American Journal of Hematology 76:134–138 (2004)

Acute Basophilic Leukemia: Case Report

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The term "basophilic leukemia" has been in use for 75 years. However, consistent diagnostic criteria are lacking. This is due to the rarity of the disease and to the routine unavailability of special tests that are often required to confirm a diagnosis. We report an unusual case of acute basophilic leukemia in a child who was referred to our Center, arriving with partially treated acute lymphoblastic leukemia. Basophilic differentiation on light microscopy was evident from the coarse basophilic granules in blasts, a progressive maturation of blasts toward basophils, and toluidine positivity on cytochemistry. Blasts showed a myeloid immunophenotype ($CD13^+$, $CD33^+$, $CD117^+$) with a characteristic dual positivity for CD34 and CD25, highly suggestive of basophilic nature of the blasts. Conventional cytogenetic studies revealed translocation t(8;21)(q22;q22). A diagnosis of acute basophilic leukemia with t(8;21) was made. Review of pre-therapy slides showed features consistent with AML-M2 with basophilia. There were no basophilic blasts. With these features, a diagnosis of acute basophilic leukemia secondary to AML-M2 was made. In our patient, basophilic leukemia appears to have evolved from selective clonal proliferation of "basophil-committed blasts" during the course of the disease in a case of AML-M2 with basophilia. Am. J. Hematol. 76:134–138, 2004.

Key words: acute basophilic leukemia; immunophenotyping; cytogenetics

INTRODUCTION

Acute basophilic leukemia is a relatively rare form of acute leukemia accounting for 4–5% of all cases of acute nonlymphocytic leukemia [1,2]. Most cases of basophilic leukemia have been reported to have developed from other hematological disorders, such as chronic myeloid leukemia (CML) and myelodysplastic syndromes (MDS) [3–6]. Here we report a case of acute basophilic leukemia with t(8;21) in a child, secondary to AML-M2 with basophilia.

CASE REPORT

A 6-year-old child was referred from outside to our Center as partially treated acute lymphoblastic leukemia (ALL). On examination, the child had pallor, low-grade fever, and moderate hepatosplenomegaly. There was no lymphadenopathy, cutaneous involvement, or signs of hyperhistaminemia. His hemoglobin was 7 g/dl, platelet count was 22×10^9/l, and total leukocyte count was 76×10^9/l, which included 50% blasts. Of these, 18% had coarse basophilic granules, there were 18% basophilic precursors, 6% mature basophils, 15% maturing myeloids including 1% eosinophil (Figs. 1 and 2). There were 10% lymphocytes. Bone marrow aspirate revealed a cellular marrow with 40% blasts including 10% with coarse basophilic granules, 14% maturing basophils, and 14% eosinophils. There was an obvious maturation toward basophils with precursor cells exhibiting pale cytoplasm, variable number of basophilic granules, and immature nucleus with fine chromatin pattern. Auer rods were not seen. The blasts showed coarse granular positivity for myeloperoxidase (MPO), diffuse reaction with acid phosphatase (AP), and were negative for non-specific esterase (NSE). Basophilic granules in the blasts and basophils exhibited metachromasia with toluidine blue (Fig. 3).

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Received for publication 23 December 2002; Accepted 15 August 2003

Published online in Wiley InterScience (www.interscience.wiley.com).
DOI: 10.1002/ajh.10446

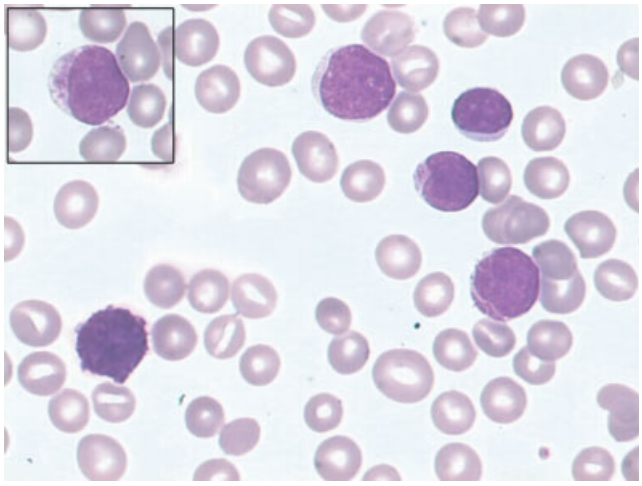

Fig. 1. Peripheral blood smear showing agranular blasts, blasts with coarse basophilic granules and a mature basophil. Inset shows an early basophilic precursor (Jenner-giemsa, original magnification 1000×). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Immunophenotyping with three-color flow cytometry was performed on peripheral blood using standard whole blood lysis technique [7]. Blasts were gated based on their dim CD45 (RPE-Cy5, Serotec) and low side-scatter characteristics (Fig. 4). The following monoclonal antibodies were used to characterize the immunophenotype of the blasts: CD2, CD3, CD4, CD7, CD10, CD11b, CD13, CD14, CD15, CD19, CD22, CD25, CD33, CD34, CDw65, CD117, and human leukocyte antigen HLA-DR. The reactivity of antibodies was measured on Epics Elite Flow Cytometer (Coulter Corporation, Hialeah, FL) using the corresponding negative isotypic controls. The blasts were positive for CD34, HLA-DR, CD117, CD33, CD13, and CD25 (Fig. 4). Cytogenetic studies performed on bone marrow aspirate using standard culture methods and GTG banding revealed t(8;21)(q22;q22). A FISH analysis for this translocation was not done. A diagnosis of acute basophilic leukemia with t(8;21) was made.

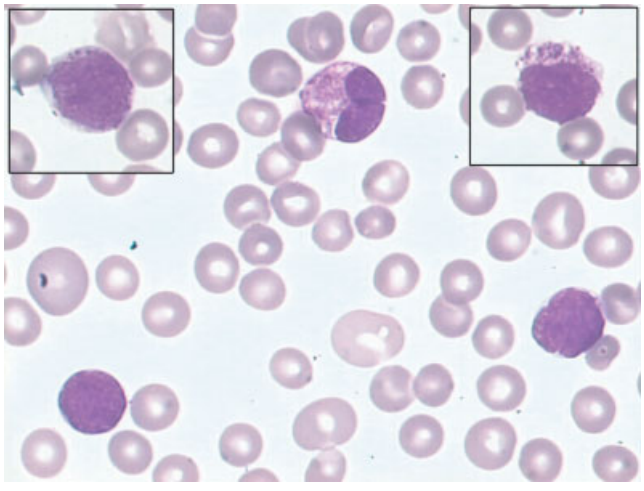

Fig. 2. Peripheral blood smear showing a blast with coarse basophilic granules (Inset left), basophilic precursor (Inset right), and maturing basophil (Jenner-giemsa, original magnification 1000×). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

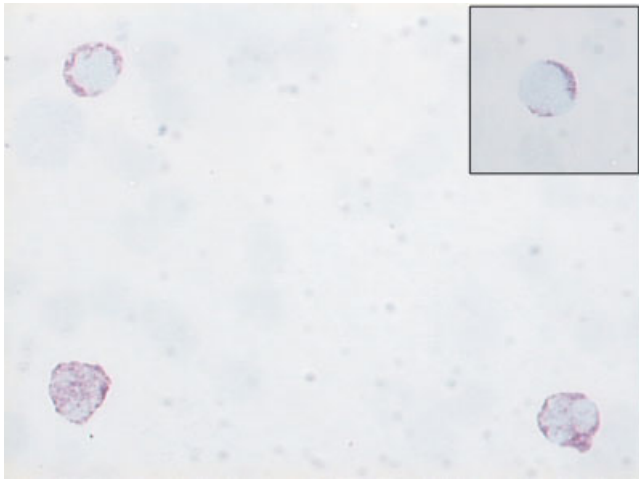

Fig. 3. Peripheral blood smear with basophilic precursors and mature basophils exhibiting metachromasia with toluidine blue. Inset shows a blast with metachromatic granules (Toluidine blue, original magnification 1000×). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Review of pre-therapy slides, which then became available, revealed a cellular marrow with increased blasts and prominence of mature basophils and eosinophils. There were no basophilic blasts. An occasional Auer rod was noted. Pre-therapy cytochemical and immunological work-up was not available for review.

The features at presentation taken together with those of the pre-therapy slides, led us to diagnose t(8;21) positive acute basophilic leukemia secondary to AML-M2 with basophilia.

The child was treated with daunorubicin and cytosine arabinoside-based chemotherapy. His day-21 marrow was hypocellular with 3–4% blasts and 40% mature basophils. Peripheral smear showed 2% blasts. Re-induction with high dose cytosine arabinoside was started. Patient developed septicemia but eventually recovered and is in remission for past 4 months.

DISCUSSION

"Basophilic leukemia" was first described as early as in 1906 by Jaochim in two patients with extreme basophilia and clinical features of myelocytic leukemia [8].

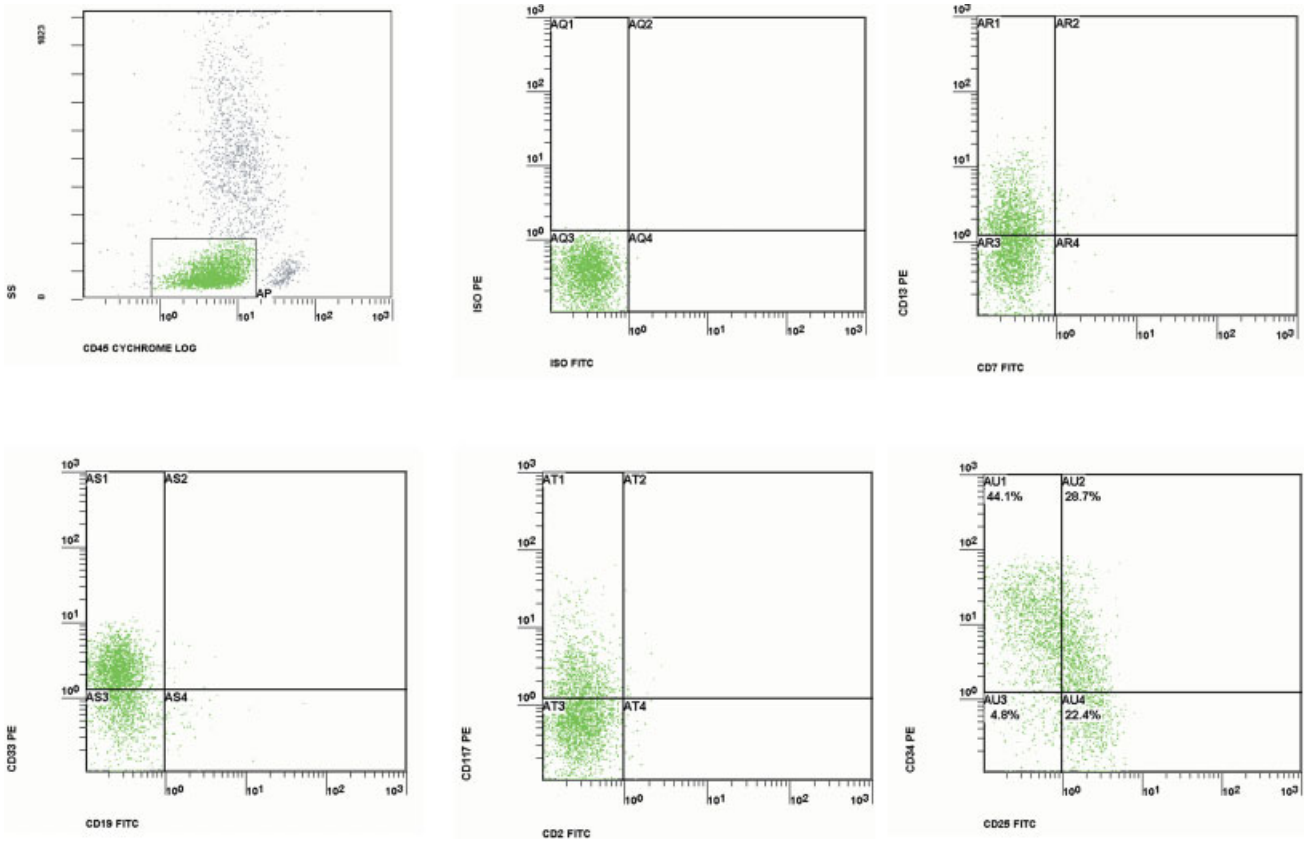

Fig. 4. Dot plots showing immunoreactivity pattern of blasts. (A) Blasts gated by dim CD45 and low side scatter characteristics. (B) Negative isotype control. (C–E) Blasts showing positivity for CD13, CD33, and CD117. (F) Blasts showing characteristic dual positivity for CD34 and CD25 with CD34 positive progenitor cells progressively acquiring CD25 and then losing CD34, corroborating with morphological maturation of blasts towards basophils. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

However, acute basophilic leukemia was not recognized as a separate entity in the FAB classification [9–11], possibly owing to its rarity and lack of consistent diagnostic criteria. In fact, most cases previously reported as basophilic leukemia represented a variant of CML or developed secondary to MDS [3–6]. De novo acute basophilic leukemia was first described by Wick et al. in 1982 and subsequently similar cases have been reported by others [1,12–19]. In the recent WHO classification of myeloid malignancies, acute basophilic leukemia has been integrated as a distinct entity and defined as an acute myeloid leukemia in which primary differentiation is to basophils [20].

Morphologically, acute basophilic leukemia is a somewhat heterogeneous group, with cases having none to conspicuous basophilic differentiation on light microscopy. Blasts are either agranular or exhibit coarse basophilic granules in the cytoplasm. Mature basophils may or may not be seen [1,12]. Cytochemically, blasts are often negative for MPO and NSE, show metachromasia with toluidine blue and diffuse reaction with AP. Acute basophilic leukemia blasts express a myeloid phenotype and are usually positive for CD9 and CD25, which are baso-associated markers [20,21]. Acute basophilic leukemia, per se, is not associated with any specific chromosomal abnormality [20]. However, cytogenetic studies are required in all such cases to rule out blast crisis of CML as most cases develop secondary to CML. Our patient had distinct morphological differentiation towards basophils with a continuum from "basophilic" blasts to immature basophils to mature basophils, metachromasia with TB and diffuse positivity with AP. In addition, there was eosinophilia in bone marrow and positive reaction with MPO. The strong MPO positivity was atypical for basophilic differentiation. This has been described in only a few cases [1,18] and probably indicates mixed myeloid nature of the blasts. In the present case, blasts displayed a myeloid phenotype ($CD13^+$, $CD33^+$, $CD117^+$) along with positivity for CD25. CD9 was not tested for in this case.

Differentiation of basophils from mast cells is not difficult but may be problematic when dealing with leukemic populations, and therefore, mast cell

leukemia should be considered in the differential diagnosis of basophilic leukemia [22]. On immunophenotyping, both basophils and the mast cells display a myeloid phenotype. However, while mature basophils are positive for CD25 and negative for CD117, mast cells are positive for CD117 and negative for CD25 [23]. A characteristic dual positivity of blast cells for CD34 and CD25 with CD34-positive progenitor cells progressively acquiring CD25 and then losing CD34, corroborated with the morphological maturation of blasts towards basophils (Fig. 4). A similar demonstration of CD117 with maturation would have been useful in further differentiating maturing basophils from mast cells in our case. This was, however, not possible as CD34 and CD117 were not analyzed together at the time of initial examination. In difficult cases, electron microscopy may help in discriminating basophils from mast cells [21]. CD25, though characteristic is not specific for basophil lineage of blast cells. CD25 positivity has been observed in blast cells of CML and few cases of myeloblastic and BCR/ABL-positive lymphoblastic leukemia [24]. In the present case, the characteristic cytomorphological features, the myeloid immunophenotype of blast cells with distinct maturation pattern with CD25 and CD34 along with Philadelphia negativity on cytogenetic studies favored a diagnosis of basophilic leukemia and ruled out basophilic blast crisis of CML, ALL, and non-basophil lineage AML.

Cytogenetic studies in our case revealed t(8;21) (q22;q22), which is an unusual finding in acute basophilic leukemia. Cases with t(8;21) and basophilia have earlier been reported [25,26]. In one, the cytomorphological features were those of AML-M2 with basophilia [25], and in the second, additional chromosomal abnormality t(9;22) was present along with clinical and hematological features of CML [26]. On review, the first bone marrow of our patient had morphological features compatible with AML-M2 with increased basophils and eosinophils. Basophilic blasts were not appreciable. At the time of the second bone marrow examination, eosinophilia and basophilia persisted, and basophilic blasts and precursors also proliferated. One plausible explanation is that this case was AML-M2 to begin with, and during the course of the disease, following a partial or incomplete therapy, a selective clonal proliferation of "basophil committed blasts" resulted in frank acute basophilic leukemia. Cytogenetic studies were of crucial value in this case as Philadelphia negativity effectively ruled out basophilic blast crisis of CML and t(8;21) further strengthened the diagnosis of acute myeloid leukemia. It is likely that this case is a hybrid acute leukemia (myeloid/basophilic), which probably arose from a multipotent progenitor cell.

FISH analysis for t(8;21) on the bone marrow was not performed, and hence it was not possible to check if eosinophils and other bone marrow cells were part of the leukemic clone.

To summarize, we have described a case of t(8;21) positive acute basophilic leukemia secondary to AML-M2 and highlighted the importance of immunological and cytogenetic studies in making a correct diagnosis in such cases.

ACKNOWLEDGMENT

Help from the Department of Medical Oncology and from Dr. R. Kumar in the preparation of this paper is gratefully acknowledged.

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