Case Report
Basophilia with Blasts – A Diagnostic Dilemma

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Citation

Submitted: Apr 5, 2020; Accepted: Sep 6, 2020; Published: Sep 20, 2020

Abstract: Basophilia is commonly seen in inflammatory and autoimmune conditions. Primary malignancies of basophils are rare, however basophilia is seen in few haematological malignancies. It is most commonly seen in myeloproliferative neoplasms. Presence of basophilia helps to differentiate chronic myeloid leukemia (CML) from acute myeloid leukemia (AML). The association of basophilia with AML is rare. We present a case of 68 year old male with complaints of fever and worsening of itching, pain and swelling in right lower limb and left upper limb. On physical examination he had mild hepatosplenomegaly and no lymphadenopathy. Complete blood count showed leucocytosis. Increase in blasts and basophil was noted on peripheral smear and bone marrow examination. Flow cytometry on bone marrow aspirate showed blasts to be of myeloid origin. A distinct population of mature basophils was also noted. After exclusion of all morphological mimickers, a final diagnosis of AML with basophilia was made. The presence of basophilia in AML may warrant a search for an underlying chromosomal abnormality to assess the prognosis of the patient. Only few cases of AML with basophilia have been reported so far and it remains a diagnostic challenge.

Key Words: Acute myeloid leukemia, Basophils, Flow cytometry

Introduction:
Basophils are the least common blood cells and basophilia is an alarming sign. In healthy individuals, they account for only about 0.5% of the total white blood cells in the peripheral blood and about 0.3% of all the nucleated cells in the bone marrow. (1) Basophilia is seen in infective and immune – mediated conditions. It can be associated with hematolymphoid malignancies, most commonly chronic myeloid leukemia (CML), others being acute basophilic leukemia (ABL) and mast cell leukemia (MCL). All these conditions present with basophilia in association with increased blasts. Rarely basophilia is seen in acute myeloid leukemia (AML). It is uncommon and has a poor prognosis. (2) The differentiation of all these entities remains important for treatment and prognosis of the patient.

Case Report
A 68 year old male came with complaints of fever for 15 days along with worsening of itching, pain and swelling in right lower limb and left upper limb. He was a known case of diabetic, for 25 – 30 years, on treatment. Local examination of the affected limbs showed ulcers over the right foot with erythema and excoriation of the surrounding skin. His general physical examination was unremarkable. Ultrasound scan of the abdomen showed mild hepatosplenomegaly. Lymphadenopathy was not present. Routine blood investigations were done. Hemogram showed anemia with haemoglobin of 11.3 g/dL and leucocytosis with white blood cell count of 32 x 10^3/mm^3. Platelets were adequate. Differential count on the peripheral smear showed blasts - 12%, basophils - 46%, neutrophils - 23%, band - 01%, metamyelocyte - 01%, myelocytes - 02%, promyelocyte - 01%, eosinophil - 01%, monocyte - 01% and lymphocytes - 12%.

Bone marrow examination done, revealed hypercellular marrow particles with suppressed erythropoiesis and abnormal myeloid maturation (Fig. 1). Blasts were 38% (of the total nucleated cell count) and basophils - 28%. Other cells were myeloid precursors - 07%, neutrophils and bands - 10%, eosinophils - 14%, and erythroid precursors - 03%. Blasts were large with high nuclear-cytoplasmic ratio, with clumped chromatin, prominent nuclei and moderate cytoplasm. Megakaryocytes were adequate with mild dysmegakaryopoiesis. Cytochemistry showed positivity for Myeloperoxidase (MPO) and Sudan Black B (SBB) stains in blasts. Periodic acid Schiff stain (PAS) was negative in blasts.
A differential diagnosis of CML in blast crisis was considered. However, molecular studies for BCR-ABL fusion gene were found negative.

Fig. 1: Bone marrow aspirate showing blasts, basophils and myeloid precursor. (MGG stain, 100X)

Fig. 2: Blasts show low side scatter and dim CD45 expression. Basophils (P2) show low side scatter and moderate CD45 expression.

Fig. 3: Blasts show homogenous bright expression of CD34

Fig. 4: Blasts show heterogenous bright expression of HLA-DR. CD117 is negative.

Fig. 5: Blasts show homogenous bright expression of CD13 and CD33.

Fig. 6: Blasts show heterogenous bright expression of aberrant CD7. Blasts are negative for CD25. Basophils (green, P2) show homogenous dim expression of CD25.
Flow cytometry was performed on bone marrow aspirate. Low side scatter with dim CD54 cells were gated as blasts. A distinct population, (20%) showing low side scatter with moderate expression of CD54 was observed and labelled as P2 (Fig. 2). The blasts were positive for stem cell markers CD34 and HLA-DR and negative for CD117 (Fig. 3, 4). Myeloid markers cMPO, CD13 and CD33 were positive in the blasts (Fig. 5). CD25 was negative in the blasts and was positive in population P2, confirming them as mature basophils. Ablerrant expression of CD57 was also noted in the blasts (Fig. 6). Blasts were negative for monocytic and B and T lymphoid cell markers. A final diagnosis of AML with basophilia was made. The skin manifestations of the patient, at the time of presentation, were attributed to the release of enormous amounts of histamine from the markedly increased basophil population.

Discussion

The association of basophilia with AML is very rare. Parwaresch, et al have stated that Ehrlich first noted basophils in AML in 1879. (3) It is commonly associated with t(6;9)(p23;q34). Other associated cytogenetic abnormalities may be t(8;21)(q22;q22), t(3;6)(q21;p22), and t(9;22)(q34;q11). (2) Morphologically, basophilia is seen in FAB AML-M2 and M4. (4) Chronic myeloid leukemia in blast crisis is morphologically indistinguishable from AML with basophilia, and was the most strongly suspected diagnosis in our patient. However, it was ruled out by a negative BCR-ABL gene rearrangement. Atypical CML (aCML) is a distinct subtype of CML that characteristically lacks the Philadelphia chromosome. Over time, the diagnostic criteria for aCML has evolved with cytogenetic and molecular studies and it remains to be a diagnosis of exclusion from all other clinically similar entities. The 2017 revision of World Health Organisation (WHO) classification of myeloid neoplasms and acute leukaemia defines the absence of basophilia (<2%) and less than 20% blasts in the blood and bone marrow as a requirement for diagnosis of aCML to be made. (5) Atypical CML was therefore excluded.

Marked basophilia is also a feature of Philadelphia chromosome positive AML as noted by Singh MK, et al. However, it shows p190 BCR-ABL transcript, instead of p210 which is seen in CML. (4) Acute basophilic leukaemia (ABL) is another entity morphologically resembling AML associated with basophilia. It is uncommon and comprises <1% of all leukemias. (6) It is not associated with any specific cytogenetic abnormality. (7) The blasts in AML are morphologically undifferentiated. Duchayne, et al noted that the presence of coarse basophilic granules in blasts may be the first step to diagnosis of ABL. (6) Cytochemically, ABL blasts have diffuse pattern of staining for acid phosphatase and block positivity with PAS stain. They are negative for MPO, SBB, chloroacetate esterase (CAE) and non-specific esterase (NSE). (7) In our patient, blasts were positive for MPO and SBB stain and negative for PAS stain indicating a myeloid origin. On immunophenotyping, ABL blasts express myeloid markers CD13 and CD33, and are positive for CD123, CD203c and CD11c. (7) Han X, et al stated mature basophil are positive for CD45 (dimmer than lymphocytes and brighter than myeloblasts) and CD 25, and are negative for stem cell markers (CD34, CD117, HLA-DR), CD19, CD64, (1.8) This was in corroboration with findings in our patient showing mature basophil population showing dim expression of CD25 (Fig. 1, 6). Basophilic differentiation of blasts, in our patient was ruled out by absence of CD25 expression in blasts. (Fig. 6) Another morphological mimicker of AML with basophilia is MCL. It is very rare and accounts for < 1% of all mastocytosis. (8) On cytochemistry, blasts in MCL are negative for both PAS and MPO stains and give strong positive reaction with CAE. (9) Lou XH, et al noted that mature basophils are positive for CD25 and negative for CD117. Mast cells are positive for CD117 and negative for CD25. (10) In our patient blasts were negative for both CD25 and CD117 and hence MCL was ruled out.

Conclusion

Basophilia along with increase in blasts is an indication to many morphologically similar differential diagnoses. Basophilia in association with AML should be differentiated from all other clinical conditions as it carries a worse prognosis. Accurate diagnosis of this entity is crucial because these patients may benefit from early allogeneic stem cell transplantation.

References