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Morphological and Immunophenotypic Clues to the WHO Categories of Acute Myeloid Leukaemia

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Acute myeloid leukaemia · Immunophenotyping · Morphology · World Health Organisation classification

Abstract
Diagnosis and classification of acute myeloid leukaemia (AML) require cytogenetic and molecular genetic investigation. However, while these evaluations are pending, morphology supplemented by immunophenotyping can provide clues to the diagnosis of specific cytogenetic/genetic categories of AML. Most importantly, acute promyelocytic leukaemia can be diagnosed with a high degree of certainty. However, provisional identification of cases associated with t(8;21), inv(16), t(1;22), and *NPM1* mutation may also be possible. In addition, transient abnormal myelopoiesis of Down's syndrome can generally be diagnosed morphologically.

Introduction

The diagnosis of the World Health Organisation (WHO) categories of acute myeloid leukaemia (AML) requires the careful integration of clinical history, morphology, and cytogenetic/molecular genetic analysis, supplemented by immunophenotyping in the residual category of AML, not otherwise specified [1]. However, results of cytogenetic and molecular genetic analyses may not be available immediately so that there is a role for morphology plus immunophenotyping in rapidly indicating a likely diagnosis. In the case of acute promyelocytic leukaemia (APL), in which the diagnosis is clinically urgent, the combination of these two modalities permits a diagnosis with a high degree of certainty. In some other types of AML, morphological and immunophenotypic features may provide an indication as to the cytogenetic anomaly likely to be present [2]. The latter nevertheless has to be confirmed by karyotypic analysis or fluorescence in situ hybridisation (FISH). Moreover, new entities characterised by molecular anomalies will require even more time-consuming targeted or whole-genome analyses. The WHO categories that will be discussed here are shown in Table 1.

AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*

This category of core-binding factor (CBF) leukaemia usually shows differentiation to mature neutrophils. Neutropenia is uncommon and there may be neutrophilia. Neutrophils can be dysplastic. Sometimes there is eosino-

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Table 1. WHO 2016 categories of AML

AML with recurrent genetic abnormalities	AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1* APL with t(15;17)(q24.1;q21.2); *PML-RARA* AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11* AML with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3* AML with t(6;9)(p23;q34.1); *DEK-NUP214* AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM* Acute megakaryoblastic leukaemia with t(1;22)(p13.3;q13.1); *RBM15-MKL1* AML with t(9;22)(q34.1;q11.2); *BCR-ABL1* AML with *NPM1* mutation AML with biallelic *CEBPA* mutation AML with *RUNX1* mutation
AML with myelodysplasia-related changes	
Therapy-related myeloid neoplasms[1]	
AML, not otherwise specified	AML with minimal differentiation AML without maturation AML with maturation Acute myelomonocytic leukaemia Acute monoblastic/monocytic leukaemia Acute erythroid leukaemia Acute megakaryoblastic leukaemia Acute basophilic leukaemia Acute panmyelosis with myelofibrosis
Myeloid sarcoma	
Myeloid proliferations associated with Down syndrome[2]	Transient abnormal myelopoiesis Myeloid leukaemia associated with Down syndrome[1, 2]

[1] Encompasses myelodysplastic syndromes as well as AML.
[2] WHO terminology.

philic differentiation. Typically, some of the blast cells have an indentation in the nucleus, representing the Golgi zone, and often there is a long thin or fusiform Auer rod sometime within the nuclear "hof" (Fig. 1). The diagnosis may be suspected from the cytological features.

Immunophenotyping shows the classical expression of markers of immaturity, CD34 and CD117, together with CD13 and CD33 (Fig. 2). Cytoplasmic myeloperoxidase (MPO) is present. Maturation of a proportion of the blasts towards the neutrophil lineage translates into some expression of CD15 and/or CD65 but not CD11b. Many cases show aberrant weak expression of the B-lineage antigen, CD19 [3–5]. Expression of CD56 by blast cells is frequently observed and has been reported to be associated with a poorer prognosis [6]. CD56 is also present on immature granulocytes from these patients [7]. Assessment of cytology plus immunophenotype can often suggest this diagnosis.

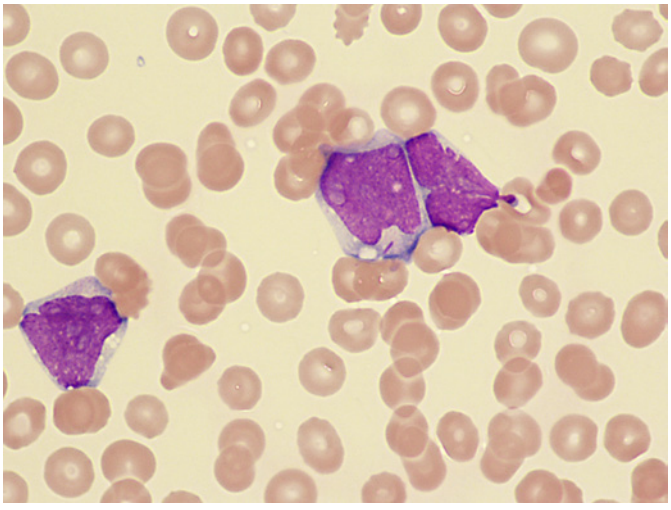

Fig. 1. Peripheral blood film in AML with t(8;21) showing an Auer rod in a nuclear "hof." MGG ×100.

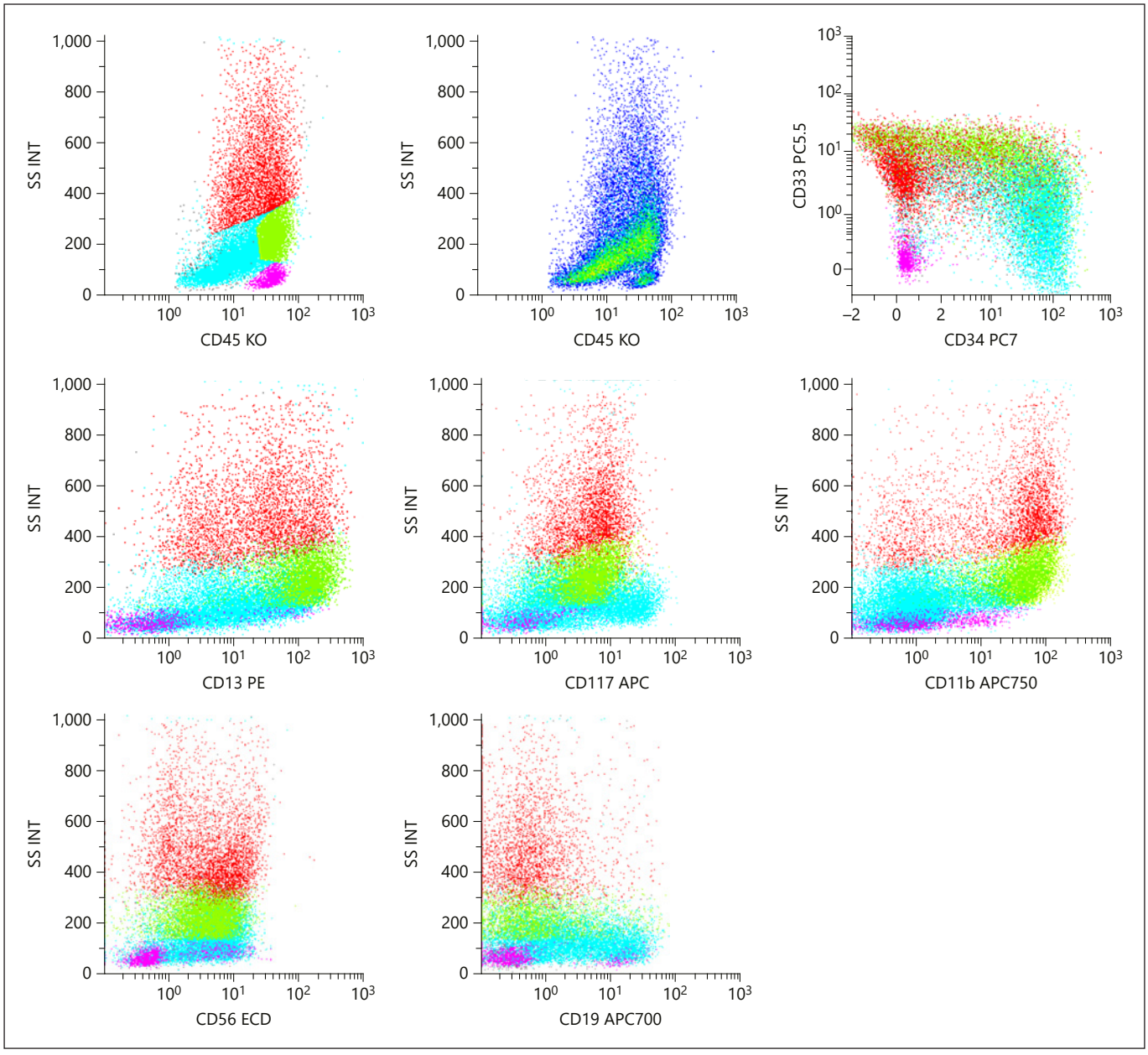

Fig. 2. Immunophenotypic features of AML with t(8;21), bone marrow aspirate. Side scatter (SS) is plotted against antigen expression. Red, neutrophils; green, monocytes (confirmed as such by expression of CD14 and CD36 [data not shown] as they could otherwise have been interpreted as degranulated neutrophils); cyan, blast cells; magenta, lymphocytes. There are two distinct populations of monocytes and blast cells, although almost with a continuum. The blast cells express CD34 and weak CD33, as well as CD13 and CD117, but not CD11b (which stains monocytes and neutrophils). Blast cells, monocytes, and part of the neutrophil population express CD56. There is aberrant expression of CD19 by the blast cells.

APL with t(15;17)(q24.1;q21.2); *PML-RARA*

A distinction must be made between cases of APL with classical morphology and the variant forms. Classical APL has hypergranular promyelocytes, some of which contain multiple Auer rods. Giant granules can also be present. The nucleus is bilobed but, because of the hypergranularity, this may not be readily apparent. The blood count, with a marked thrombocytopenia despite a relatively low white cell count and reasonably well-preserved

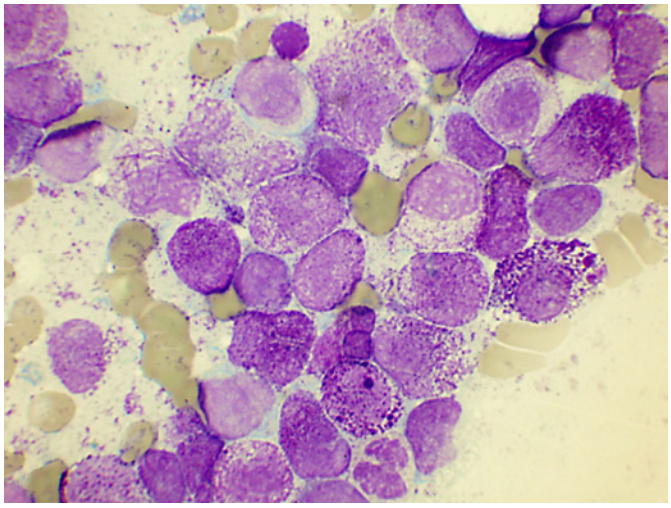

Fig. 3. Bone marrow film in hypergranular APL showing hypergranular promyelocytes, one with multiple Auer rods. MGG ×100.

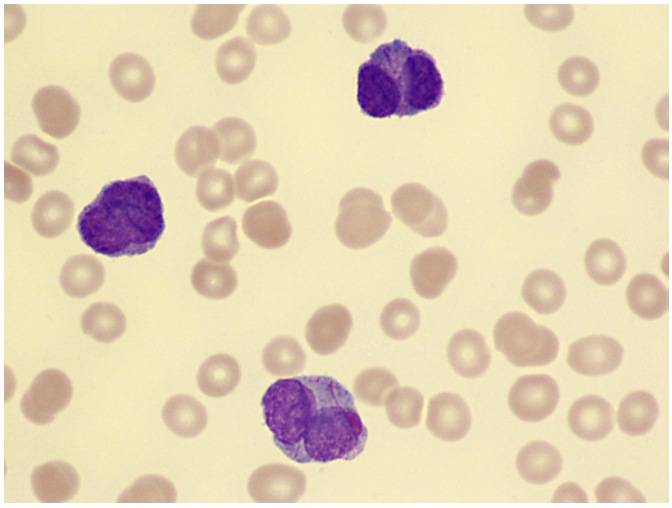

Fig. 4. Peripheral blood film in the hypogranular variant of APL showing three bilobed promyelocytes; granules are scanty but Auer rods are present. MGG ×100.

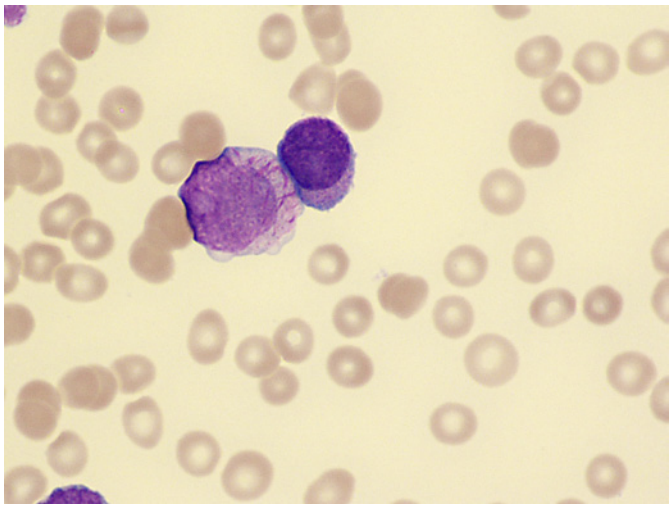

Fig. 5. Peripheral blood film in the hypogranular variant of APL showing a bilobed promyelocyte with multiple Auer rods. MGG ×100.

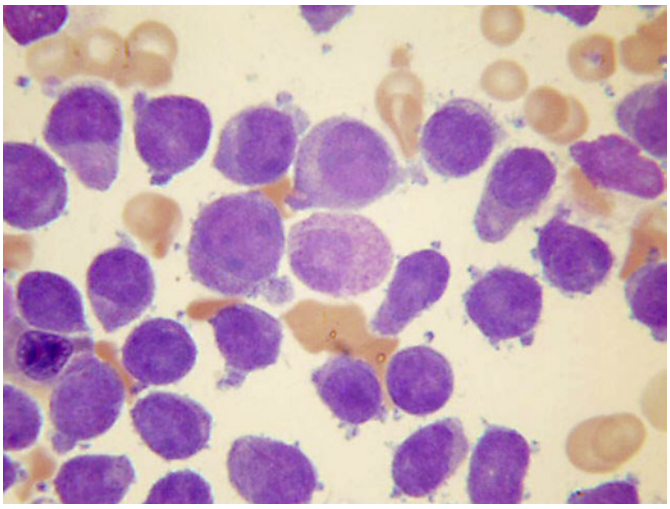

Fig. 6. Bone marrow film in the hyperbasophilic variant of APL showing abnormal, hyperbasophilic promyelocytes with cytoplasmic blebs that resemble those of megakaryoblasts. MGG ×100.

haemoglobin concentration, supports the diagnosis and should lead to further testing for disseminated intravascular coagulation. Leukaemic promyelocytes may be rare in the peripheral blood (or even absent) so that a careful search is needed followed by urgent examination of the bone marrow (Fig. 3). The cytological features are so characteristic that, when circumstances necessitate, treatment with ATRA (all-*trans*-retinoic aid) can be started without waiting for further supporting evidence. However, demonstration of the typical immunophenotype (see below) makes the diagnosis even more firmly based.

The hypogranular/microgranular variant of APL is also distinctive with a bilobed nucleus (Fig. 4). There is often a negative image between the lobes, which represents the Golgi zone containing granules that are below the level of resolution of the light microscope. A careful search may reveal some cells that are hypergranular or contain Auer rods (Fig. 5). The WBC is typically higher

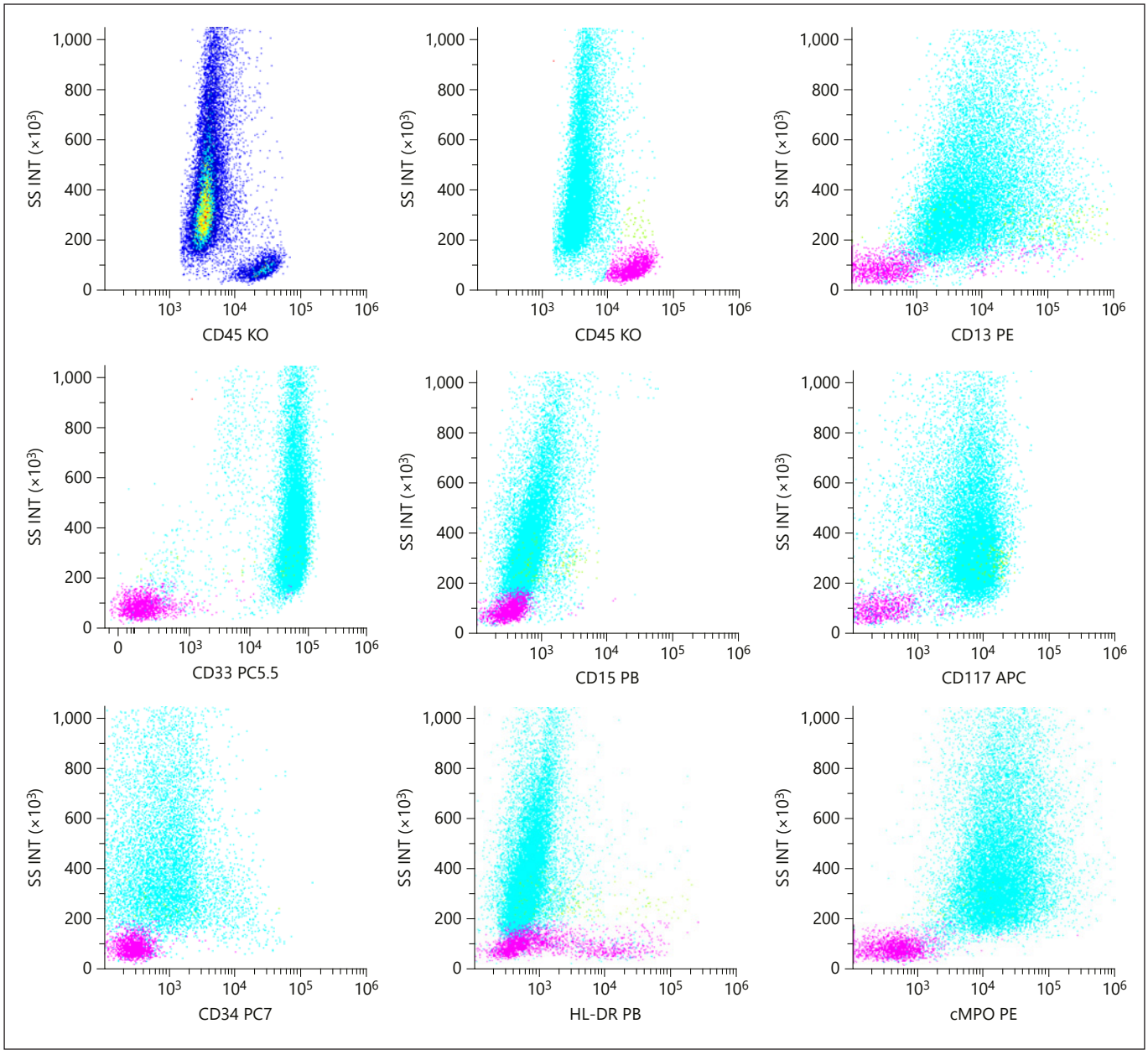

Fig. 7. Immunophenotypic features of APL, bone marrow aspirate. Side scatter (SS) is plotted against antigen expression. Cyan, blast cells; magenta, lymphocytes. There are no monocytes or granulocytes in this diagnostic sample. The blast cells mimic the position of neutrophils but lack CD15 (and CD16 and CD11b, not shown). They express CD117 together with CD13 and CD33 but lack CD34 and HLA-DR. They also strongly express MPO.

than in the hypergranular variant. Cytochemical staining shows strong MPO and Sudan black B positivity. The cytological features should arouse suspicion of this diagnosis, often quite a strong suspicion. A coagulation screen and urgent immunophenotyping are important in supporting the diagnosis and permitting the initiation of treatment while awaiting cytogenetic/molecular genetic confirmation.

The third cytological variant is the hyperbasophilic variant in which cytoplasm is more scanty, is basophilic, and shows cytoplasmic blebs (Fig. 6). Granules may or may not be visible. Confusion with the cytological fea-

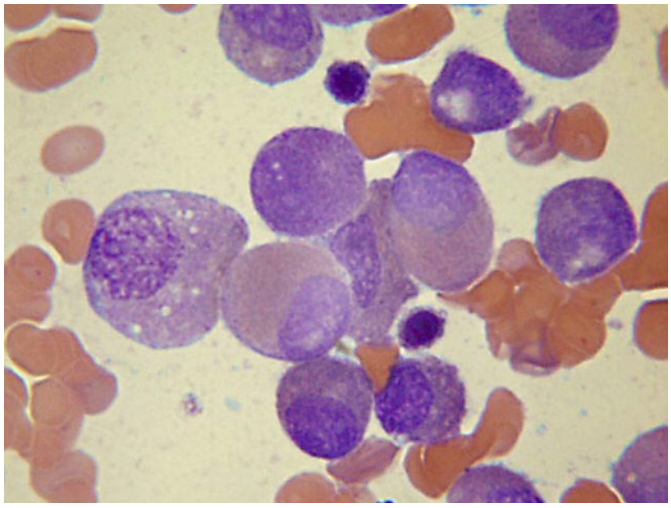

Fig. 8. Bone marrow film in AML with t(11;17)(q23.2;q21.2) showing hypergranular promyelocytes but without Auer rods. MGG ×100.

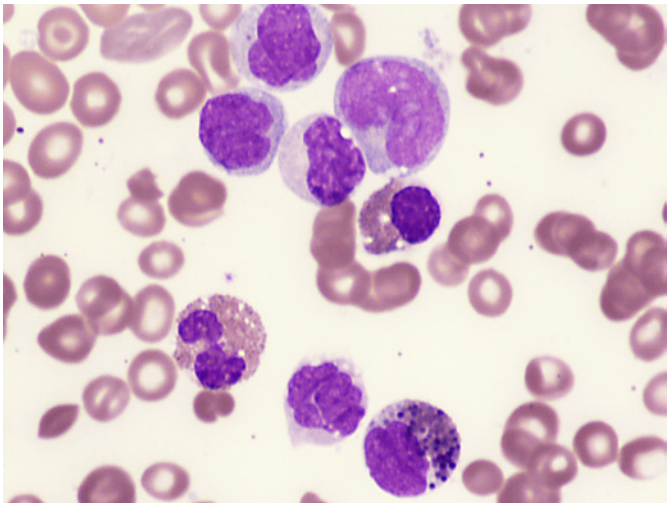

Fig. 9. Bone marrow film in AML with inv(16) showing myelomonocytic differentiation. There are two mature, vacuolated eosinophils, one of which has a non-lobed nucleus. An eosinophil myelocyte has some granules with basophilic staining characteristics. MGG ×100.

tures of acute megakaryoblastic leukaemia is possible so that coagulation screening and immunophenotyping have a role in making a rapid provisional diagnosis.

The immunophenotype, considered by some as unnecessary, is however very characteristic while slightly tricky [8]. On the canonical CD45/side scatter (SSC) cartography, the first impression may be that of an absence of progenitors/blasts with large numbers of slightly degranulated neutrophils (Fig. 7). In fact, this "flame-like" image of cells with intermediate expression of CD45 reflects the granularity of the leukaemic cells. These cells express typical myeloid markers such as CD13, CD33, and often CD117. However, they typically lack CD34 expression. Testing for this quadruplet of fundamental markers will thus strengthen the diagnosis. Strong expression of MPO is also demonstrated by flow cytometry. Of other classically tested antigens, leukaemic cells of APL fail to express CD15 and CD16, which would be present on neutrophils. Another key feature is the absence of HLA-DR, which is often present on myeloid blasts of different types of AML. There is also lack expression of beta2 integrins (CD18 beta-chain and CD11a, CD11b, or CD11c alpha-chains). Testing for CD41, CD42 and/or CD61 will permit exclusion of megakaryoblastic leukaemia in the hyperbasophilic variant [9].

Assessment of the cytological and immunophenotypic features enables this diagnosis to be made reliably, and within hours, in the great majority of cases, before confirmation of the t(15;17) by FISH or conventional cytogenetic analysis.

The cytological features of AML with variant *RARA* translocations are less distinctive. Cases associated with t(11;17)(q23.2;q21.2)/*ZBTB16-RARA* typically show more maturation beyond the promyelocyte stage, with neutrophils being dysplastic; Auer rods may be absent (Fig. 8).

AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*

The peripheral blood features of this category of CBF AML are not distinctive. Usually, the characteristics are those of acute myelomonocytic leukaemia, but there is variation from case to case. There is sometimes eosinophilia with the mature eosinophils showing little cytological abnormality. The bone marrow morphology is more distinctive, usually with an increase in eosinophils and their precursors, the latter showing large proeosinophilic granules, which have basophilic staining characteristics (Fig. 9). Abnormal eosinophil precursors are almost always present, even when the number of eosinophils is low. The diagnosis can often but not always be suspected from the cytological features.

The immunophenotype is that of myeloid blasts, with frequent expression of monocytic markers such as CD4,

CD36, or CD38 among those most often tested [10, 11]. Part of the blastic population may express neutrophil markers such as CD15 and/or CD65. The neutrophilic/monocytic differentiation trend of these blasts also translates into clear expression of CD11b, an antigen that is generally more strongly expressed by monocytes than by neutrophils. CD2 is often positive. Assessment of the cytological (particularly in the bone marrow) and immunophenotypic features suggests this diagnosis in the majority of cases, before FISH and/or conventional cytogenetic analysis disclose the inversion or translocation.

AML with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3*

Cytological features are usually those of acute monoblastic leukaemia but sometimes of acute monocytic or acute myelomonocytic leukaemia. There are no specific cytological clues to this diagnosis.

The immunophenotype shows the presence of monocytic markers, without expression of CD19. Some cases are CD4 positive. There may be some asynchrony in the expression of CD33 (positive) and CD13 (negative), and CD34 is often lacking. Monocytic differentiation may also be deduced from some co-expression (often weak) of CD15 and/or CD65, usually in the absence of CD14 [4]. There are no strong morphological or immunophenotypic clues to this diagnosis.

AML with t(6;9)(p23;q34.1); *DEK-NUP214*

This category of AML sometimes presents as AML with maturation and sometimes as acute myelomonocytic leukaemia. There are often dysplastic features. Sometimes there is basophilic differentiation, and in these cases the cytogenetic diagnosis may be suspected (Fig. 10). Both peripheral blood and bone marrow basophils can be increased. Some patients also have an increase in bone marrow eosinophils.

The immunophenotype of AML carrying this anomaly has been reported by Oyarzo et al. [12] as that of immature myeloid progenitors co-expressing in most cases CD34, CD117, CD33, and CD13 together with CD9 and CD38. In a previous smaller series, Alsabeh et al. [13] reported a more variable expression of CD34. This diagnosis may be suspected in cases with increased basophils but otherwise there are no strong morphological or immunophenotypic indicators.

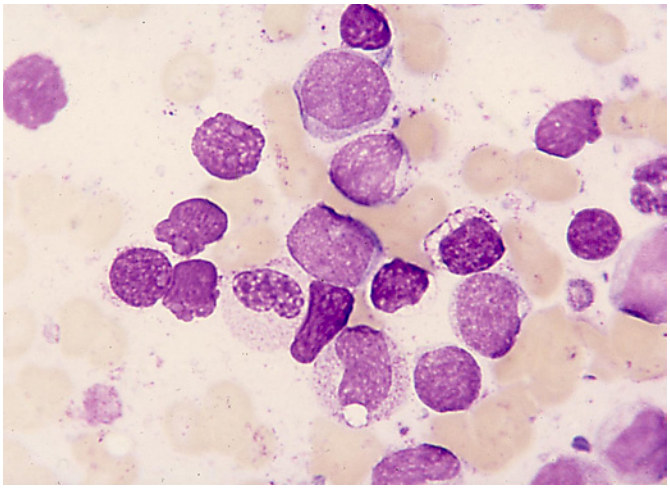

Fig. 10. Bone marrow film in AML with t(6;9) showing blast cells, two bands form neutrophils and two dysplastic mature basophils with scanty granules and vacuolated cytoplasm. MGG ×100.

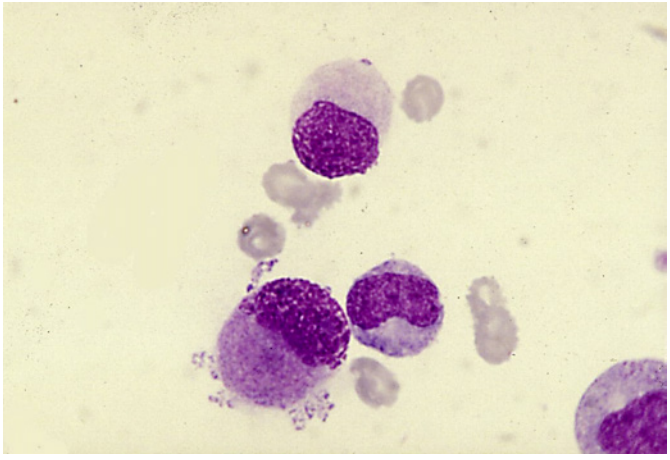

Fig. 11. Bone marrow film in AML with inv(3) showing two micromegakaryocytes, the larger of which is budding platelets. MGG ×100.

AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*

This category of AML often has dysplastic megakaryocytes (Fig. 11) and, unusually among cases of AML, can have a normal or even an increased platelet count. Differentiation can be granulocytic, myelomonocytic, or monoblastic/monocytic, but megakaryocytic differentiation is over-represented. Trilineage myelodysplasia can be present.

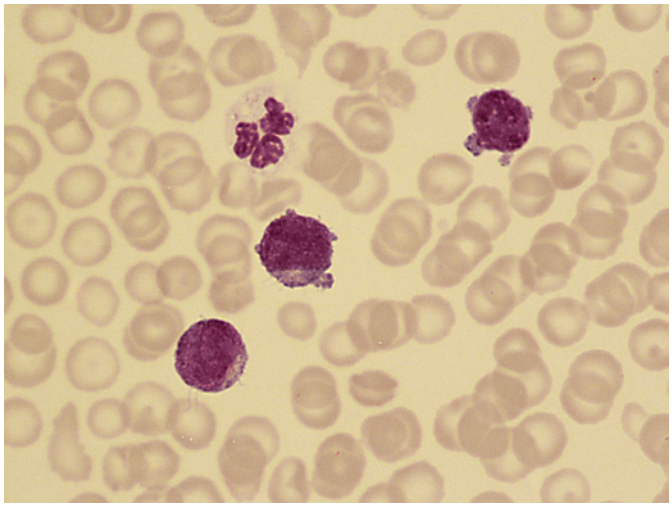

Fig. 12. Peripheral blood film in acute megakaryoblastic leukaemia associated with t(1;22) showing megakaryoblasts, two of which are budding platelets. MGG ×100.

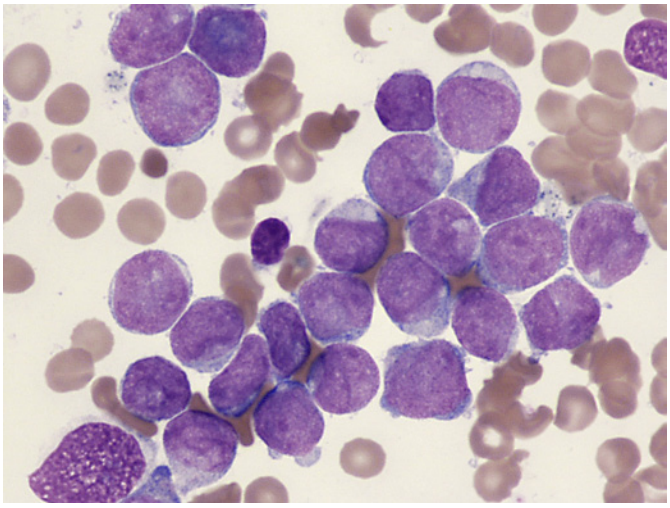

Fig. 13. Bone marrow film in AML with *NPM1* mutation and *FLT3* internal tandem duplication. Some of the blast cells show indentation of the nucleus, creating a cup shape. MGG ×100.

The immunophenotype is that of immature myeloid cells co-expressing CD34, CD117, CD13, and CD33 with MPO often being negative [14, 15]. Expression of CD7, CD11c, CD11b, and CD123 is frequent, but positivity for CD56 is seen less often [14]. When megakaryocytic differentiation is present, it can be confirmed by CD41, CD42, and/or CD61 positivity. Monocytic forms may express CD14.

Only cases with a normal or increased platelet count and with dysplastic megakaryocytes are likely to be suspected on morphological and immunophenotypic grounds. Otherwise, making a distinction from AML with myelodysplasia-related changes is difficult.

Acute Megakaryoblastic Leukaemia with t(1;22)(p13.3;q13.1); *RBM15-MKL1*

This subtype of AML typically occurs in infants and this, combined with the cytological features (basophilic blast cells with cytoplasmic blebs), can lead to a strong suspicion of the diagnosis (Fig. 12). Immunophenotyping is useful in confirming the megakaryoblastic differentiation [16]. There is expression of CD41, CD42, and/or CD61. Search for expression of these antigens can be prompted by the morphology of the blast cells. If there is no connexion with a morphology platform, at least one of these specificities should be included in the immunophenotyping panel in all cases of AML in infants [9]. In the event of unexpected faint or absent surface labelling, a stronger signal can be obtained by investigation of intracytoplasmic expression of these megakaryocyte-associated markers. Consideration of the cytological and immunophenotypic features in the context of the age of the patient often leads to suspicion of this diagnosis.

AML with t(9;22)(q34.1;q11.2); *BCR-ABL1*

This is a provisional WHO category of AML. There are no specific cytological features.

Immunophenotyping shows expression of myeloid antigens with aberrant expression of CD7 and CD19 appearing to be common. However, in cases expressing CD19 it is important to exclude a diagnosis of mixed phenotype acute leukaemia [9]. Distinctive cytological or immunophenotypic features that would permit suspicion of this entity have not yet been identified.

AML with *NPM1* Mutation

This subtype of AML can have either: (i) the cytological features of acute myeloblastic leukaemia with or without maturation (with Auer rods sometimes being present) and with expression of MPO, or (ii) the cytological features of acute myelomonocytic or monocytic/monoblastic

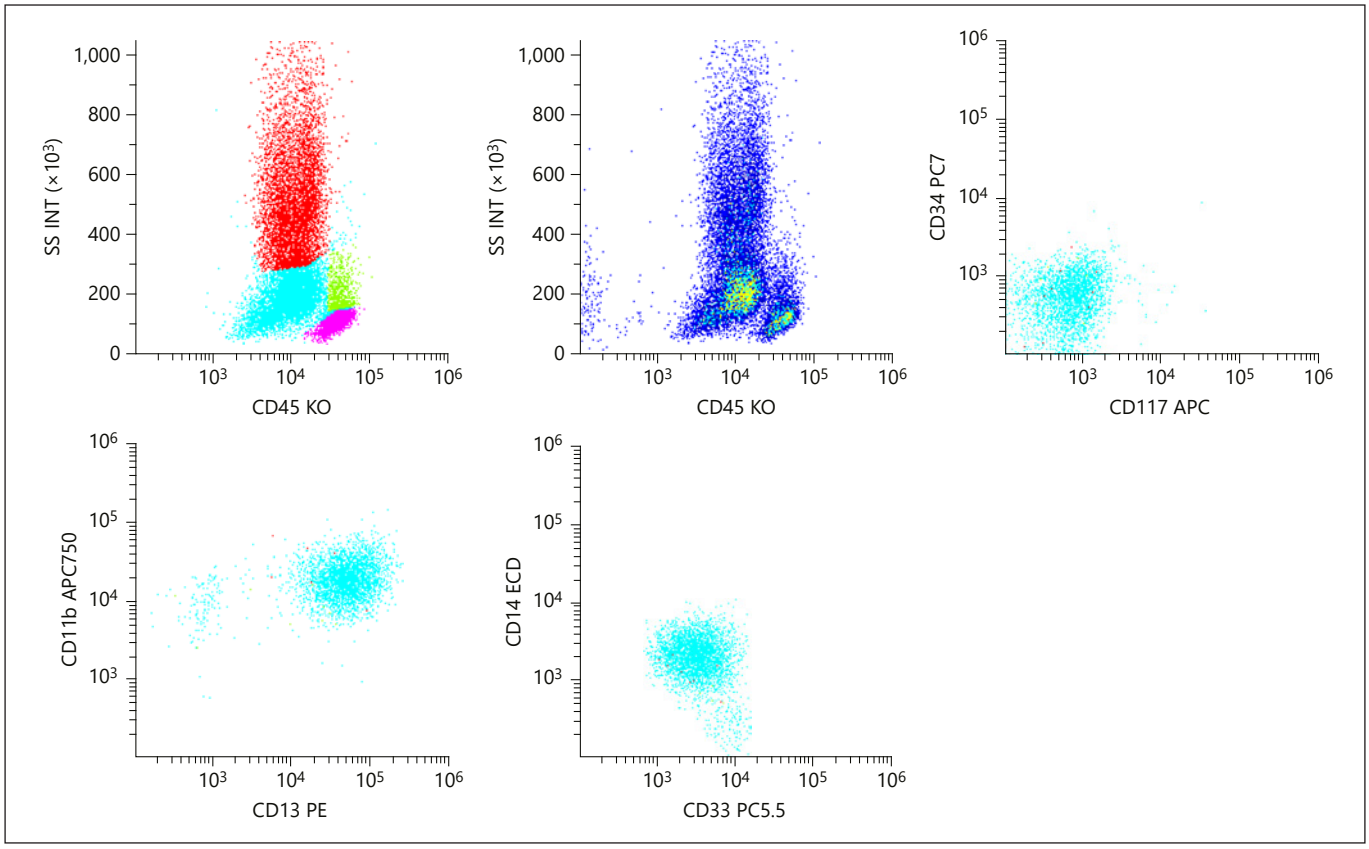

Fig. 14. Immunophenotypic features of *NPM1*-mutated AML, bone marrow aspirate. Side scatter (SS) is plotted against antigen expression. Red, neutrophils; green, monocytes; cyan, blast cells; magenta, lymphocytes. The blast cells lack CD34 and CD117, but express CD33, CD13, CD11b, and CD14.

leukaemia with expression of non-specific esterase. In one large series, the former was seen in about two thirds of patients and the latter in the remaining third [17]. There is correlation between the cytological category and the immunophenotype. A distinctive feature that can be present is the presence of leukaemic blasts with cup-shaped nuclei. This is seen particularly in cases with coexisting *FLT3*-internal tandem duplication [18, 19] (Fig. 13).

Immunophenotyping shows expression of CD33, CD117, and MPO in cases with myeloblastic differentiation. Cases with monocytic differentiation (Fig. 14) typically show expression of CD64, CD14, and/or CD11b. Overall, about two thirds of cases do not express CD34 and about one third do not express HLA-DR, yielding an "APL-like" immunophenotype [17]. In one large series, 32% of cases were negative for both CD34 and HLA-DR, these falling very largely into the group with myeloblastic differentiation; such cases were more likely to express CD56 and show weak or negative expression of CD13 [17]. The expression of CD4 or CD19 has also been reported in a series of AML patients with mutated *NPM1* and normal karyotype [20].

It is possible to suspect this diagnosis on cytological and immunophenotypic grounds when cup-shaped nuclei are present with HLA-DR, CD34, or both being negative or, in the absence of the typical cytological features, when there is an immunophenotype resembling that of APL, CD34-negative, HLA-DR negative, but with the SSC expected of normal myeloid progenitors [21].

AML with Biallelic *CEBPA* Mutation

There are no cytological clues to this diagnosis, although Mannelli et al. [22] reported a frequent association with erythroid dysplasia. The same authors performed an extensive immunophenotypic exploration of their cases, comparing them with wild-type *CEBPA* and monoallelic *CEBPA* mutation. They noted a high expression of antigens indicative of immaturity (CD34, CD117,

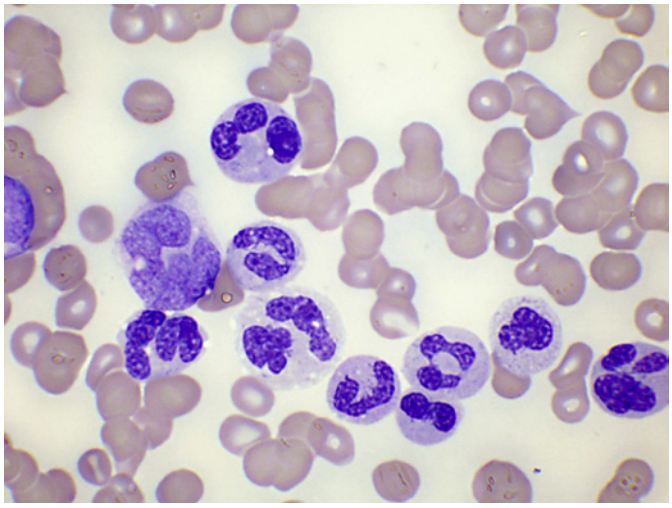

Fig. 15. Peripheral blood film in AML with myelodysplasia-related changes showing hypogranular neutrophils. Two of these, one with two nuclei, appear to be tetraploid. MGG ×100.

and HLA-DR) together with strong MPO and asynchronous expression of antigens typical of more mature cells, CD15 and CD65. CD7 and CD56 were also frequently expressed. Interestingly, CD64 was found to be expressed not only by blasts, but also by neutrophils (unusual and mostly characteristic of activated neutrophils and of monocytes). The erythroid dysplasia detectable morphologically was reflected in flow cytometry with features of immature erythroblasts being observed, respectively CD117 and CD105 (endoglin) positivity associated with low levels of CD36 and CD71 [22]. By analysing SSC and the expression of six antigens on blast cells, neutrophils, monocytes, and erythroid cells, these authors were able to predict *CEBPA* biallelic mutation and thus target molecular analysis [22]. The cytological features are not distinctive but detailed immunophenotypic analysis can permit suspicion of this diagnosis.

AML with *RUNX1* Mutation

There are no cytological features suggestive of this anomaly although this genetic subtype is over-represented among cases of MPO-negative AML. In a large Taiwanese study, Tang et al. [23] found 4 out of 10 patients with French-American-British (FAB) M0 AML to have a *RUNX1* mutation.

The same authors also reported that the blast cells usually expressed CD34, CD13, and HLA-DR, whereas expression of CD33 and CD15 was less common than in other cases of AML (77 and 28%, respectively), suggesting immature cells; CD56 was also expressed less often, being seen in only 13% of cases. CD19 was not expressed in any case.

AML with Myelodysplasia-Related Changes

Cytology provides one of the criteria for recognition of this category of AML (Fig. 15), with clinical history and specific cytogenetic abnormalities also being of relevance. Immunophenotypic features are variable but are those reported in myelodysplastic syndromes, the major anomalies being reduced side scatter reflecting hypogranularity of neutrophils, aberrant differentiation patterns, loss of haematogones, and aberrant expression of CD56 or CD7 [24]. In cases without a preceding myelodysplastic or myelodysplastic/myeloproliferative neoplasm, multilineage dysplasia can suggest the diagnosis but this cannot be confirmed until t(6;9), mutated *NPM1*, and biallelic *CEBPA* mutations are excluded.

Therapy-Related Myeloid Neoplasm

Diagnosis of therapy-related AML is dependent on the clinical history and morphological assessment. The WHO classification does not distinguish therapy-related AML from therapy-related myelodysplastic syndrome, since both are prognostically adverse. Multilineage dysplasia is common in both. The immunophenotypic abnormalities are non-specific but can include aberrant and asynchronous antigen expression.

Acute Myeloid Leukaemia, Not Otherwise Specified

Morphology and immunophenotyping are crucial for the diagnosis and further categorisation of AML, not otherwise specified, but not in isolation. Other more specific WHO categories must be excluded by molecular/cytogenetic analysis before this diagnosis can be made.

Acute basophilic leukaemia can be recognised cytologically (Fig. 16) and confirmed by the usual expression of CD123, CD203c, and CD11b in addition to other myeloid antigens. CD22 may be expressed [9]. HLA-DR is negative [9].

Acute megakaryoblastic leukaemia can sometimes but not always be suspected from cytological features (moderately basophilic, agranular cytoplasm with cytoplasmic

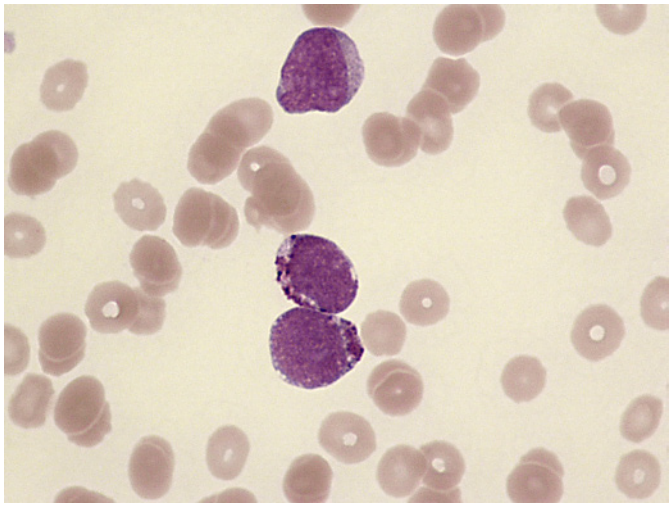

Fig. 16. Peripheral blood film in acute basophilic leukaemia showing three blast cells, two of which have basophilic granules. MGG ×100.

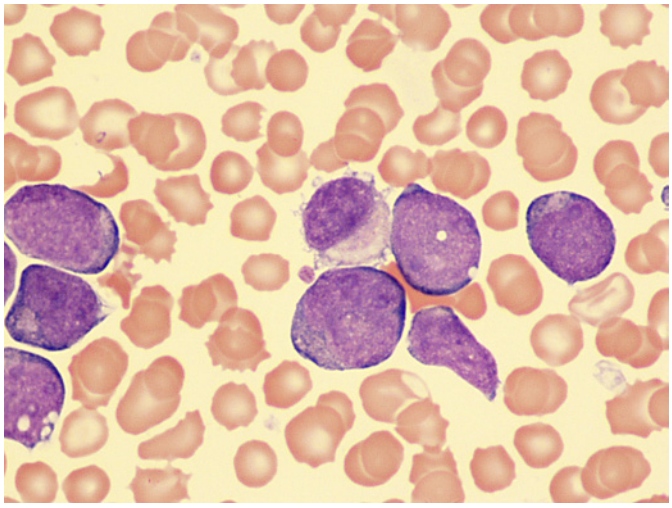

Fig. 17. Peripheral blood film in transient abnormal myelopoiesis of Down's syndrome showing blast cells and, in the centre, a micromegakaryocyte. MGG ×100.

blebs), with confirmation being by demonstration of expression of CD41, CD42, and/or CD61. However, the diagnosis of AML, not otherwise specified cannot be made until t(1;22) has been excluded.

Pure erythroid leukaemia can often be suspected morphologically since the primitive erythroblasts have round nuclei, very basophilic cytoplasm, and frequently vacuoles, which represent glycogen and thus can be elongated rather than round. Confirmation is by demonstration of the expression of CD235a (glycophorin A) and often also CD36 and strong CD71. Investigating for CD105 expression can also be useful in some cases, allowing for the fact that this marker is only transiently present during normal erythroid maturation [25]. On immunohistochemistry, E-cadherin is useful since it is expressed earlier than CD235a.

Diagnosis of acute panmyelosis with myelofibrosis is dependent on morphology, but specifically on histology rather than cytology. Bone marrow aspiration is often difficult so that immunohistochemistry, showing multilineage involvement, is generally more important than flow cytometry.

Myeloid Sarcoma

Cytology and immunophenotyping are important in the recognition of AML presenting as myeloid sarcoma. Morphology may be myeloblastic, myelomonocytic, or monoblastic/monocytic. Sometimes there is eosinophilic or neutrophilic differentiation.

Immunophenotyping is crucial in making a distinction from other tumours and thus making the diagnosis. Because of the nature of the biopsy specimen, this is more likely to be by immunohistochemistry than by flow cytometry, the latter requiring cell-dissociation of the sample.

Myeloid Proliferations Associated with Down's Syndrome

Transient abnormal myelopoiesis of Down's syndrome (TAM) is cytologically distinctive. Megakaryoblasts are characteristic and there can be prominent megakaryocytic differentiation with the presence of giant and hypogranular platelets (Fig. 17). However other lineages are also abnormal, with circulating mature and immature erythroblasts and myeloblasts often being present. Sometimes there is basophilic differentiation. Because of the pleomorphism of the neoplastic population, confusion with acute megakaryoblastic leukaemia with t(1;22) is not likely.

AML associated with Down's syndrome occurs during the first 5 years of life, in children with and without a history of preceding TAM. It is often acute megakaryoblastic leukaemia, although other lineages are also involved [26]. Immunophenotyping can be useful to identify the lineages involved.

The cytological features or TAM are so characteristic that the diagnosis can usually be made from the blood film and clinical features. Immunophenotyping and bone

marrow examination are not needed. Immunophenotyping is usually carried out in AML associated with Down's syndrome but the diagnosis can in fact be made from the clinical and haematological features.

Conclusion

This review summarises published data and our own experience on the role of morphology and immunophenotyping in permitting the rapid suspicion of a specific cytogenetic/genetic category of AML. Identification of APL is the most clinically important, with there being a need to recognise not only the highly characteristic features of the hypergranular variant, but also the features of the microgranular/hypogranular and hyperbasophilic variants. Morphological and immunophenotypic features, together with the detection of coagulation anomalies, can indicate the need for rapid specific treatment prior to availability of cytogenetic/molecular confirmation. Other cytogenetic/genetic categories can be suspected from cytology and immunophenotype, these helping to guide appropriate confirmatory cytogenetic and molecular investigations.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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