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HAEMATOLOGY IMAGES

When acute promyelocytic leukaemia changes its face in the peripheral blood

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An 85-year-old man was referred for gingival bleeding in the context of untreated dental abscess. The blood count showed pancytopenia (Haemoglobin: 72 g/L, platelets: 22 × 10^9/L, white blood cells: 0.6 × 10^9/L and neutrophils: 0.1 × 10^9/L) with 44% blasts with a round irregular nucleus and slightly granular basophilic cytoplasm (upper left image, May-Grünwald-Giemsa, original magnification ×100) suggesting acute myeloid leukaemia. No Auer rods were identified on the peripheral blood (PB) sample. Haemostasis tests showed slightly decreased fibrinogen (1.9 g/L) and increased D-dimers (> 4000 ng/mL), but the normal prothrombin time and partial thromboplastin time were not suggestive of a severe coagulopathy. Flow cytometry confirmed 38% blasts with coexpression of myeloid markers myeloperoxidase (MPO), CD117, CD13, CD33 and immaturity marker CD34 (lower left image). Finally, bone marrow (BM) examination showed 88% abnormal promyelocytes (upper right image) diagnosing acute promyelocytic leukaemia (APL). Flow cytometry confirmed 63% abnormal promyelocytes with characteristic high SSC signal, strong MPO and no CD34 expression (lower right image). Furthermore, 5% blasts similar to those described in PB, exhibited low SSC signal and coexpression of CD34 and MPO (lower right image). Conventional cytogenetic and molecular testing (reverse transcriptase multiplex ligation-dependent probe amplification) performed in BM, revealed 46,XY,t(15;17)(q24;q21) karyotype and detected *PML*::*RARA* bcr3, respectively, confirming the diagnosis of APL with *PML*::*RARA*. *FLT3*-ITD mutations (qualitative polymerase chain reaction followed by fragment analysis) were detected but not *ASXL1*, *DNMT3A*, *FLT3*-TKD, *IDH1/2* and *NPM1* (next-generation sequencing). Combined treatment with all-trans-retinoic acid and arsenic trioxide was started and the patient was in complete remission at the end of the induction phase. Currently, he is starting the consolidation phase (Figure 1).

This uncommon APL case, with predominant blasts in PB and abnormal promyelocytes in BM, highlights the variability in morphological and phenotypic profiles of leukemic cells across anatomical sites. Differences in homing properties of blasts and abnormal promyelocytes might explain these differences, depending on CD34 and CD45 expression [1, 2], although it has not been yet described in APL to our knowledge. Some coexistence of leukemic populations has been reported, especially in mixed-phenotype acute leukaemia [3–5], but the differences in anatomical compartments remain unclear. Such morphologic and phenotypic variations can result in diagnostic errors or delays, especially in life-threatening emergencies such as APL. While some studies support the use of flow cytometry in PB because of its high sensitivity and specificity [6, 7], our experience shows that BM assessment remains essential. Furthermore, in the era of deep learning, some trained models have shown good effectiveness in APL diagnosis on PB and BM aspirates [8]. Nonetheless, this case underscores a potential

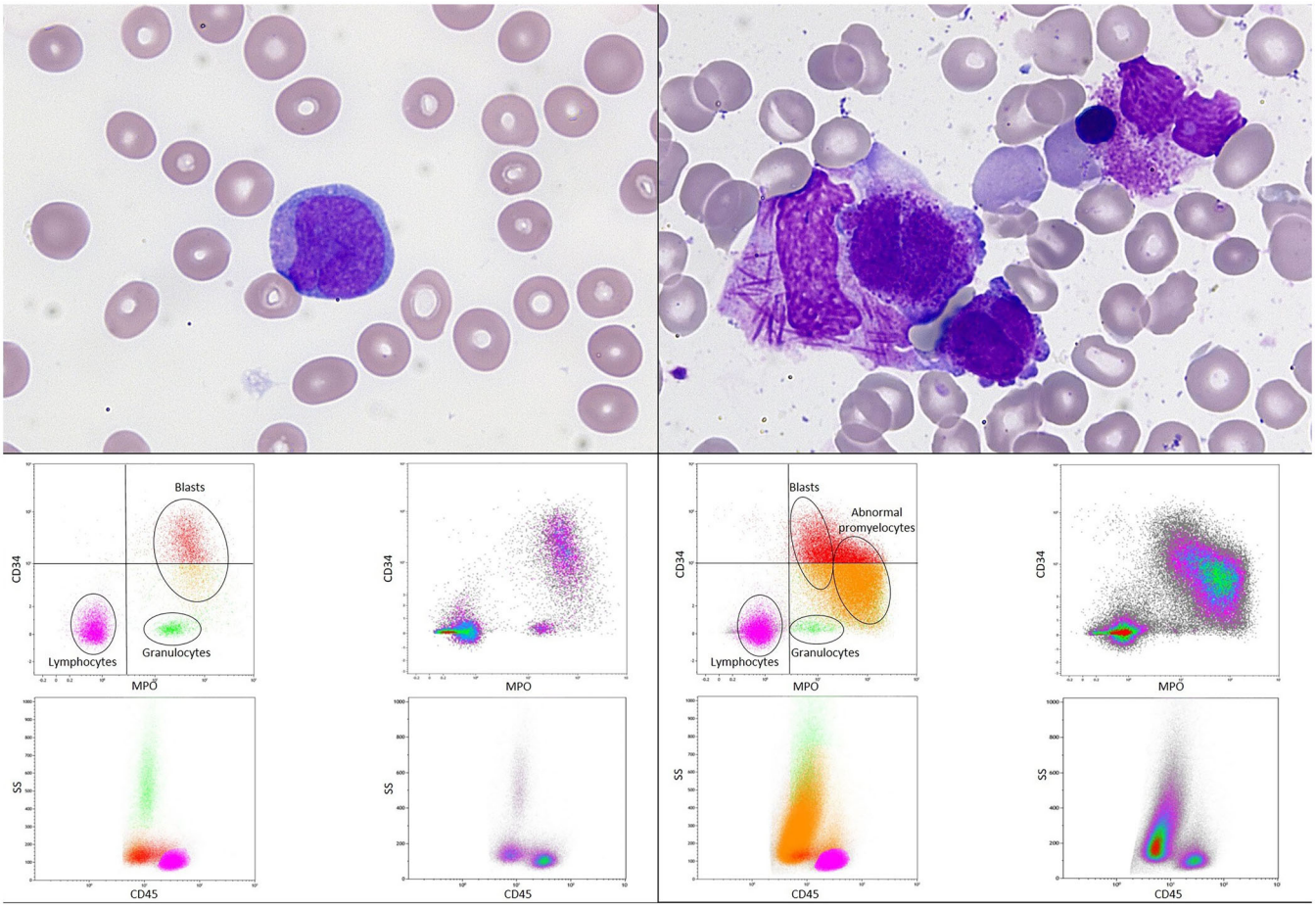

FIGURE 1 Upper left image: Blood film examination, May-Grünwald-Giemsa stain, 100x objective, depicting a blast with a round irregular nucleus and slightly granular basophilic cytoplasm. Lower left image: Flow cytometric immunophenotyping in peripheral blood revealing blasts with a low SSC signal and coexpression of myeloid markers myeloperoxidase (MPO), CD117, CD13, CD33 and the immaturity marker CD34. Upper right image: Bone marrow examination, May-Grünwald-Giemsa stain, 100x objective, depicting abnormal promyelocytes and faggot cells. Lower right image: Flow cytometric immunophenotyping in bone marrow revealing abnormal promyelocytes with a characteristic high SSC signal, strong MPO expression, and no CD34 expression, as well as blasts similar to those described in peripheral blood with a low SSC signal and coexpression of CD34 and MPO.

limit to the use of such devices and highlights the absolute necessity of the supervision of an experienced cytomorphologist.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

This manuscript respects the ethical policy of CHU Toulouse for the treatment of human research participants.

PATIENT CONSENT STATEMENT

The authors did not obtain written informed consent from the patient but the patient did not object to his data being used for research purposes (as required by the ethical policy of CHU Toulouse). Written permission for reproduction from the copyright owners will be provided if the submission is accepted.

CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

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