Chronic Basophilic Leukemia; a rare myeloproliferative disorder and the role of flow cytometry for its diagnosis

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Abstract

Chronic basophilic leukemia (CBL) is a rare disorder and according to the published data, few cases have been reported as primary CBL. Morphologic findings in CBL, mostly mimic chronic eosinophilic leukemia and basophils have unusual and dysplastic morphology. A 47 years-old patient comes to the hospital with gastrointestinal symptoms and bloating. Complete blood count (CBC) showed leukocytosis and marked eosinophilia. After evaluating the PB smear, abnormal leukocytes with hypersegmented nuclei along with increase in eosinophils were observed. For further investigation patient was referred to hematology clinic and underwent bone marrow aspiration and biopsy. After the morphological examination, flow cytometry was performed on the aspiration sample to accurately diagnose the disease. Flow cytometric findings were in favor of CBL. Morphological findings is unreliable for basophils detection and for definite diagnosis, flow cytometry is reliable method to precise detection of basophils and CBL.

Key Words: Basophils, Chronic Basophilic Leukemia, Chronic Eosinophilic Leukemia, Flow cytometry, Myeloproliferative

Introduction

Chronic basophilic leukemia (CBL) is not recognized as a new entity or classified as a unique myeloproliferative disorder (MPD) in the new WHO classification (1). According to the literature review, a few cases have been reported as primary CBL and this disorder has still remained an extremely rare condition (2). An important challenge in diagnosing chronic basophilic leukemia is misdiagnosis of CBL with chronic eosinophilic leukemia (CEL) due to the remarkable increase in eosinophils, and abnormal basophils morphologies like hypersegmentation and hypogranulation (3). In an extensive screening to search for new groups of rare MPDs, Paradanani et al. reviewed electronic databases from 1975 to 2003. It was observed four cases with high percent of basophils in differential counting and two cases with basophilic leukemia manifestations (4). The bone marrow (BM) examinations of the two latter cases revealed trilineage hyperplasia with active presence of basophils and eosinophils, besides the increased numbers of dysplastic megakaryocytes without clustering. A remarkable increase in basophil counts is a common manifestation in chronic myeloid leukemia (CML) (5). In the accelerated phase of CML, the morphology of basophils is usually typical with frequent presence of many basophilic granules in the cytoplasm without nuclear hypersegmentation, but dysplastic features are also common manifestations. (5). On the contrary, in reported cases as primary CBL, the peripheral blood (PB) represented dysplastic basophils with hyperlobulated nucleus besides hypogranular cytoplasm (with fine granules). The Hypersegmented basophils were also observed in BM smear of these patients (6). According to the presented data, CBL patients might be classified under the category of MPD not otherwise specified (MPD-NOS) or CEL, so that both are because of the misdiagnosis and underestimation of CBL. Lack of specific signs in patients with primary CBL or secondary basophilia mimicking CBL, it makes difficulty for the accurate diagnosis.

Case presentation

A 47-year-old woman was admitted to internal clinic at Razi Hospital in Rasht, (Guilan province, Iran). At the time of presentation, the patient did not have any underlying disease or family history of leukemia. The clinical presentation was gastrointestinal symptoms and bloating with laboratory findings of leukocytosis (50000/µL) and eosinophilia more than 50.0%. Therefore, she was referred to a hematology clinic. At the first step of evaluation, anti-fasciola medications were utilized. However, the complication did not improve and after one week, albendazole was prescribed. Due to the persistent clinical findings and leukocytosis, the patient was referred to the hematology clinic for second time. Here, the patient presented splenomegaly, so for more extensive evaluations, BM aspiration and biopsy were performed. Also, molecular assessing of Jak2, BCR-ABL, cMPL, CALR, PDGFRa, PDGFRb and FGFR1 for ruling out MPDs was carried out, so that all these tests were negative. After examining the BM specimen, chronic myelomonocytic leukemia (CMML) was the probable diagnosis. Patient managed with hydroxyurea, prednisolone, cytosar, imatinib, and splenectomy. After a while, other complications like retina bleeding occurred; therefore, for preventing of these conditions and interdiction of severe thrombocytopenia and anemia, the treatment was continued using imatinib with no further drugs. This led to palliation of clinical and laboratory (leukocytosis) findings for three months. Once again, BM aspiration and biopsy was repeated. This time, MPD was suspected, so prednisolone, hydroxyurea, imatinib, and cyclosporine were prescribed, however, her clinical findings were still persistent. For further evaluations, aspiration and biopsy of the BM was performed for the third time and the specimen was referred to our laboratory. In this step, in addition to leukocytosis, anemia and thrombocytopenia, fatigue manifested. PBS examination showed the increased leukocytes with eosinophilia besides hypersegmented (with individual nuclear lobes) and hypogranular leukocytes. Few of these cells showed fine granulation

(Figure 1). Blasts were less than 1.0% and the other types of leukocytes were rarely seen. BM smear showed similar findings with dysplastic megakaryocytes. After precise observation of these findings, flow cytometry was performed on BM sample with the following markers: HLA-DR, CD3, CD5, CD19, CD10, CD13, CD33, CD14, CD64, CD117, CD38, CD25, CD34, and CD45. On the basis of dot plot in forward versus side scatter, medium sized leukocytes with lower side scatter were observed (Figure 2) and this pattern was similar to AML-M4/M5 blastic flow cytometry pattern. These specific cells were positive for CD13, CD33, CD38, CD25, $CD45^{mod}$, and negative for other myeloid and lymphoid markers (Figure 2).

According to the morphological and immunophenotyping findings, about 42.0% basophil and 30.0% eosinophil were identified in BM sample confirming the diagnosis of MPD-NOS (CBL). In order to improve clinical symptoms, mepolizumab was added to other mentioned drugs. After observing the skin masses, the possibility of chloroma was suggested and following the administration of interferon, the clinical symptoms subsided and the patient was placed as a candidate for BM transplantation.

Discussion and Conclusion

Basophils are distinct hematopoietic cells and in some myeloid neoplasms, including CML, basophilia is seen. Basophils are markedly increased in the accelerated phase of CML and in some patients may produce clinical findings (7). CBL is a rare disorder and in order to avoid unnecessary treatment, precise evaluation of clinical manifestations and use of new laboratory methods is mandatory (4).

In the present case, morphological findings were not suitable to differentiate CBL from CEL, and besides the increase of eosinophils, basophils did not have typical morphology. For the mentioned reasons, misdiagnosis would be so probable. Most of the basophils in this case were hypersegmentated and their nucleuses had individual lobes. Hypogranulation and presence of few fine granules were others special findings. These strange morphologies besides eosinophilia would enhance suspicion of CBL detection. The morphological findings are not reliable enough, and flow cytometry evaluation was mandatory for definite diagnosis. Basophils have moderate CD45 expression and low side scatter pattern (8), and express CD123, CD9, CD22, CD13, CD33, CD36, CD38, CD25 and $CD45^{mod}$ (9), but eosinophils do not express CD25, CD38 and are positive for CD45 (bright expression), CD13, CD33, CD15, CD11b, CD11c, which all can conduct us for a more specific and time-saving diagnosis of CBL.

The findings of the present case were in part similar to those of case 6 and accelerated phase of same patient reported by Chehreli et al, In that the increased basophils in the PB and BM,
basophils and eosinophils dysplasia, eosinophilia, hypercellularity of BM, and dysplastic megakaryocytes were evident (10,11).

In the 6-month follow-up of this case, despite receiving the mentioned drugs, no improvement was seen. Based on these findings and also the findings of above mentioned reviews and proposed diagnostic criteria (2), it is suggested that patients who have these presentations, should be evaluated for the expression of CD13, CD33, CD38, CD25, CD45, forward scatter and side scatter. The present data add to the previously reported data as proposed criteria for the diagnosis of primary BCL.

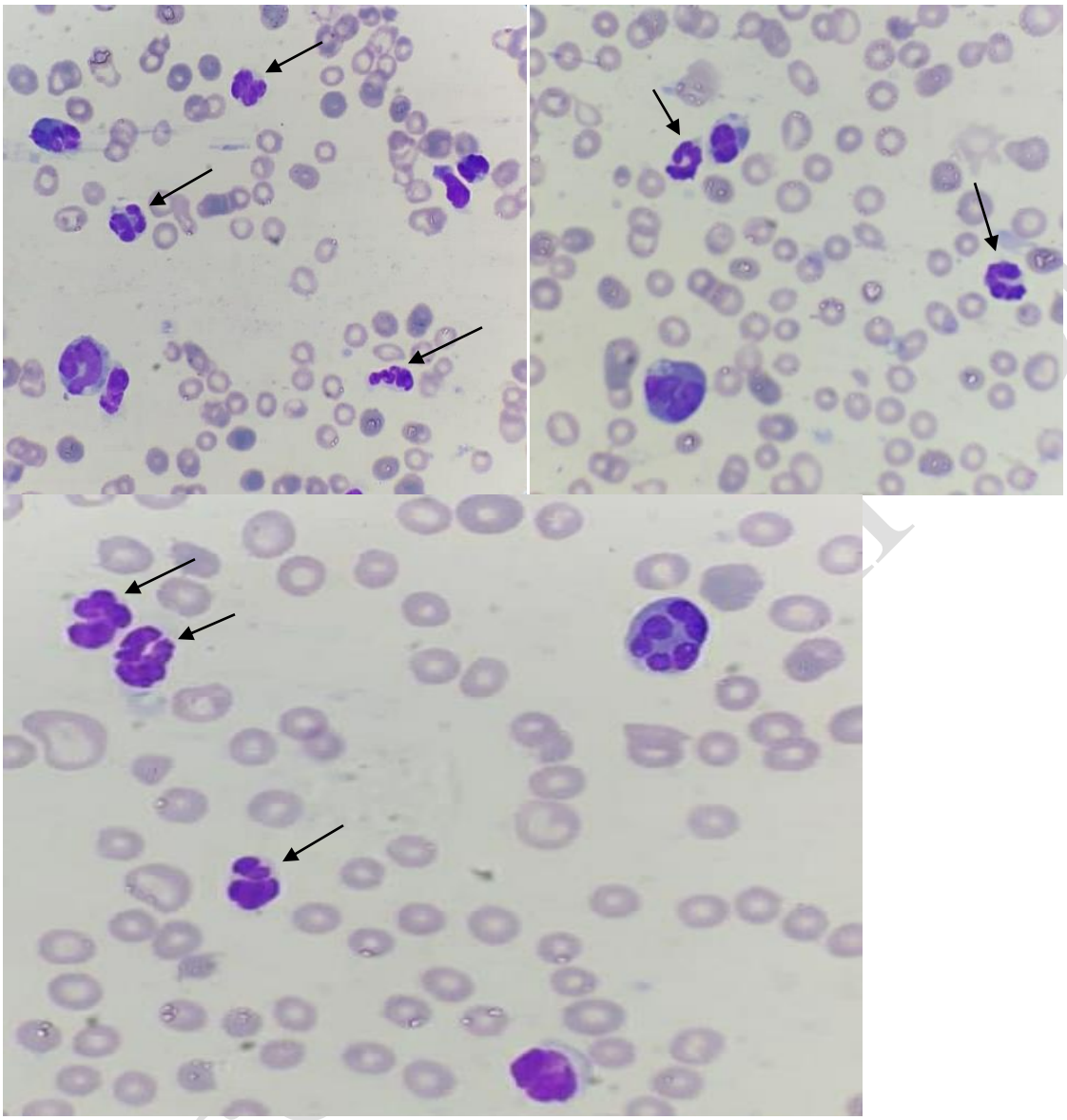
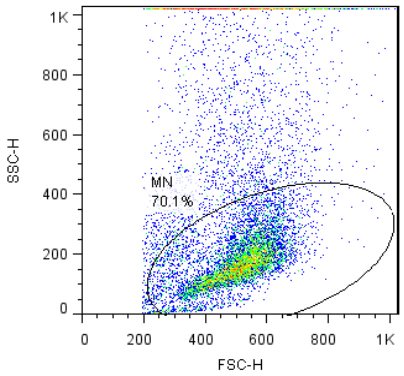
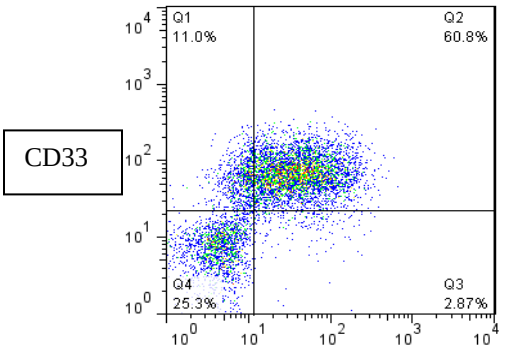


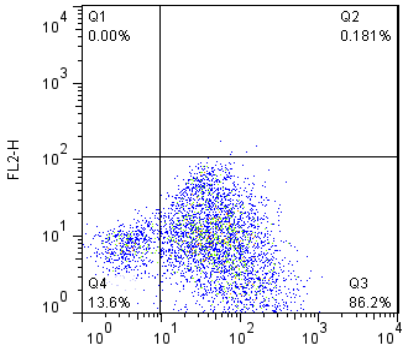
Figure 1. BM smears show increase in eosinophils and the presence of many hypogranular and hypersegmented leukocytes (arrow).



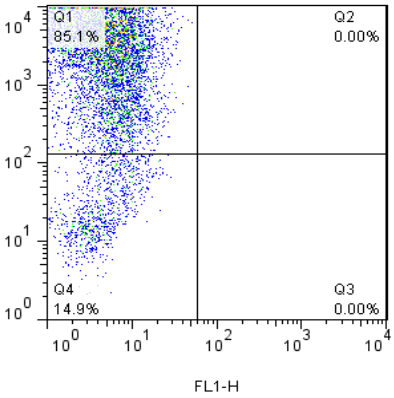


CD33

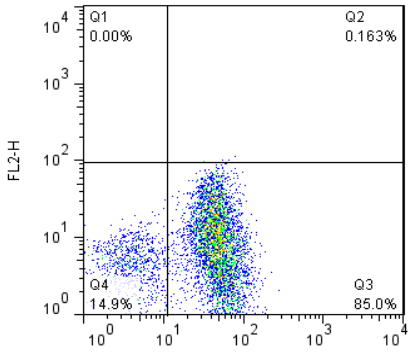
CD13



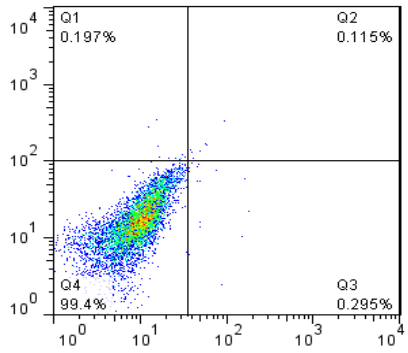
CD38



CD45



CD25



CD64

CD14

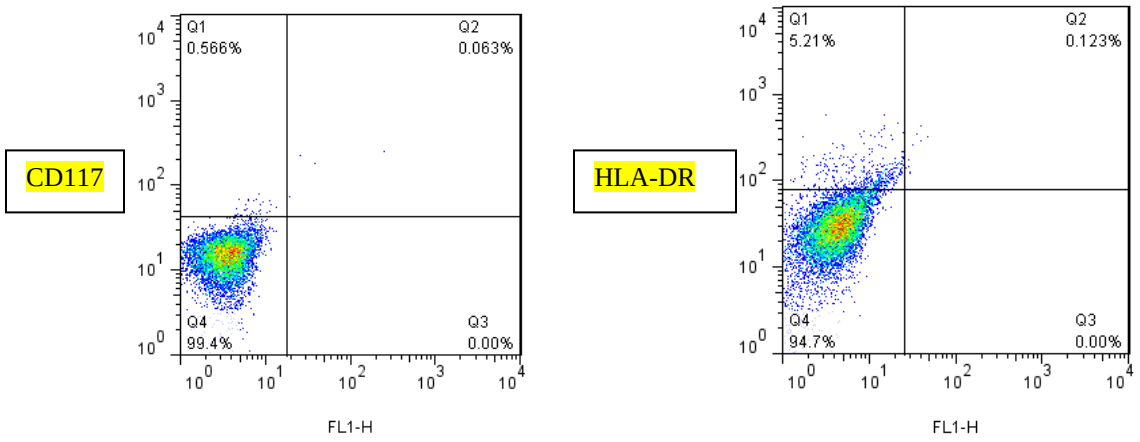


Figure 2. Flow cytometry dot plot reveals expression of CD13, CD33, CD25, CD38, CD45 mod. CD14 and CD64 were negative in the selected population.

Conflict of interest

The authors declare they have no conflict of interest

Author Contributions

The Authors equally contributed for this article

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Ethics approvals

Consent was obtained from the patient and the patient was assured that her information would remain confidential.

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