

Diguglielmo syndrome

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ABSTRACT

Acute Erythroid Leukemia (AEL) / Acute Myeloid Leukemia M6 (AML M6) is a rare disorder of hematopoietic system and accounts for 1-3% of acute leukemia and 15% of myeloid leukemia. It is characterized by uncontrolled proliferation of erythroblasts and myeloblasts. We report a case in a 70 year lady who presented with non classical symptoms and the diagnosis is based on purely peripheral smear, bone marrow findings and cytochemistry. The present case is a testament not only for rarity of disease but also a reminder that erythroleukemia can present in non-classical manner.

Keywords: Acute erythroid leukemia, AML M6, Erythroblasts, Prognosis, Cytochemistry

INTRODUCTION

Erythroleukemia is characterized by prominent component of erythroblasts. According to new World Health Organization (WHO) classification, erythroleukemia is classified based on the presence or absence of a significant myeloid component. Erythroid/myeloid leukemia (M6a) has 50% or more erythroid precursors in the nucleated population and 20% or more myeloblasts in the non-erythroid population. In the less common pure erythroid leukemia (M6b), 80% of the marrow cells are immature erythroid precursors, without significant number of myeloblasts. A third type (M6c) has been characterized by 30% or more non-erythroid blasts and 30% or more pronormoblasts.¹

We present a case of Erythroleukemia (erythroid/myeloid) (M6a) diagnosed with complete hemogram, peripheral smear, bone marrow examination, Periodic acid Schiff stain, Myeloperoxidase stain.

CASE REPORT

A 70-year old known hypertensive female presented with low grade fever, generalised weakness, pallor and dry cough since 15days. Complete hemogram was done and data was tabulated in Table 1. Peripheral smear revealed moderate anaemia, marked thrombocytopenia, leucocytosis with 80% blasts which resemble erythroblasts with peripheral rimming

of red cell cytoplasm and few blasts had granules. Bone marrow aspiration was done and revealed erythropoiesis showing 70% of all nucleated bone marrow cells as erythroblasts. These blasts are large having grey blue cytoplasm with large nucleus and 2-3 prominent nucleoli. There are marked dyspoietic features in the form of anisonucleosis with altered nuclear to cytoplasmic ratio. Frequent budding forms, karyorrhexis, mitotic figures, gigantoblasts with multiple irregular nuclei are seen. Proerythroblasts and micronormoblasts are seen. Myelopoiesis showed more than 20% non erythroid cells as myeloblasts. Few Auer rods were seen. Rest of the myeloid series is markedly decreased. Megakaryocytes are markedly decreased. Periodic Acid Schiff stain revealed block positivity and paranuclear granular positivity in erythroblasts. Myeloperoxidase stain revealed positivity in more than 20% myeloblasts.

Table 1: Hemogram findings of the patient

COMPLETE BLOOD PICTURE	PATIENT VALUES
Haemoglobin	6.8 gm/dl
Red blood cell count	2.0 million/cumm
White blood cell count	29,800 cells/cumm
Platelet count	45,000/cumm
Differential count	80% blasts

DISCUSSION

Erythroleukemia accounts for 2% to 4% of cases of AML. The most common immunophenotypic markers for erythroleukemia are glycophorin 7, spectrin, carbonic anhydrase I, ABH blood group antigens and the transferring receptor (CD71). There is a bimodal age distribution for erythroleukemia, with a small peak below 20 years and a broader peak in the seventh decade. Approximately one half of cases of erythroleukemia are therapy related. Cytogenetic abnormalities are found in over 70% of patients, and abnormalities of chromosomes 5 and 7 are common. The

prognosis for erythroleukemia is generally poor, with a recent reported overall survival of 8 months, but depends upon age, secondary leukemia, cytogenetic abnormalities, and subtype of erythroid leukemia. Median survival was inferior in M6b (1.8 months) compared to M6a (18.8 months, $P < 0.002$) and M6c (7 months, $P < 0.01$). Allogeneic Stem cell transplantation appears to confer the best long-term survival in erythroleukemia; particularly with unfavorable cytogenetics and/or therapy-related.¹ Antihemoglobin antibody and antihuman erythroleukemic cell line antibody often are positive. The more predominant the erythroid component and the lower the proportion of myeloblasts, the better the response to therapy.² The main differentials entertained in a case of erythroleukemia(erythroid/myeloid) are refractory anemia with excess blasts, AML with myelodysplasia related changes, AML with increased erythroid precursors, megaloblastic anemia and reactive erythroid hyperplasia following therapy or administration of erythropoietin. Other AML subtypes particularly megakaryoblastic, acute lymphoblastic leukemia and lymphomas also need to be distinguished from AML-M6.³ Increased survival was associated with minor chromosomal aberrations and an increase in myeloblasts.⁴ Di Guglielmo reported the original case of acute erythroleukemia in 1917; he described it as a syndrome composed of immature erythroid and myeloid elements characterized by a pure normoblastic proliferation.⁵ The signs and symptoms of AML M6 are nonspecific and are attributed to the replacement of bone marrow elements by neoplastic cells. Patients rarely present with symptoms lasting longer than six months, and they are usually diagnosed within 1-3 months after the onset of symptoms.⁶ The current WHO criteria for establishing the diagnosis of AEL reduce the frequency of this entity, as cases once classified as the erythroleukemia subtype are now reclassified as other types of AML, particularly AML with myelodysplasia related changes and therapy related AML. This reclassification also may have prognostic significance for patients with the erythroleukemia subtype of AEL. Molecular studies are needed for a better understanding of the pathogenesis of AEL, and for developing diagnostic and prognostic markers.⁷

CONCLUSION

AML-M6 is a heterogeneous disease with poor response to standard chemotherapy that carries a poor prognosis. 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.. 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.

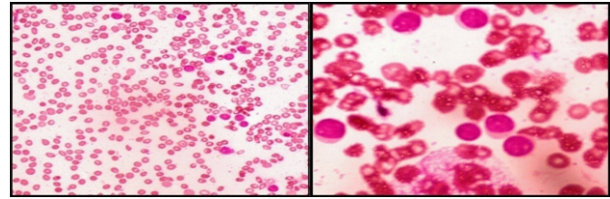


Figure 1: Peripheral blood smear reveals blasts (Leishman stain 40x & 100x)

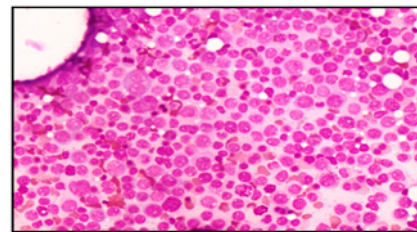


Figure 2: Bone marrow aspiration reveals >70% Erythroblasts (H & E- 40x)

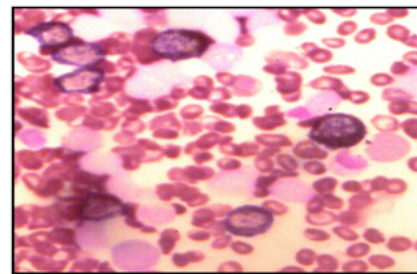


Figure 3: Bone marrow aspiration: Positivity in Myeloblasts (Myeloperoxidase stain- 100x)

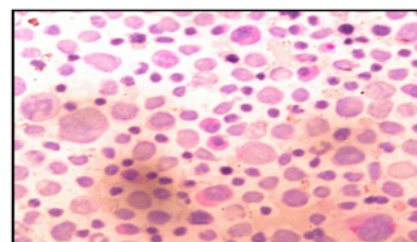


Figure 4: Bone marrow aspiration: Positivity in Erythroblasts (Periodic acid schiff stain- 100x)

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