

Pure Erythroleukemia: A Case Report And Literature Review

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Citation

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Abstract

Pure erythroleukemia is a rare hematopoietic neoplasm, seldom reported in literature. Varied reports suggest a prevalence of 3-5% of all AML. We report one such case, presenting with non classical symptoms in a 65 year old lady. Peripheral smear examination and complete hemogram revealed a pancytopenic profile with circulating basophilic erythroblasts. Bone marrow study yielded erythroid hyperplasia with abundance of PAS positive proerythroblasts and dyspoiesis in other lineages. Pure erythroleukemias are known to carry a poor response to standard chemotherapy. The present case is a testament not only to the rarity of the disease but also for a reminder that such an aggressive neoplasm can indeed present in the most inconspicuous manner.

INTRODUCTION

Erythroleukemia is a rare disorder characterized by uncontrolled proliferation of erythroblasts and myeloblasts. Ever since its description almost a century ago it remains an elusive diagnosis, comprising approximately 3-5% of all acute myeloid leukemias. In 1969 Dameshek and Baldini postulated that the disease had 3 phases in the bone marrow: an erythemic phase, an erythromyeloblastic phase, culminating in an acute myeloblastic leukemia.¹

In 1985, FAB group subdivided it into leukemia and myelodysplastic syndrome, only to be further modified by Kowal Vern and associates as M6a & M6b (pure erythroleukemia)²

The current WHO classification recognizes 2 subtypes based on the presence or absence of a significant myeloid component. The first subtype, pure erythroleukemia (FAB subtype B) represents a neoplastic proliferation of immature cells (undifferentiated or proerythroblastic) committed exclusively to the erythroid lineage (>80% of bone marrow cells) with no evidence of a significant myeloblastic component. The second subtype, erythroleukemia (FAB subtype A) is defined by the presence of >50% erythroid precursors among all nucleated cells in the bone marrow and > 20% myeloblasts in the non erythroid cell population.

We report a unique case of pure erythroleukemia in a 65 year old lady, presenting with non classical symptoms.

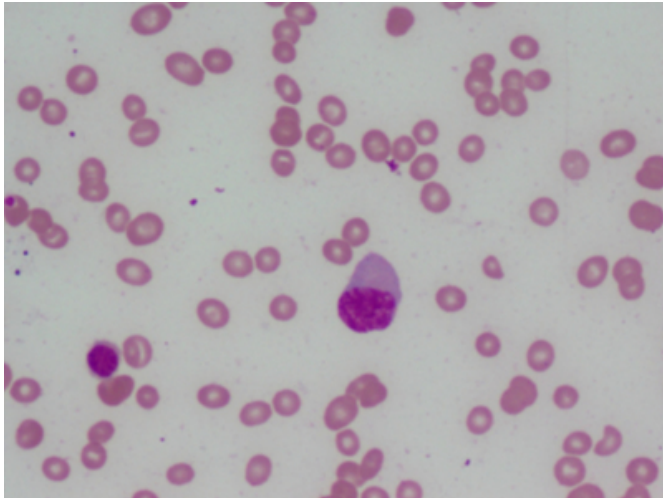
CASE REPORT

A 65 year old woman, housewife by occupation, presented to the outpatient clinic with complaints of loss of appetite and increasing fatigue since 6 months. She was a non alcoholic and also denied any history of drug intake or toxin exposure. Systemic examination was normal and there was no history of fever, night sweats, weight loss or bleeding tendencies. Physical examination revealed pallor without any obvious distress apart from moderate dyspnea. There was no palpable lymphadenopathy or hepatosplenomegaly.

Hematological investigations showed a pancytopenia profile, with a white blood cell count of $3.3 \times 10^3/\mu\text{l}$, hemoglobin of 4.4gm/dl and a platelet count of $1.9 \times 10^3/\mu\text{l}$ respectively. Peripheral smear showed 29% basophilic erythroblasts and numerous nucleated red blood cells (Fig. 1).

Figure 1

Figure 1: Peripheral smear showing a basophilic erythroblast and a nucleated RBC

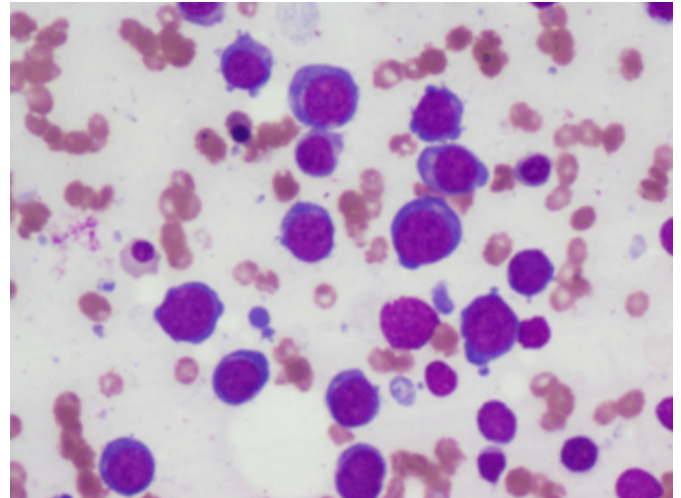


The special tests ordered by the concerned physician showed a negative HAM test and a positive sucrose lysis test. Biochemical parameters were insignificant except for an elevated serum LDH and AST.

The smear findings were concluded as acute leukemia and a bone marrow study was requested to subtype the neoplasm. A flow cytometric analysis of the peripheral blood was also advised for the same. The bone marrow analysis (Fig.2) yielded hypercellular aspirates with increase in erythroid precursors showing an abnormal pattern of maturation. The proerythroblasts comprised 29% of all nucleated cells while other erythroblasts were 53%. The total erythroblast count was 82% of all nucleated cells. Myeloblasts comprised 56% of non erythroid cells. Megakaryocytes were suppressed with few dyspoietic forms.

Figure 2

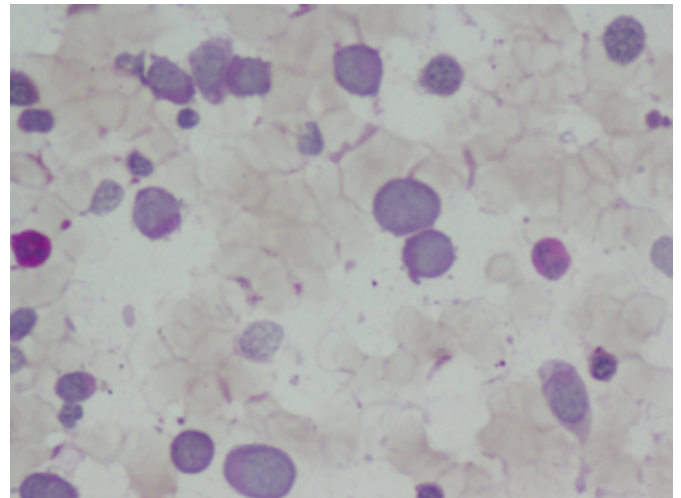
Figure 2: Bone marrow aspirate showing numerous erythroblasts



Special stains: PAS was positive in few abnormal erythroblasts (Figure 3). No sideroblasts were seen on Perl's Prussian blue stain.

Figure 3

Figure 3: PAS stain showing positivity in few erythroblasts



Flow cytometric analysis was not performed due to economic constraints. The patient was non-compliant with regard to the cost of chemotherapeutic regimen and was subsequently discharged after receiving palliative care in the form of blood transfusions and oral medications.

DISCUSSION

The malignancies which are a derivative of erythrocytic lineage have been mired in speculations right from their inception. Erythroleukemia represents 3 to 5% of adult AML cases, with few exceptional cases also reported in the pediatric age group.³ Previous exposure to toxins or alcohol

or both have been associated; but our patient was a non alcoholic, with no drug history. Although no clinical feature is specific to it, severe pallor, bleeding manifestations and rheumatic complaints have been reported in increasing frequency versus other AMLs⁴. The median age at diagnosis is fifth to sixth decade of life⁵.

Another feature described in conjunction with erythroleukemia is an antecedent history of MDS along with chromosomal abnormalities identified on cytogenetic analysis, common being chromosome 5 and /or 7 and complex karyotypes⁶. Aberration of chromosome 19 has also been reported in one study. No cytogenetic study could be done on this patient due to high cost of the tests. The median survival has been pegged between 4 to 14 months by few studies⁸. Our patient could not be followed up due to aforementioned reasons.

The characteristic hematologic features of pure erythroleukemia include normocytic normochromic anemia, punctuated by a preponderance of nucleated RBCs, with the most immature and basophilic precursors in the majority. Atypical nucleated RBCs are also encountered & reticulocytes are few, with a gradual reduction with disease progression⁹. Leucopenia and thrombocytopenia are not uncommon. Rare reports of reticuloendothelial cells in the peripheral blood have also been noticed.

Bone marrow examination usually reveals an increase in erythroid series with myeloid suppression and predominantly shows medium to large erythroblasts with deep basophilic cytoplasm often agranular and frequently displays poorly demarcated vacuoles that are often PAS positive. In many instances, the blasts may be smaller, resembling lymphoblasts

Multilineage dysplasia has been seen in many cases. Megakaryocytes are often dysplastic with nuclear segmentation abnormalities. Rarely megakaryoblasts may be seen in circulation. Dysgranulopoiesis has been reported in 50% cases¹⁰.

Special stains accentuate the differentiation from other lineages by being MPO negative, but displaying positivity for acid phosphatase, alpha naphthyl acetate esterase and PAS (block like staining pattern). In our case, PAS positivity was noted in few abnormal erythroblasts.

Interestingly, Prussian blue stain demonstrates increased iron stores sometimes with ring sideroblasts. No sideroblasts were seen in our case. Few authors have described

occasional MPO positivity in erythroid cells in erythroleukemia¹¹

In flow cytometric analysis and immunophenotyping the erythroblasts in erythroleukemia stain positive with CD36 and glycophorin A. This is not a specific feature in favor of M6 as glycophorin A is a late erythroid marker and hence can be completely negative in AML-M6. CD36 on the other hand is also non specific as it is also expressed by monocytes and megakaryocytes. The more differentiated form of pure erythroleukemia can be detected by the expression of glycophorin A, absence of myeloperoxidase and other myeloid markers. The blasts are often negative for HLA-DR and CD34 but may be positive for CD117¹⁰.

Infiltration of extrahematopoietic organs like adrenals, pancreas, lungs, myocardium, testis, spleen and trachea have also been reported in literature⁹.

DIFFERENTIAL DIAGNOSIS

The main differentials entertained in a case of pure erythroleukemia are MDS (RAEB), AML with MDS related changes, AML with increased erythroid precursors, megaloblastic anemia and reactive erythroid hyperplasia following therapy or administration of erythropoietin.

Other AML subtypes particularly megakaryoblastic, ALL and lymphomas also need to be distinguished from AML-M6b.

CONCLUSION

Pure Erythroleukemia is a rare hematopoietic neoplasm carrying a poor prognosis to standard chemotherapy. Morphological diagnosis is often difficult due to its close resemblance to various other neoplastic and non-neoplastic hematological conditions. A thorough bone marrow examination with an accurate differential count of all nucleated cells and a blast count of non erythroid cells is a must for a proper diagnosis. Glycophorin A can be a useful immunohistochemical marker for further confirmation. In our case there were no typical clinical features of AML-M6 like organomegaly and the diagnosis was purely based on bone marrow morphology and cytochemistry.

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