diagnosed as AIHA before AML..

Keyword: AIHA, AML

Poster No: 00104 Abstract:0279

ESSENTIAL THROMBOCYTOSIS AS A CAUSE OF ARTERIAL COMPLICATIONS

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Essential thrombocytosis (ET) is a clonal disease characterized by thrombocytosis, splenomegaly and proliferation of megakaryocytes in the bone marrow(1).The disease may be asymptomatic or may present with severe complications such as thrombosis and haemorrhage.It is usually diagnosed through the incidental finding of increased platelet counts during routine check-up.ET is a slowly progressive disease but it can lead to life-threatening complications.Unusual course of a patient with ET is presented here.

A 61-year-old female patient with no previous complaint was intubated after a hypertensive pulmonary oedema attack three months ago and was followed up in the intensive care unit. One month later she was hospitalised for acute myocardial infarction in the coronary intensive care unit.After coronary angiography and renal artery angiography revealed, PTCA and stent implantation was done for the right renal arterial stenosis.

The patient was referred to the haematology for consultation because of detected high platelet levels (Plt: 820.000/mm^3) during a routine cardiology outpatient visit.On physical examination she was normotensive with regular heart rate of 76 beats/min.Systemic examination was unremarkable except a 4 cm palpable spleen below the left costal margin.Her WBC was 13.000/mm^3, haemoglobin was 14.8 g/dl, and platelet count was 820.000/mm^3, blood chemical analysis including immunoglobulins was normal except increased levels of LDH, uric acid, calcium. direct and indirect coombs tests were negative.

Thrombophilia testing including homocysteine, protein C, protein S and factor V Leiden was unremarkable.JAK2-V617F mutation was positive.Bone marrow biopsy was hypercellular consistent with chronic myeloproliferative disease favouring ET.Hydroxyurae together with acetyl salicylic acid was begun.

ET is a clonal disorder affecting mostly women in adult ages.Increased bone marrow megakaryocytes and peripheral thrombocytosis accompanied by splenomegaly and 30-70% JAK 2 gene mutation positivity are the cardinal physical and laboratory findings.(2,3,4,5).A retrospective study performed by Vannuchi et al. showed an increase of cardiovascular events in association with the JAK2 gene mutation(6). JAK-2 gene mutation was linked to increased bleeding and thrombosis in a retrospective study with 90 patients(7).Our case had all the risk factors described in these studies and showed a poor clinical course.Outside the context of this particular patient, one should also consider that the complications that occurred during the course of thrombosis and therapeutic agents used in the treatment of these complications might lead to temporary increase in platelet counts.Thus the increased platelet counts may be the result rather than the cause in thrombosis.But in our patient the diagnosis (ET) was established and the disease seems to be the underlying disease.In patients with recurrent arterial thrombosis ET should be included in the differential diagnosis.

Keyword: acute myocardial infarction, essential thrombocytosis

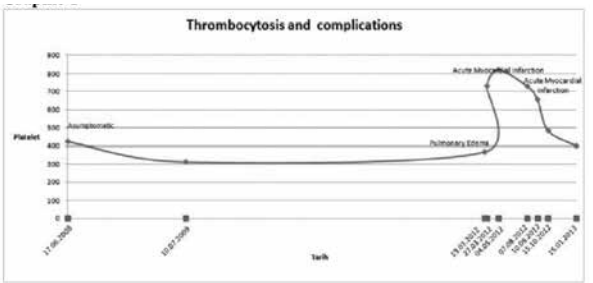

Figure 1: Thrombocytosis and complications

Poster No: 00105 Abstract:0283

MANAGEMENT OF TWO JUVENILE MYELOMONOCYTIC LEUKEMIA PATIENTS ACCORDING TO CLINICAL AND GENETIC FEATURES

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Juvenile myelomonocytic leukemia (JMML) is a rare clonal myeloproliferative disorder of

childhood. Major progress has been achieved in diagnosis and understanding the pathogenesis of JMML by identifying the genetic pathologies that occur in patients. Mutations of RAS, NF1, PTPN11, and CBL are found in approximately 80% of the JMML patients. Distinct clinical features have been reported to be associated with specific gene lesions. The advent in genomic studies and recent identification of novel genetic mutations in JMML are important not only in diagnosis but also in prognosis and clinical management of the disease. Herein we present two patients with JMML harboring different mutations, NRAS and C-CBL respectively, with distinct clinical features and different clinical coarses.

The first patient was a male who had the diagnosis of JMML when he was 16 months old. He had recurrent febrile lower and upper respiratory tract infections, bloody diarrhea attacks, periodic febrile episodes lasting 4-5 days and relapsing and remitting vasculitic leisons. The symptoms didn't fade with cytoreductive treatment. Genetic work-up revealed somatic NRAS mutation. As soon as full matched unrelated donor was found, the patient was referred to another center for allogeneic HSCT.

The second patient had the diagnosis of JMML when she was 17 months old. She had recurrent lower respiratory tract infections, typical facial features, marked developmental delay. Genetic analysis revealed germline heterozygous C-CBL mutation. The findings of the patient was consistent with the CBL syndrome which is a newly defined entity characterized by impaired growth, shared phenotypic features like broad forehead, mild hypertelorism, short upturned nose, prominent philtrum, thick lips, mild retrognathism, developmental delay, and predisposition to JMML. As this patient harbored germline C-CBL mutation and has a chance of spontaneous resolution, HSCT was not planned as initial treatment. A cytoreductive treatment with 6-mercaptopurine was started and she had shown clinical improvement in the follow-up period.

In conclusion, JMML is phenotypically and genotypically a heterogenous disease. Recent developments in identifying the molecular lesions have revealed the importance of genotype phenotype correlation in this disease which is very important for tailoring the management.

Keyword: childhood, juvenile myelomonocytic leukemia

Poster No: 00106 Abstract:0310

MANAGEMENT OF ESSENTIAL THROMBOCYTHEMIA WITH INTERFERON ALFA- SINGLE CENTER EXPERIENCE

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Background: The Philadelphia-negative chronic myeloproliferative neoplasms encompass essential thrombocythemia (ET), polycythemia vera (PV) and primary myelofibrosis (PMF). A major break-through in the understanding of the pathogenesis of this neoplasm's occurred in 2005 by the discovery of the JAK2 V617F mutation A number of studies have shown that the "tumour burden" may be monitored at the molecular level in JAK2-positive patients using highly sensitive real-time quantitative PCR. During the last 25 years several studies have shown that interferon-alpha (IFN-alpha) induces complete haematological remissions in a large proportion of the patients. However, its use in clinical practice has unfortunately been limited due to side effects with high drop-out rates in most studies. Recently, IFN-alpha has been shown to induce deep molecular remissions and also normalization of the bone marrow in PV, which may be sustained even after discontinuation of IFN-alpha therapy. The aim of the study is to present our experience in treatment of this subset of patients with IFN-alpha therapy

Design and methods: In University Clinic of Hematology during 2005-2010year, 35 patients, with

essential thrombocythemia diagnosed according WHO classifications were treated with Interferon-Alfa 2b subcutaneous. Treatment scheme was consisted of two phases: a) induction phase with interferon alpha 3million units (MU) per day and b) a maintenance phase. The pretreatment mean platelet counts were 923 x10 9/l and megacariocytes in bone marrow were increased in all cases. Splenomegaly was present in 15% of the patients, and 5pts have had vascular complication like thrombosis in pretreatment phase.

Results: During the induction phase, the results showed that using 21MU of IFN Alfa weekly (3MU/day) platelet counts were 500 x10 9/l in 100% of the patients. During the maintenance phase 25pts required 3MU three times a week, and 10 pts required 9MU three times a week. V617F mutation of JAK2 gene was positive in17pts. During a long-term treatment of 5 years subjective side effects were tolerable. Until now 31 pts have stable platelet counts below 500 x10 9/l and only 2 had died because of acute myocardial infarction and two had died because of acute mesenteric thrombosis.

Conclusions: We conclude that Interferon-Alfa can correct thrombocythosis in pts with essential thrombocythemia over a period of years and prevent morbidity attributable to this disease.

Keyword: Essential thrombocythemia, Interferon-Alfa

Poster No: 00107 Abstract:0313

EVALUATION OF THE AMOUNT OF THE NEOPLASTIC CLONE IN THE BONE MARROW SAMPLES OF MYELOPROLIFERATIVE DISORDERS AND ITS RELATION WITH THE DISEASE STATUS

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Biology and disease status of Myeloproliferative disorders (MPD) can be interpreted by the amount of neoplastic clone. This evaluation can be made on JAK2 mutated cases by using sensitive molecular methods.

In this study, we aimed to investigate JAK2 exon 14 (JAK2V617F), JAK2 exon 12 and MPLW515L, MPLW515K, MPLA506T and MPLA519T mutations, on pathology archival material using Next Generation Sequencing Technologies. The amount of the mutated clone was compared with the histopathological parameters and the clinical data in order to evaluate the relationship between disease presentation and the "allele burden" status on bone marrow samples. For this purpose, the bone marrow biopsies and smears of 56 patients with median age 57,8 (22-80) (45.8% male, 54.2% female) diagnosed as MPD (ET, PV, PMF) between 2001-2011 in Ankara University Faculty of Medicine Department of Pathology were selected for the study. The clinical and laboratory data were collected from the hospital records. Roche 454 GS Junior system was performed for detection of JAK2 and MPL mutations sequencing.

Our series showed compatible age, gender and laboratory findings with the stages of the diasease groups. JAK2 exon 14 V617F mutation was examined in %79,2 of the patients (ET 84.2%, PV 91.7%, PMF 64.7%). One of the cases carried JAK2 exon 12 mutation. MPL exon 10 mutation was examined only on one ET case (%2,9) case also carrying JAK 2 exon 14 mutation. "Allel burden" which represents the amount of JAK2V617F mutated clone ratio was lowest among PMF cases, followed by ET. The ratio was highest among PV cases. A positive relation between cellularity (p=0.032), white blood cell count (p=0.007) and allel burden status was examined. The amount of mutated allel was less than %10 for five patients.

Our results confirmed that the ratio of Jak mutated cases for different clinical presentations of MPD is higher than the literature when the bone marrow samples were examined by pyrosequencing. Cellularity in the bone marrow biopsies and white blood cell count in blood are the most reliable reflectors of the amount of neoplastic clone for MPD as expected.

Keyword: MPD, Jak2 mutation

Poster No: 00108 Abstract:0327

PATHOPHYSIOLOGY OF PLATELET MEDIATED THROMBOSIS AND BLEEDING IN THROMBOCYTHEMIA

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Erythromelalgic thrombotic thrombocythemia (ETT), caused by a thrombotic occlusion of the acral digital (erythromelalgia) and the cerebral end-arterial circulation (migraine-like microvascular cerebral transient ischemic attack; MIAs) are the far most frequent aspirin-sensitive microvascular complication in ET and PV. If left untreated, major thrombosis of the peripheral, cerebral and the coronary circulation do occur usually in the absence of pre-existing vascular disease as a main cause of death. In cases of reactive thrombocytosis, erythromelalgia, MIAs and major thrombosis do not occur, indicating not only a quantitative but also a qualitative hypersensitive platelet defect in thrombocythemia. It is postulated that hypersensitive platelet in thrombocythemia are caused by the JAK2V617F or MPL515 gain of function mutations in thrombocythemia. Correction of the hemotocrit to normal in PV (<42 in female, < 0.45 in male) on top of low dose aspirin or reduction of platelet number in ET and PV to normal by platelet by agents (interferon or anagrelide) reduces the minor and major thrombotic complication to near zero. An association between spontaneous hemorrhages and pronounced thrombocythemia (hemorrhagic thrombocythemia: HT) is caused by an acquired von Willebrand Disease (AVWS due to platelet induced proteolysis of the von Willebrand fator (VWF)) at platelet counts in excess of $1000x10^9$/l. Correction of the platelet counts to below $1000x10^9$/L alleviates bleeding and largely corrects the AVWS-defect. Reduction of platelet count to near normal or normal is associated with the complete relief of bleeds, but the risk on aspirin preventable minor erythromelalgic ischemic distress and major thrombosis persist in ET and PV patients. The von Willebrand factor (VWF) is the link to explain the paradoxical occurrences of both ETT and HT at the same time in one the same ET or PV patient. We hypothesize and could produced good evidence, that interactive activation of hypersensitive platelet/ADAMTS13/VWF complex formation at high shear stress in the end-arterial microcirculation does

initiate platelet thrombi formation and VWF proteolysis. It is a matter of the increased degree of thrombocythemic platelet counts whether erythromelalgic thrombotic (at platelets in excess of $350x10^9$/L) or bleeding (at platelet count in excess of $1000x10^9$/L) do occur. There is a third component of a peculiar type of bleeding related to 'increased platelet-mediated blood clot retraction' disturbance with erythrocyte fall out, that causes painful subcutaneous hematomas with a central swelling (clot) after a blow, trauma and/or surgery.

Keyword: MIAs

Poster No: 00109 Abstract:0328

BONE MARROW RETICULINE FIBROSIS (RF) AND RETICULIN-COLLAGEN FIBROSIS (RCF) IN MYELOFIBROSIS IS NOT A DISEASE BUT SECONDARY TO THE CLONAL MEGAKARYOCYTIC/GRANULOCYTIC PROLIFERATION IN MYELOPROLIFERATIVE DISORDERS

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Myelofibrosis is not specific for a disease and seen in patient with hairy cell leukemia, Ph-positive chronic myeloid leukemia (CML), in essential thrombocythemia (ET), polycythemia vera (PV), primary (dys)megakaryocytic granulocytic myeloproliferation (PDGM), and many other conditions. The term chronic idiopathic myelofibrosis (CIMF) or primary myelofibrosis (PMF) is derived from reticulin staining of bone marrow biopsies which only shows you in the microscope black fine or coarse fibers and is only of minor prognostic significance. According to the 1990 Hannover Bone Marrow Classification for CML and MPD, Georgii concluded that CIMF is secondary, misleading and scientifically not sound.

Myelofibrosis (MF) itself is not a disease because reticulin and collagen fibrosis are produced by polyclonal fibroblasts in response to cytokines released from the clonal granulocytic and megakaryocytic proliferative cells in both PV and CMF. The sequential occurrence of reticuline fibrosis (RF) and irreversible reticulinn/collagen fibrosis (RCF) is well documented in JAK2V617F mutated PV and PDGM, in MPL515 mutated PT, in BCR/ABL-positive thrombocythemia and CML and in many other conditions. The transition of RF into RCF is rare in heterozygous JAK2V617F positive ET and does occur in about one third of heterozygous/homozygous or homozygous JAK2V617 positive PV and does occur in the majority of patients with JAK2 wild type PDGM during long-term follow-up.

Grading of reticulin fibrosis using the reticulin silver stain according to the polycythemia vera study group (PVSG) and UK guidelines is world-wide used. A scoring system based on morphometric analysis (point intersection with an ocular grid) and quality of fibers (reticulin and collagen fibers) and the bone marrow fiber density (fine or course reticulin and some or course bundles of collagen) has been proposed by German institutes of pathology (Hannover Bone Marrow Classification of MPD and CML). The different scoring systems for RF, RCF and MF use different criteria for grading of reticulin and collagen, are subjective and not always comparable by lack of strict criteria. A standardized semiquantitative grading of reticulin and collagen fibrosis in the bone marrow, myelofibrosis (MF) is proposed by a panel of pathologists.

Keyword: JAK2V617, CML

Poster No: 00110 Abstract:0329

CLASSIFICATION AND NATURAL HISTORY OF BCR/ABL- POSITIVE THROMBOCYTHEMIA AND CHRONIC MYELOID LEUKEMIA AS COMPARED TO THE BRC/ABL-NEGATIVE MYELOPROLIFERATIVE DISORDERS; ESSENTIAL THROMBOCYTHEMIA (ET)

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The Philadelphia chromosome ((Ph1) originates from a translocation (t) of a large part of 22q to the long arm of chromosome 9, and the translocation (t) of a small part of 22q to 9q: the t(9:22)(q34:q11). The Ph1 chromosome breakpoints on chromosome 22 in CML patients appeared to be clustered within a limited region, the breakpoint cluster region (BCR) on chromosome 22. The BCR/ABL fusion gene is found in classical CML patient with the t(9:22)(q34:q11) translocation but also in CML patients with complex chromosomal translocations. The BCR/ABL fusion gene has a high tyrosinekinase activity. Ninety five percent of patients with the clinical phenotype of CML are BCR/ABL+; 90% are Ph1+/BCR/ABL+; and 5% are Ph1-/BCR/ABL+. Five percent are Ph1-/BCR/ABL-, and diagnosed as atypical CML, juvenile CML, chronic neutrophilic leukemia or chronic myelomonocytic leukemia. Three phenotypes of BCR/ABL-positive disease can be distinguished; CML with megakaryocyte predominance (CML.M) and CML of common type (CML.CT) and BCR/ABL-positive essential thrombocythemia (ET) without features of CML. In BCR/ABL-positive thrombocythemia, platelets are small and indolent (non-reactive) and megakaryocytes are smaller than normal with hypolobulated nuclei. In contrast, platelets and megakaryocytes in Ph1–negative ET and PV are large. According to strict morphological, biochemical, and molecular criteria, BCR/ABL-positive CML is a malignant disease (neoplasia) with an obligate transition into acute leukemia. BCR/ABL-positive ET may progress to overt CML and usually show a high tendency to myelofibrosis and blastic transformation near to 100%. Despite high platelet count around $1000x10^9$/L and far in excess of 1500x109/l, patients with BCR/ABL-positive thrombocythemia do not present erythromelalgic thrombotic or bleedings manifestations. In the MPDs ET and PV, erythromelalgic thrombotic events are frequent due hypersensitive large platelets with a high risk of platelet-mediated inflammation and thrombosis in the end-arterial circulation. caused by the JAK2V617F point mutation.

Keyword: BCR/ABL, CML

Poster No: 00111 Abstract:0330

PATHOPHYSIOLOGY OF PLATELET-MEDIATED MICROVASCULAR DISTURBANCES AND MAJOR THROMBOSIS IN ESSENTIAL THROMBOCYTHEMIA AND POLYCYTHEMIA VERA: REVERSAL BY ASPIRIN, PLATELET REDUCTION, BUT NOT BY ANTICOAGULATION

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Essential thrombocythemia (ET) and polycythemia vera (PV) frequently present with erythromelalgia and acrocyanotic complications, migraine-like microvascular cerebral and ocular transient ischemic attacks (TIAs) and/or acute coronary disease. The spectrum of TIAs in ET range from poorly localized symptoms of transient unsteadiness, dysarthria and scintillating scotoma to focal symptoms of transient monocular blindness, transient mono- or hemiparesis or both. The attacks all have a sudden onset, occur sequentially rather than simultaneously, last for a few seconds to several minutes and are usually associated with a dull, pulsatile or migraine-like headache. Increased hematocrit and blood viscosity in PV patients aggravate the microvascular ischemic syndrome of thrombocythemia to major arterial and venous thrombotic complications. Phlebotomy to correct hematocrit to normal in PV significantly reduces major arterial and venous thrombotic complications, but fails to prevent the platelet-mediated erythromelalgia and TIAs. Complete long-term relief of the erythromelalgic microvascular disturbances, TIAs and major thrombosis in ET and PV patients can be obtained with low dose aspirin and platelet reduction to normal, but not with anticoagulation. Skin punch biopsies from the erythromelalgic area show fibromuscular intimal proliferation of arterioles complicated by occlusive platelet-rich thrombi leading to acrocyanotic ischemia. Symptomatic ET patients with erythromelalgic microvascular disturbances have shortened platelet survival, increased platelet activation markers β-thromboglobulin, (β-TG) platelet factor 4 (PF4) and thrombomoduline (TM), increased urinary thromboxane B2 (TXB2) excretion, and no activation of the coagulation markers thrombin fragments F1+2 and fibrin degradation products. Inhibition of platelet cyclooxygenase (COX1) by aspirin is followed by the disappearance and no recurrence of microvascular disturbances, increase in platelet number, correction of the shortened platelet survival times to normal, and reduction of increased plasma levels of β-TG, PF4, TM and urinary TXB2 excretion to normal. These results indicate that platelet-mediated fibromuscular intimal proliferation and platelet-rich thrombi in the peripheral, cerebral and coronary end-arterial microvasculature are responsible for the erythromelalgic ischemic complications, TIAs and splanchnic vein thrombosis. Baseline platelet P-selectin levels and arachidonic acid induced COX1 mediated platelet activation showed a highly significant increase of platelet P-selectin expression (not seen in ADP and collagen stimulated platelets), which was significantly higher in JAK2V617F mutated compared to JAK2 wild type ET.

Keyword: TIAs

Poster No: 00112 Abstract:0331

1975 PVSG, 2008 WORLD HEALTH ORGANISATION (WHO) AND THE 2008 EUROPEAN CLINICAL, MOLECULAR AND PATHOLOGICAL (ECMP) CRITERIA FOR THE DIAGNOSIS AND CLASSIFICATION OF MYELOPROLIFERATIVE DISORDERS

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The present critical appraisal integrates the world wide used criteria of the Polycythemia Vera Study Group (PVSG), thrombocythemia Vera (TVSG) and the 2007 World Health Organization (WHO) into a new set of 2008 WHO bone marrow features and European clinical molecular and pathological (WHO-ECMP) criteria for the diagnosis and classification of JAK2V617 muated trilinear myeloproliferative disorders essential thrombocythemia (ET), polycythemia vera (PV), and JAK2 wild type primary (Dys)megakaryocytic granulocytic myeleproliferation (PMGM/PDGM) and primary advanced agnogenicmyeloid metaplasia with myelofibrosis (PAMM). The 1975 PVSG, the 2008 WHO and the 2008 WHO-ECMP classifications agree upon the diagnostic criteria for PV and PDGM or primary myelofibrosis (PMF). The clinical diagnosis of ET according PVSG and TVSG criteria comprises three variants of JAK2V617F mutated ET when the 2008 ECMP criteria are applied. These include normocellular ET phenotype 1, ET phenotype 2 with features of early PV (prodromal PV), and ET phenotype 3 with a hypercellular bone marrow due to megakaryocytic, granulocytic myeloproliferation (MGM), but with no anemia and with the absence of leukoerythroblastosis. ET 2 or prodromal PVwill progress to overt PV. Evolution of myelofibrosis is rare in normocellular ET 1 and does occur in patients with ET 3 (ET.MGM) and in PV after long-term follow-up.

The detection of JAK2V617F in granulocytes with sensitive PCR techniques plays a key-role in the diagnostic work-up and staging of patients with ET, PV and PMF or MMM. Spontaneous endogenous erythroid colony (EEC) formation, low serum erythropoietin (EPO) levels and JAK2 mutations are highly specific for early and overt PV but not sensitive enough for true ET and CMF. The JAK2V617F mutation burden in heterozygous mutated ET and in heterozygous/homozygous or homozygous mutated PV is of major clinical and prognostic significance. The combination of a careful clinical work-up, JAK2V617 mutation screening and pre-treatment bone marrow histopathology is highly sensitive and specific to classify and stage each the MPDs ET, PV, PDGM and PAMM as a sound basis for prognosis assessment and therapeutic implications. Myelofibrosis (MF) itself is not a disease because reticulin fibrosis (RF) and reticulin/collagen fibrosis (RCF) are secondary serious irreversible event induced by polyclonal fibroblasts in response to cytokines released from the clonal granulocytic and megakaryocytic proliferative cells in ET.MGM, PV and PDGM.

Keyword: PMGM, PDGM

Poster No: 00113 Abstract:0332

COMPARISON OF WORLD HEALTH ORGANISATION (WHO) AND EUROPEAN CLINICAL, LABORATORY AND PATHOLOGIC (ECMP) CRITERIA FOR THE DIAGNOSIS AND STAGING OF PREFIBROTIC MYELOPROLIFERATIVE NEOPLASIA CARRYING THE JAK2V617F MUTATION

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The clinical diagnoses based laboratory tests including blood cell counts, serum erythropoietin (EPO), endogenous erythroid colony formation (EEC), and JAK2 mutation for the diagnosis of myeloproliferative neoplasm (MPN) without use of bone marrow pathology were essential thrombocythemia (ET) in 6 and polycythemia vera (PV) in 4 patients. Three PV patients were homozygous and one PV and all ET cases revealed a heterozygous JAK2V617F mutation of less than 40%. The bone marrow histopathology diagnosis by expert pathologists without use of clinical data was PV in seven (of which 3 ET with features of early PV) and PV in four. The European Clinical Molecular and Pathology (ECMP) criteria distinguish three sequential stages or phenotypes of JAK2V617F mutated ET: normocellular ET-1; ET-2 with clinical and bone marrow features of PV (prodromal PV) in 3 ET-3 with a hypercelular dysmorphic megakaryocytic and granulocytic myeloproiferation (ET.MGM).

Bone marrow histopathology is a powerful tool to differentiate MPN of various molecular etiologies from all variants of primary or secondary erythrocytosis and reactive thrombocytosis with a sensitivity and specificity near to 100%. Three cases with prodromal PV developed a slow onset PV after long-term follow-up of about 10 years. Red cell counts are below $6x10^{12}$/L in separates JAK2V617F mutated normocellular ET and prodromal PV but clearly above $6x10^{12}$/L in overt PV at diagnosis and at time of transition of prodromal PV into overt PV thereby obviating the need to use red cell mass when bone marrow histopathology is included in JAK2V617F mutated MPN.

Keyword: prodromal PV

Poster No: 00114 Abstract:0333

EUROPEAN CLINICAL, MOLECULAR AND PATHOLOGICAL (ECMP) CRITERIA FOR THE DIAGNOSIS AND CLASSIFICATION OF PREFIBROTIC MYELOPROLIFERATIVE NEOPLASMS

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The clinical and bone marrow features of the prefibrotic JAK2V617F mutated myeloproliferative neoplasms (MPN) can be subclassified as normocellular ET, ET with features of early PV (prodromal PV), classical polycythemia vera (PV), and ET with hypercelular megakaryocytic granulocytic myeloproliferation (EMGM) as the three main JAK2 V616F mutated phenotypes of one distinct trilinear MPN. The morphology of clustered pleomorphic megakarocytes and bone marrow cellularity on histopathology evaluation are overlapping in ET, prodromal PV and PV carrying the JAK2V617F mutation. Pleomorphism of megakaryocytes becomes more pronounced or even dysmorphic in PV and EMGM as the bone marrow cellularity (80-100%) and JAK2V617F mutation load increase on top of other molecular and biological variables during long-term follow-up. Increased erythrocyte counts at a cut off level of $6x10^{12}$/L separates ET and prodromal PV from overt PV and can replace increased red cell mass for the diagnosis of PV. The JAK2 wild type ET carrying one of the thrombopoietin receptor or MPL515 mutation is featured by increase of clustered small and giant megakaryocytes with hyperlobulated stag-horn-like nuclei, in a normal cellular bone marrow, and has no laboratory and bone marrow features of prodromal PV or overt PV at diagnosis and during follow-up. A third entity of pronounced JAK2 wild type thrombocythemia presents with prefibrotic primary dysmegakaryocytic and granulocytic myeloproliferation (PDGM) characterized by a hypercellular dual myeloproliferation of granulopoiesis and dense clustered enlarged immature dysmorphic megakaryocytes with bulky (bulbous) hyperchromatic nuclei, which are never seen in JAK2V617F mutated ET, prodromal PV, EMGM and PV, and also not in prefibrotic MPL515 mutated ET.

Keyword: JAK2V617F

Poster No: 00115 Abstract:0334

CHANGING CONCEPTS ON MYELOPROLIFERATIVE DISORDERS (MPDS), CHRONIC MYELOID LEUKEMIA (CML) AND THROMBOCYTHEMIA IN VARIOUS MPDS: FROM DAMESHEK 1950 AND VAINCHENKER 2005 TO THE 2008 ECMP CRITERIA FOR DIAGNOSIS AND CLASSIFICATION OF THE MPDS

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The PVSG classification (1975) clearly distinguished the Philadelphia (Ph1) chromosome positive chronic myeloid leukemia (CML) from the Ph1-negative myeloproliferative disorders (MPD.) The World Health Organisation (WHO) is a compromise between clinical PVSG criteria and WHO bone marrow bone features for essential thrombocythemia (ET), polycythemia vera (PV) and primary myelofibrosis (PMF) or primary advanced agnogenic myeloid metaplasia (PAMM). Very early latent and intermediate stages of PV and ET are not considered by the WHO classification and diagnosed as unclassifiable MPD indicating the need to fundamentally modify the WHO classification. Applying the proposed WHO bone marrow criteria reveals that the PVSG defined clinical diagnosis of ET comprises various clinical conditions including 3 phenotypes of thrombocythemia at the bone marrow level: normocellular ET, early PV mimicking ET (prodromal PV) and prefibrotic hypercellular ET associated prefibrotic hypercellular bone marrow due to increased megakaryocytic-granulocytic myeloproliferation (MGM) or prefibrotic (PMF-0) of elusive molecular etiology. As PMF-0 is a contradictio in terminis, we changed in 1999 the term chronic megakaryocytic granulocytic myelosis (CMGM) into prefibrotic essential megakaryocytic granulocytic myeloproliferation (EMGM) with various degrees of myelofibrosis MF-0, MF-1, MF 2, and MF 3, and its association

with various degrees of clinical and laboratory features of primary myeloid metaplasia of the spleen.

Half of PVSG/WHO defined ET patients show spontaneous endogenous erythroid colony formation (EEC), low serum erythropoietin (EPO) levels, and carry the JAK2V617F mutation, indicating prodromal PV when the European Cinical, Molecular and Pathological (ECMP) criteria are applied. EEC and low serum EPO are specific JAK2V616F mutated MPN, but not sensitive enough as isolated markers for the diagnosis of PV. The positive predictive value of a JAK2V617F PCR test for the diagnosis of WHO defined PV is high (95%). About half of the PVSG/WHO defined ET and EMGM are JAK2V617F positive (sensitivity 50%). So-called heterozygous MPN with allele load less than 50% in fact are hetero/homozygous in PV and true heterozygous in ET at the EEC blood and bone marrow level. The JAK2V617F mutation load is related to MPD disease burden: heterozygous in normocellular ET and prodromal PV and hetero/homozygous in ET.MGM, trilinear PV, and advanced PV. The proposed WHO-ECMP on top of JAK2V617F and MPL515 mutation screening will much better characterize the early, intermediate, overt and advanced clinicopathological stages of normocellular ET, prodromal PV, trilinear PV, ET.MGM and its various degrees of fibrosis on bone marrow histology in patients with JAK2V617F positive and JAK2 wild type MPD.

Keyword: Thrombocythemia

Non-Hodgkin's Lymphoma

Poster No: 00116 Abstract:0085

DETAILED ANALYSIS OF DIFFUSE LARGE B CELL LYMPHOMA PATIENTS: A SINGLE CENTER, RETROSPECTIVE STUDY REPORTING ON YOUNG PATIENTS

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Objectives: The aim of this single-center, retrospective study was to investigate the impact of rituximab on DLBCL, to reconsider the validity of the IPI, and to evaluate the prognostic role of the cell of origin(CoO) in a relatively young cohort of patients.

Materials-Methods: We retrospectively analyzed 312 de novo DLBCL patients; 54 received CHOP and 258 received R-CHOP.

Results: Rituximab increased 3-and 5-year OS rates from 71% to 77.3% and %67 to 74.5%, respectively(p=0.264). Rituximab significantly improved the 3-and 5-year PFS(41%vs.70% and 36%vs.65%,respectively;p<0.001).

Among young, low risk patients(aaIPI=0&1) in our cohort(n=129); 107 patients received R-CHOP and 22 patients received CHOP treatment. Three- and 5-year OS rates were 90% for R-CHOP and 72% for CHOP group(p=0.048). Similarly, 3- and 5-year PFS were 93%vs53% and 5-year PFS were 91%vs53% for R-CHOP and CHOP groups, respectively(p<0.001).

The studies on young high risk patients are scarce. Analyzing 71 young, high risk patients(aaIPI =2&3),the majority received R-CHOP(n=58);the 3- and 5-year OS were both 71%, and 3 and 5-year PFS rates were 75% and 64%. For the high-intermediate aaIPI group, the 2-year OS rates were 83% and PFS rates 79%. In the high aaIPI group, 2-year OS rates were 59% and PFS rates 75%. Comparing 2-year survival results with the literature, we may conclude that our OS data for high IPI group was worse than transplantation results, although the results of high-intermediate IPI group were comparable with high dose therapy literature.

CoO data were available in 190 patients.The 3-year OS rates in GC and non-GC subgroups were 79% and 64%, respectively.The 3- and 5- year overall survival rates were significantly better in GC group (p=0.014). In multivariate analysis all IPI parameters except extranodal involvement were significantly associated with prognosis. Even though CoO was significant in univariate analysis, it was no longer significant in multivariate analysis.

Conclusion: This retrospective cohort study confirmed the validity of IPI scoring in the rituximab era and showed that rituximab leads to improved survival rates even in poor risk DLBCL patients. In our hands, CoO, as defined by immunohistochemistry, occurred as an IPI independent prognostic factor in univariate but not in multivariate analysis.The survival advantage and a lower mortality rate in GC group were independent of rituximab usage.In the literature, it is obvious that the high dose chemotherapy has no OS advantage but some PFS advantage in young high risk population. In our analysis,OS data for high aaIPI group was worse than first line high dose treatment with autologous stem cell support in rituximab era,although the results of high-intermediate IPI group were comparable with high the literature. To our knowledge, this is the first study which investigated the impact of R-CHOP in the context of CoO and IPI in a relatively young cohort of patients.

Keyword: Diffuse large B cell lymphoma, young high risk cohort

Figure 1

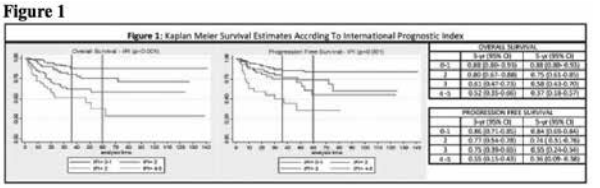

Table 1: Patient Characteristics

	All Patients (n=312)	*Loss of the Follow-up (n=30)*	*Survivors (n=205)*	*Dead (n=77)*	*P value**
SEX F/M	143/169	17/13	96/210	39/46	0.123
Mean/median Age (range)	51.3 / 52 (17-83)	54.9 / 55	48.3 / 47.5	58 / 60 (32-83)	0.104
SUBGROUP: GCB/ NON-GCB/Unknown	104/86/122	7/7/16	77/49/79	20/30/27	0.023
TREATMENT: CHOP/R-CHOP	54/258	10/20	25/180	19/58	0.042
STAGE: 1/2/3/4	75/66/86/85	10/4/9/7	58/50/49/48	7/12/28/30	<0.001
AGE: <60/>=60	208/104	19/11	151/54	38/39	<0.001
LDH: Normal/High	145/162	17/13	108/93	20/56	<0.001
ExTRANODAL: <2/>=2	220/92	24/6	152/53	44/33	0.002
PERFORMANCE: >70/<70	263/49	27/3	183/22	53/24	<0.001
B SYMPTOMS: Absent/Present	220/91	26/3	146/59	48/28	0.062
BMI: Absent/Present	252/57	22/6	173/32	57/19	0.090
BULKY (>5cm): Absent/Present	179/129	29/9	116/87	43/33	0.754
IPI: 0-1/2/3/4-5	139/68/59/43	18/5/5/2	106/48/32/18	15/15/22/23	<0.001
aaIPI: 0/1/2/3	67/62/53/18	7/5/4/2	56/46/37/8	4/11/12/8	0.002

GC: Germinal Center B cell Non-GC: Non-Germinal Center B Cell LDH: Lactate Dehydrogenase BMI: Bone Marrow Involvement at initial diagnosis * Comparison between surviving and dead patients μ Karnofsky performance scale

Table 2: OS and PFS rates in different subgroups

	Median Follow-up Period	OS- 3year (95% CI)	OS- 5year (95% CI)	PFS- 3year (95% CI)	PFS- 5year (95% CI)
GCB Subgroup (n=104)	38 months	0.79 (0.69-0.86)	0.76 (0.69-0.86)	0.70 (0.60-0.78)	0.61 (0.48-0.71)
NON-GC Subgroup (n=86)	31 months	0.64 (0.53-0.74)	0.64 (0.51-0.72)	0.61 (0.49-0.70)	0.61 (0.49-0.70)
Comparison between GCB and NON-GCB Subgroups		p=0.014	p=0.014	p=0.573	p=0.573

Poster No: 00117 Abstract:0088

CLADRIBINE TREATMENT IN HAIRY CELL LEUKEMIA: SINGLE CENTER EXPERIENCE

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Objective: Hairy cell leukemia is a disease that is indolent and B-cell chronic lymphoproliferative. The disease occurs around the age of 52. The disease is four times more common in men. This one is a rare type of leukemia in all leukemia that has a ratio of 2%. Typical hairy cells in the peripheral blood and bone marrow, neutropenia and monositopeni, splenomegaly are usually available at diagnosis. Today, cladribine (2-klorodeoksiadenozin, 2-CdA) and pentostatin are used at first-line treatment.

Materials-Methods: Between 2000 and 2012, 15 patients treated were evaluated retrospectively in our clinic with the diagnosis of hairy cell leukemia. 11 patients (74%) were male and 4 (26%) were female. Median age was 51 (35-66) years. Pancytopenia in 12 patients and bicytopenia in 3 patiens were determined. The 12 patients had splenomegaly (Splenectomy had been performed in 2 patients outside the center) and 3 patients had hepatomegaly. The mean spleen size 18 (9-27) cm. All patients were diagnosed with hairy cell leukemia after examination of the blood, assessment of bone marrow biopsies, peripheral blood and / or bone marrow flow cytometry analysis and tartrate resistant acid phosphatase (TRAP) staining.

Results: All patients were treated with cladribine. Cladribine 0.1 mg / kg / day (for 7 days as a continuous IV infusion) was administered. A relapse developed in 5 of 15 HCL patients (33%), 2 of them after splenectomy, 3 of them(20%) had relapsed after cladribine treatment. 2. cycle cladribin was given to the patients who had relapsed. One patient have been followed without medication due to being asymptomatic. After follow-up cladrabin treatment, the polycythemia emerged in one of our patients. Intermittent, phlebotomy was performed. 14 patient are followed in complete remission. Due to the good general condition and laboratory values, the patient are follewed up without medication. One of our patients could not be reached.

Discussion: Hairy cell leukemia is a slowly progressive disease. Today, cladribine that is purine nucleoside analogue (2-CdA) or pentostatin are used for the first-line treatment. Purine nucleoside analogues and a complete remission rate are approximately 80% to 90. The results of treatment with cladribine in our clinic are same compared with the literature and are quite good. A complete remission were obtained in the ratio of 77% with cladribine treatment in our patient group. Number of patients who had relapsed were 40% in the literature, same as 33% patients had relapsed in our group

Keyword: Hairy cell leukemia, Cladribine

Poster No: 00118 Abstract:0090

CLINICAL FEATURES AND TREATMENT OUTCOMES OF PRIMARY BREAST LYMPHOMA; MULTI-INSTITUTIONAL ANALYSIS OF 63 PATIENTS IN KOREA

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There has been sparse information about primary breast lymphoma (PBL). Recently, several studies suggested some common features: predominant diffuse large B-cell lymphoma (DLBCL) histology, significant risk of central nervous system (CNS) relapse.

The aim of this study is to investigate the clinical features and outcomes of PBL and also to find the factors associated with CNS relapse.

We analyzed the data of 63 patients diagnosed with PBL from 1994 to 2009, who were identified from our nationwide survey. The median age was 45 years (range, 20-73) and all were female. The Ann Arbor stage was I(37, 59%)/II(22, 35%)/III(4, 6%). ECOG performance status was 0 or 1 in 58 patients (92%) and serum LDH level was elevated in 23 (37%).

The most common subtype identified was DLBCL (49, 78%), with the second most common subtype being extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT; 6, 10%). Follicular lymphoma was identified only in one. T-cell lymphoma consisted of peripheral T-cell lymphoma, unspecified (PTCL-U; 4, 6%) and anaplastic large-cell lymphoma (ALCL), anaplastic lymphoma kinase (ALK) positive (1, 2%); ALCL, ALK negative (2, 3%). T-cell lymphoma had significantly more unfavorable characteristics such as presence of B symptom and poor performance status.

The majority of patients (91%) received systemic chemotherapy +/- radiotherapy as a curative treatment. Primary surgical resection +/- axillary node dissection was performed in 29 patients (46%). Five of the 6 patients with MALT lymphoma were only treated with surgical resection.

With a median follow-up of 49.6 months (range, 4.4-186.0), estimated 5-year PFS and OS was 53.1% (95%CI, 45.9-60.3) and 64.8% (95%CI, 57.8-71.8). The PFS and OS of the B-cell lymphoma were significantly better than those of the T-cell lymphoma (PFS, 57.3% vs 17.9%, P=0.007, respectively; OS, 71.3% vs 17.9%, P=0.001, respectively). In multivariate analysis for OS, T-cell phenotype (hazard ratio [HR], 3.41; 95% CI, 1.12-10.31) and low-intermediate/high-intermediate IPI (HR, 3.89; 95% CI, 1.26-12.06) were independent prognostic factors for worse OS.

Twenty-one patients experienced progressive disease following first-line therapy. Of these, 7 experienced CNS relapse, and cumulative incidence of CNS relapse at 3-year was 13.1% (95% CI, 8.5-17.7). In multivariate analysis, serum LDH level was only independent predictor for CNS relapse (HR, 10.31; 95% CI, 1.20-88.65). Interestingly, six patients (10%) received prophylactic intrathecal chemotherapy using methotrexate, and there was no CNS progression in these patients.

DLBCL is the most predominant subtype in agreement with previous series. Distant extranodal failures, especially in the CNS, are a major problem. And, elevated serum LDH level was identified as a risk factor for CNS relapse. Thus, despite the role of CNS prophylaxis are still not clear, it should be considered in PBL patients with elevated serum LDH level.

Keyword: primary Breast Lymphoma, CNS relapse

Poster No: 00119 Abstract:0092

SYSTEMIC CAPILLARY LEAK SYNDROME IN A RELAPSED DIFFUSE B LARGE CELL LYMPHOMA PATIENT

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Systemic capillary leak syndrome (SCLS) a rare clinical entity characterized by plasma extravasation as a result of vascular collapse, generalized edema, hypoalbuminemia. 84-year-old female patient with diffuse large B-cell lymphoma was diagnosed in Ann-Arbor stage IVB RCHOP a total of 6 cycles of chemotherapy. Complete remission was obtained after a total of 6 cycles of chemotherapy. After a year of chemotherapy, the patient was admitted to emergency service due to general condition impairment, respiratory distress, generalized edema and poor oral intake. Physical examination revealed confusion, the skin and under the skin with generalized edema, hypotension (80/40mmhg), Laboratory tests Hb: 8.6 g / dl, WBC: 5990 / mm^3 plt: 151000/mm 3 MCV: 88 cr: 0.96 Total protein: 4.4 g / dl, albumin 2.2 g / dl, spot urine examination and 24-hour urinary protein excretion was not observed. The patient was thought to SCLS. 400mg/kg/gün with IVIG terbutaline, theophylline, and prednisolone was performed. About 15 days, in spite of steroid therapy, the patient's general condition and the lack of widespread subcutaneous edema reduction in whole-body PET CT examination was performed and this examination splenomegaly with splenic FDG uptake (SUVmax 14) was defined as the diagnosis of lymphoma in patients relapsed. Rituximab 375mg/m^2/gün performed. Steroid dose was reduced gradually. After one cycle rituximab, the patient's total protein 5,5 g / dl, albumin 3,2g/dl and Hb:11,2g/dl. Patients with rituximab administered once every 21 days for 6 cycles in total. Whole body PET-CT taken after the treatment, in the spleen normal size and no FDG uptake. Over the 6 months after the last dose of rituximab patients in complete remission are followed.

The majority of patients with SCLS, clinical etiology was not identified. Sepsis, systemic mastocytosis, multiple myeloma hematological malignancies such as lymphoma and multipl myeloma were reported.

As a result, when investigating the etiology of a rare condition in which an existing SCLS should be screened for malignancy especially with history of lymphoma.

Keyword: Non Hodgkin's Lymphoma, systemic Capillary Leak syndrome

Poster No: 00120 Abstract:0111

ERDHEIM-CHESTER DISEASE PRESENTED WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT: CASE REPORT

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Erdheim–Chester disease (ECD) is non-Langerhans form of histiocytosis of unknown origin. It is a systemic and heterogeneous disease mainly involving the bones, lungs, skin, retro-orbital tissues, central nervous system (CNS), pituitary gland, large vessels, kidneys,

retroperitoneum, and heart. The clinical picture may vary from asymptomatic bone lesions to multisystemic and life-threatening forms with poor prognosis, especially in case of specific CNS or cardiovascular involvements. It is mainly diagnosed by typical pathologic features with the biopsy specimen displaying the xanthomatous or xanthogranulomatous infiltration of tissues by CD68+ CD1a- spumous histiocytes, which distinguished from Langerhans cell histiocytosis. Herein, we present a patient with ECD who had intra cerebral tumor-like lesion, which have occasionally been reported.

Case: A previously healthy 35–year-old woman, except visual impairment in left eye due to cataract for last 2 years, presented to the neurology department with complaints of weakness and headache 5 months ago. Headache was throbbing type on temporofrontal region and last in 5 minutes. Any pathological sign was found on physical examination. Cranial magnetic resonance imaging (MRI) revealed a 3x3.5 cm mass on the level of left basal ganglion, which was heterogenic contrasted on central part. Due to edema and mass, 3. Ventricular and the left frontal horn of lateral ventricular were compressed. Dekzamethazon treatment was initiated. The patient was referred to neurosurgery department for biopsy from that mass. The biopsy revealed infiltration of CD 68+ S 100+ CD1a- non-Langerhans histiocytes which were consistent with ECD. The patient was referred to our department. The physical examination of the patient was normal. Although deksamethazon dose was lowered the patient was still receiving it about one month. Laboratory studies revealed an elevated C-reactive protein (>4.4 mg/L) and erythrocyte sedimentation rate (45 mm/ hour), and decreased hemoglobin level (10.1 g/dl) which was compatible with iron deficiency anemia. The other laboratory studies including urea and electrolytes, lipids, urinary studies, liver function and antinuclear antibodies were all within normal limits. Radiologic studies including direct x ray and 99Technetium of long bones, thoracal and abdominal CT and heart echocardiography were normal. Dexamethazon was stopped and 3 million units in 3 days for a week interferon α-2a and oral iron treatments were started. Interferon treatment was well tolerated. There was a marked regression on cranial MRI scan after 3 months. The mass was almost completely disappeared and the impression of the mass and edema were not seen.

Steroids has been the most common medical treatment in this disease. But, in recent years, IFNa has also been reported as very effective therapy in some studies. IFN-a was a very effective treatment in our ECD patient with cranial involvement, which is rarely seen.

Keyword: Erdheim–Chester disease, Interferon α-2a

Poster No: 00121 Abstract:0156

LANGERHANS CELL HISTIOCYTOSIS IN ADULT PATIENTS: SINGLE INSTITUTION EXPERIENCE

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Objective: Langerhans cell histiocytosis (LCH) is characterized by abnormal proliferation of histiocytes. It is rare disease with an incidance of 1 -2/ million. Although it is more frequent in children at 1-3 years old, it can be diagnosed in all ages. Disease can be presented by multifocal or localized organ infiltrations. Although all systems and organs mıght be infiltrated, main sites for disease is bone, especially skeletal bones.

Treatment options differs according to its presentation as local or multifocal. At local disease, only radiotherapy can be effective modality but patients with multifocal disease should be treated with systemic chemothepies or with combination.

Method: At this study, we aimed to retrospectively analyse our adult LCH patients diagnosed between 1992-2012.

Results: Twenty-one patients, 13 male and 8 female, were retrospectively analyzed. Median age was 29(range, 18-53). All of the patients had bone involvement and bone pain has been most prominent complaint according to the involvement site. We documented poliuria and polidipsia in one patient due to hypophysis involvement in addition to bone. 13 (%15 female, %85 male) patients were presented with local disease and 8(%25 male, 75 female) patients had multifocal disease. The characteristics of the patients were given at table 1. The patients with local disease were treated with only radiotherapy and then followed up. The patients with systemic disease were treated with both radiotherapy and chemotherapy. During the treatment period,any grade 3-4 hematological side effects were not documented.

The median period of follow-up was 19 (range, 4-120) months. We determined 7 relapses in 4 patients. All of the relapses were detected with bone lesions and they were treated with radiotherapy successfully. Median overall survival was 19 months. 6 patients were lost to follow up. No deaths were recorded during follow up.

Conclusion: At this retrospective study with relatively limited number of patients, we reported that adult onset LCH patients were mostly presented as a focal disease with bone pain. The radiotherapy was an effective tretatment modality at these patinets. Although, LCH is a rare disease in adult age groups, it should be considered in patients with bone lesions.

Keyword: langerhans cell, histiocytosis

Table 1: Characteristics of the patients

Sex	
female (%)	8 (38)
male (%)	13 (62
Age (median, range)	29(18-53)
Presentation of the patient	
Localized (%) (male/female)	13 (62) (11/2)
Multifocal (%) (male/female)	8 (38) (2/6)
İnvolved organs	
bone	21
lung	2
external audotory canal	1
hypopysis	2
cranial nevre involvement	1
Mucosal involvement	1
İnvolved bone	
cranial bones	13
Tibia	1
Acetabulum – femur	6
Vertebra	2
costa	1
Humerus	1
clavicula	1

Poster No: 00122 Abstract:0159

SURVIVAL OF DLBCL PATIENTS TREATED WITH R-CHOP

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Aim: In this study we aimed to search R-CHOP treatment responses and event free survival (EFS) of patients with DLBCL. We also aimed to compare our results with literature, and to explain the reasons of differences.

Method: Total 130 patients were investigated. The study was performed retrospectively. Treatment responses were compared according to disease stage and event free survival was analyzed. Non responders, partial response, progression of disease, relapse of disease and death in treatment were considered as event. Survival analyses were calculated by Kaplan Meier's method. Differences in survival between prognostic groups were evaluated in univariate analysis by log-rank test. The differences of treatment responses were evaluated by Chi-square method and p value <0.05 was considered statistically significant.

Results: The mean age was found 58.48 years and 52.46 years for females and males respectively. The basic characteristics of patients are shown in table 1. The patients were followed minimum 1.23 month and maximum 190.53 months after treatment. Complete response (CR), partial response (PR), non-responder and death were found 70.8%; 5.4%; 12.3% and 11.5% respectively. Relapsed disease (RD) is evaluated in 22.3% of patients. In the stages I, II, III and IV the CR rate is observed 82.7% (43), 94.45 % (17), 64.7% (22) and 38.5 % (10) respectively. The EFS was found significant between disease stages, IPI scores, age and B symptoms (p=0.000) (Figure). The median EFS are shown in table 2.

Discussion: Near the same response rates are found in GELA study with RCHOP treatment (76%, 7%, 9%, 1%, 10% and 10% for CR, PR, Progressive disease, Stable disease, RD and death, respectively). On the other hand Pfreundschuh M et al. found 86% CR rates in their study which was higher than our result. However in this study the mean age was 47 years and all patients had low IPI scores unlike our study.

We found similar CR rates as RICOVER 60 study. In this study investigators showed significant survival times patients with normal serum LDH level, early stage, age <60 years and low IPI score.

Conclusion: Stage, IPI score, age and B symptoms are still maintaining their importance effect on treatment response and EFS in DLBCL. Patients who have advanced stage and high IPI scores should be followed carefully at diagnosis.

Keyword: DLBCL, event free survival

Figure 1

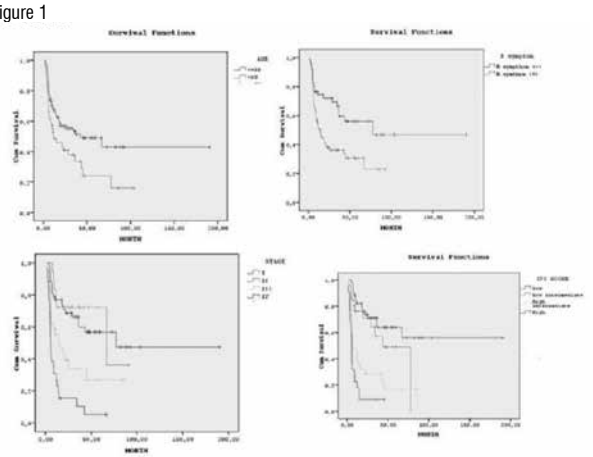

Table 1. Basic characteristics of patients

	n	%
Age <=60	81	62,3
Age >60	49	37,1
Stage		
I	52	40,0
II	18	13,8
III	34	26,2
IV	26	20,0
IPI		
0	23	17,7
1	28	21,5
2	26	20,0
3	31	23,8
4	21	16,2
5	1	,8
B symptom		
Negative	51	39,2
Positive	79	60,8
Extranodal involvement		
E positive	66	50,8
E negative	64	49,2
LDH		
Normal	45	34,6
High	85	65,4

Table 2. Median Suvival

	Median Survival (Month)
Age	
<=60	44,71
>60	11,40
Stage	
I	76,4
II	69,69
III	15,95
IV	5,57
IPI	
Low	186
Low-intermediate	46,46
High-intermediate	8.50
High	4,71
B symptom	
Negative	76,11
Positive	13,37
LDH	
Normal	69,00
High	14,44

Poster No: 00123 Abstract:0167

PRIMARY EFFUSION LYMPHOMA IN AN ELDERLY, HIV & EBV NEGATIVE PATIENT: CASE REPORT

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Introduction: Primary effusion lymphoma(PEL) is a HHV8 associated lymphoproliferative disease characterized by effusions in body cavities,lack of tumor mass,and is commonly seen in HIV and EBV(+),AIDS patients[1]. PEL can also occur in the absence of AIDS,particularly in elderly patients,mostly from areas with high endemic HHV8 infection such as Mediterranean region[2].Here we present a case of EBV and HIV(-),HHV8(+) PEL patient.

Case: A 79 year-old male patient was presented with dyspnea,bilateral ankle edema,and abdominal distension. He had decreased breathing and heart sounds,ascites. The serology for HIV,HBV,and HCV was negative.The PCR analysis of the serum for HSV1 and HSV2, EBV DNA was also negative.

Cytologic evaluation of ascites and pleural fluid showed large atypical cells with dark blue cytoplasm,prominent nucleoli,without forming cohesive clusters,macrophages and neutrophils (Figure1).The H&E sections revealed large atypical lymphocytes some with plasmacytoid morphology.IHC performed on the cell block showed that the large atypical cells were positive HHV-8,CD138,MUM-1,CD38 and negative for CD20,CD79a,Pax5,EMA,Alk-1,kappa,lambda,T cell markers (CD3,CD5,CD43,CD4,CD 8,CD7),CD30,calretinin,and cytokeratin. In situ hybridization for EBV-encoded RNA was negative. The flow cytometric analysis of the pleural fluid revealed seventy percent of the viable cells were brightly positive for CD38 and CD138,dimly positive for CD45,negative for CD3,CD2 ,CD5,CD4,CD8,CD34,CD10,CD11c,CD23,HLA-DR,CD117 ,CD33,CD13,CD57,CD64,CD25,CD56,CD24,CD16,CD15, CD58,glycophorin A,CD61,CD14,CD19,CD20,CD22,surfa ce and cytoplasmic kappa and lambda proteins.The PCR of the pleural fluid was EBV-DNA(-) and HHV8 DNA(+).

HHV8(+) EBV(-) PEL was diagnosed. HHV8 replication,especially important in the induction and maintenance of KS,PEL and MCD,is reduced by oral valganciclvir[3].The patient started on oral valganciclovir 450mg twice daily as he was not suitable for cytotoxic chemotherapy. At the 1st week of the treatment,the blood HHV8 DNA was 16.013 eq-gen/ml(4.20log) and decreased to 3.754 eq-gen/ml(3.57log) at the 4th week by RT-PCR.

Discussion: PEL can occur in the absence of AIDS, mostly from areas with high endemic HHV8 infection such as Mediterranean region[2].The survival varies from 1 week to 5 years. However,it is obvious that the prognosis is poor and the disease responds poorly to chemotherapy. PEL should be in the differential diagnosis of the anasarca type edema especially in the elderly immune suppressed population.

Keyword: Primary effusion lymphoma, HIV (-) EBV(-) HHV8(+)

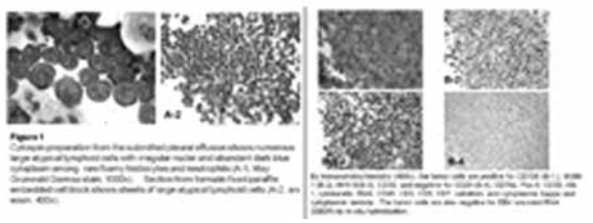

Figure 1

Poster No: 00124 Abstract:0174

ZIDOVUDINE-BASED LYTIC-INDUCING CHEMOTHERAPY FOR EPSTEIN-BARR VIRUS-RELATED LYMPHOMAS

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Treatment of Epstein Barr virus (EBV)-related lymphomas with lytic-inducing agents is an attractive targeted approach for eliminating virus infected tumor cells. Zidovudine (AZT) is an excellent substrate for EBV-thymidine kinase; can induce EBV lytic gene expression and apoptosis in primary EBV+ lymphoma cell lines. We hypothesized that the combination of AZT with lytic-inducing chemotherapy agents would be effective in treating EBV+ lymphomas. We report a retrospective analysis of 9 patients with various subtypes of aggressive EBV+ non-Hodgkin's lymphoma treated with AZT-based chemotherapy.

Ten patients with aggressive EBV+ NHL subtypes were treated with first-line methotrexate (MTX) (3.0-4.5 g/m^2 IV on day 1) and AZT 1.5 g IV q12 hours (days 2-5) every 3 weeks or upon recovery of blood counts at the discretion of the physician. This regimen was used alone or alternated with dose adjusted EPOCH (DA-EPOCH) or hyper-CVAD chemotherapy. Four patients had PBL, 3 had BL, 1 had DLBCL, and one had a solid PEL variant. Of 8 patients who were HIV+, 6 had a CD4 cell count of less than 200/μL at the time of lymphoma diagnosis. Seven patients had stage IV disease. Two patients received radiotherapy in addition to chemotherapy. Seven of 9 patients (78%) achieved a CR, and 2 patients (22%) had refractory disease. During a median follow-up period of 47.3 months (range 1.3-95.2), 3-year OS and PFS were 77.8% (95% CI: 54.8% - 100.0%) and 67.5% (95% CI, 43.0%-100.0%). The regimen was highly tolerable with only 2 patients (20%) experiencing grade 3-4 adverse events including mucositis and neutropenic fever.

AZT-based combination approaches could add efficacy to standard lymphoma chemotherapy and improve the treatment of γ-herpesvirus related lymphomas.

Keyword: non-Hodgkin lymphoma, EBV

Poster No: 00125 Abstract:0180

PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: A CASE REPORT

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Objective and Introduction: Primary central nervous system lymphoma (CNS) is a very rare hematologic malignity that belongs to the group of non-Hodgkin Lymphoma (NHL). It represents 1% of all the lymphomas and is of B lymphocyte origin. It is more commonly observed with immune disorders. Here we present a case of primary CNS lymphoma in a patient with a healthy immune system

Case: A 67-year-old female patient presented with complaints of speech disorder and inability to walk. Cranial magnetic resonance (MR) investigation requested for diagnostic purposes detected a lesion that is 41 x 23 x 30 mm in size in lateral adjacency to the frontal horn in the left frontal lobe. Stereotactic brain biopsy revealed the presence of diffuse large B-cell NHL. The patient, who had normal ophthalmologic examination results, and negative anti-HIV and hepatitis test results was diagnosed with primary CNS lymphoma. The whole-body PET/CT detected no pathologic-size lymph nodes. Bone marrow aspiration and biopsy showed a normocellular bone marrow. Cranial MR showed no leptomeningeal involvement. After receiving radiotherapy for 11 days as performed at the radiation oncology unit, we administered her the De Angelis protocol. This protocol included the following: methotrexate (MTX) 2000 mg once weekly at the 1st, 3rd, 5th, 7th and the 9th weeks; folinic acid 4 x40 mg administered for 3 days after MTX; vincristine 2 mg once weekly at the 1st, 3rd, 5th, 7th and the 9th weeks and dexamethasone started at a dose of 16 mg at the 1st week and continued by weekly 2-mg dose reductions. Meanwhile, MTX 12 mg was administered via intrathecal route at the 2nd, 4th, 6th, 8th and 10th weeks. Radiotheraopy was administered between the 11th and 15th weeks followed by 3000 mg/m^2 cytosine arabinoside 2x1 at the 16th and 19th weeks. The 41x23x30-mm lesion revealed by the cranial MR taken at the time of diagnosis was observed to regress to 17 x 10 x 11 mm in size at the control cranial MR following the DeAngelis protocol and also motor aphasia and muscle weakness that were present at the time of diagnosis completely returned to normal. The whole-body PET/CT performed after the treatment revealed normal results.

Discussion: It's interesting that lymphoma of the brain occurs when the brain doesn't have a lymphatic system. Lymphoma in the CNS may manifest as the spread of the systemic lymphoma or primarily. While the most common site of involvement is the brain in the primary CNS lymphoma, the meninges, eyes and the spinal cord may also be affected. In our case, lymphoma was detected primarily in the brain, left frontal lobe. The patient developed no complications during treatment. The control PET/CT was normal; the patient is under follow-up without receiving any treatment. We present this patient as a case of CNS lymphoma with a normal immune system, who experienced a regression in the marked neurologic complaints with treatment, in order to contribute to the literature.

Keyword: central nervous system lymphoma, primary

Poster No: 00126 Abstract:0183

CONCOMITANT FOLLICULAR LYMPHOMA IN A CASE OF SMALL-CELL LUNG CANCER

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Introduction and Objective: Small-cell lung cancer represents 15-25% of all the lung cancers. Since dieresis time is very high, the tumor grows very rapidly; and this condition is considered as a systemic disease since it exhibits distant organ metastasis in the early period. Here we present a patient, who was receiving treatment for small-cell lung cancer and was referred to our department upon developing pancytopenia following treatment and was detected to have follicular lymphoma at the investigations performed for the etiology of the pancytopenia.

Case: A 57-year-old female patient has been diagnosed with small-cell lung cancer a year ago and received 10 days of thoracal radiotherapy following four courses of carboplatin +etoposide chemotherapy and two courses of Campto chemotherapy. Upon failure to achieve improvement in pancytopenia, the patient was referred to our department for further hematologic investigation. The hemogram revealed the following: leukocytes: 900, hemoglobin 8gr/dl and platelets:16.000; the peripheral smear revealed anisocytosis, marked leukopenia, normochromic normocytic erythrocytes and a platelet count of 15.000-20.000. The patient underwent bone marrow aspiration and biopsy. Aspiration revealed a hypocellular bone marrow. Biopsy showed no findings of small-cell lung cancer metastasis by cytokeratin staining, however the case was observed to have CD20, PAX5, bcl-2 positive cluster-type lymphoid cells.Based on these findings, the bone marrow biopsy result was reported as follicular lymphoma bone marrow involvement by the pathology department. The tomographies performed revealed multiple intra-abdominal thoracal lymph nodes. Since the patient had last-stage small-cell lung cancer, she refused treatment and was discharged without any treatment prescribed.

Discussion: Pancytopenia may be related to various reasons including infections, auto-immune diseases, chemotherapy, radiotherapy, solid tumors, hematologic malignity, chronic liver diseases, hypersplenism, aplastic anemia, storage diseases and megaloblastic anemia. In this patient with small-cell lung cancer, chemotherapy-radiotherapy history, bone marrow involvement due to medication or disease were primarily considered in case of pancytopenia. Upon failure to achieve improvement in pancytopenia following chemotherapy and radiotherapy, the patient was referred to our department and the investigational bone marrow biopsy revealed follicular lymphoma bone marrow involvement and no cancer metastasis was detected. There are no reports on association of small-cell lung cancer and follicular lymphoma in the literature. We present this patient since such association is very rare.

Keyword: follicular lymphoma, small cell lung cancer

Poster No: 00127 Abstract:0191

DO BCL-6 AND CD138 EXPRESSIONS CORRELATE WITH PROLIFERATIVE CAPACITY IN DIFFUSE LARGE B CELL LYMPHOMA?

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Objective: Diffuse large B cell lymphoma is a heterogeneous disease and can be cathegorized into prognostically significant subgroups as germinal center B-cell-like, and activated B-cell-like, by using immunohistochemical panels. One of these panels include CD10, bcl6, MUM1, and CD138 expression patterns for subdividing diffuse large B cell lymphoma. CD138 expression alone is accepted as an independent poor prognostic factor, whereas bcl-6 expression is associated with a better outcome. Since high Ki67 index is associated with increased growth fraction and correlates well with poor prognostic factors in majority of human cancers, we aimed to assess the correlation of CD138 or bcl-6 immunoreactivities and Ki67 index in our diffuse large B cell lymphoma case series.

Methods: Twenty nodal and 22 extranodal de novo diffuse large B cell lymphoma cases were included in the study. Study group was consisted of 26 male and 16 female patients with a mean age of 54.6 ±22.3 (range 8-95). None of the patients had a known history of HIV infection. Pathological diagnosis of all cases were confirmed by an experienced pathologist based on recent WHO classification. Tissue sections were cut from tissue macroarray blocks of formallin fixed, paraffin embedded pretreatment tumor samples. Ki67 index was determined as positive stained cell percentages using monoclonal MIB1 antibody. For CD138 and bcl-6 expressions, immunoreactivity in >10% of lymphoma cells were defined as positive. Mann Whitney U test was used to compare the difference of Ki67 indices and continious variables between positive and negative staining groups. Chi square tests were used to analyze cathegorized variables.

Results: Out of 42 DLBCL samples, 29 (69.0%) were defined as positive and 13 (31%) were defined as negative for bcl-6 staining. Ki67 indices varied in a wide range between 45% and 95%. Mean Ki67 indices of bcl-6 positive cases were slightly lower than the mean Ki67 indices of bcl-6 negative cases, however, the difference was not statistically significant (p=0.19). The distributions of patient demographics between bcl-6 positive and negative cases were similar. Bcl-6 expression frequency was slightly more common in extranodal disease (77.3%, n=17 vs 60.0, n=12) but did not reach the significancy level (p>0.05). All cases were defined as negative for CD138 expression in our study group. Therefore we could not analyze its association with proliferative capacity of lymphoma cells.

Conclusion: Although it has been implied as a poor prognostic marker, our results revealed that CD 138 expression is not common in DLBCL. Therefore, its utility in recognizing patients to have a more aggressive disease, is limited. In contrast, Bcl-6 expression is observed in majority of the cases, however, we did not find a significant difference in proliferative capacity of the lymphoma cells with regard to bcl-6 immunostaining, which suggests its inability to discriminate a prognostic subgroup alone.

Keyword: Lymphoma, immunohistochemistry

Poster No: 00128 Abstract:0195

PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN IMMUNOCOMPETENT INDIVIDUALS: A SINGLE CENTER EXPERIENCE

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Introduction: Primary central nervous system lymphoma (PCNSL) is defined as the involvement of brain, leptomeninges, cerebrospinal fluid, eyes or spinal cord by non-Hodgkin lymphoma without evidence of a systemic lymphoma. After the introduction of highly active antiretroviral therapy into clinical practice and close monitorization with heightened awareness in immunosuppressed individuals, the incidence of PCNSL decreased substantially in these patients. Today, the frequency of PCNSL is much higher in immunocompetent individuals. Whether the disease has a different course in immunocompetent patients is still unclear. The role of various immunophenotypic markers in predicting adverse outcome for this particular group is debated.

Objectives: To investigate the clinical and immunohistochemical findings of immunocompetent PCNSL cases diagnosed at the study center, and evaluate the influence of potential prognostic factors on overall survival (OS) of patients.

Methods: All consecutive cases diagnosed with PCNSL between 1997 and 2012, at Cerrahpasa Medical School, were investigated and only the patients who were immunocompetent at the time of diagnosis were enrolled in this study. Data regarding clinical features and follow-up were obtained from patient records. The strength of the association between OS time and potential prognostic variables was investigated by Kaplan-Meier OS curve and log-rank test. A Cox proportional hazards model was developed to investigate the relationship between five prognostic variables, which had been shown to have an impact on survival in different studies, and OS.

Results: 39 cases were included in the study. Mean age at diagnosis was 51.8 years with a male/female ratio of 1.17/1 (21:18). The majority of the cases presented with headache (n=12), paresthesias/hemiparesis (n=9),

seizures (n=6), and signs of raised intracranial pressure (n=5). Parietal lobe was the most commonly involved site (11/39), followed by temporal lobe (8/39), frontal lobe (7/39), and cerebellum (4/39). Multifocal involvement was evident in 23% of the cases (9/39). 33 cases (%84.6) belonged to non-germinal center subtype. All of the patients had a high Ki-67 index, ranging from 80 to 100% (mean, 93.5%). EBV was positive in 2 cases only. Median follow-up and survival times were 16 and 18 months, respectively. In univariate analysis, patients who received combined chemotherapy and radiotherapy had a significantly better OS when compared to chemotherapy alone (p<0.001)(Table 1). On multivariate analysis, combined therapy was found to be an independent factor affecting the OS (HR=0.088, 95% CI=0.028–0.277)(Table 2).

Conclusion: Combined therapy was superior to chemotherapy alone, but none of the immunophenotypic markers had a statistically significant influence on OS of patients with PCNSL. Prospective studies with large patient series are needed to elucidate prognostic factors, as well as optimum treatment regimens.

Keyword: primary central nervous system lymphoma, immunocompetent

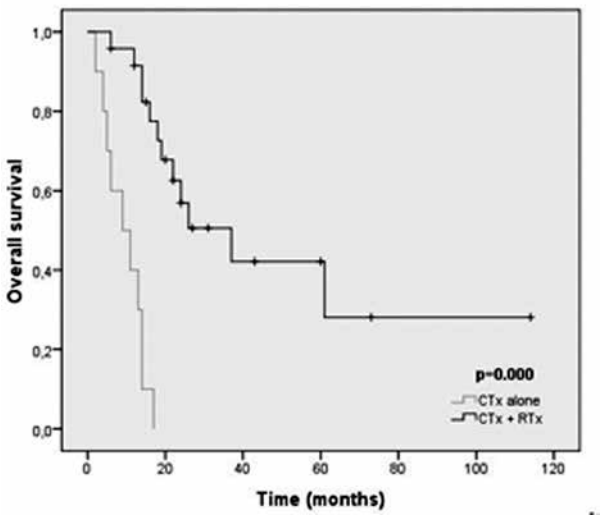

Figure 1. Kaplan-Meier overall survival curve of patients with primary central nervous system lymphoma. Patients who received combined chemotherapy and radiotherapy had significantly better overall survival when compared to those who received chemotherapy alone (p<0.001). Two-year survival rate for patients who received combined therapy was 33% while all patients who received single therapy were dead of disease at 17 months follow-up.

Table 1. Univariate Analysis for Various Clinicopathologic Variables (Log-Rank test)

Prognostic Factor	*No (%)*	*Median survival (months)*	*p-value*
Age >= 60 years < 60 years	8 (22.8) 27 (77.2)	16 18	0.940
Gender Male Female	18 (51.4) 17 (48.6)	14 22	0.170
Multifocal involvement Yes No	9 (25.7) 26 (74.3)	14 19	0.503
Deep-site involvement Present Absent	11 (31.4) 24 (68.6)	19 18	0.383
Bcl-2 Positive Negative	15 (42.8) 20 (58.2)	17 19	0.835
Bcl-6 Positive Negative	15 (42.8) 20 (58.2)	14 18	0.107
CD10 Positive Negative	6 (17.1) 29 (82.9)	19 17	0.494
MUM1 Positive Negative	27 (77.1) 8 (23.9)	17 19	0.856
EBV Positive Negative	2 (5.7) 33 (94.3)	6 19	0.131
GC status GC phenotype NGC phenotype	6 (17.1) 29 (82.9)	19 17	0.494
Treatment CTx alone CTx + RTx	10 (29.4) 24 (70.6)	9 37	0.000

GC, germinal center; NGC, non-germinal center; CTx, chemotherapy; RTx, radiotherapy

Table 2. Mulitvariate Cox regression analysis for prognostic factors

Prognostic Factor	HR (% 95 CI)	p-value
Age >= 60 years	1.376 (0.509–3.715)	0.529
Multifocal involvement	0.566 (0.168–1.916)	0.361
Deep-site involvement	0.464 (0.141–1.523)	0.206
Bcl-6 positivity	1.567 (0.620–3.958)	0.342
Combined therapy	0.088 (0.028–0.277)	0.000

HR, hazard ratio; CI, confidence interval

Poster No: 00129 Abstract:0199

CORRELATION OF MICROVESSEL DENSITY AND TUMOR CELL KINETIC PARAMETERS IN DIFFUSE LARGE B CELL LYMPHOMA

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Objectives: Increased proliferation and apoptosis are shown to be correlated with aggressive behavior in majority of the human cancers including diffuse large B cell lymphoma. Tumor microenvironment plays a critical role in the development and progression of the disease and modifies survival and proliferative capacity of the malignant cells partly by regulation of angiogenic processes. In this study we aimed to evaluate the correlation of microvessel density (MVD) and tumor cell kinetic parameters in diffuse large B cell lymphoma.

Methods: Pretreatment tumor samples of 42 diffuse large B cell lymphoma cases (20 nodal and 22 extranodal) were included in the study. MVD score was semiquantitatively assessed as low and high after immunostaining with CD31 antibody. Proliferative indices were assessed by using monoclonal MIB1 antibody. Apoptotic cells were labelled by the terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) technique. Positive stained cell percentages were used for apoptotic and Ki67 indices. The associations between MVD

score and Ki67 or apoptotic indices were analysed by Spearman's correlation test.

Results: In 27 (64.3%) cases, MVD scores were defined as high, and in 15 (35.7%) cases MVD scores were defined as low. Ki67 indices varied in a wide range between different DLBCL samples (range 45% - 95%). We observed a significant correlation between MVD and Ki67 index ($r=0.312$; $p<0.04$). However, there was no statistically significant correlation between apoptotic index and MVD. There was no correlation between MVD and clinical parameters such as age, localization, or gender.

Conclusion: The prognostic value of increased MVD has been shown in various tumors. However, the data about its value in DLBCL is limited. We found a positive correlation between MVD and proliferative capacity of the tumor cells, which suggests the utility of vascularization as a prognostic marker for this heterogeneous disease group. We were also interested in the associations of MVD and apoptotic index, however, our study did not show a significant correlation between them. In addition, the apototic indices were low in all cases, which revealed that irrespective of the clinicopathological features, anti-apoptotic mechanisms play a major role in DLBCL pathogenesis. Although mean MVD scores were slightly higher in patients with young ages, or in extranodal disease, the differences did not reach the significancy level. Our results did not show any significant correlation between MVD and other clinical parameters.

Keyword: Lymphoma, Microvessel Density

Poster No: 00130 Abstract:0200

MULTIPLE AXILLARY LYMPH NODE INVOLVEMENT BY LYMPHOMATOID GRANULOMATOSIS IN A YOUNG PATIENT: A CASE REPORT

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Background: Lymphomatoid granulomatosis is a rare clonal B cell proliferative disorder of extranodal sites with a prominent reactive T cell component. Although it is a lymphoid disorder, most comon sites of involvement are lung, central nervous system, and skin, whereas lymph node and spleen involvement is exceptional. Histologically it is characterized by angiocentric and angiodestructive lymphoid infiltrates admixed with mononuclear inflammatory cells and scattered large B cells. We report an unusual case of lymphomatoid granulomatosis presented with multiple lymphadenomegalies and lung nodules.

Case: A 28-year-old Turkish man was admitted to a regional hospital for complaints of fever, cough, night sweats, and fatigue. He was referred to our hospital after his chest X-ray showed multiple pulmonary nodules at initial evaluation. Physical examination revealed bilateral axillary lymphadenomegalies, hepatosplenomegaly and a subcutaneous nodule at anterior wall of the chest. Thoracal CT scan demonstrated diffuse pulmonary parenchymal nodules that vary in size, and also mediastinal and axillary lymphadenomegalies reaching up to 2 cm in diameter. With the suspicion of a high grade lymphoma, a diagnostic lymphadenectomy was performed from axillary region.

Histopathologic examination showed a partial effacement of the lymph node architecture by sheets of large atypical cells admixed with large pleomorphic cells. At high power, numerous large transformed lymphoid cells and scattered pleomorphic Hodgkin-like cells were seen in a background of small lymphocytes and immunoblasts. CD20 immunostaining revealed diffuse cytoplasmic membranous expression in Hodgkin-like cells and large transformed cells.

Discussion: LYG is an unusual extranodal angiocentric/angiodestructive lymphoproliferative disease primarily affecting the lung. Histopathologic features are distinctive; scattered large atypical EBV-positive B cells in a background of reactive T cells, plasma cells and histiocytes. The term 'lymphomatoid granulomatosis' reflects its broad clinicopathological spectrum range from granulomatous inflammation and vasculitis to malignant lymphoma. Despite its name, granulomatous inflammation is mostly limited to skin lesions and it is infrequent in other sites.

Histologic grading can be assigned according to the number of large atypical cells including Hodgkin-like cells. Grade I lesions contain a few (0-5/high power field) EBV-positive large cells and consist of an angiocentric lymphoid proliferation. Grade II lesions contain 5-20 large cells per high power field. In grade III lesions EBV-positive large cells may form sheets and necrosis is prominent.

Awareness of this rare lymphoproliferative disease will permit its recognition and avoid mistreatment of LYG patients.

Keyword: Lymphoma, lymphomatoid granulomatosis

Poster No: 00131 Abstract:0201

PRIMARY GASTRIC LYMPHOMAS: INTEROBSERVER AGREEMENT BETWEEN PATHOLOGISTS

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Introduction: Primary gastric lymphoma (PGL) is a rare tumor that constitutes 1-5% of all gastric malignancies. Presenting symtoms of the patients are usually non-specific and B-type symptoms including palpable mass and gastrointestinal bleeding are seen only in minority of the cases. Considerably low diagnostic rate of barium-contrast studies and various non-specific endoscopic patterns make biopsy the most important tool in diagnosis of PGL. Due to the progressive increase in the incidence of PGL during last decades and improvement of diagnostic endoscopy in optics, pathologists encounter this tumor much more than they did. PGL is a treatable cancer in a high percentage of cases, thus, pathologists should be able to diagnose this tumor accurately from gastric biopsy specimens.

Objective: Detecting the discrepancies and concordance between gastropathologist, hematopathologist and general pathologist in the diagnosis of primary gastric lymphomas.

Materials-Methods: 47 patients were diagnosed as PGL at Cerrahpasa Faculty of Medicine between 2000-2008. Hematoxylin-eosin stained slides of these patients were retrieved and two gastropathologists, one hematopathologist and one general pathologist evaluated the

parameters including tumoral infiltration pattern, infiltration area, infiltrative cell type, Russel and Dutcher cell bodies, lymphoepithelial lesion, intraepithelial lymphocyte amount, reactive lymhoid follicles and follicular colonization without knowing anything about the immunohistochemical results. Spearman correlation coefficient was used to evaluate agreement between pathologists. rs value between 0-0.3 was accepted as no agreement, 0.3-0.5 as weak, 0.51-0.74 as intermediate,0.75-1 as strong agreement.

Results: Concordance between pathologists for all parameters are summarized in the table. Overall, there was a weak concordance for tumoral infiltration pattern, but for diffuse large B cell lymphoma alone, concordance could not be detected at all. There was a strong agreement for glandular localization, but it was not observed for other localizations including foveola, muscularis mucosa and submucosa. Additionally, there was a weak accordance for monocytoid cells, intermediate accordance was seen in large cells, no accordance was detected for transformed cells and centrocytes. Pathologists did not make a strong agreement for Dutcher and Russel bodies. A weak concordance was shown in lymphoepithelial lesion. Intraepithelial lymphocytes, reactive lymphoid follicles and follicular colonization did not have a significantly high level of agreement between pathologists.

Conclusion: Since the immunophenotyping is not a specific tool in the diagnosis of PGL, morphologic evaluation has a critical importance in the diagnostic process. Our study highlighted the level of concordance and discrepancies in the evaluation of diagnostic parameters between pathologists.

Keyword: primary gastric lymphoma, pathologist

Tablo 1. Interobserver agreement between pathologists for different morphological variables (Spearman Correlation test)

	r value, MALT lymphoma (n=18)	*r value, DLBCL (n=21)*	*r value, all cases (n=43)*
Tumoral infiltration pattern	0.42	0.02	0.34
Tumor localization	-*	-*	Foveolar: 0.19, Muscularis m: 0.28 Submucosal:0.28 Glandular: 0.89
Monocytoid cells	-*	0.19	0.49
Large cells	-*	0.42	0.71
Transformed cells	-*	0.01	0.12
Centrocytes	-*	0.27	0.29
Dutcher bodies	0.1	0.14	0.16
Russell bodies	0.35	0.24	0.40
Lymphoepithelial lesion	0.07	0.34	-*
Intraepithelial lymphocyte count	0.39	0.05	0.17
Presence of reactive lymphoid follicles	0.45	0.33	0.28
Presence of follicular colonization	-*	-*	0.11

* Spearman correlation test could not be performed because more than one observer had the same answers for all specimens.

Poster No: 00132 Abstract:0214

AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME: AN ORPHAN DISEASE

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Introduction: Lymphadenopathy (LAP) is a very common presenting symptom observed in different infectious and neoplastic diseases of childhood. However, it can be a challenging diagnostic dilemma in children when the underlying etiology is not obvious. Autoimmune lymphoproliferative syndrome (ALPS) is a non-neoplastic disease characterized by widespread LAP, hypergammaglobulinemia, lymphocytosis, and splenomegaly. Increased CD4-/CD8- (double negative) T cell population is a characteristic and diagnostic finding in ALPS. Herein, we present a case with ALPS who had been erroneously diagnosed and treated as peripheral T cell lymphoma.

Case: 22-month-old male patient admitted to clinic with fever and widespread LAP. He had a history of recurrent upper respiratory tract infections (tonsillitis, otitis media) since he was 2 month old. Cervical and inguinal LAP were excised and evaluated as reactive hyperplasia in lymph nodes. Immunodeficiency syndromes were taken into differential diagnosis and laboratory evaluation revealed positive direct Coombs test. Thorax CT showed multiple thoracic and supraclavicular LAP and repeated biopsy, taken from supraclavicular lymph node, revealed diagnosis of “peripheral T cell lymphoma-unspecified”. Bone marrow biopsy and peripheral blood smear were normal. 10 months after the initial presentation, he was internalized with diffuse LAP and hepatosplenomegaly. He was regarded as stage 3 moderate risk non-Hodgkin lymphoma and TRALL-BFM 2000 chemotherapy protocol was initiated. After completion of a 24-month chemotherapy cycle, he received 12.66 Gy prophylactic whole brain radiation therapy. One year after the completion of therapy, multiple LAP at supra- and infradiaphragmatic areas were evident. Excisional biopsy of supraclavicular lymph node revealed diffuse paracortical expansion and “starry-sky” appearance with infiltration by CD3+ CD4/CD8 double negative T cells. The initial lymph node specimens were reviewed and the similar ALPS morphology was observed. CD3+CD4-CD8- (double negative) T cell count was found to 37.2% in peripheral blood with flow cytometry and 1 mg/kg/day (15 mg) prednisolone therapy was given. LAP regressed with treatment. Then prednisolone was replaced with sirolimus, and he is now on sirolimus treatment for 1.5 year period with clinical and hematological remission. The mother gave birth to a new female baby and she developed hepatosplenomegaly with pancytopenia when she was 3 month old. Flow cytometric analysis of the sister was compatible with ALPS with a double negative T cell count of 21%.

Discussion: ALPS should be thought in differential diagnosis of LAP of unknown etiology especially when it first becomes apparent after birth. ALPS might be

confused with T cell lymphomas microscopically, thus it should be excluded before making the diagnosis of lymphoma in pediatric age group.

Keyword: ALPS, NHL

Poster No: 00133 Abstract:0218

HAIRY CELL LEUKEMIA PRESENTING WITH ISOLATED SKELETAL INVOLVEMENT SUCCESSFULLY TREATED BY RADIATION THERAPY AND CLADRIBINE: REPORT OF A CASE

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Hairy cell leukemia (HCL) characterized by infiltration of peripheral blood, bone marrow (BM) and spleen by 'hairy cells' represents 2% of leukemias. Skeletal involvement resulting in lytic or mixed lytic/blastic lesions in HCL is rare, with frequencies ranging from 0% to 13%.

A 55-year-old male was admitted with 3-month history of severe pain in right femur extending to his right leg. On physical examination, there was no lymphadenopathy or organomegaly. Blood count was as follows: haemoglobin:13 g/dl, WBC: 6030/mm³ and platelet:267000/mm³. Biochemical tests showed increased ESR (50 mm/h) and hypergammaglobulinemia; LDH was normal. Anteroposterior radiographs of both femurs revealed mixed lytic-sclerotic lesions and lytic destructive process with eccentric localization and narrow zone of transition at diaphysis of left femur extending to left subtrochanteric region. On MRI scan, multiple hypointense metastatic bone lesions on T1-weighted coronal imaging and hyperintense metastatic lesions on T2-weighted coronal imaging dominantly located in both femoral heads, necks and trochanters with largest of diameter 2 cm were present. Abdominal MRI revealed 1 cm wide heterogeneous metastatic lesion at left side of posterior L2 and L3 vertebrae corpus on T1-weighted axial imaging. Histopathological examination of biopsy from right femoral lesion showed diffuse neoplastic infiltration consisting of cells with round, oval, regular nuclei and medium-sized, clear cytoplasm. Neoplastic cells expressed CD20, LCA, CD79 alpha, TRAP, CD11c, CD68 and annexin. Diagnosed with HCL, patient was referred to our hematology department. Blood smear showed 54% neutrophils, 40% lymphocytes and 6% monocytes. Lymphocytes appeared normal. Bilateral BM aspirates revealed normal bone marrow elements with no hairy cells. Flow cytometry of BM aspirates revealed no abnormal clone of lymphoid cells or aberrant antigen expression. Bilateral BM trephine biopsies showed normocellular BM. On PET scan, there was increased FDG uptake in axial skeleton, sacrum, pelvis and bilateral femurs (Figure 1a). Patient underwent radiotherapy to bilateral proximal femur at a dose of 20 Gy and obtained complete clinical response with resolution of pain. Four weeks after completion of radiotherapy, 7-day course of 0.1 mg/kg/day cladribine was administered. Follow-up PET scan performed 8 weeks after chemotherapy showed marked metabolic response with decrease in uptake of multiple metastatic lesions on bilateral proximal humerus, right lamina of C6 vertebrae and bilateral first ribs (Figure 1b). Repeat PET scan 12 months after chemotherapy showed normal recovery of skeletal disease, with no evidence of residual enhancement. There is no disease recurrence 14 months after chemotherapy.

Skeletal involvement is infrequent in HCL and almost associated with extensive involvement of BM. Isolated skeletal involvements with no BM involvement or splenomegaly as in our case is a rarely reported entity.

Keyword: Hairy cell leukemia, skeletal involvement

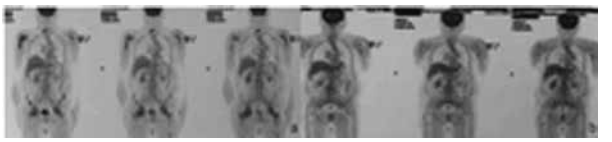

Figure 1. a. On PET scan, there was increased FDG uptake on lateral sides of right 2nd and 3rd ribs, posterior sides of right 9th and 10th ribs, lateral sides of left 2nd, 5th, 6th and 7th ribs, corpus sterni, corpus of D1, D5, D6, L1 and L2 vertebrae, processus spinosus of D12, L3 and L4 vertebrae, right pedicle of C6 and D11 vertebrae, both femoral head, neck and diaphyseal regions, sacrum and pelvic bones. b. Follow-up PET scan showed marked metabolic response with decrease in uptake of multiple metastatic lesions on bilateral proximal humerus, right lamina of C6 vertebrae and bilateral first ribs

Poster No: 00134 Abstract:0220

A CASE OF SIMULTANEOUSLY OCCURRING DIFFUSE LARGE B CELL LYMPHOMA AND SQUAMOUS CELL LUNG CANCER

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Diffuse large B-cell lymphoma (DLBCL) and squamous cell lung cancer (SCLC) has been rarely seen together at the same time. Due to the common planned treatment for SCLC and DLBCL, this case, in which both malignities has been seen simultaneously, is found appropriate to the presentation. Sixty two years old man who followed with the diagnosis of chronic obstructive lung disease was admitted with a diameter of 4 cm left axillary lymphadenopathy (LAP). According to our investigations, opacity with a diameter of 45 mm in his right lung parahilar has been monitored in his chest X-ray. Then chest computerized tomography (CT) has been performed and multiple lymphadenopathy in the left axilla with the largest 39x27 mm, mediastinal multiple LAP with the largest 20x11 mm, 44x35 mm mass in the parahilar side of the right upper lobe, three nodules in the lower lobe of the right lung with the largest 13 mm, two nodules in the lower lobe of left lung with the largest 8 mm were observed. In addition, 45x47 mm (SUV max 9.3) nodule in the upper lobe of the right lung, 3 nodules in the lower lobe of the right lung with the largest 25x16 mm (SUV max 9.3), 37x32,5x22 mm (SUV max: 22) LAP in the left axilla were detected in the PET-CT. According

to tru-cut biopsy to axillary LAP, DLBCL was diagnosed with CD20+, CD79a+, CD5-, CD3 - diffuse cell infiltration. CT-guided biopsy was performed of lesion of lung parenchyma. Squamous cell carcinoma was diagnosed with keratin5+, keratin14+, P63+ malignant epithelial tumor. Treatment of patient has been decided with pneumologists. Rituximab, carboplatin, paclitaxel-containing chemotherapy was planned collectively. Treatment of patient is ongoing.

Keyword: Diffuse large B-cell lymphoma, squamous cell lung cancer

Poster No: 00135 Abstract:0225

A LGL CASE DEVELOPING LONG TERM AFTER ALLOGRAF REJECTION

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The chronic use of immunosuppressive agents in solid organ transplantation increases the long-term risk of malignancy. This reports describes a T-cell Large Granulocytic Leukemia (LGL) case developed following chronic renal allograft rejection. Case: 48 year-old male patient who had been diagnosed with chronic renal failure 21 years before. He had received dialysis for 9 years and then had a renal transplantation. At the end of the first year of the transplant chronic rejection had occurred. He receieved 1U/week eritrocyte transfusion for a year since he had a erythropoetin unresponsive anemia. He has been a dialysis since last five years. At the last 6 months the patient re-developed erythropoetin unresponsive anemia and a need for transfusion. In the physical exam skin was urochromic with pale conjunctiva and mucosas, liver and spleen are palpable under 3 cm of costal margin and a left radial aneurysmatic fistula. Hb 6.7 gr/dl, WBC: 3630 U/L, MCV: 80, platelets:149000 U/L and reticulocyte was <%1. Ferritine: 1890 ng/ml and B12: 281. In abdominal USG liver was 160 and spleen was 154 mm. Bone marrow was normocellular with a noticeable decrease in erithyroid prpgenitor cells and with lymphocyte cell percentage was 28% and these cells have prominent granular cytoplasma. In flow-cytometric analysis CD3: 90%, CD4: 6%, CD8: 82% and CD20 was 3%. T-clonality was positive. With these findings the patient was diagnosed with T-LGL.

T- cell LGL is a heterogeneous disorder characterized by a persistent (>6 months) increase in the number of peripheral blood large granular lymphocytes, without a clearly identified cause. In most cases the clinical course is indolent. There is frequently severe neutropenia with or without anemia. Severe anemia due to red cell aplasia has also been reported in association with T-LGL. Moderate splenomegaly is the main physical finding. The etiology of T- cell LGL has not been entirely elucidated, but chronic antigenic stimulation with exogenous antigens or putative endogenous autoantigens may be responsible for inducing the activation and clonal expansion of effector CD8+ LGL. In chronic allograft injury of renal transplantation, there is evidence to show that CD4 + and CD8 + T cells play roles. The proposed mechanism of malignancy developing in the post transplantation period is usually immunosuppression. T-cell stimulation following transplantation may also contribute to the post-transplant malignancy development.

Keyword: LGL, renal transplantation

Poster No: 00136 Abstract:0226

BONE MARROW INVOLVEMENT OF A PATIENTS WITH ANAPLASTIC LARGE CELL LYMPHOMA; MORPHOLOGIC AND IMMUNOPHENOTYPIC FEATURES

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Anaplastic large cell lymphoma (ALCL), which is a T cell lymphoma type, usually presents with nodal involvement. Leukemic from is extremely rare. In spite of well known CD30 positivity which is usually detected with immunohistochemistry, there is scary literature about immunophenotypig which is performed with flow cytometry. We herein report the morphologic and immunophenotyping features of a case of ALCL presented with a leukemic relapse.

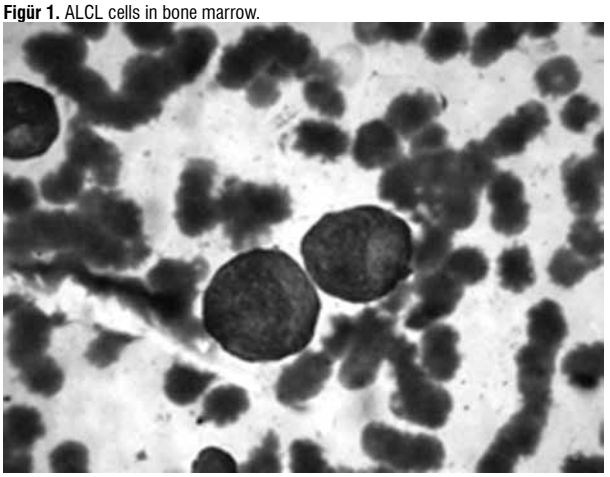
A 16 year-old girl who admitted to our hospital with suddenly appeared high fever, sore throat, and mild cervical lyphadenomegaly. The patient was originally diagnosed with ALK-positive ALCL of the cervical lymph node. Bone marrow biopsy was negative at that time. She was treated with CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone) chemotherapy for eight cycles and had a remission confirmed with PET-CT. Relapse appeared two months after end of the chemotherapy.

After admission, the health condition of the patient did get worse in a few days. Anemia, thrombocytopenia and leucocytosis characterized with appearance of increased atypical mononuclear cells in peripheral blood appeared and she had generalized edema with severe hypoalbunemia. We performed bone marrow aspiration and biopsy. Bone marrow aspirate smears demonstrated 55% atypical, highly pleomorphic cells (Fig 1A and 1B)). A majority of those cells were intermediate to large in size, with light to dark blue cytoplasm often with numerous azurophilic granules. It was difficult to discriminate them from myeloid or monocytic blasts without immunophenotypig. Immunophenotyping of by flow cytometry showed CD2 -, CD3-, CD4-, CD5-, CD7+, CD8+, CD10-CD19 -, CD34 - (Fig 2).

As a result, we demonstrated morphologic and immunophenotypic features of ALCL in bone marrow.

Keyword: anaplastic large cell lymphoma, immunophenotype

Figür 1. ALCL cells in bone marrow.



Poster No: 00137 Abstract:0230

LOSS OF CD20 ANTIGEN EXPRESSION AFTER RITUXIMAB THERAPY OF CD20 POSITIVE B-CELL LOW-GRADE NON HODGKIN LYMPHOMA

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Background: Rituximab is a key molecular targeting drug for CD20 positive B-cell lymphomas. Recently, resistance to Rituxumab has been recognised to be a considerable problem in re-treatment patients.The mechanism of resistance to Rituximab retreatment in non-responding patients is unknown, but it is possible that loss of CD20 expression in the relapsed NHL could be important in some cases.

Aims: Here we present a patient with CD20 positive low grade B-cell NHL that lost the CD20 expression at relapse after Rituxumab therapy.

Case presentation: A 39-year-old female was admitted at our hospital with a diagnosis of Non-Hodgkin lymphoma (CLL/SLL). Immunohystochemical analysis on diagnostic samples of the axilar lymph node biopsy showed CD20 positive expression with proliferative centres positive for Ki67 that responds to pseudofolicular variant. The patient was treated according to R-CVP protocol (Rituxumab 375mg/m² on day 1, Vincristine 2 mg on day 2, Cyclophosphamide 400mg/m² and Prednisolon 50mg daily on days 2-6, every 28 days, eight courses). Maintenance therapy with Rituxumab was continued on three months intervals. At ten months from initial therapy conclusion, a relapse of the lymphoma was found. The second-line therapy according to R-CHOP protocol was started (Rituxumab 375mg/m² on day 1, Vincristine 2 mg, Cyclophosphamide 750mg/m², Doxorubicin 50mg/m² on day 2 and Prednisolon 100mg daily on days 2-6). Partial remission was achieved after 8 cycles of therapy that lasted one year when further recurrence of the lymphoma occurred consisting of lymph nodes enlargement and WBC 94000/mm³. The patient was then treated with 6 new cycles of chemo-immunotherapy according to FCR protocol (Rituxumab 375mg/m² on day 1 and Fludarabine 25mg/m² and Cyclophosphamide 250mg/m² on days 2-4). The achieved partial response lasted 4 months when new lymph node enlargement and leucocytosis of up to 220000/mm³ occurred. Flow cytometric analysis of peripheral blood demonstrated loss of CD20 expression on malignant lymphocytes, while CD19 and CD5 were positive in 80% cells. Father therapy with high-dose Methyl-prednisolon was started.

Conclusions: Our observation confirmed the hypothesis already described in literature, that a CD20 negative phenotypic change could occur in certain number of patients with CD20 positive B-cell lymphomas. As such, CD20 expression by both flow cytometry or immunochisochemistry should be undertaken to document CD20 expression prior to considering repeated courses of Rituxumab in relapsed Non-Hodgkin lymphomas.

Keyword: Non Hodgkin lymphoma, CD20 antigen

Poster No: 00138 Abstract:0235

HUMAN IMMUNODEFICIENCY VIRUS (HIV)-NEGATIVE AND HUMAN HERPES VIRUS-8 (HHV-8)-POSITIVE PRIMARY EFFUSION LYMPHOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

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Primary effusion lymphoma (PEL) is a rare type of non-Hodgkin lymphoma that presents with serosal effusion in body cavities, without obvious tumor masses. Although PEL occurs in immunocompromised patients that are human immunodeficiency virus (HIV) positive, it also occurs in immunocompetent human herpes virus-8 (HHV-8)-positive patients. Herein we present an immunocompetent, HIV-negative, CD-20-negative, HHV-8-positive patient with pleural effusion that was diagnosed as PEL. The CHOP protocol and talc pleurodesis were administered. HHV-8 plays a causative role in PEL and is important for differentiating PEL from other types of lymphoma. As such, in addition to pleurodesis antiviral treatment should be considered for optimal treatment outcome.

Keyword: Human herpes virus-8, Primary effusion lymphoma

Poster No: 00139 Abstract:0236

PRESENTATION: CASTLEMAN DISEASE WITH POLYMYOSITIS

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Introduction: Castleman Disease or Angiofollicular Lymph Hyperplasia is a rare illness that can occur clinically in an unicentric or localized form with an isolated enlargement of the lymph nodes (often located in

mediastinum) or in a multicentric form as a systemic disease with generalized lymphadenopathy and organomegaly. It occurs histologically in three forms: hyaline vascular, plasma-cellular and transitional (mixed) form. This case-report presents a patient with a multicentric appearance of the disease, histologically plasma-cellular form including polymyositis.

Case: The patient, 71 years old, was admitted in May 2010 with fever, sweating, loss of body weight, pain, weakness in the muscles, and generalized lymphadenopathy (large lymph nodes in the neck and in both axillas and individual lymph nodes in the groins). A CT scan showed a slightly enlarged liver,the hilum and retroperitoneal lymph nodes were up to 20mm in size and an enlarged spleen of up to 18cm. He did not have enlarged mediastinal lymph nodes. The lab findings showed he had SE 90, a moderate immune hemolytic anemia (+direct Coombs test) HGB 115 g / L, thrombocytopenia 76x10/9/L, total protein 137g / L, albumin 25 g / L, an increase of polyclonal IgG 52.4 g / L, preserved global renal function, CRP 52, HBsAg, HCV, HIV negative. Biopsy of the neck lymph nodes and histopathological findings indicate that it was a case of plasmacytoid form of the M. Castleman, ruling out lymphoproliferative disease. According to the clinical apperance it is a case of multicentric Castleman disease.Immunological tests showed the existence of a systemic connective tissue disease, most likely type Polymyositis, ANA (IgG) +homogeneous 1:160, ANA-HEp2 (IgG) 1:320 cytoplasm + nucleoplasm + diffuse 1:160, ANA Jo (IgG) + 62, 5U/ml, EMG Findings: grade I polyneuropathy. We introduced a corticosteroids-based therapy (1mg/kg). After seven days we noticed a disappearance of the general symptoms and after three weeks a regression of lymphadenopathy and hepato-splenomegaly, as well as a normalization of hemoglobine and platelet count. After five weeks there was a correction of SE, a normalization of albumin levels and the therapy showed no further increase of polyclonal IgG. The patient then maintained a successful recovery under a 20 mg Prednison therapy and was regularly monitored by hematologists and immunologists.

Conclusion: a further monitoring of the disease will show us whether this is a case of Castleman's disease as a primary or secondary phenomenon

Keyword: Castleman, Polymyositis

Poster No: 00140 Abstract:0238

NON-HODGKIN'S LYMPHOMA: IS 1G/M2 METHOTREXATE AS EFFECTIVE AS 5 G/M2 IN ADVANCED STAGE NONLYMPHOBLASTIC NON-HODGKIN LYMPHOMA?

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Background: Survival rates in non-Hodgkin's lymphoma (NHL) have increased significantly in the last decades.

Objectives. This study aims to assess the demographic data and treatment results of children with non-lymphoblastic NHL treated in a single institution.

Methods: 106 children (74 male, 32 female), treated in Istanbul University, Oncology Institute, between 9/1989-12/2012 were evaluated retrospectively.

Results: The median age was 8(2-19) years. Histopathologic subtypes: 81 Burkitt and Burkitt like, 25 large cell. The primary location was abdomen in 51, mediastinum 4, head/neck 31, 20 other (bone 8, breast 2, ovaries 2, skin 2, paravertebral 2, other 4). Bone marrow was involved in 10, CNS in 2. Forty patients had stage I+II, 44 stage III, and 22 had stage IV disease. Until 1991, nonlymphoblastic NHL received COMP. After then, all received BFM protocols. Non-lymphoblastic NHL patients received BFM protocols with 5 g/m^2 methotrexate (MTX) until 1995 and 1 g/m^2 MTX thereafter. 23 patients died, 7 due to toxicity. Ten year survival and event-free-survival in the whole group was 76 and 76 % respectively. Ten year survival was 100, 94.3, 71.3 and 50% in stage I, II, III, and IV. Considering only advanced stage non-lymphoblastic NHL patients, 10 year survival was significantly higher in patients receiving BFM regimen with 1 g/m^2 MTX, than in ones receiving COMP or BFM protocol with 5 g/m^2 MTX (10 year survival 81%, 46.7%, 44.4% respectively). Burkitt type patients had also significantly higher 10-yr survival with 1 gr/m^2 MTX than 5 gr/m^2 or COMP treatment (78.5%, 41.7% and 40%). When deaths due to toxicity are excluded from the analysis, 10-yr survival is significantly higher in 1 gr/m^2 than 5 gr/m^2 and COMP treatment (88%, 51.3% and 50.9% respectively).

Conclusions: Survival rates in the whole group are in parallel with advances attained in the world in NHL. The significantly higher survival rates achieved in patients with advanced stage non-lymphoblastic patients receiving modified BFM (1g/m^2MTX) may be due to the decreased toxicity seen in this group and to the advances in supportive care in the last decade. In another major center in the same university that uses the same protocol with 5 g/m^2 MTX in the same time period, similar survival rates suggest that 1 g/m^2 MTX which is cheaper and less toxic is also as effective as 5 gr/m^2 in these patients.

Keyword: Non-Hodgkin Lymphoma; Burkitt Lymphoma; Methotrexate; Advanced stage

Poster No: 00141 Abstract:0244

PRIMARY OVARIAL NHL IN ELDERLY FEMALE - A CASE REPORT

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Considering lack of primary lymphoid tissue in the ovary, ovarial lymphoma is a rare event.This location of the lymphoma participates with 0,5% of total NHLs and 1,5% of total ovarial neoplasia.Predominant subtype of the ovarial lymphoma is DBCL,occuring in the younger females,usually aged 35-45.In the population of elderly females, follicular lymphomas and SLL are more frequent. Usual clinical presentation includes palpable abdominal mass with abdominal pain. B symptoms are present in 10-33% cases.Bilateral ovarial involvement has been reported in 36-71%

Female patient aged 74 was hospitalized in January 2010 with abdominal pain and B symptoms (sweating and loss of 25 kgs body weight in six months). Personal history included fivefold ACBy pass four years before, Diabetes mellitus, two labors, menopause in the age of 50.

Physical examination revealed paleness, without either peripheral lymphadenopathy or palpable abdominal

organomegaly, but with a palpable tumor mass in the lower pelvis, 10 cm in diameter. ECOG PS 3.

Laboratory data included mild anaemia (Hb 109 g/L), normal total and differential leucocyte count, mild thrombocytosis (477 x 10^9/L), positive inflammatory syndrome (ESR 56/h, CRP 18 mg/L, ferritine 891 ug/L, borderly elevated LDH – 452 U/L). Abdominal CT scan revealed a tumor mass sized 11x10 cm in the lower pelvis, involving right ovary and spreading towards the uterus, small and large intestine, right kidney with the signs of the first degree stasis. Other analyses were within the normal range, thoracal CT and bone marrow histology without pathological features.

Abdominal surgery was performed in March 2010 and revealed tumor mass involving the right ovary and spreading to the external uterus wall, small and large intestine. Operative performance included: Hysterectomia totalis cum adnexectomiam bill et hemicolectomiam l dex cum ileocoloanastomisis termino-terminalis. Histopathological diagnosis: NHL DBCL of the anaplastic type, with Ki 67 positive in > 90% cells. Clinical staging classified the patient as IV cl stage, with IPI – 5(high risk).

After the surgery,patient received chemotherapy according to the R-CHOP regime, total eight cycles resulting with the complete remission.

28 months after the completion of the chemotherapy, complete remission persists.

Primary ovarial NHL shares the same therapeutical modality as well as the prognosis with other NHLs.

Keyword: ovarial lymphoma

Poster No: 00142 Abstract:0256

99MTC-HYNIC-RITUXIMAB: A PROMISING MOLECULAR IMAGING AGENT IN NON-HODGKIN´S LYMPHOMAS

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Background: Anti-CD20 (Rituximab®), a chimeric monoclonal antibody directed against B lymphocites surface CD20 antigen is a major therapeutic agent in CD20+ non-Hodgkin´s lymphomas (NHL).

Objectives: Labeling 99mTc -Rituximab through bifunctional chelant agent Suc-HYNIC. Evaluate this as a potential imaging agent in NHL.

Methodology: Rituximab was derivatized through Suc-HYNIC and labeled with 99mTc using Tricine/ SnCl2.2H2O. Radiochemical purity was determined by ITLC-SG and HPLC. In vitro stability was evaluated in solution and serum up to 24 h. Specificity of binding was performed in Raji cells. Biodistribution was evaluated in BALB/c normal mice at 4 and 24 h (n = 5).

Results: HYNIC-rituximab was easily separated from free HYNIC with >=90% recovery of the initial antibody. Efficacy of 99mTc-HYNIC-Rituximab binding was > 90 %. Radiochemical purity was >90% in solution and serum, remaining stable after incubation at 37º during 24 h. Specificity of 99mTc-HYNIC-rituximab binding to CD20 antigen was demonstrated, as shown in Fig.1. Biodistribution of the conjugate is similar to that of labeled antibodies, remaining stable in vivo with a low uptake in thyroid and stomach, as shown in fig 2.

Conclusion: 99mTc-HYNIC-rituximab represents a promising molecular imaging agent in NHL. Experiments in tumoral models will be the next step in our research.

Acknowledgements: Roche, Pro.In.Bio.

Keyword: Rituximab, 99mTc

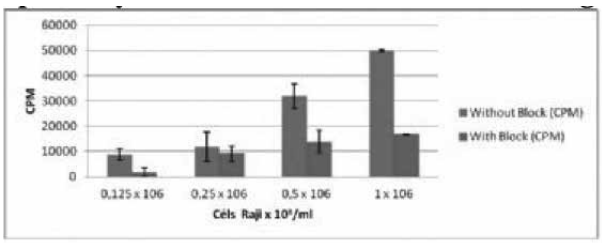

Figure 1.Specificity of 99mTc-HYNIC-rituximab binding to CD20 antigen

Table 1. Biodistribution

Tissue	*1h*	*4h*	*24h*
Blood	18,35 ± 0,33	16,61 ± 1,78	10,65 ± 1,94
Liver	5,35 ± 3,85	7,37 ± 1,09	9,37 ± 3,00
Heart	3,11 ± 1,03	6,93 ± 0,77	4,89 ± 1,35
Lungs	3,61 ± 1,81	6,38 ± 0,99	4,78 ± 1,61
Spleen	1,78 ± 0,54	4,89 ± 0,78	3,92 ± 1,91
Kidneys	3,04 ± 1,56	6,22 ± 1,33	4,73 ± 1,55
Thyroid	0,95 ± 0,57	0,93 ± 1,10	0,21 ± 1,01
Muscles	0,47 ± 0,23	1,30 ± 0,37	0,69 ± 0,33
Bone	0,92 ± 0,42	1,55 ± 0,44	1,14 ± 0,46
Stomach	0,22 ± 0,43	0,74 ± 0,70	0,70 ± 0,46
Gastrointestinal	1,26 ± 0,70	6,89 ± 2,92	3,94 ± 0,53

Percentage of dose injected/g (%DI)/g)*

Table 2. Biodistribution2

Tissue	1h	4h	24h
Guts	2,70 ± 0,92	12,22 ± 4,05	7,30 ± 1,95
Bladder+Urine	3,02 ± 0,16	14,08 ± 3,32	23,63 ± 2,21

Percentage of dose injected (%DI)*

Poster No: 00143 Abstract:0260

A RARE CASE OF LYMPHOMATOID GRANULOMATOSIS PRESENTED WITH AUTOIMMUNE HEMOLYTIC ANEMIA

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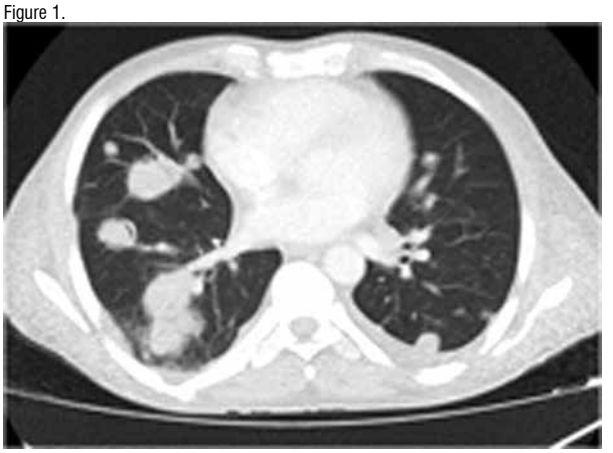
Introduction: Lymphomatoid granulomatosis (LYG) is a rare angiocentric and angiodestructive lymphoproliferative disease involving extranodal sites. It is an EBV-driven disease and pulmonary involvement occurs in over 90% of patients. Patients frequently present with symptoms related to respiratory tract. Here, we report a patient diagnosed as LYG 1,5 years after the presenting symptom of autoimmune hemolytic anemia.

Case: A 47 years old male admitted to our hospital with a fatigue. At this admission, laboratory tests were as: WBC: 5960 /mm^3, Hb: 8.5 gr/dL, MCV: 97.1, Plt: 177.000 /mm^3, LDH: 320 U/L, and few small pulmonary nodules were seen on posterior-anterior chest X-ray. On thoraco-abdominopelvic computed tomography (CT), multiple hypodense nodular pulmonary parenchymal lesions (largest one is 3x2.5 cm) were seen, and the longitudinal length of liver was 17.5 cm, spleen's was 13.5 cm. Wedge biopsy of the pulmonary nodule was performed and reported as "coagulation necrosis continued with lung parenchyma". RF, ANA, dsDNA, p-ANCA and c-ANCA, anti-CCP, HBsAg, anti-HCV, anti-HIV were (-). After 1.5 months of the biopsy, Hb level fell to 4,9 gr/dL and the patient was consulted to our hematology department. During this period, direct coombs (+) immune hemolytic anemia was determined with IgG type warm antibodies. 1 mg/kg/day methyl prednisolone was prescribed, but anemia did not respond to this treatment. Three months later, splenectomy was performed and reported as extramedullary hematopoiesis. After splenectomy, symptomatic anemia continued with Hb levels between 4.5 – 5.5 gr/dl. Whereupon, azatiopurin was prescribed and Hb levels were around 7 gr/dL. After 5 months of azatiopurin treatment, B symptoms and multiple lympadenopathies were developed and on thoraco-abdominopelvic CT; multiple conglomerated cervical, axillary, mediastinal, abdominopelvic lympadenopathies, multifocal solid lesions in liver and lungs were seen (Picture). Anti-CMV-IgG, anti-toxoplasma-IgG were (+) and monospot heterophile antibody test was (-). Excisional cervical lymph node biopsy was performed and reported as "lymphomatoid granulomatosis, grade III". The patient died due to sepsis a few days after the biopsy.

Discussion: The most common underlying diseases of secondary autoimmune hemolytic anemia are lymphoproliferative disorders and immune diseases. LYG is a rare EBV-driven lymphoproliferative disorder and as in our patient, immune hemolytic anemia was the presenting symptom of the disease. The patients with immune hemolytic anemia without any etiologies at the time of diagnosis should be followed for the possible underlying diseases, especially for the lymphomas.

Keyword: lymphomatoid granulomatosis, immune hemolytic anemia

Figure 1.



Poster No: 00144 Abstract:0262

HISTIOCYTIC SARCOMA ASSOCIATED WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a rare, potentially life-threatining disease. HLH most often affects infants, but cases in adults also have been reported. Primary HLH denotes the presence of an underlying genetic disorder and secondary HLH denotes presence of the HLH phenomenon occurring secondary to another condition like viral illnesses, autoimmune diseases, and lymphomas. The diagnosis of HLH is depends to the following criteria: 1. fever, 2. splenomegaly, 3. cytopenia in at least two cell lines, 4. tissue demonstration of hemophagocytosis, 5. hypertriglyceridemia and/or hypofibrinogenemia, 6. hepatitis, 7. low or absent natural killer cell activity, 8. Serum ferritin level >500 µg/L, 9. soluble CD25 (sIL-2 receptor) >2400 U/mL. Here, we report a case of HLH secondary to histiocytic sarcoma (HS).

Case: A 62 years old male admitted to our hospital with a multiple cervical masses. On physical examination: fever: 38.3ºC, blood pressure: 100/75 mmHg, there were multiple cervical conglomerated lympadenopathies and splenomegaly. Laboratory tests were as: WBC: 980 / mm^3, neut.: 430 /mm^3, Hb: 10 gr/dL, Plt: 18000 /mm^3, LDH: 2301 U/L, AST: 178 U/L, ALT: 25 U/L, ferritin: 1124 µg/L, triglycerides: 237 mg/dL, fibrinogen: 99 mg/dL. Low natural killer cell activity was determined by flow cytometry. HBsAg, anti-HCV, anti-HIV were (-). On bone marrow examination, a hypercellular bone marrow with histiocytes phagocytizing platelets and normoblasts were seen (picture). Excisional cervical lymph node biopsy performed and reported as "histiocytic sarcoma". Consequently, the patient was diagnosed as HLH secondary to HS. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy was started, but the patient died at 4th day of treatment because of respiratory failure and sepsis.

Discussion: HLH is a potentially fatal disorder due to cytokine dysfunction, resulting in uncontrolled accumulation of activated T-lymphocytes and activated histiocytes in many organs. HLH may be primary or secondary

to a number of different infections, autoimmune disorders, or coincident with a number of malignancies. HLH should be suspected in those with fever, splenomegaly, cytopenias, elevated triglyceride and ferritin levels, and hemophagocytosis demonstrated in bone marrow, spleen, or lymph nodes. Treatment should be initiated immediately with the HLH-2004 protocol when the patient fulfills the clinical criteria for HLH, since delay of therapy may lead to irreversible multi-organ failure. On the other hand, HS is an extremely rare non-Langerhans histiocyte disorder of unknown cause. Cytopenias are seen in approximately one-third of HS cases, a minority of which will demonstrate hemophagocytosis on bone marrow biopsy as in our patient. There is no standardized therapy for HS. CHOP like regimens can be used for multisystem disease.

Keyword: Hemophagocytic lymphohistiocytosis, histiocytic sarcoma

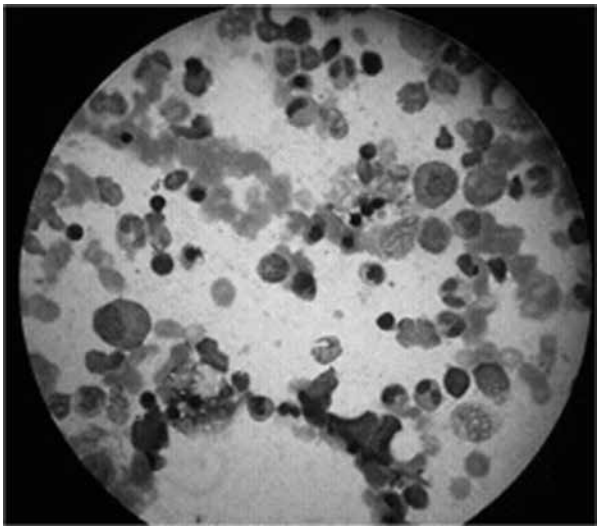

Figure 1. Histiocytes phagocytizing platelets and normoblasts on bone marrow.

Poster No: 00145 Abstract:0263

WE REPORT ON PRIMER MEDIASTINAL B CELL LYMPHOMA WITH ELEVATED SERUM LEVEL OF BETA HCG

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Primary mediastinal B cell lymphoma (PMBL), first recognized in the 1980s, has been accepted as a distinct subtype of diffüse large B cell lymphoma in the World Health Organisation classification. It represents approximately %2-3 of all non-hodgin lymphoma cases. It is mostly seen in female patients and presents with a bulky anterior mediastinal tumor. Twent-year-old female patient was admitted to our hospital with cough, sore throat, fatigue, fever, significant weight loss and a mediastinal bulky tumor. She was diagnosed as as primary mediastinal B cell lymphoma with the biopsy of anterior mediastinal mass.Because the patient was at child-beaing age she was evaluated with serum beta-hCG level before R-CHOP chemotherapy. The result was 12.53 mIU/mL (normal range 0-5 mIU/ml) and after that the pregnancy has been exluded with ultrasonographic screening and gynecological examinations. Other etiological factors of beta-hCG elevation were investigated and the etiological factor could not be detected. After the chemotherapy, serum level of beta- hCG was repeated as normal serum b-hcg levels with the reduction of the mass (beta-hCG:<0.1 mIU/mL). Patient achieved full remission after 6 cycles of R-CHOP chemotherapy and beta-hCG values were within normal limits at that time. In reviewing the literature; the case which Fraternal-Orciani G et al had been reported also showed high beta-hCG levels in the patological specimens by immunochemistry. On top of that elevation of serum beta-hCG at the time of diagnosis and decrease in the level after treatment, we thought elevated levels of beta-hCG may be disaese related in our case. As a result, elevated levels of b-hcg may be rarely seen in female PMBCL patients at the child bearing age. Therefore this case is presented for the aim of contribite the literature.

Keyword: Primary mediastinal B cell lymphoma, serum beta-hCG level

Poster No: 00146 Abstract:0266

CLINICAL FEATURES AND TREATMENT OF SPLENIC MARGINAL ZONE LYMPHOMA

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Aim: Splenic marginal zone lymphoma (SMZL) is a rare B-cell malignancy, with no standard treatment other than splenectomy. The aim of this retrospective single-center study was to evaluate the clinical characteristics and prognosis of SMZL.

Patients: Between 2008 and 2013, we analyzed a total of 36 patients being considered as appropriate diagnostic criteria for SMZL in our hematology clinic. Among them only 21 individuals who had at least 3 months follow-up period were included. There were 13 (62%) female and 8 (38%) male patients. Median age was 58.8 years (range, 37-88 years). The median time of follow-up was 19.3 months (range, 3-97.7 months).

Results: We retrospectively assessed 21 patients from single center, who received splenectomy, either alone or with chemotherapy. The presence of splenomegaly (95.2%) was recorded as the most frequent symptom at diagnosis. Of the patients, 18 (85.7%) had bone marrow involvement and 6 (28.6%) had lymph nodes involvement. Tumor involvement of peripheral blood defined as the presence of absolute lymphocytosis or 5% of tumor lymphocytes in peripheral blood was detected in 5 patients (23.8%). Because of the high frequency of bone marrow involvement, most patients in the series were Ann Arbor stage IV. Data concerning the presence of hypogammaglobulinemia was obtained from only 9 patients (42.9%).Obviously, 20 patients underwent splenectomy. In 7 patients (33.3%) chemotherapy was received apart from splenectomy (Table-1).The number of patients reaching clinical complete remission after splenectomy with/out therapy was 18 (85.7%) and partial remission 3(14.3%). The probability of 5 year-overall survival was 87.5%±11.7%. When we analyzed the patients with

splenectomy alone the probability of overall survival was 83.3%±15.2%.

Conclusion: In conclusion, although the options of new treatment modality in SMZL have been debated today, splenectomy seems to be safe and effective in controlling long-term disease.

Keyword: splenic marginal zone lymphoma, splenectomy

Table 1. Patients's characteristics and clinical outcome

Gender (M/F) (n)	8/13
Median age (years (range))	58.8 (37-88)
Haemoglobin concentration (g/dl)	10.6±1.9
Platelet count (x109/L)	147.1±67.9
Leucocyte count (x109/L)	7.6±4.4
Lymphocyte count (x109/L)	3.6±4.0
Lactate dehydrogenase(UI/L)	412.2±170.2
Albumin (g/dl)	3.4±0.7
Hypogammaglobulinemia(n)	9
Therapy received Splenectomy only(n)	13
Splenectomy + chemotherapy(n)	7
CHOP	1
R-CHOP	2
Rituximab alone	1
Fludarabine alone	2
R-Fludarabine	1
Chemotherapy only (n) Rituximab alone	1

Poster No: 00147 Abstract:0270

EXTRANODAL NK CELL LYMPHOMA NASAL TYPE

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Extranodal NK/T cell lymphoma (ENKL), nasal type is a rare type of non-Hodgkin's lymphoma originating in the nasal cavity or in the paranasal sinuses (1,2). Rarely, other sites of the upper aerodigestive tract (e.g. nasopharynx, palate), the skin, the gastrointestinal tract or the testis may be involved (1,2). Tissue biopsies often contain necrotic material making precise diagnosis difficult; thus excisional biopsy is usually required for correct diagnosis (3).

A 35 year–old male was admitted to the Department of Infectious Diseases due to an infected palatal ulceration of about 11/2 months. He was consulted with Haematology Department for bicytopenia that appeared after initiation of antibiotherapy. Recurrent punch biopsies from velum revealed fungal infection which did not responded to antifungal therapy. On examination there was a deep ulcerated-necrotic lesion from right velum to nasal cavity (Figure 1). Systemic examination was unremarkable. Chest radiography and electrocardiography were normal.

Blood chemical analysis was normal except elevated liver function tests, high ESR (99 mm/hr) and CRP (5.1 mg/dl. His Hb was 8.6 g/dl, WBC was 3,58/mm^3. Platelet counts were within normal limits. Blood smear showed no abnormality. Proteinuria was also noted. Negative results for ANA,Anti-ds DNA, ANCA, RF, c-ANCA,p-ANCA ruled out Wegener's granulomatosis and vasculitis. Rheumatologic parameters were negative Recurrent cultures taken from the lesion were reported as a fungal infection.

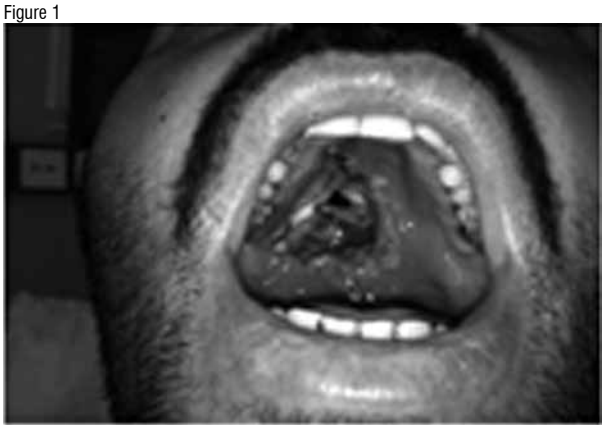
Immunoglobulins levels excluded immunodeficiency. Negative microbiological findings ruled out infectious nature of the lesion. VDRL, TPHA tests were found negative. Cranial CT was normal, paranasal sinus CT showed obliteration in right osteomeatal complex and a soft tissue mass which causes filling completely the right maxillary sinus and partially both of the ethmoids and left maxillary sinus. Repeat biopsy from the ulcerated-necrotic showed inflammatory granulation, vascular proliferation and active chronic inflammation. Tuberculosis tested via PCR and acid-fast staining bacilli was negative on tissue biopsy. Bone marrow biopsy obtained due to bicytopenia was reported to be normocellular without atypical infiltration.

To prevent necrosis deep debridement was advised. Morphological and immunophenotypic findings of the excisional biopsy revealed ENKL. Oncological PET-CT showed high- dense FDG staining in the nasal cavity around the velum, on right tonsillar part, and in cervical lymph nodes. High-dose chemotherapy with autologous hematopoietic stem cell transplantation was planned but the patient died on the seventh day of the treatment.

Mid facial involvement with ulcerations should alert physicians to think of NK cell lymphoma. Diagnosis may be difficult and late due to necrosis in the tissues.

Keyword: NK cell lymphoma, nasal

Figure 1



Poster No: 00148 Abstract:0282

POLYPLOIDY IN SMALL LYMPHOCYTIC LYMPHOMA(SLL) / CHRONIC LYMPHOCYTIC LEUKEMIA(CLL) WITH RELATIVE P53 DELETION DETECTED BY FISH: A CASE REPORT

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SLL is a diffuse form of non-Hodgkin's lymphoma representing the neoplastic proliferation of well-differentiated B lymphocytes, with focal lymph node enlargement or generalized lymphadenopathy and splenomegaly.

Here we present a case of 55-year-old women who applied with presented multiple bilateral cervical lymphadenopathies. Her leukocyte 14 400 /uL, Hg: 11.6 gr/dL, platelet. 205000/Ul. Bone marrow and lymphadenopathy biopsies showed SLL or CLL. Radiological screening showed generalized lymphadenopathy in different parts of her body. Flow cytometric analysis of the biopsy material sampled from bone marrow and lymphadenopathy biopsies are similar: CD5+/CD19+/CD23+/CD79A+/CD20-(partially positive in lymphadenopathy biopsy). She had limited response to R-CHOP and ESHAP therapies. She had a better response to CAMPATH chemotherapy. Her Fluorescence in situ hybridization (FISH) revealed a polyploidy with relative p53 deletion that could not be detected by conventional cytogenetic. There were 4 centromeric chromosomes 17 signal but only 2 p53 region signal. In this study, bone marrow and peripheral blood cells were collected analyzed by FISH with DNA probes for chromosomes 5, 7, 8, 13, 14, 21, and X. All of them showed different percentages of trisomy and tetrasomy which was supporting polyploidy. This is the first reported case of small lymphocytic lymphoma with polyploidy and relative p53 deletion that is reported till date. Our findings indicate the utility of FISH analysis in cytogenetic monitoring of small lymphocytic lymphoma patients are important to discover new cytogenetic aberrations.

Keyword: SLL/CLL' polyploidy with 17p deletion

Poster No: 00149 Abstract:0285

ANALYSIS OF THE EFFICACY AND SIDE EFFECTS OF BEXAROTENE IN THE TREATMENT OF MYCOSIS FUNGOIDES: A REPORT OF FIVE CASES

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Backround**:** Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphomas in adults.It is a low-grade cutaneous lymphoma characterized by skin-homing CD4+ T cells. It is notable for highly symptomatic progressive skin lesions, including patches, plaques, tumors, and erytheroderma in which has a poor prognosis in advanced stages. Management of MF should use a "stage-based" approach; treatment of early-stage disease (IA-IIA) typically involves skin directed therapies that include topical corticosteroids, phototherapy (psoralen plus ultraviolet A radiation or ultraviolet B radiation), topical chemotherapy, topical or systemic bexarotene, and radiotherapy.

Objective: The present study was aimed to evaluate the efficacy and effects of bexarotene, treatment and disease progression in MF patients.

Method: Five patients diagnosed with MF in different stages, who received PUVA and steroid treatment before including the study. Bexarotene (initial dose 300 mg/day, decreasing to 225 or 150 mg/day if signs of toxicity appeared). All received atorvastatin and levotroxin sodium. We measured AST, ALT, billuribin, triglyceride, VLDL, LDL, FT3, FT4 and TSH levels at the beginning and monthly for 3 months. We compared the the results of biochemical parameters with beginning and after 3 months of the bexarotene treatment.

Results: AST level was increased above the normal level (N; 5-32 U/L) in 1, TG (N; 10-200 mg/dl) and LDL(N; 57-129 mg/dl) in 4 of the 5 MF patients. FT3 level (N; 1.71-3.71 pg/ml) was decreased from the normal level in 1 and FT4 (N; 0.7-1.48 pg/ml) level 2 of the 5 patients (Table 1). Patient 3 started bexarotene treatment 15 days ago. We observed bexarotene caused partially clearing of the cutaneous lesions of MF for 3 months.

Conclusion: Our study together with the other studies with bexarotene has shown that this agent is effective in the treatment of MF in patients who have failed on a number of other therapies and can produce long-lasting response. The common side-effects of hypertriglyceridemia, hypercholesterolemia and hypothyroidism associated with bexarotene therapy require monitoring, but can readily be managed with concomitant medication, using a strategy similar to that suggested above. However, patients should be aware of the importance of making changes to their diet and lifestyle. It should be stressed on patients that their diet and lifestyle also have a key role to manage MF with bexarotene treatment.

Keyword: Bexarotene, Mycosis fungoides

Poster No: 00150 Abstract:0290

THE ROLE OF RITUXIMAB AND OPTIMAL TREATMENT MODALITY IN PRIMARY GASTRIC DIFFUSE LARGE CELL LYMPHOMA: A STUDY BY THE ANATOLIAN SOCIETY OF MEDICAL ONCOLOGY

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Background: In this study we have compared treatment modalities for gastric lymphoma and examined independent factors contributing to survival and whether rituximab is effective drug in gastric lymphoma.

Patients and Methods: This retrospective study included 146 primary gastric diffuse large B-cell lymphoma (DLBCL) patients diagnosed at a multicenter analysis. A combination chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) plus rituximab was applied to 109 of the patients. Thirty-one patients had received chemotherapy without rituximab.

Results: The median follow-up period was 25.5 months. The 5-year EFS (Event Free Survival) and OS (Overall Survival) rates for the patients were 55% and 62.3%. In multivariate analysis of OS and EFS, we have identified low albumin, complete response to treatment, nonsurgical treatment, and stage I-II disease as factors independently contributing to the survival. There was no statistically significant difference in terms of survival between the different treatment modalities (EFS and OS) (p = 0.707 and p = 0.124 respectively). Also, no statistically significant difference regarding the OS was found between the chemotherapy modalities with and without rituximab (p=0.332). Significantly better EFS was observed in the group that had received chemotherapy without rituximab (p=0.041). In the subgroup analysis, the addition of rituximab to the treatment did not result in statistically significant changes in the EFS or OS for the group of 63 patients who received chemotherapy alone (p= 0.145 and p=0.384).

Conclusions: The benefit of rituximab treatment in gastric DLBCL is still a controversial subject. Additional prospective trials are definitely required in order to clarify the use of rituximab in the treatment of gastric DLBCL.

Keyword: Gastric lymphoma, rituximab

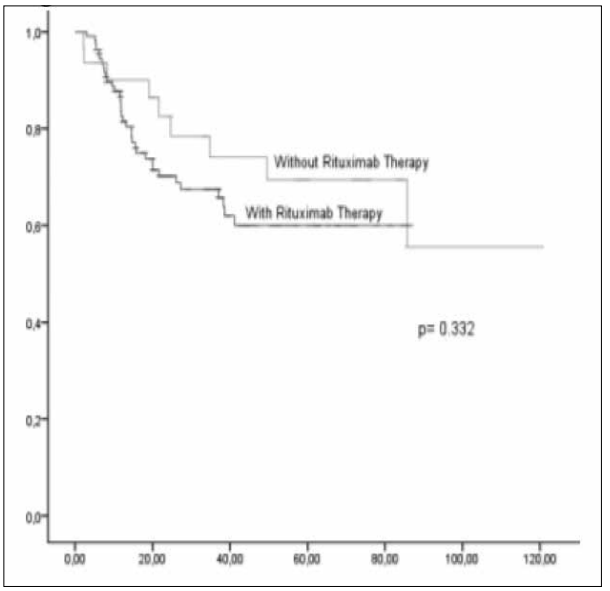

Figure 1: Comparison of the Overall survival curves of patients with and without Rituximab therapy

Poster No: 00151 Abstract:0307

RITUXIMAB MAINTENANCE THERAPY IN DIFFUSE LARGE B-CELL LYMPHOMA-SINGLE CENTAR EXPERIANCE

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Introduction: Rituximab maintenance treatment after achieving response to induction therapy appears to be an effective approach to extending response duration in follicular lymphoma patients. In literature, investigators have reported improved event-free(EFS) and progression-free survival (PFS) with maintenance rituximab in patients with newly diagnosed follicular lymphoma. But in diffuse large B-cell lymphoma patients Rituximab administered as induction therapy in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) significantly prolonged event-free survival. However, continued use of rituximab after R-CHOP failed to demonstrate benefit. High-dose therapy followed by autologous stem cell transplantation is the treatment of choice for patients with relapsed DLBCL who are still responding to salvage therapy. Although rituximab is effective, but its role in salvage therapy after autologous transplant remains unclear. Maintenance therapy with rituximab in patients with complete remission after autologous transplant may be a useful novel approach capable of eradicating minimal residual disease. However, there are currently no data confirming this hypothesis.In line with these facts we conducted this retrospective study to investigate benefit from rituxomab maintenance therapy in patients with aggressive lymphoma after induction therapy and after autologous transplantation.

Methods: Our study enrolled 50 CD20+ DLBL patients diagnosed and treated at the University Clinic of Haematology in the period between January 2002 and January 2010. The most common initial treatments was R-CHOP. Patients were required to have a CR following initial treatment to continue with Rituximab maintenance therapy which was administered as 375 mg/m^2 doses every 3 months for 2 years. Eight patients with aggressive subtype- non Germinal centre DLBCL were treated with high-dose chemotherapy/autologous stem cell transplantation (HDT/ASCT) and received rituximab maintenance therapy every 2 months for 2 years.

Results: Most patients had disease stage according to Ann Arbor >= III. Event-free and overall survival were 97.6 months and 100.8months. To date,37/50 patients are in continuous clinical remission, only 8 patient have relapsed, and 5 patient had died. Maintenance therapy was generally good tolerated: in 5 pts a WHO grade 3 toxicity event occurred which were arrhythmia, leucopenia, and infection. In one pt two WHO grade 3 toxicity events were observed (infection, neuropathy).

Conclusions: Rituximab maintenance therapy is effective and well tolerated in this setting. Evaluation of a larger patient population, together with a longer follow-up, will determine whether this treatment approach has curative potential in aggressive lymphoma.

Keyword: DLBCL, Rituximab maintenance treatment

Poster No: 00152 Abstract:0314

EPSTEIN-BARR VIRUS (EBV) POSITIVE DIFFUSE LARGE B CELL LYMPHOMA OF THE ELDERLY; EXPERIENCE OF A SINGLE CENTER FROM TURKEY

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In the 2008 World Health Organization (WHO) Classification of tumours of haematopoietic and lymphoid tissues 'EBV positive diffuse large B cell lymphoma (DLBCL) of the elderly' is included as a new provisional entity; and it is defined as the EBV+ clonal B-cell lymphoid proliferation occurring in patients older than 50 years of age, without any known immunodeficiency or prior lymphoma. This new entity had been introduced after the studies from Far East, based on Asian population; several studies coming from different geographical locations of the world followed them. In this study, we aimed to determine and evaluate the morphological, immunophenotypic, and clinical characteristics of the cases diagnosed as 'EBV positive diffuse large B cell lymphoma of the elderly' in a single center, to assess the diagnostic and morphological criteria in comparison with the literature.

EBV status was detected by Epstein-Barr early RNA (EBER) in situ hybridization analysis. The EBER expression in the majority of tumour cells (> 20 %) was required to consider the cases as EBV+ DLBCL of the elderly. By immunohistochemistry, a panel of antibodies for CD10, Bcl-2, Bcl-6, IRF4/MUM1, CD30 and Ki67 was performed.The cases were classified as germinal center B-cell (GCB) or non-germinal center B-cell (non-GCB) phenotype according to 'Hans criteria'.

Eight patients who fulfill the criteria were re-evaluated. Five patients were male, and three were female with a median age of 67.6 years (range 60-87 years). Four patients presented with lymph node involvement; others presented with bone and surrounding soft tissue infiltration, bone marrow, and spleen infiltrations. Five of the cases revealed predominantly monomorphic morphology with sheets of large cells, one also contained focal areas consistent with polymorphous subtype; and three patients revealed a polymorphous infiltrate. When the cases were classified according to 'Hans criteria', five patients were non-GCB cell phenotype, and three cases were classified as GCB cell phenotype. All of the four cases with polymorphous morphology revealed to be non-GCB cell phenotype and all expressed IRF4/MUM1. Two patients died with disease, four patients are alive and in complete remission following R-CHOP therapy, followed up for 42, 36, 31, and 38 months after the initial diagnosis, two patients have just recently been diagnosed and started receiving chemotherapy. Further studies including larger series are needed to fully understand the details of this disease, which can lead to new treatment modalities.

Keyword: Epstein Barr virus, large B cell lymphoma

Poster No: 00153 Abstract:0319

PROMOTER METHYLATION OF *GADD45*γ IN DIFFUSE LARGE B-CELL LYMPHOMA

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Background: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) and is highly heterogenous from both clinical and molecular perspectives. The growth arrest and DNA damage-inducible (GADD) 45 gene family which consists of three members, *GADD45a*, *GADD45β*, and *GADD45γ* are implicated in modulating the cellular response to various types of genotoxic/physiological stress. Although it has been reported that *GADD45γ* is frequently methylated in various solid tumors, there is no detailed information about the methylation frequency of the gene in DLBCL.

Objectives: The aims of this study are to detect the methylation frequency of *GADD45γ* in DLBCL and to assess the association between this epigenetic aberration and transcriptional inactivation of the gene at the protein level. We investigated *GADD45γ* promoter methylation and its protein expression in 40 patients with DLBCL and 40 patients with reactive lymphoid hyperplasia.

Methods: Genomic DNAs were extracted from all FFPE tissue samples in both groups using a commercial kit (QIAamp DNA Mini kit, Qiagen). After bisulphite treatment, methylation-sensitive high resolution melting (HRM) analysis was used to determine the frequency of *GADD45γ* methylation. GADD45γ protein expression in both groups was determined by immunohistochemistry.

Results: The methylation frequencies of *GADD45γ* in DLBCL and non-cancer group were 55% and 40%, respectively. There was a significant difference in GADD45γ protein overexpression in both groups (P=0.000). Eighteen (45%) methylated samples did not express the GADD45γ protein, whereas eight (20%) protein overexpression was seen in unmethylated samples in DLBCL. Although the frequency of methylation in patients with extranodal DLBCL was higher than those in patients with nodal DLBCL, there was no statistically significant difference between the two groups (P=0.508). GADD45γ protein overexpression in patients with extranodal DLBCL was almost three times higher than those in patients with nodal DLBCL (P=0.323).

Conclusion: The findings suggested that *GADD45γ* is frequently methylated and the epigenetic silencing of *GADD45γ* by DNA methylation does not fully explain its decreased expression in DLBCL. Therefore, more detailed studies are required to determine other epigenetic changes that were responsible for the silencing of *GADD45γ*, rarely mutated, in DLBCL.

Keyword: Diffuse large B-cell lymphoma, GADD45γ

Poster No: 00154 Abstract:0322

CD5(-) BLASTOID MANTLE CELL LYMPHOMA PRESENTING AS AN ORBITAL MASS: A CASE REPORT

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Introduction: Mantle cell lymphoma (MCL) is a B-cell neoplasm with a nodal or extranodal presentation, composed of monomorphic small to medium-sized lymphoid cells,usually co-expressing CD5 and Cyclin D1. A minority of cases which are CD5(-) compose a group with diagnostic difficulty. Blastoid MCL is an agressive morphologic variant. Orbital and adnexal region MCL presents in elderly males. The orbit and eyelid are frequently involved. There is a very high proportion of systemic involvement in general with MCL of the orbital and adnexal region. Most patients present with stage IV disease and have multiple relapses and short survival time.Here we report a case of CD5(-) blastoid mantle cell lymphoma presenting as an orbital mass.

Case: A 62-year-old man presented with a progressive right palpebral swelling of three months duration. His right eye was protruded. Orbita MRI revealed a 5x3.5 cm orbital mass originating from the lacrimal gland, extending to retrobulber region, and pressing the ocular bulb and optic nerve. İnsicional biopsy of the mass was consistent with a lymphoid neoplasm composed of middle sized lymphoid cells. Neoplastic cells had a diffusely infiltrating pattern and strong CD20 and Cyclin D1 expression. CD5 was negative. Positron Emission Tomography showed hypermetabolic lymph nodes in cervical, bilateral axillary and inguinal regions. Bone marrow was involved. Spleen and liver was not enlarged. The patient was treated with radiotherapy and chemotherapy (R-CHOP) and complete regression of the mass was achieved in control MRI, after three months following initial diagnosis.

Conclusion: Lymphoid neoplasms should be included in the differential diagnosis of orbital masses and pathologists should be alert of neoplasms with unusual immunophenotypes such as CD5 (-) MCL in order to reach a correct diagnosis.

Keyword: mantle cell lymphoma, orbita

Poster No: 00155 Abstract:0323

PRIMARY MULTIFOCAL EXTRANODAL DIFFUSE LARGE B CELL LYMPHOMA; A CASE REPORT

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Diffuse large B-cell lymphomas (DLBCL) account for approximately 40% of adult non-Hodgkin's lymphomas. Approximately one quarter to one third of DLBCLs originate from tissues other than lymph nodes. We herein report a patient with multifocal extranodal involvements who presented like primary ovarian carcinoma. A 63 year old woman living in an underserved area of Turkey was referred to our center for multiple abdominal masses determined with ultrasonography. She had a history of skin lesions on her neck and subcutaneous nodules on the abdomen and breasts for several months. A preliminary diagnosis of dermatofibrosarcom was done with skin biopsy before referral to our center. On physical examination she had skin lesion on the back of neck (Figure 1) and subcutaneous nodules on abdomen and breasts. She had normal blood count. CA-125 was 36,4 IU/ml (0-35). Thoracoabdominal tomography revealed a solid lesion of 129x124 mm in pelvis with no certain margins from uterus and ovaries, 3 cm parailiac nodular solid lesion, subcutaneous nodular metastatic lesions, bilateral surrenal 2 cm lesions, left renal 61x48 mm nodular solid lesions and right breast metastases. She underwent total hysterectomy with bilateral salpingo-oophorectomy, lymph node dissection and omentectomy with a preliminary diagnosis of ovarian carcinoma. Pathology was consistent with non-germinal center phenotype DLBCL. Normal ovarian tissue wasn't observed outside of neoplastic areas. Neoplastic cells were positive for CD20, BCL-2, BCL-6, and negative for CD10 CD3 and CD30. Ki67 index was 80-90%. A skin biopsy was also consistent with DLBCL. Additional work up with magnetic resonance imaging revealed 31x26x24 mm mass lesion destructing left orbita medial wall displacing medial rectus muscle. She also had a 55x41 mm mass lesion posterior to left scalen muscle. None of the imaging studies showed any lymph node involvement. A FDG PET/CT scan additionally showed gastric involvement. Bone marrow biopsy was negative for lymphoma involvement. Patient had high risk IPI. She received R-CHOP chemoteharpy and intrethecal CNS prophylaxis. All her subcutaneous nodules resolved dramatically after first cycle, skin lesions totally faded after second cycle (Figure1). She now has an excellent performance status. Primary extranodal lymphomas constitute one third of DLBCLs and treatment is no different than nodal lymphomas. Our patient had primary multifocal extranodal DLBCL presenting like ovarian carcinoma. Primary ovarian lymphoma is extremely rare accounting for 0,2% of all lymphomas in women. For our patient, it is not possible to know she had a primary ovarian lymphoma as she had multifocal involvements, thus there is also a probability that it might have spread from ovaries to different organs over several months.

Keyword: diffuse large B-cell lymphoma, primary extra nodal

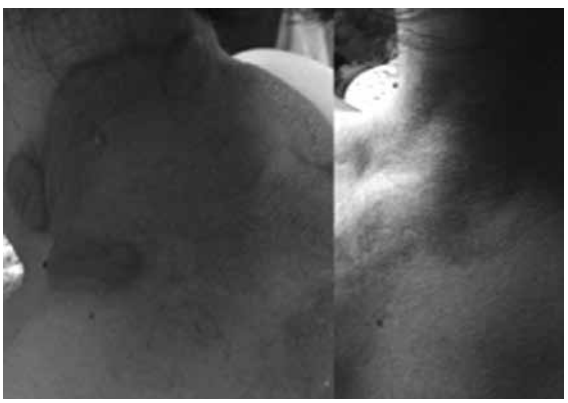

Figure 1 Skin lesion before (left) and after (right) 2 cycles of R-CHOP chemotherapy

Poster No: 00156 Abstract:0325

MARGINAL ZONE B-CELL LYMPHOMA OF THE MUCOSA- ASSOCIATED LYMPHOID TISSUE (MALT) OF THE THYROID GLAND: A CASE REPORT

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Introduction: Primary lymphoma of the thyroid gland is a rare malignant tumor constituting 1% to 2% of all thyroid malignancies and less than 2% of lymphomas. Most lymphomas of the thyroid gland are high grade lymphomas, particularly large B-cell and immunoblastic types. Low grade marginal zone lymphoma of MALT represent %15-20 of all primary thyroid lymphomas. Thyroid lymphoma affects predominantly females over 70 years of age with a history of Hashimoto's thyroiditis (HT). Hashimoto's thyroiditis is considered as a risk factor for thyroid lymphoma development. The onset of malignant lymphoma likely is a consequence of the chronic antigenic stimulation of B lymphocytes that take place in the autoimmune disorder; this chronic stimulation probably leads to a population of lymphocytes that are more susceptible to neoplastic transformation.

Case: 40 year-old woman with a prior history of HT presented with a complaint of rapidly growing painless neck mass. Fine needle aspiration biopsy was suspicious for malignancy favoring papillary carcinoma, Hurthle cell variant. Total tyhroidectomy was performed and pathologic examination revealed neoplastic lymphoid infiltration with characteristic lymphoepithelial lesions of MALT lymphoma and neoplastic cells had striking plasmacytic differentiation. Fully developed chronic lymphocytic thyroiditis characterized by reactive lymphoid follicles with germinal center formation and Hurtle cell change was encountered adjacent to neoplastic lymphoid infiltration. There were numerous reactive T lymphocytes accompanying neoplastic B cells. There was no malignant change in the epithelial component.

Conclusion: Primary marginal zone lymphoma of MALT of the thyroid gland is a rare disease that continues to produce diagnostic dilemmas. We report a case of primary MALT lymphoma of the thyroid with a prior history of HT, and highlight the morphologic features that are spesifically thought to aid in the differentiation of reactive nonneoplastic lymphoid proliferations from neoplastic lymphoid infiltrations of the thyroid gland.

Keyword: MALT lymphoma, thyroid

Poster No: 00157 Abstract:0326

CD30(+) PERIPHERAL T CELL LYMPHOMA MISDIAGNOSED AS METASTATIC CARCINOMA BY FINE NEEDLE ASPIRATION BIOPSY OF THE LYMPH NODE: A CASE REPORT

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Introduction: Peripheral T-cell lymphomas (PTCLs) generally affect older individuals (>50 years of age), with males affected more frequently than females. Most patients present with lymphadenopathy. Cytologic evaluation of the affected lymph node by fine needle aspiration biopsy (FNAB) may result misdiagnoses because of the morphologic resemblance of pleomorphic neoplastic cells with other nonlymphoid tumors like carcinoma. PTCLs are characterized by a spectrum of lymphoid forms, frequently associated with marked nuclear irregularity. Cell marker studies further assist in distinguishing lymphoma cells from other malignancies.

Case: A 57 year-old woman presented with a lump in her breast. Mammary ultrasound revealed a cystic mass of 1cm in diameter. In addition to the breast lump, physical examination revealed cervical lymphadenomegaly, and FNAB of the lymph node was performed. The cytologic diagnosis was a metastatic carcinoma of the lymph node. Then the patient underwent excessive investigations including positron emission tomography (PET) aiming to find the primary tumor of unknown origin. PET findings suggested cervical and inguinal lymphadenopathy consistent with a malignancy and malign melanoma was the possible diagnosis. Excisional biopsy of the inguinal lymph node and subsequent pathologic examination solved the diagnostic dilemma resulting from conflicting results and revealed a lymphoid neoplasm composed of CD30(+) peripheral T cells.

Conclusion: A case of PTCL with CD30 expression, which was misdiagnosed as metastatic carcinoma by the FNAB of the lymph node, is presented. Clinical and pathologic features of PTCL are reviewed, and pitfalls of lymph node FNAB are emphasized.

Keyword: peripheral T cell lymphoma, misdiagnosis

Palliative Care–Supportive Therapy

Poster No: 00158 Abstract:0112

THE IMPACT OF ELTROMBOPAG ADMINISTRATION ON THE CLINICAL COURSE OF SEVERE REFRACTORY FATAL ACQUIRED APLASTIC ANEMIA

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Objective: Severe aplastic anemia (SAA) has an aggressive clinical course and represents a "difficult-to-treat" situation with current medications. Eltrombopag is a c-mpl receptor agonist oral thrombopoietin-mimetic drug mainly active in immune thrombocytopenic purpura (ITP). We would like to share our experience about eltrombopag in two patients with refractory fatal acquired SAA.

Case #1: A 19 -year-old male patient was admitted to our emergency room with the complaints of nasal bleeding and ecchymosis. Laboratory studies revealed pancytopenia. After his diagnosis was confirmed with bone marrow aspiration and biopsy as aplastic anemia steroid 1 mg/kg and 5 mg/kg cyclosporin were started. During his follow up acute vision loss developed and retinal hemorrhage was detected and platelet transfusion was started daily in an attempt to raise the platelet count over since enough response was not obtained with immunsupressive treatment. Following the horse ATG at dose of 40 mg/kg for 4 days, he became more cytopenic and needed more frequently transfusions especially platelet suspensions. Despite multiple platelet transfusions, his platelet counts remained below 50x109/L and eltrombopag 50 mg/day started to patient. After one week of the eltrombopag initiation, the patient's platelet counts remained above 50x109/L without any

transfusion support. However, septic shock complicated the clinical picture and the patient died.

Case #2: A 44-year-old female patient with the history of bronchial asthma admitted to our emergency service with the complaint of epistaxis, bleeding from ears and visual loss. In her complete blood count Hb: 6.2 g/dL, leukocyte count: 2.2 x109/L, platelet count: 4x109/L and reticulocyte count: 1% with normal coagulation parameters. Her bone marrow aspiration and biopsy was consisted with aplastic anemia and cyclosporine-A were started. Because of her intracranial hemorrhage we did not plan ATG. During this period, she remained profoundly thrombocytopenic, requiring twice per day platelet transfusions to achieve platelet count below $100x10^9$/L and we started 50 mg/day eltrombopag. Two weeks after the initiation of the eltrombopag, her platelet transfusion requirement was reduced with platelet counts reaching the 80.000/uL range without transfusions. Her control MRI showed regression of intracranial hemorrhage. Her donor screening tests revealed a related HLA match donor, accordingly allogeneic HSC transplantation was planned. During her hospitalization abdominal pain and fever developed. Her abdominal CT scan was consistent with typhlitis without perforation. Antimicrobial therapy was started. After two days she became septic and died.

Conclusion: Both cases with SAA presented here suggested that eltrombopag could reduce transfusion requirements in patients with platelet transfusion dependent-aplastic anemia. However, the drug had no impact on the morbidity or mortality in our patients with SAA.

Keyword: aplastic anemia, eltrombopag

Poster No: 00159 Abstract:0125

EFFICIENCY OF ANTIFUNGAL TREATMENT IN PATIENTS WITH HIGH RISK FEBRILE NEUTROPENIA

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Objectives: Febrile neutropenia (FEN) is a life-threatening complication that is common in patients with hematological malignancies. In order to treat these infections early and right time are preferred instead of targeted antifungal therapy.High-risk group: the expected duration of neutropenia and the period of 10 days or longer than most of the PNL count $<100/mm^3$ is an underlying hematological malignancy (acute leukemia, lymphoma, etc.) the presence of which had been scheduled to receive intensive chemotherapy has taken or prior history of hospitalization the fact that uncontrolled cancer, the presence of additional factors is designated as negative.

The aim of this retrospective study is to evaluate efficiency of antifungal treatment in patients with high-risk febrile neutropenia.

Methods: Between January 2005 and March 2012, FEN of 78 febrile neutropenic patients was retrospectively analyzed in Manisa Celal Bayar University, Department of Hematology

Results: 43 (55%) patients were male and 35 (45%) patients were female. The mean age was 46.7±15.06 years and the median age was 45 years (20-76). The distribution of disease is AML, ALL, chronic leukemia, lymphoma and other hematologic malignancies and ratios were 50%, 12%, 7%, 15%, 6% respectively.

In 78 patients, 135 FEN were evaluated. Within these 90 FEN were received antifungal agents. 45 FEN were not needed any antifungal treatment. The efficacy of first-line antifungal therapy was 72% (65/90 FEN). The efficacy of second-line antifungal therapy (i.e. refractory to or intolerant of prior antifungal therapy) was 97% (30/32 FEN). Empirical antifungal therapy was started early and changed by clinical, microbiological and serologic results for the high efficacy.

Conclusion: We concluded that the use of empirical antifungal therapy early according to the antifungal guidelines and changed by clinical, microbiological and serologic results should be most effective in patients with high-risk febrile neutropenia.

Keyword: Antifungal agents

Poster No: 00160 Abstract:0126

THE SIDE EFFECTS OF ANTIFUNGAL AGENTS IN NEUTROPENIC FEVER ATTACKS

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Objectives: Febrile neutropenia (FEN) is a life-threatening complication that is common in patients with hematological malignancies. In patients with persistent fever and netropenia, antıfungal agents are administered empirically for early treatment and prevention of systemic fungal infections. The aim of this retrospective study is to evaluate side effects of antifungal treatment in FEN.

Methods: Between January 2005 and March 2012, FEN of 78 febrile neutropenic patients was retrospectively analyzed in Manisa Celal Bayar University, Department of Hematology

Results: 43 (55%) patients were male and 35 (45%) patients were female. The mean age was 46.7±15.06 years and the median age was 45 years (20-76). The distribution of disease is AML, ALL, chronic leukemia, lymphoma and other hematologic malignancies and ratios were 50%, 12%, 7%, 15%, 6% respectively. In 78 patients, 135 FEN were evaluated. Within these 90 FEN were received antifungal agents. 45 FEN were not needed any antifungal treatment.

The side effect of first line antifungal therapy was 48% (43/90 antifungal used FEN). The side effect of second-line antifungal therapy was 42% (13/32). The side effects of first and second-line antifungal therapy were infusion related, metabolic and visual toxicity, hepatotoxicity, rash, diarrhea and their numbers and ratios were 3(5%), 49(86%), 2(3,6%), 1(1,8%), 1(1,8%), 1(1,8%) respectively.

Conclusion: The use of empirical antifungal therapy early according to the antifungal guidelines and monitoring by side effect should be most security in patients with high-risk febrile neutropenia.

Keyword: Antifungal agents

Poster No: 00161 Abstract:0134

MULTIPLE BIOMARKERS IN THE DETECTION OF CARDIOTOXICITY INDUCED BY CONVENTIONAL AND HIGH-DOSE CHEMOTHERAPY FOR ACUTE LEUKEMIA

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Background: Cardiotoxicity is a potentially serious complication of anticancer therapy that can significantly impair patient's quality of life. The greatest risk for development of cardiotoxicity is represented by anthracyclines (ANT) and high-dose chemotherapy (HD-CT). Various methods including cardiac biomarkers have been recommended for monitoring of cardiotoxicity in oncology.

Objectives: The aim of our study was to assess cardiotoxicity of conventional and HD-CT with multiple biomarkers of cardiac injury – glycogen phosphorylase BB (GPBB), heart-type fatty acid-binding protein (H-FABP), cardiac troponins (cTnT, cTnI), creatine kinase MB (CK-MB mass), myoglobin.

Methods: A total of 47 adult acute leukemia patients were studied – 24 patients treated with conventional CT containing ANT (mean total cumulative dose 463.2 ± 114.3 mg/m^2) and 23 patients treated with HD-CT (myeloablative preparative regimen Bu/Cy2 or Cy/TBI) followed by stem cell transplantation (SCT). All patients had normal liver and renal functions during the study. Cardiac biomarkers were measured prior to treatment (before CT/HD-CT), after first CT with ANT, after last CT with ANT in the first group; after HD-CT and after SCT in the second group. Cardiac biomarkers were measured on Evidence Randox (GPBB, FABP, cTnI) and Elecsys Roche (cTnT, CK-MB mass, myoglobin) analyzers. Values above the reference range recommended by the manufacturers were considered elevated.

Results: Before CT/HD-CT, all biomarkers of cardiac injury were below the cut-off values in all patients. GPBB increased above the cut-off (7.30 µg/L) in 4 (16.7 %) patients after first CT and in 5 (20.8 %) patients after last CT with ANT. GPBB increased above the cut-off in 5 (21.7 %) patients after HD-CT and remained elevated in 5 (21.7 %) patients after SCT. CTnI became elevated (above 0.40 µg/L) in 2 (8.3 %) patients after first and last CT with ANT. Both patients with cTnI positivity had elevated GPBB. Other tested biomarkers (H-FABP, cTnT, CK-MB mass, myoglobin) remained below the cut-off values during the study.

Conclusions: Our results suggest that GPBB could become a sensitive biomarker for detection of acute cardiotoxicity associated with conventional CT containing ANT and HD-CT followed by SCT. The predictive value for development of cardiomyopathy in the future is not known and will be evaluated during a prospective follow-up. Based on our data, a larger prospective and multicenter study would be most desirable to define the potential role of new biomarkers in the assessment of cardiotoxicity in hematooncology.

The work was supported by a long-term organization development plan 1011 (FMHS).

Keyword: cardiac biomarkers, chemotherapy

Poster No: 00162 Abstract:0150

THE DISTRIBUTION OF FUNGAL PATHOGENS ON NEUTROPENIC FEVER ATTACKS AND ANTIFUNGAL TREATMENT

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Objectives: Febrile neutropenia (FEN) is a life threatening complication that is common in patients with hematological malignancies. Invasive fungal infections (IFI) are serious cases of mortality in neutropenic patients. It is difficult to diagnose IFIs in neutropenic patients and this causes delay in diagnosis which has detrimental effects on prognosis. The aim of this retrospective study is to evaluate fungal pathogens in patients on febrile neutropenia.

Methods: Between January 2005 and March 2012, FEN of 78 febrile neutropenic patients was retrospectively analyzed in Manisa Celal Bayar University, Department of Hematology

Results: 43 (55%) patients were male and 35 (45%) patients were female. The mean age was 46.7±15.06 years and the median age was 45 years (20-76). The distribution of disease is AML, ALL, chronic leukemia, lymphoma and other hematologic malignancies and ratios were 50%, 12%, 7%, 15%, 6% respectively. In our study 27 fungal pathogens (27/90) were isolated microbiologically and/or histopathologically in.27 patients. C.albicans, C.tropicalis, C.glabrata, C.crusei, Aspergillus, yeast species were found in 12(44%), 3(11%), 2(8%), 1(4%), 3(11%), 6(22%) respectively. The most isolated fungal pathogen was C.albicas (p=0.001). After the isolation of fungal pathogens antifungal treatment were given in accordance with the guidelines to the 27 patients (7 patients; liposomal amphoterisin, 12 patients; caspofungin, 2 patients; vorikonazol, 5 patients; flukonazol and 1 patient; posakonazol)

Conclusions: Within the scope of our study we could conclude that early diagnosis of fungal pathogens in FEN is important due to early treatment of IFI. Using antifungal agents after the correct isolation brings effective antifungal treatment so we could decrease mortality in FEN.

Keyword: Fungal pathogens

Poster No: 00163 Abstract:0171

CASE OF A RETROPERITONEAL FIBROSIS PATIENT COMPLICATED WITH AUTOIMMUNE HEMOLYTIC ANEMIA

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Retroperitoneal fibrosis (RPF) is a rare disease (incidence:1/200.000) with fibrosis in retroperitoneal tissue and chronic inflamation. It commonly effects males, ages between 40-60.

A 45-year-old male patient applied to hospital with abdominal pain lasting over 20 days. We revealed blood urea 40mg/dl,creatinine 0,66 mg/dl, total bilirubine:0,48 mg/dl,hemaglobin:12,9 g/dl, leukocyte: 14,400/mm^3, platelet: 525,000/mm^3, ESR:102 mm/h and CRP: 19,9 mg/dl. We applied CT examination due to intermittant abdominal pain complaints. We revealed 9-10 cm mass lesions with soft tissue density at infrarenal area circulating both abdominal aorta and proximal common iliac artery. These lesions were interpreted as RPF or lymphoproliferative disorder. We applied dynamic contrast MRI examination and the results were commented as RPF. On the 5.day of hospitilisation, the patient complained about abdominal pain with waist and back pain. His laboratory examination, Hgb 8,1 g/dl,LDH:2595 U/L,t.bilirubine:19,3 mg/dl, i.bilirubine:12.5 mg/dl, haptoglobin: 3,9 mg/dl and DAT was positive. Although we replaced with erytrocyte suspension, hemoglobin levels decreased until 3,7 g/dl and creatinine levels increased to 3,5 mg/dl. He was taken to intensive care unite with diagnosis of acute hemolytic anemia complicated with acute renal failure. Applying steroid (1 gr/per day/3 days), intravenous immunglobin (0,5 gr/kg/day,3 days) and three cycle of plasmapheresis, hemoglobin levels increased and LDH levels decreased. We applied two cycle of hemodialysis. We continued steroid treatment with lower doses as 1 mg/per kg/per day and applied 4 more cycles of plasmapheresis. Creatinine levels of patient decreased and his urine output started to increase. We screened the patient for RF, ANA, p-ANCA, c-ANCA, ENA and anti-cardiolipin antibodies. They were all negative. His bone marrow biopsy, cytogenetic and flowcytometric examinations were normal. There was no sign of malignancy on CT and MRI of thorax and pelvic regions. After a month of the admission to hospital, his creatinine, LDH, hemoglobin, bilirubine and haptoglobin levels were all in normal ranges. His DAT was negative and we continued low doses of steroid therapy with 8 mg per day. Due to non obstructive RPF, no surgical intervention was planned. After a 6-month follow up, there was no sign of urinary systeme obstruction and hemolysis.

More than 70% of RPF cases are idiopathic. Fibrosis due to malignancy is nearly 8% of the cases. The association between autoimmune diseases and RPF is observed lately. Idiopathic RPF has a better prognosis and the best known treatment is steroids. Thanks to the steroid treatment, there can be an improvement on symptoms, retroperitoneal mass lesions and obstructive complications. Other immunsupresive treatment option are used for the patients resistant to steroid treatment. Surgical intervention is preferred for the patients with urinary system obstruction.

Keyword: Retroperitoneal fibrosis, autoimmune hemolytic anemia

Poster No: 00164 Abstract:0216

DETERMINATION OF NURSE'S KNOWLEDGE ABOUT APLICATION, CARE AND COMPLICATIONS OF PERIPHERAL VENOUS CATHETERS, PORT CATHETERS AND CENTRAL VENOUS CATHETERS

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Peripheral, central arterial, venousor port catheters are used for various purposes and also may lead various complications like infections or thrombosis. Central venous catheterization (CVC) is performed by a physician but preservation and following-up is done by the nurses. Study was carried out in Fatih University Hospital and Ankara Dışkapı Yıldırım Beyazıt University hospital including 668 nurses. We produced the questionnaire by investigating the literature for measuring the knowledge of nurses.

There were 31,8% (n=48) was in 18-25 age group, 42,4%(n=64) was 26-35 and 25,8%(n=39) was 36 and older age group and all participants were female.

When we evaluated the questionnaires about peripheral venous catheter and central venous catheter implementation, maintenance, and complications differences between university and high school graduated came out. With increase of education the success rates was increased. In terms of questionnaire results university graduated nurses had %79.1 success rate and high school graduated nurses was %62,5 respectively and the difference between these two groups was significant (P<0,05). Contrarily about port catheterization there was no difference between groups.

There was also significant difference about PVC and CVC information between nurses considering professional experience and working service (P<0,05). However there was no significant difference about port catheterization information (P>0,05).

We evaluate the achievement scores of the nurses considering their satisfaction levels. But we did not find any difference.

One third of the participated nurses (n=55) were unsuccessful and 63,6% were successful about PVC and CVC. However 91% (n=138) of the nurses were failed or have no idea related to subject. As a result of questionnaire the average score was 72,3 (max: 100, min 43,75).

There were new developments new approaches to patients in nursing profession like all others. But nurses may be cannot fallow this advancement because of intensive work or neglect. So in-service training was required for additional information and practice.

Keyword: Catheterisation, Nursing

Poster No: 00165 Abstract:0245

THE CHRONIC COURSE OF İNVASIVE FUNGAL SINUSITIS IN A PATIENT WITH MYELODYSPLASTIC SYNDROME: A CASE REPORT

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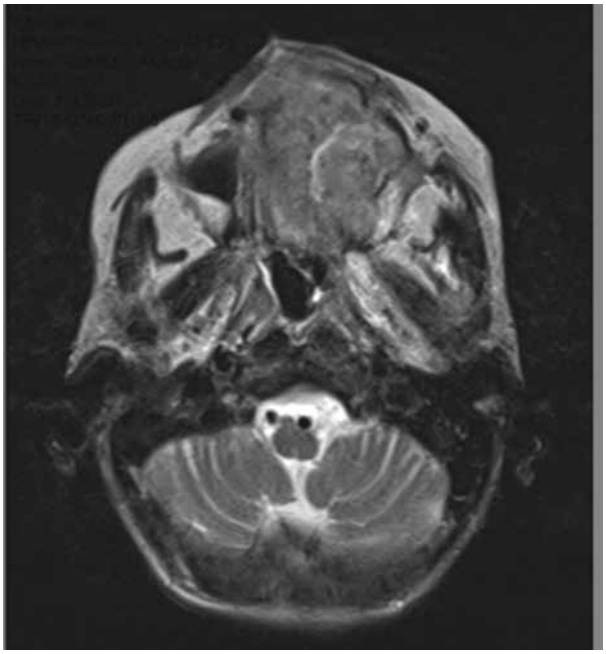
Invasive fungal rhinosinusitis is usually seen in patients with compromised immune systems. The most frequently observed in patients with diabetes, the second is often observed in patients with leukemia. There are two forms; invasive and non invasive fungal sinusitis. Invasive form can be acute fulminant, granulomatous and chronic. In this article,we present a case with chronic invasive fungal rhinosinusitis that was followed for myelodysplastic syndrome.

The patient is a women aged 82 years who had admitted to hematology with weakness and fatigue in January 2012. Laboratory studies revealed WBC count of 1190 with 100 neutrophils, hemoglobin 8.2 g/dl, an MVC count of 90 FL and a platelet count of 13000. Bone marrow aspiration and biopsy was consistent with myelodysplastic syndrome multilineage dysplasia. The patient was treated with filgrastim and erythropoietin. Despite the increased maximal doses of erythropoietin alfa therapy, patient didn't respond to treatment so stoped erythropoetin. She supported with erythrocyte and platelet suspension. Ferritin value was > 1000ng/ml during the supportive therapy so the patient was treated with deferasirox. Case was followed. Patient admitted with left cheek pain, erythema, swelling, nasal obstruction and palatal wound in January 2013. This symptoms were proceeded for two weeks. 37x35x42 mm sized mass was determined with MRI of paranasal sinus. Mass was completely filling the left maxillary sinus, extending the left nasal cavity, invasing the left side of hard palate and orbital floor, demonstrating with enviromental enhancement and primarily suggesting malignancy (Figure1).Platelet value didn't increase with random and platelet apheresis. Platelet alloimmunization developed and platelet count was 5000. Debalking oriented caldwell luc approach was performed to the patient under local anesthesia and platelets were infused during the process. Biopsies and culture were obtained from maxillary sinus. Direct examination result was inflammatory cell infiltration, result of the pathological examination was fungal infection and appearance was consistent with Aspergillus, but the fungus wasn't isolated from the culture. Patient has treated with intavenous vorikonazol currently. Loading dose is 2x6mg/kg/day and maintenance dose is. 2x4 mg/kg/day. Following and treatment of the patient is proceeding in our clinic.

As a result, invasive fungal sinusitis may be seen acute fulminant or chronic in immunosuppressed patient and can mimic malignancy. The diagnostic value of CT and MRI is limited. The biopsy specimen should be examined as well as pathological and microbiological. Pathologist and microbiologist are warned in terms of fungal infection. Fungal cultures and pathological results aren't always diagnostic. İncorrect or retarted diagnosis may delay the treatment. For this reason if there is a clinical suspicion, the right approach will be life saving as soon as possible.

Keyword: Myelodysplastic Syndrome, Chronic Invasive Fungal Sinusitis

Figure 1



Poster No: 00166 Abstract:0273

A RARE CAUSE OF GENERALIZED LYMPHADENOPATHY: ROSAI DORFMAN DISEASE

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Introduction: Rosai Dorfman Disease is a rare benign disease characterized by generalized lymphadenopathies usually involving cervical lymph nodes. Its association has been reported with other autoimmune conditions and malignancies at the time of diagnosis or during its course. Anemia, polyclonal gammapathy and high sedimentation rate are remarkable findings in the laboratory investigations. Diagnosis is made by biopsy of the involved lymph node. Although the condition is a benign entity presenting with spontaneous remissions, it also may be lethal in the case with multi organ involvement associated with other autoimmune conditions. We present here four cases followed in our center with diagnosis of Rosai Dorfman Syndrome.

Findings: All of the cases presenting to our center with cervical lymphadenopathy were male and their median age was 49 years (range: 41 – 80 years). Anemia compatible with anemia of chronic diseases was found in all cases at the time of presentation. In regard to laboratory investigations, all cases had high levels of globulin, C-reactive protein and high rate of sedimentation, and polyclonal gammopathy.Diagnoses of all patients were

made with biopsy of lymphadenopathy.In regard to follow-up of the patients, anemia worsened and increased level of creatinine was found after follow-up of 4 years without treatment. Biopsy results of the patient for whom renal biopsy was performed because of suspicion of renal involvement is still being waited, and steroid treatment was scheduled to the patient after the result of the biopsy. Hodgkin lymphoma developed in the course of one patient. Complete remission occurred with 4 courses of ABVD chemotherapy.New mass lesion was found in lung parenchyma on imaging studies following 6th course of ABVD chemotherapy.This patient whose result of lung biopsy has come as pulmonary adenocarcinoma is still receiving chemotherapy in the oncology unit for lung cancer. Steroid treatment was given to two patients with complaints of fever, weight loss, fatigue due to anemia (hemoglobin level was 8 g/dL and 6 g/dL, respectively). Fever response occurred with steroid treatment in both patients and their symptoms were controlled. High rate of sedimentation and high level of globulin normalized in the patients with anemia resolved. In one patient receiving steroid treatment, chronic renal failure developed due to accompanying cresenteric glomerulonephritis. The patient is still on chronic hemodialysis program. Steroid treatment is still continuing in both patients.

Conclusion: Although Rosai Dorfman syndrome is rare, lymphadenopathy should be kept in mind in differential diagnosis. It should be remembered that although it is a benign condition, it may be associated with other autoimmune conditions or malignancies at the time of diagnosis or during its course, and that it should be treated for symptoms due to such associated conditions and the patients should be followed for this.

Keyword: Lymphadenopathy, Rosai Dorfman Syndrome

Poster No: 00167 Abstract:0288

EFFECT OF RESIDUAL DRUGS ON THE COST OF HEMATOLOGIC TREATMENT PROTOCOLS

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Background: Hematologic treatment protocols are expensive drug therapies (1). Although the most important factor that determines the cost is the high price of drugs, amount of residual drugs can be an important factor on the cost of therapies. So we aimed to determine the effect of residual drugs on the expense of therapy.

Material-Methods: Two hundred and fortynine chemotherapy sessions of 83 patients given in one year were evaluated. According to the standard protocols after the necessary amount of drug was taken from drug flacon, volume of the residual drug was calculated. Amount of residual drug to total dose was proportioned, then according to the formal drug prices of Turkish Ministry of Health (Price list of 2011) (2), cost of residual drug was calculated. By this method both cost of one chemotherapy session and each drug were calculated separately.

Findings: In this trial, 18 hematologic chemotherapy protocols and 21 drugs which are used in these protocols were evaluated. Cost of residual drugs of 1 year was found as 142,019 TL. Among these protocols, PAD protocol had the highest cost for both per chemotherapy session and total therapy and was followed by Azacytidine. Other protocols are listed in Table 1. When the drugs are evaluated individually, Bortezomib, Rituximab and Azacytidine had the highest residual drug cost. Other drugs are listed in Table 2.

Discussion: Cancer research, prevention, treatment and follow u p of the patient are the factors that affect the cost of treatment (1). Residual drugs cause an extra financial burden to present expensive therapies. In our trial we found that presence of high dosage of drug per flacon compared to the dosage recommended by protocols, especially for new drugs, was the most important factor increasing the cost. Impossibility of the preservation of the residual drugs and the unavailability of alternative packing forms containing lower dosages are also contributing factors.

Results: In conclusion alternative commercial forms of drugs containing lesser dosage should be produced to reduce cost of these important and expensive therapies. Furthermore central chemotherapy units having systems using residual drugs can be established to minimize drug wasting.

Keyword: Cost, Treatment Protocols

Table 1. Drug's total used and residual doses and total cost of residual doses.

DRUG NAME	USED DOSE (mg)	RESİDUAL DOSE (mg)	COST (TL)
RİTUXİMAB	56942	4658	21737
CYCLOPHOSPHAMİDE	187570	80430	1601
VİNCRİSTİNE	310,6	66,4	434
PREDNİZOLON	59500	0	0
DOXORUBUCİN	11686	2134	2131
DEXAMATAZON	8800	0	0
FLUDARABİNE	4670	580	2009
DAUNORUBUCİN	3247	513	258
İDARUBUCİN	270	15	264
BORTEZOMİB	174,4	147,6	93283
CİSPLATİN	5012	132	79
ETOPOSİDE	4280	270	86
ARA-C	644265	25535	1455
METOTREXATE	15180	2320	292
BLEOMİCİN	386	126	223
DACARBAZİN	15964	1836	95
MİTOKSANTRONE	20	0	0
AZACYTİDİNE	6230	2170	17642
FOLİNİC ACİD	1360	240	92
İFOSFAMİDE	21400	3000	240
ECULİZUMAB	21600	0	0

Table 2. Increasing total drug costs and the cost per course of treatment according to chemotherapy protocols.

Treatment protocol	Count of patients	Count of cure	Increasing drug cost	cost per cure (TL)
3+7	7	7	646	99,2
ABVD	4	11	363	33
AZCYTİDİNE	2	6	17642	2940,3
R-CHOP	20	92	23653	257,1
CHOP	2	13	372	28,6
CVP	2	8	41	5,1
DHAP	2	2	12	6
ESHAP	2	2	147	73,5
FLAG	5	5	2022	404,4
FLAG IDA	4	4	706	176,5
FLUDARABIN	1	7	0	0
HIDAC	7	11	0	0
ICE	3	8	333	41,6
PAD	7	23	93776	4077,2
FC	1	1	376	376
VAD	6	21	728	34,6
HYPERCVAD	7	12	1202	100,1
SOLIRIS	1	14	0	0
TOTAL	83	249	142019	

Stem Cell Transplantation

Poster No: 00168 Abstract:0117

AUTOLOGOUS STEM CELL TRANSPLANTATION IN TREATMENT OF PATIENTS WITH MULTIPLE MYELOMA-12 YEARS SINGLE CENTER EXPIRIENCE

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Background: multiple myeloma is a malignant neoplasm of plasma cells. Autologous stem cells transplantation (ASCT) has become the first line of therapy mainly because of the low transplant-related mortality and prolongation of event free survival resulting in improved quality of life. High–dose therapy (HDT) with ASCT should be part of primary treatment in newly diagnosed patients up to the age of 65 years with adequate performance status and organ function.

Aim: the aim of this study is to present our ten years experience in treatment of patients with multiple myeloma with ASCT.

Material-Methods: during a 12- years period we have performed 44 courses of HDT and consecutive ASCT in 39 patients with multiple myeloma (5 tandem transplantation). In this study we retrospectively analyzed the epidemiological characteristics of this group of patients. Results: Female:20 Male: 22 Median age: 53 years (from 43-64). High-dose Melphalan in doses 200mg/m^2 was used as conditioning regimen, in second (tandem) transplantation 140mg/m^2. Median count of infused CD34+ cells was 3,65x108/kg. As a source of added stem cells we use phlebothomy in 3 patients. The median period from diagnosis to transplantations was 10 months. Of 39 patients, 24 (61%) are alive, 15 (39%) are have died (4 renal failure, 4 multi-organ failure, 4 infections, 3 fatal cerebral bleeding). The disease-free survival was 24 months. OS was 50 months and EFS was 38 months. Conclusions: ASCT offer better results in survival and quality of life compared with patients treated only with standard chemotherapy.

Keyword: stem cell transplantation;multiple myeloma

Poster No: 00169 Abstract:0135

MULTIPLE BIOMARKERS IN THE DETECTION OF CARDIOTOXICITY DURING STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCIES

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Background: Cardiotoxicity is a potentially serious complication of hematooncology treatment. Preparative regimen (PR) followed by stem cell transplantation (SCT) represents a high risk for development of cardiotoxicity. Various methods including cardiac biomarkers have been recommended for monitoring of cardiotoxicity.

Objectives: The aim of the study was to assess cardiac toxicity during SCT with multiple biomarkers of cardiac injury – myoglobin, creatine kinase MB (CK-MB mass), cardiac troponin I (cTnI), heart-type fatty acid-binding protein (H-FABP), glycogen phosphorylase BB (GPBB). Experience with new perspective cardiac biomarkers (GPBB, H-FABP) in this setting is very limited.

Methods: A total of 53 patients (mean age 49.9 ± 12.3 years, median 54 years, 33 males) transplanted for various hematological malignancies were studied. The diagnoses were as follows: AML 27, MM 12, NHL 5, HL 4, ALL 3, CML 1, MDS 1. Thirty transplants were autologous, 23 allogeneic. Cardiac biomarkers were measured on Randox Evidence analyzer the day after completion of preparative regimen (after PR) and the day after infusion of stem cell grafts (after SCT). Values above the reference range recommended by the manufacturer were considered elevated.

Results: We found significant elevations in GPBB (above 7.30 µg/L) in 8 (15.1 %) patients after PR and in 9 (17.0 %) after SCT. H-FABP increased slightly above the

cut-off after SCT in 1 (1.9 %) patient. Other cardiac biomarkers (myoglobin, CK-MB mass, cTnI) remained within the reference ranges in all patients. We found a significant correlation between elevation in GPBB and diastolic left ventricular (LV) dysfunction on echocardiography (r = 0.603; p <0.0001). No patient manifested clinical cardiotoxicity in the peritransplant period.

Conclusions: Our results suggest that administration of PR followed by SCT could be associated with myocardial injury manifested by increased release of GPBB from cardiomyocytes which could correlate with diastolic LV dysfunction on echocardiography. In asymptomatic patients, these findings could be considered a sign of acute subclinical cardiotoxicity. Whether these acute changes will have predictive value for development of treatment-related cardiomyopathy in the future is not clear and will be evaluated during a prospective follow-up. Further studies in a larger number of patients will be needed to confirm our results and define the potential role of new biomarkers of cardiac injury in this context.

The work was supported by a long-term organization development plan 1011 (FMHS).

Keyword: cardiac biomarkers, stem cell transplantation

Poster No: 00170 Abstract:0142

WHEN AND HOW SHOULD A PATIENT WITH MYELODYSPLASTIC SYNDROME BE TRANSPLANTED?

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Patients with lower risk MDS tend to have a more indolent, yet still progressive course. In fact, the presence of severe neutropenia or thrombocytopenia may be an indication for HCT, particularly in younger individuals even with a low International Prognostic Scoring System (IPSS) score since none of the non-HCT therapies have been shown to be curative. Red blood cell transfusion dependence should also be considered in this context. Transfusion dependence is also linked to marrow fibrosis, which is associated with more rapid progression of MDS, and we showed recently that MDS patients with marrow fibrosis who are transplanted at a more advanced disease stage have an inferior outcome compared to patients without fibrosis. Whether chelation therapy of iron overload improves outcome after HCT, has yet to be determined.

The decision to proceed to HCT is easier in patients with advanced/high risk disease. Patients with RAEB-1 or RAEB-2 patients in WPSS categories intermediate, high and very high risk, and patients with intermediate to very poor risk cytogenetics (by 5-group classification) should definitely be considered for HCT.

Patients with therapy-related MDS should also be offered transplantation as it has been shown that, once adjusted for the patient's karyotype, the probability of transplant success is similar to that in patients with de novo MDS.

Optimal timing of HCT for MDS has remained a controversial issue. The probability of relapse increases progressively with increased IPSS or WPSS scores, the major determining parameters being karyotype and myeloblast count. Patients with high or intermediate-2 risk by IPSS who have HLA-identical sibling donors and are prepared for HCT with high intensity conditioning regimens, appear to benefit from early HCT, while patients with low or intermediate 1 risk may have a longer life expectancy if HCT is delayed until evidence of disease progression.

Post-HCT relapse has remained a challenge, particularly in patients with high risk disease, especially those with poor risk cytogenetics. Intensification of the conditioning regimens has decreased post-HCT relapse, but has also increased toxicity and NRM. Very little, if any, toxicity was observed with a regimen composed of Flu (3 × 30 mg/m^2) and 2 Gy of TBI, but the cumulative incidence of relapse was more than 50% at 3 years. Others used a regimen of Flu + melphalan and noted a relapse incidence of less than 25% at 3 years, but a NRM of 40%.

Encouraging results have been reported recently with regimens including treosulfan. In a trial conducted at our Center 60 patients with MDS or AML were prepared with a regimen of Fludarabine (30 mg/m^2 × 5) and treosulfan (12g or 14 g/m^2 × 3) for HCT from HLA-matched related or unrelated donors.

Additional studies will need to determine the impact of novel non-transplant therapy on the decision about and the timing of HCT.

Keyword: Mds, transplantation

Poster No: 00171 Abstract:0158

HODGKIN LYMPHOMA BUT NOT NON-HODGKIN LYMPHOMA IS INDEPENDENT RISK FACTOR FOR POOR STEM CELL MOBILIZATION

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Objective: Poor mobilization is an important problem in autologous stem cell transplantation. The ratio of poor mobilization was higher in lymphoma patients. In this study we tried to identify the possible risk factors for poor mobilization at lymphoma patients.

Method: We retrospectively analyzed 57 lymphoma patients who were treated by autologous stem cell transplantation between 1998 – 2011. We searched the relation between mobilization and different variables (diagnosis, type of the disease, age, sex, weight, bone marrow involvement, radiotherapy, treatment protocols, the number of the chemotherapy cycles and the rituximab administration) by the multivariate test (logistic regression). p values less than 0.05 were considered as significant. The data were analyzed using computer software (SPSS 16.0, SPPS, Inc., Chicago, IL). Mobilization insufficiency was defined as the peripheral blood CD34+ cell count less than 10/µl during the post-mobilization period or collected CD34+ cell count less than 2.5x106/kg

Results: The 57 patients diagnosed as lymphoma (38 non- Hodgkin and 19 hodgkin lymphoma) were composed of 34 males and 23 females. Their median age was 44 (range, 19 - 66) years old. A poor mobilization was documented in 13 patients. (22.8 %; 5 Hodgkin lymphoma patients: 25% and 8 non-Non Hodgkin lymphoma patients: 21.6 %). Bone marrow involvement (OR = 46.34, p = 0.003), being diagnosed as Hodgkin lymphoma (OR = 24.33, p = 0.03), and treatment with more than 10 cycles of chemotherapy (OR = 14.92, p = 0.02) were found as risk factors for poor mobilization. When we excluded patients with bone marrow involvement, the ratio of poor mobilization was 11.5 % for non – Hodgkin Lymphoma and 22.2 % for Hodgkin Lymphoma.

Discussion: For the lymphoma patients the most important factor for poor mobilization was bone marrow involvement. In this present study, we documented that the increased risk for poor mobilization at non-Non Hodgkin lymphoma patients was due to bone marrow involvement. We could conclude that the increased risk of poor mobilization at Hodgkin lymphoma patients (OR = 24.3) was independent of bone marrow involvement unlike non-Hodgkin lymphoma patients. At these patients other factors like the nature of the disease, the chemotherapeutic drugs specific to Hodgkin lymphoma, or the characteristics of the patients should be investigated for poor mobilization

Keyword: mobilization, lymphoma

Poster No: 00172 Abstract:0175

FACTORS AFFECTING LYMPHOCYTE RECOVERY AFTER BONE MARROW TRANSPLANTATION

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Recovery of the immune system is of paramount importance for the success of allogeneic stem cell transplantation (ASCT). The incidence of post-engraftment infections is mainly due to a delayed reconstitution of lymphocytes. Several groups including ours reported that early lymphocyte recovery after ASCT was associated with improved outcomes. The factors affecting lymphocyte recovery after bone marrow transplantation (BMT) and its influence on outcomes are not well studied.

554 pts with acute leukemia (452 AML/MDS and 102 ALL) who underwent ASCT from bone marrow grafts at MD Anderson Cancer Center between 01/1999 and 12/2010 were included. Eighteen pts who had primary graft failure were excluded. Demographics, remission status at the time of BMT, preparative regimen, graft-versus-host disease (GVHD) prophylaxis, donor type, graft CD34+ and CD3+ cell contents, data on engraftment, response, GVHD, progression, and survival were gathered from institutional databases. Early lymphocyte recovery (ELR) was defined as achieving absolute lymphocyte count of 1000/μL (ALC1000) by day 100. Haploidentical donor was defined as a related donor with >=3 HLA allele mismatches.

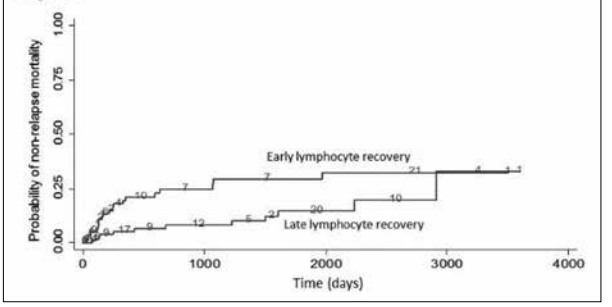
Pt age, graft CD34+/CD3+ cell content, and remission status did not affect lymphocyte recovery. ALL diagnosis, TBI-based or fludarabine-melphalan (>140 mg/m^2, FM>140) ablative regimens, post-BMT cyclophosphamide for GVHD prophylaxis, and not receiving ATG were significantly associated with late lymphocyte recovery on univariate analysis. There was a trend of late lymphocyte recovery after BMT from haploidentical donors compared to matched ones. A Cox proportional hazards model confirmed the adverse effect of TBI-based/FM>140 ablative regimens and haploidentical donors on lymphocyte recovery. A strong association between ATG use and early lymphocyte recovery among patients who received reduced intensity or busulfan-based ablative conditioning was also observed (p=0.06).

Pts who developed acute GVHD, received a second graft infusion, or relapsed prior to day 100 were excluded from the analyses assessing the influence of ELR on BMT outcomes. Among the remaining 246 patients, being in complete remission (CR) at the time of BMT and ELR were associated with significantly lower non-relapse mortality (NRM) on univariate analysis (Figure). There was a strong trend of higher NRM in patients who received TBI-based ablative conditioning (p=0.07). Pt age, graft cellular content, and GVHD prophylaxis type did not affect NRM. A Cox proportional hazards model confirmed ELC (HR: 0.2 [0.1-0.5]) and CR status (HR: 0.3 [0.2-0.7]) to be independent prognostic factors for NRM.

In conclusion, early lymphocyte recovery is an independent prognostic factor for NRM after BMT and is influenced by conditioning regimen but not by the bone marrow graft cellular content.

Keyword: Stem cell transplantation

Figure 1



Poster No: 00173 Abstract:0185

FLAMSA-BASED SEQUENTIAL CONDITIONING THERAPY AS SALVAGE TREATMENT FOR HEAVILY PRETREATED PATIENTS WITH LEUKEMIA: A SINGLE CENTRE EXPERIENCE

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Aim: The aim of this retrospective single-centre study was to examine the allogenic HSCT results based on FLAMSA cytoreductive therapy followed by a reduced intensity or myeloablative conditioning regimen.

Patients: Between 2007 and 2012, a total of 20 patients (17 de novo or secondary AML, 2 ALL, 1 Mantle cell lymphoma; all with active refractory disease) were treated with the FLAMSA (fludarabine, amsacrine, and cytarabine) followed by a reduced intensity regimen (n=19) or myeloablative regimen (n=1) (Table 1). The median age was 41 years (range 28-48.5 ys); three patients were females and 17 males. In our cohort, three patients underwent the second allo-HSCT due to relapse of acute myeloid leukemia. Donors were HLA-identical siblings in 11 and unrelated donors in 10 patients. The allograft source was peripheral blood stem cells in 17 patients; two patient received cord blood and one patient received bone marrow.

Results: Twelve patients reached complete remission (CR). Of these eight patients relapsed, but CR was re-achieved in two patients after chemotherapy and donor-lymphocyte infusions. After a median follow up of 102 days (95% CI), the incidence of non-relapse mortality was 30 %. Median time from diagnosis to alloHSCT was 18.2

months (range: 8.0-24.3 months). The median number of transplanted cells was 5.38x106 CD34+ cells/kg (range 1.3-9.9 x106). Eleven patients (55%) died from reasons not related to leukemia before day +100 (Table 1). Acute GvHD occurred in nine patients, reaching grade I in 1, grade II in 1, and grade III and IV in 7 cases. Of the 10 patients who survived more than day 100 chronic GvHD developed in 7 patients. The estimated 1-year overall survival from the transplantation was 40%±11% (median: 3.4 months, 95%CI).

Conclusion: Although 60% of CR rate makes this approach attractive, high rates of relapse and TRM needs to be improved new transplant modalites.

Keyword: FLAMSA, allogenic HSCT

Table 1. Patients's characteristics and transplant outcome

Gender (M/F) (n)	17/3
Median age (years (range))	41 (28-48.5)
Diagnosis (n)	
AML (De novo/Secondary)	14/3
ALL	2
Mantle cell lymphoma-leukemic form	1
Treatment cycles prior to transp. (median±SD)	3 (1-8)
Sorror comorbidity index (median±SD)	2 (0-7)
Donor type (n)	
HLA-matched sibling or related donor	10
HLA-macthed unrelated donor	10
HLA-mismatched unrelated donor	8
Unrelated cord blood	2
Conditioning regimen	
ATG+TBI	1
Cy+ATG+TBI	11
Cy+TBI	6
Flu+Bu	1
Treosulfan+VP16+ATG	1
Prophylaxis for GvHD	
CSA+MMF	13
CSA+Mtx	6
Tacrolimus	1
Engraftmant kinetics (median±SD)	
Neutrophil (0.5x10e9/L)	16 (10-39)
Platelet (20x10x10e9/L)	15 (11-48)
Transplant-related mortality	6 (30 %)
Day +100	1 engraftment failure
Causes of death	2 sepsis
	1 congestive heart failure and sepsis
	1 GVHD and fungal infection
	1 Acute GVHD and myocardial infarction
One-year overall survival	40±11%

Poster No: 00174 Abstract:0186

GRANULOCYTIC SARCOMA AT CHRONIC MYELOID LEUKEMIA PATIENT WHO WAS TREATED WITH ALLOGENEIC TRANSPLANTATION

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Introduction: Granulocytic sarcoma is an extramedullary tumoral lesion consists of immature myeloid cells. It can accompany with acute myeloid leukemia, chronic myeloproliferative neoplasm and myelodysplastic syndrome. It can be seen at the diagonosis or during the follow up period. Here, we report a case of chronic myeloid leukemia who was treated with allogeneic stem cell transplantation and relapsed with granulocytic sarcoma.

Case: A 33-year old male patient was diagnosed as Ph (+) CML in 2003 September. He was treated with hydroxyurea and interpheron. In 2004 February 400 mg/day imatinib mesilate treatment was initiated. In January 2007, the dose of imatinib was titrated to 800mg /day due to progression of disease to accelerated phase. In 2007 September, allogeneic stem cell transplantation from HLA full-matched related donor was performed due to lack of response. Full donor chimerism and complete cytogenetic response was obtained after the transplantation without major molecular response and 100 mg/ day Dasatinib was administered. We achieved major molecular response six months after the dasatinib treatment and he was followed up with major molecular and complete cytogenetic responses until April 2012. At that time, rapidly progressive tumoral lesion of 20x15 cm was observed at his right shoulder. The biopsy revealed granulocyctic sarcoma. The bone marrow biopsy revealed remission with a cyctogenetic analysis of 46XX. The bcr –abl analysis of bone marrow with RT-PCR method was also negative. He was treated with radiotherapy and standard doses Ara C + İdarubicine induction chemotherapy for 2 cycles and more than 90% regression was achieved. But the lesion grew up rapidly in a few weeks and FLAG-İda chemotherapy was initiated. He died of sepsis during the time of chemotherapy.

Conclusion: Relapse of disease with only granulocyctic sarcoma is rare in patients who treated with allogeneic stem cell transplantation. Even though, without systemic disease involvement, granulocytic sarcoma has an aggressive course, usually no response was achieved to combination therapies. Donor lymphocyte infusions or retransplantation can be used as a treatment option.

Keyword: granulocytic sarcoma

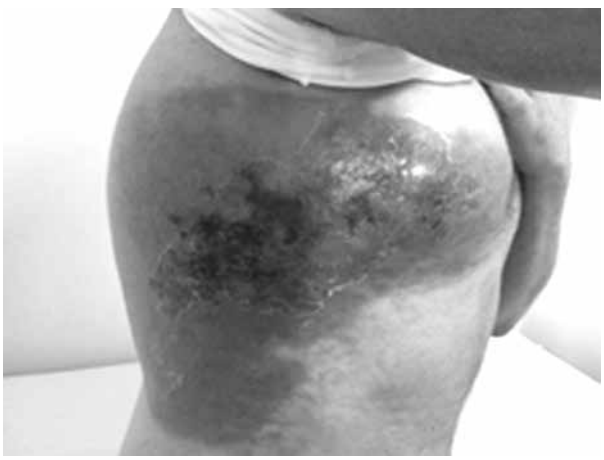

Figure 1. Granulocytic sarcoma at presentation

Poster No: 00175 Abstract:0208

EXTENSIVE CHRONIC GVHD TRIGGERRED BY LENALIDOMIDE MAINTENANCE AFTER NONMYELOABLATIVE ALLOGENEIC STEM CELL TRANSPLANTATION IN A PATIENT WITH MULTIPLE MYELOMA

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Allo-SCT may be the only treatment in MM with potential chance of cure. Immune-modulator novel anti-myeloma agents with potential to induce graft-versus-myeloma (GVM) effect and hence improve disease outcome are of special therapeutic interest.

A 53 year old man diagnosed with stage III-A IgG kappa MM in April 2005 received 6 courses of VAD and PR was obtained. One year later, for relapse, thal/dex was started and resulted in PR after 2 months. In January 2007, ASCT with 200 mg/m^2 melphalan was performed and VGPR was achieved after 6 months. In March 2009, 2nd relapse was treated with 8 courses of vel/dex and resulted in VGPR. For 3rd relapse in July 2010, 2 courses of len/dex achieved PR and was completed to 12 courses. 4th relapse in October 2011 was treated with 4 courses of V/TCD and PR was obtained. He underwent nonmyeloablative (NMA) allo-SCT from matched related donor in February 2012 with fludarabine and melphelan as CR and CSa and MTX as GVHD prophylaxis. On day +30, complete chimerism was shown. Because of renal dysfunction, CSa was replaced by MMF on day +75. By day +100, patient had no active MM, but MMF was tapered due to positive serum immunofixation test and 5-10% plasma cells in bone marrow. By day +120, M-protein increased from 0.54 to 0.83 g/dl and MMF was discontinued to further induce GVM. One month later, due to mild anemia and an increase in M-protein to 0.88 g/dl, lenalidomide maintenance 10 mg/day on days 1-21, q 28 days and dexamethasone 40 mg/week was started. After 2 cycles on 7th month of allo-SCT, patient presented with papular skin changes on anterior torso, hyperkeratotic changes on lower labial mucosa, symptoms of dry eyes and elevated liver enzymes. Schirmer's test was positive and liver biopsy showed severe bile duct injury and infiltration of some portal tracts by mononuclear cells. Due to extensive chronic GVHD, len/dex was stopped and methylprednisolone 2 mg/kg/day was started. Within 3 weeks, there was regression in skin rash, mucosal changes and liver enzymes. Patient is still under follow up with no active disease.

Both thalidomide and bortezomib are effective in relapse after allo-SCT, without excessive stimulation of GVHD. Impressive results were obtained with lenalidomide as salvage therapy for symptomatic disease after allo-SCT. Hovon 76 trial showed lenalidomide maintenance after allo-SCT improved response in 37% of patients with a 1-year PFS of 69%. Yet, this trial reported early lenalidomide treatment after an NMA allo-SCT is not feasible due to development of GVHD, which caused to stop treatment prematurely in 43% of patients. Increased frequency of HLA-DR+T cells and regulatory T cells with lenalidomide is accounted for GVHD. In lenalidomide associated GVHD, most common sites of involvement were skin and liver. Yet, liver involvement had not been confirmed by biopsy. To our knowledge, this is the first case, in which liver GVHD due to lenalidomide maintanance was histologically proven.

Keyword: Extensive chronic GVHD, lenalidomide maintenance

Poster No: 00176 Abstract:0212

SUCCESSFULL TREATMENT OF RELAPSED HODGKIN LYMPHOMA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION WITH BRENTUXIMAB VEDOTIN: REPORT OF TWO CASES

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Hodgkin lymphoma (HL) relapsing after allogeneic stem cell transplantation (alloSCT) presents a major clinical challenge.

Case 1: A 21-year-old man was diagnosed with NS HL in 2009. Over following 3 years, he was treated with multiple chemotherapy regimens and myeloablative alloSCT from matched related donor was performed in active disease status with BEAM as conditioning regimen (CR). Three months after alloSCT, primary refractory disease was diagnosed by PET CT and histopathological studies. At that time, complete chimerism was shown. Immunosuppressive medication was stopped and CEP chemotherapy and DLI was started. Yet, after 3 cycles, there was no response. Decision was made to initiate treatment with brentuximab vendotin 1.8 mg/kg q 3 weeks followed by DLI. After infusion, patient complained of erythema of eyes and tingling of fingers, which responded to administration of diphenhydramine and steroids. At 2nd cycle of brentixumab, steroids and diphenhydramine were given as premedication and no infusion related complication ensued. DLI was discontinued due to development of severe liver and mild skin chronic GVHD (cGVHD). Corticosteroid, mycophenolate mofetil and extracorporeal photopheresis (ECP) were initiated. During follow-up, antiviral treatment was given for CMV viremia. PET CT after 4 cycles of brentixumab showed near complete metabolic and anatomic response. Two months after ECP, complete and partial response were obtained for skin and liver cGVHD, respectively. Patient has completed 6 cyles of brentixumab and will continue to a maximum of 16 cycles.

Case 2: A 32-year-old male with primary refractory HL despite multiple chemotherapy regimens, radiation, autologous stem cell transplantation was treated with non-myeloablative alloSCT from matched unrelated donor 11 years after initial diagnosis. Flu/Cy was used as CR. Three months after alloSCT, first complete metabolic response was obtained. 18 months after alloSCT, relapse occurred and brentuximab vedotin 1.8 mg/kg q 3 weeks was begun. At initiation of therapy, patient had no sign of cGVHD and was not under immunsupression. Infusion was well tolerated with no need for premedication. PET scan after 2 cycles of brentuximab showed complete metabolic response. After 6 cycles, grade 1 peripheral neuropathy developed. Patient is currently under follow up and completion of therapy to a maximum of 16 cycles is planned.

Our cases support the potential clinical benefit of brentuximab suffering relapsed HL after alloSCT. It is important to interpret results of the present observation in context of a broader group of HL patients relapsing

after alloSCT. Interestingly, there is preclinical data implying targeting CD30 on T cells may abrogate GVHD, so one could hypothesize brentuximab vedotin could yield a 2-fold benefit for patients with relapse and GVHD, though there are no clinical data to date supporting this premise.

Keyword: brentuximab vedotin, relapsed Hodgkin lymphoma after allogeneic stem cell transplantation

Poster No: 00177 Abstract:0272

ANTITHYMOCYTE GLOBULINE (ATG) OR ANTILYMPHOCYTE GLOBULINE (ALG) FOR TREATMENT OF STEROID REFRACTORY ACUTE GRAFT VERSUS HOST DISEASE (GVHD)

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Introduction: Currently there is no consensus of treatment for steroid-refractory acute GvHD. Antithymocyte globulin (ATG) is the most common form of immunosuppression used in this setting. We report our institution's experience treating steroid resistant acute GvHD in 26 patients between Jan 2000 and Dec 2012. Median age was 33 years (19-54y). The gender of patients was 10 females and 16 males. The patients' and donors' characteristics and response to the treatment were shown in Table.

Results: Acute severe GvHD (grade III-IV) developed median 22 days (8-70 days) after the transplantation (n=23) or donor lymphocyte infusion (n=3). For secondary treatment of acute GvHD, ATG (ATG fresenius®) (n=22) or ALG (equine Pastuer Merriux®) (n=4) with corticosteroids was usually administered by intravenous infusion at a dose of 10 mg /kg/day consecutively five days. From the beginning of acute GvHD to the first doses of infusion of ATG or ALG was median 19 days (5-78 days). The estimated one- and two-year overall survivals were 15.4±7.1% and 7.7±5.2%, respectively. Complete remission was seen in 11 patients (42.3%). When we compared to patients with/out response to the treatment, the type of organ involvement such as gastrointestinal system or liver were not associated with the responses to anti-globuline. Survival did not change according to response of the treatment and using anti-globulin type, ATG vs ALG. In responsive group (n=11), all the patients died of several reasons such as infection (n=7), chronic GvHD (n=3) and upper gastrointestinal bleeding (n=1). In non-responsive group (n=16) 14 patients were death. Thirteen out of them systemic infection added to acute progressive GvHD in early period. But one patient died of sudden death nine years after acute GvHD. Only one patient is alive today.

Conclusion: Steroid refractory acute GvHD is one of the severe mortal complications of allogeneic HSCT. In our retrospective evaluation ATG or ALG seems to be effective on GvHD, even though anti-globulin treatment did not change the survival due to opportunistic infections.

Keyword: Graft versus host disease, transplantation

Table 1. Characteristic and responses

Features	N=36
Patients	
Median age (range), years	33 (19-54)
Gender (M/F)	16/10
Donors	
Median age (range), years	31 (11-55)
Gender (M/F)	12/14
The pair of gender	
Female donor → Female recipient	3
Female donor → Male recipient	9
Male donor → Male recipient	8
Male donor → Female recipient	6
Diagnosis	
Acute Leukemia (AML/ALL)	13 (10/3)
Chronic myeloid leukemia	8
Mylodisplastic syndrome	2
Multiple myeloma	1
Pure red cell aplasia	1
Primary myelofibrosis	1
Donor type	
Identical sibling	23
Identical related	1
Unrelated	2
Conditioning regimen	
Ablative/Reduced intensity	22/4
Stem Cell Source	
Peripheral blood	19
Bone Marrow	6
Peripheral blood+Bone marrow	1
GvHD prophylaxis	
Ciclosporin A plus methotrexate	22
Ciclosporin A plus mycophenolate mofetil	4
Organ involvement	
Gastrointestinal system (G) ±skin	15 (12)
Liver (L) ±skin	1 (0)
G plus L ±skin	10 (8)

Poster No: 00178 Abstract:0278

WHICH SHOULD BE TAKEN INTO CONSIDERATION WHEN DMSO IS USED FOR CRYOPRESERVATION VOLUME OR CELL COUNT?

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Dimethylsulfoxide (DMSO) is toxic to the cells. Although it is used for cryopreservation, it has not been approved by FDA. 10% concentration is used for cryopreservation mostly.However, 5% concentration and combinaton with HES and albumin is also used.There is no standart procedure for cryopreservation.

Aim: To evaluate the viability and engrafment kinetics of the products those contain %10 DMSO but different amounts of DMSO and CD34 + hematopoietic stem cells. Materials-Methods: 60 patients whom underwent autologous transplantation were evaluated.Thecorrelation between the amount of DMSO and other parameters was tested by Spearman correlation test. A statistical software (STATA 11.0, TX-USA) was used.The average age of the patients is 52,64 (24-73). Male to female ratio was 38:21.

Results: The diagnosis of the patients were Multipl Myeloma, n=31, Non Hodgkin Lymphoma n= 24, Hodgkin Lymphoma n= 4, Acute myeloid leukemia n=1. The number of patients who have product in 1, 2, 3 and 4 cryobags were n=28, n=23, n=8 and n=1 respectively.All of the products contain 10% DMSO. The amount of total DMSO was 22,49 (7-48ml). The total CD34+ cell count was 6,3x10e6/kg(2,5-18x10e6/kg). The DMSO amount

per CD34+ hematopoetic progenitor cell is 4.72 ml (0,39-17.78ml). The viability of the cells were 80.84 % (73-89%). The blood LDH level on the first day after transplantation is 1051.22 IU/L (205-6237)Although it was not statistically significant, the viability of cells was inversely correlated with the amount of DMSO (Spearman's rho = -0.1363, P=0.3121). A significant correlation was found between the amount of DMSO and the LDH level on day one after the transplantation (Spearman's rho = 0.5945, P<0.001).Neutrophils engrafted on day 11 (8-23day) and platelets engrafted on day 14 (9-37 day) in all patients.

Conclusion: Although most centers use 10% DMSO, the adverse effect of the toxicity on the cells can increase to unexpected levels after a critical amount.

Keyword: cryopreservation, viability

Poster No: 00179 Abstract:0289

EFFECT OF RITUXIMAB ON LYMPHOCYTE RECOVERY AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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It has been previously shown that early recovery of lymphocytes predicts superior survival after autologous stem cell transplantation. On the other hand it is well known that rituximab treated patients has a B lymphocyte depletion for a period (around two years). Here we studied the effect of Rituximab therapy on lymphocyte recovery after autologous stem cell transplantation. Total 59 patient were analyzed. 23 of them received Rituximab prior to the transplantation (15 diffuse large B cell lymphoma, 5 mantle cell lymphoma, 1 marginal zone lymphoma and 2 t-cell rich B cell lymphoma) and 26 did not receive Rituximab before transplantation (27 Hodgkin lymphoma and 9 t-cell NHL). In both groups patients received median three courses of chemotherapy prior the transplantation. Median cycle of Rituximab was 6 months (3-12 months) in Rituximab group. Median time elapsed from last Rituximab dose to transplantation was 5 (1-37) months. Absolute lymphocyte count was 200 (0-2600)/µL in rituximab group and 300 (0-5300) in Rituximab naïve group at day 15 after reinfusion (p=0,2). Absolute lymphocyte count was 2000 (350-7800)/µL in Rituximab group and 1800 (300-5200) in Rituximab naïve group at day 100 after reinfusion (p=0,508). Our results suggest that Rituximab had no apparent effect on lymphocyte recovery of patients diagnosed with lymphoma undergone autologous stem cell transplantation. Additionally its in-vivo purging effect could have beneficial effect on the transplantation results.

Keyword: Stem cell transplantation, rituximab

Poster No: 00180 Abstract:0291

AN UNEXPECTED CAUSE OF PERSISTANT NEUTROPENIC FEVER IN A MYELODYSPLASTIC SYNDROME PATIENT: MESENTERIC PANNICULITIS

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Mesenteric panniculitis (MP) is a rare disorder characterized by inflammatory process in the mesenteric fat. Although the disease is considered idiopathic and benign, it has been associated with autoimmunity, trauma, neoplastic etiologies. Patients may present with abdominal pain, fever or intestinal obstruction. Following histological diagnosis, treatment depends on indiviual patient status and includes surgery, immunosuppressive therapy or conservative approach. Herein, we report a patient with MDS who had an unexpected diagnosis of 'mesenteric panniculitis' as the cause of persistant neutropenic fever.

A 57-year-old male diagnosed with MDS-RCMD was admitted for allogeneic HSCT. He complained of right upper quadrant pain and one month long fever reaching to 390C. He had previously recieved several antimicrobials and antifungal therapies for febrile neutropenia with no success. Microbiological and radiological investigations were performed to identify origin of fever. No microbiological agent was identified. Chest CT was normal. However, contrast enhanced abdominal CT showed a lesion with 101x52 mm in inferior neighbourhood of pancreas composed of inhomogeneous fatty tissue (Figure). Inflamed mass surrounded mesenteric vascular structures and was in close vicinity of superior mesenteric vein and artery. Findings were suggestive of mesenteric panniculitis. Due to deep localisation of the lesion and refractory thrombocytopenia, biopsy could not be performed. Colonoscopy, tumor markers and rheumatological serology were normal. Methylprednisolone (MPred) 1 mg/kg/day was started. Fever completely resolved and there was 90% relief of abdominal pain. MPred was subsequently tapered and stopped on 10th day as conditioning regimen (BU/CY) was initiated. However, fever recurred immediately following drug withdrawal. MPred was restarted and resulted in defervescence. On day +17, MPred was stopped again due to fever recurrence occurring one day later. Cultures remained negative and fever was attributed to mesenteric panniculitis. Steroid was reinitiated and resulted in rapid defervescence. Patient was discharged on MPred treatment. Control CT performed 6 weeks after initial evaluation showed mild decrease in size of mass lesion with a diameter of 82x46 mm. At last follow up on day +60, fever did not recur under steroid treatment. In our case, lack of histological evaluation is a matter of debate however the lesion appeared inflammatory. This case is interesting because MP treatment was steroid dependent and despite myeloablative and immunosuppressive conditioning regimen, there was only response to steroid therapy. To our knowledge, there is no report of a case of MP undergoing HSCT. Long term follow up of this patient will help to clarify contribution of HSCT to the course of MP.

In conclusion in febrile neutropenic patients with persistant fever as an unexpected, extraordinary and rare cause 'MP' should be included in differential diagnosis.

Keyword: Mesenteric panniculitis, HSCT

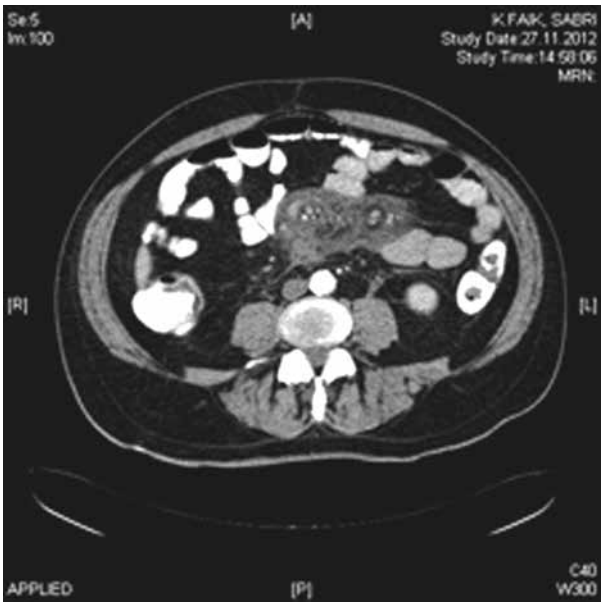

Figure 1. Apperance of inflamed mass lesion on abdominal CT scan

Poster No: 00181 Abstract:0293

ALLOGENIC PERIPHERAL STEM CELL TRANSPLANTATION AFTER REDUCED-INTENSITY CONDITIONING WITH BUSULFAN, FLUDARABINE,AND ATG IN MYELOFIBROSIS

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Busulfan, fludarabine, and antithymocyte globulin as a reduced-intensity conditioning is widely used for allogeneic stem cell transplantation (SCT). We report the results of reduced-intensity conditioning followed by allogenic peripheral SCT in 5 patients with primary myelofibrosis at diagnosis. All patients have intermediate group regarding Cervantes Risk Scoring System. The median age was 50 (35-57) years. Although all patients were transfusion-dependent, among five patients one had severe transfusional hemosiderosis due to ineffective iron chelation therapy. Stem cell source was HLA-matched sibling donors for all patients. The patients received conditioning regimen consisted of fludarabine 150-180 mg/m^2, busulfan 9,6 mg/kg, and antithymocyte globulin (ATG Fresenius) 15 mg/kg followed by peripheral blood stem cell allografting. The dose of stem cell infused was minimum 4x10^6 CD34+ cell/ µL. They received cyclosporine and mucophenolate mofetil for GVHD prophylaxis. Leukocyte engraftment occurred by day +13 (8-17) and platelet engraftment + 14 (12-22) post transplant. While four patients had full donor chimerism by day +30, one patient had on day +180. The incidence of acute and chronic GVHD were 16 % and 50 % respectively. Transplant related mortality was 16%. With the median follow-up of 15.6 (1.4-38.3) months, estimated one year event-free survival was 83 % and the overall survival was 83 %. One patient had severe back pain associate with mucophenolate and required drug interruption. One patient who had high EBMT transplant risk score developed venoocclusive disease and died on day +41 because of multi-organ failure. In conclusion, Flu-Bu-ATG protocol, as a reduced-intensity dose regimen, can provide effective disease control in myelofibrosis with acceptable non-relapse mortality and toxicity profile.

Keyword: Myelofibrosis, Allogeneik PSCT

Poster No: 00182 Abstract:0302

BONE MARROW HISTOLOGY DOES NOT PREDICT THE MOBILIZATION SUCCESS WHICH IMPLIES THE IMPPORTANCE OF "ON DEMAND" USE OF PLERIXAFOR

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Introduction: Patients with advanced or treatment-refractory Hodgkin disease and non-Hodgkin lymphoma (NHL) and patients with multiple myeloma (MM) may be successfully treated with high-dose chemotherapy followed by autologous transplantation of PBSC. Successful engraftment of PBSC is well correlated with the number of CD34 + stem cells infused. PBSC are mobilized into the peripheric blood by treating patients with granulocyte-CSF (G-CSF) for 5–7 days or with disease-specific, non-myeloablative chemotherapy,often in combination with G-CSF before leukapheresis.

The minimum number of CD34 + cells required for a single auto-SCT is generally considered to be 2–2.5_106 CD34 + cells/kg.

Plerixafor (formerly AMD3100) is a CXCR4 chemokine antagonist that has been shown to increase the number of circulating CD34+cells in healthy volunteers and cancer patients when administered alone or with G-CSF. When plerixafor (0.24 mg/kg) was given after 5 days of G-CSF (5 mcg/kg/day 2x1) to NHL and MM patients, the apheresis yields were significantly higher when compared with patients receiving G-CSF alone.

Methods-Results: We report August 2010 - February 2013 between four patients (M / F: 3/1, mean age: 52, age range 34-67) data were compiled.

One of these patient, who was MM, autologous stem cell transplantation were evaluated for the second time.

Multiple myeloma diagnostic frequency range (n = 1), Hodgkin's lymphoma (n = 1), non-Hodgkin's lymphoma (n = 1), chronic lymphocytic leukemia (n = 1) was determined.

In order to achieve the target stem cell, an average of 2 days (n = 4) apheresis was sufficient, in 1 patient, 3 days, 2 days in 2 patients, 1 patient has 1 day of apheresis.

Content of stem cell apheresis product of 4.03 million / kg (0 to 12.94 million / kg), respectively.

Mobilization could not be successful in 2 patients. These patients diagnose were MM and KLL.

MM diagnosed patient respond after 4 cycles of VAD complete response status.Then he had a autologous stem cell transplantation.After 3 months his disease repeat

and he evaluated for the second time of autologous stem cell transplantation.

The second patient KLL diagnosed patient had eight cycles of CHOP therapy after 4 cycles of Rituximab he had a complete remission. After the first repeat of the disease he had 2 cycles with minimal response to the Cyclophosphamide + G-CSF, after 4 cycles of Fludarabine + Cyclophosphamide he had partial response then he evaluated for the second time of autologous stem cell transplantation.

In none of the patients developed grade 4 adverse event during kemomobilizasyon.

Conclusion: Bone marrow histology may predict mobilization failure. In the era of plerixafor, according to the peripheral CD34+ cell count, preemptive use of plerixafor can overcome this problem but not always. Preemptive use provides reduced cost and morbidity.

Keyword: plerixafor, Bone marrow

Poster No: 00183 Abstract:0308

RESULTS OF AUTOLOGOUS PSCT FOLLOWED BY HIGH DOSE MITOXANTRONE AND MELPHALAN IN PATIENTS WITH LYMPHOBLASTIC LYMPHOMA

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Lymphoblastic lymphoma (LBL) is an uncommon malignancy accounting for <2% of non-Hodgkin's lymphoma. This type of lymphoma is considered a precursor B-cell/T-cell neoplasm and thought to be the nodal/extranodal presentation of acute lymphoblastic leukemia. Despite high initial remission rates with Hiper-CVAD, 40-60% of adults eventually relapse. Several studies have examined the role of both autologous and allogeneic peripheral stem cell transplantation (PSCT) in first and second remission, as well as in patients with refractory disease.

Patients and Metod: We evaluated the outcome of 5 patients (1 F, 4 M) with T cell LBL after high dose therapy following autologous PSCT between 2005 and 2012 in the Clinical Unit. Treatment regimens were hiper-CVAD in three patients and CHOEP in one patient. All of them had chemosensitive disease and went into complete remission prior to transplantation. One patient was primary refractory to the CHOP treatment and he was in partial remission (PR) after ESHAP salvage therapy. The Conditioning regimens were mitoxantrone 60 mg/m^2 and melphalan 180 mg/m^2 in five patients for otologus transplantation.

Results: Median follow-up of the patients were 11 months (range 4–33 months). For all patients, estimated 100 day, one year and two years event-free survival were 80 %, 80% and 60% and the overall survival were 100%, 80% and 80% respectively. One patient who has in PR prior to transplantation relapsed at 18 month and died at 33 month. The patient who has bulky and central nervous system involvement at diagnosis relapsed at 3 month and died at 8 month post transplantation.

Conclusion: Despite the small number of patients in this study, high dose mitoxantrone and melphalan followed by autologous PSCT seems to be an effective treatment option that can achieve complete remission for patients with LBL.

Keyword: Lymphoblastic lymphoma, autologous PSCT,

Poster No: 00184 Abstract:0335

STEM CELLS TRANSPLANTATION

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Chronic graft-versus-host disease (cGvHD) is a major complication of allogeneic hematopoietic stem cell transplantation. Post-transplant thrombocytopenia in patients with cGvHD has been associated with poor outcome and its etiology is unclear. We investigated whether thrombopoiesis, assessed via measurement of the absolute immature platelet number (AIPN), is impaired in cGVHD patients, and whether the level of thrombopoiesis correlates with severity and activity of cGvHD as assessed via the NIH organ scoring system. We utilized a cohort of 110 well-characterized cGVHD patients, including 83 (75%) with severe cGVHD per NIH global score. Higher AIPN was associated with active therapeutic intent (p=0.026), lower Karnofsky score (p=0.0013), worse joint/fascia cGVHD (p=0.0005) and worse skin cGVHD (p=0.0044). AIPN correlated with platelet counts and was not correlated with ANC, WBC, CRP, lymphocytes, albumin, total and average NIH scores, or number of prior systemic therapies. AIPN values for cGvHD patients substantially overlapped those of the normal population. Higher AIPN, as marker of active thrombopoiesisis, was associated with worse severity and activity of cGVHD, especially skin and joints/fascia manifestations. There is no evidence of hypo production of platelets in this cohort of moderate or severe cGvHD patients. Future studies should further investigate the role of thrombopoiesis in cGVHD.

Keyword: cGVHD, NIH global score

Poster No: 00185 Abstract:0336

CHRONIC LYMPHOCYTIC LEUKEMIA KIR GENE POLYMORPHISM IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

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Chronic lymphocytic leukemia (CLL) is associated with some cellular and humoral immune abnormalities leading to insufficient antitumor response. Natural killer (NK) cells play pivotal role in tumor development, response to infection and autoimmune diseases. The activities of these cells are regulated with several receptor systems. One of these receptors is killer immunoglobulin-like receptor (KIR). KIR polymorphism results heterogen tumor responses among population. The development of specific KIR gene phenotypes in leukemia patients result immune escape of leukemic cells from NK cells. In the present study we aimed to determine KIR gene polymorphism among CLL patients and to compare with healthy controls. The study included a total of 68 CLL patients and 64 healthy subjects. When we compared different KIR gene frequencies between CLL patients and controls, we observed statistically higher frequency of an inhibitor gene, KIR2DL3 in CLL cohort (p=0.02). The activator KIR2DS1, KIR2DS3, KIR3DS1 ve inhibitor KIR2DL5 gene frequencies were higher among low-intermediate risk CLL patients compared to high risk patients (p=0.03, p=0.01, p=0.03 ve p=0.01, respectively). The number of activator genes were significantly higher in high risk CLL patients compared to low-intermediate patients (p=0.04).

In conculusion, we speculate that the inhibitor gene KIR2DL3 might impede lysis of leukemic cells by supressing activity of NK cells and by this way contribute to disease pathogenesis. The low frequencies of KIR2DL5, KIR2DS1, KIR2DS3, KIR3DS1 genes among high risk CLL patients as compared to low-intermediate patients suggest that these genes might prevent disease progression and result a more indolent behaviour. On the other hand the lower median number of activator genes in high risk CLL patients supports the idea that activator KIR genes prevents disease progression in CLL.

Keyword: Chronic lymphocytic leukemia, KIR genes

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AUTHOR INDEX

A

B

C

Ç

D

E

F

G

H

I-İ

J

K

L

M

N

O

Ö

P

R

S

Ş

T

U-Ü

V

W-X

Y

Z