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CASE REPORT

Basophilia and megakaryoblastic differentiation in a case of acute myeloid leukemia: An unusual morphological combination

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Abstract
Basophilia is commonly associated with chronic myelogenous leukemia, notably in the accelerated phase or during blast crisis. It is also associated with other myeloproliferative neoplasms. However, its association with acute leukemia is very rare and is described in association with acute basophilic leukemia and few acute myeloid leukemias (AMLs) with recurrent genetic abnormalities such as t(6;9)(p23;q34). Herein, we describe the morphological features and discuss the differential diagnosis of a case of AML with the blasts showing previously unreported unusual combination of megakaryoblastic and basophilic differentiation along with peripheral blood and bone marrow basophilia.

Basophils are granulocytes that measure 10—15 μm in diameter with dark blue or purplish coarse cytoplasmic granules with a multilobed nucleus. They represent less than 2% (<0.13 × 10^9/L) of peripheral blood leukocytes in adults. Basophilia (basophils > 2%) is seen in a variety of reactive and neoplastic conditions. It is commonly associated with chronic myelogenous leukemia (CML), notably in the accelerated phase or during blast crisis. It is also associated with other myeloproliferative neoplasms such as polycythemia vera, idiopathic myelofibrosis, essential thrombocythemia, and systemic mastocytosis. Its association with acute leukemia is however very rare except in those cases of CML presenting in blast crisis [1]. We herein describe the morphological features of a unique previously

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unreported association of acute myeloid leukemia (AML) with basophilic and megakaryoblastic differentiation and basophilia.

Case report

A 17-year-old girl presented with fever and abdominal pain of 1-week duration. The fever was of high grade and intermittent in nature, associated with chills and rigor. The abdominal pain was associated with watery diarrhea and vomiting. The patient reported a history of dyspnea on exertion, easy fatigability, palpitation, loss of weight, and appetite during the past 1 month. Physical examination revealed pallor, mild hepatomegaly, and nonsignificant cervical lymphadenopathy. There was no splenomegaly. Imaging studies of the chest and abdomen showed multiple nodules and patchy consolidation of bilateral lungs, mild bilateral pleural effusion and pericardial effusion, mild ascites, hepatomegaly, and mildly enlarged hilar and mediastinal lymph nodes. Hemogram revealed anemia (hemoglobin 76 g/L), normal leukocyte count with blasts (total leukocyte count 4.1×10^9/L; blasts 2×10^9/L), basophilia (7%; 0.3×10^9/L), and thrombocytopenia (platelet count 78×10^9/L). Peripheral blood smear showed 49% blasts, giant platelets, and circulating micromegakaryocytes. The patient underwent a bone marrow (BM) examination and biopsy. BM examination revealed cellular smears with erythroid hyperplasia (myeloid:erythroid ratio 1.3:1). Six percent of erythroid cells (Fig. 1D) showed megaloblastosis and dyserythropoiesis in the form of nuclear budding, irregularity, abnormal chromatin clumping, binucleation, and multinucleation as well as periodic Schiff-positive cytoplasmic globules. There were no ringed sideroblasts. Dysgranulopoiesis was also present in less than 10% of cells. Megakaryocytes were increased along with numerous micromegakaryocytes. Blasts constituted 26% of all nucleated cells. Nearly 20% of the blasts were positive for myeloperoxidase (MPO; Fig. 1E), but were negative for periodic acid Schiff stain on cytochemistry. Thirty percent of blasts had coarse, dark bluish purple granules, which showed metachromasia with toluidine blue stain consistent with basophilic differentiation (Fig. 1A, B, and E), whereas another 20% of blasts showed morphology suggestive of megakaryoblasts (Fig. 1A and C). These blasts were negative for MPO. Mature basophils constituted 10% of all nucleated cells in the BM. Trephine biopsy showed hypercellular marrow spaces with interstitial increase of blasts admixed with prominent number of erythroid cells. Reticulin stain showed focal fibrosis amounting to World Health Organization (WHO) Grade 1 to 2.

A multiparametric flow cytometry (FCM) was then performed. The cells were acquired on BD FACS Canto II and analyzed using BD FACS Diva software. The antibodies used were CD1a, CD2, CD3 (cytoplasmic and surface), CD4, CD5, CD7, CD8, CD10, CD11c, CD13, CD14, CD19, CD20, CD22, CD33, CD34, CD38, CD41 (surface and cytoplasmic), CD45, CD61 (surface and cytoplasmic), CD64, CD117, HLA-DR, kappa, lambda (surface), TCR$\alpha\beta$, TCR$\gamma\delta$, and TdT (BD Biosciences, San Jose, CA, USA). The gated events/cells in the blast/progenitor region ($CD45^{dim}$ positivity and low side scatter) constituted nearly 40% of all single events. These cells showed expression of CD13, CD33, CD34, CD36, CD38, CD117, and HLA-DR. Approximately 16% of the blasts also expressed CD41 and CD61, indicating megakaryocytic differentiation. The nonspecific positivity of CD41 and CD61 due to platelet aggregation on blasts was excluded, as similar numbers of megakaryoblasts were detected using cytoplasmic CD41 and CD61 as well (Fig. 2). The blasts were negative for CD11c, CD14, CD64, and B- and T-lymphoid cell markers. Multiplex reverse-transcriptase polymerase chain reaction and gel electrophoresis performed for various fusion transcripts such as *BCR-ABL1* [t(9;22)(q34;q11.2)], *RUNX-RUNX1T1* [t(8;21)(q22;q22)], *CBFβ-MYH11* [inv(16)], and

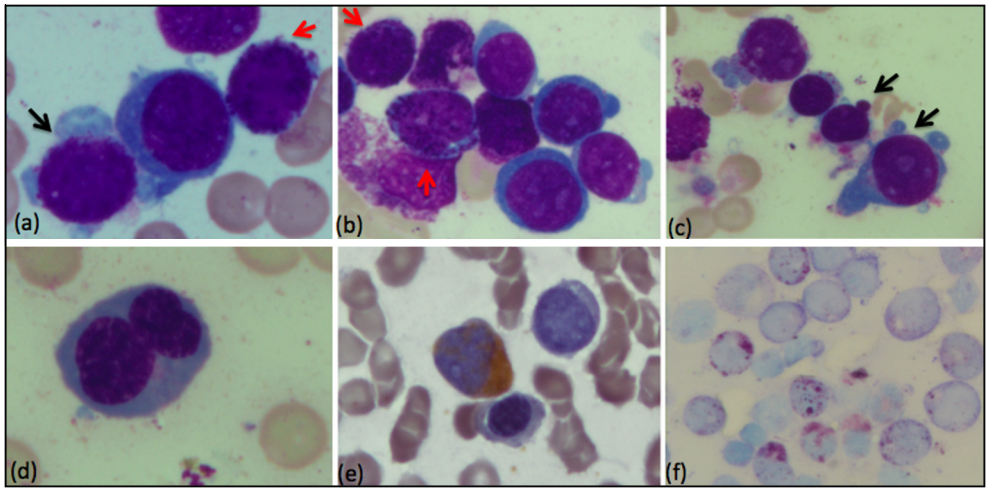

Figure 1 (A–C) Bone marrow aspirate smear showing blasts with high nuclear-cytoplasmic ratio, opened up chromatin, one to two prominent nucleoli, and basophilic granular cytoplasm. There were no Auer rods. Some of the blasts show coarse basophilic granules (red arrows), whereas some others show coarse chromatin and scanty cytoplasm with cytoplasmic blebs (black arrows) suggestive of megakaryoblasts (A–C; May–Grünwald–Giemsa stain; 100×); (D) dyserythropoiesis (May–Grünwald–Giemsa stain; 100×); (E) blasts are positive for myeloperoxidase (myeloperoxidase cytochemical stain; 100×) and (F) blasts showing metachromasia (toluidine blue stain; 100×).