Case Report

A rare case of acute myeloid leukemia-M6 in a 2-year-old child with complex karyotype

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ABSTRACT

Acute erythroid leukemia is a very rare entity in children. Here is a case of erythroleukemia with complex cytogenetics in a child aged 2 years. On immunophenotyping, CD45 versus side scatter (SSC) demonstrated blast population (29%) with intermediate SSC and moderate CD45 expression. The myeloid nature of blast population was confirmed by moderate expression of cytoplasmic myeloperoxidase, CD117, CD13 and CD33. Another population of cells (28%) with low to intermediate SSC and negative CD45 expression revealed dim expression of CD235a (64%) indicating lysis resistant abnormal erythroid progenitors. Conventional cytogenetic analysis by G-banding revealed complex cytogenetics.

Key words: Acute erythroid leukemia, child, immunophenotyping, complex cytogenetics

INTRODUCTION

The terms acute erythroleukemia, and acute myeloid leukemia-M6 (AML) are defined in the French-American-British (FAB) classification as proliferations of dysplastic erythroid elements mixed with blasts of myeloid origin, but pure erythroid leukemias are not included. The recent WHO classification has a category of AML not otherwise categorized, which includes acute erythroid leukemia (AEL) (M6) of two subtypes: M6a-erythroleukemia (erythroid/myeloid) and M6b (pure erythroid leukemia). AEL is defined as leukemia with erythroid precursors presenting ≥50% of all nucleated bone marrow cells. For acute myeloid leukemia-M6a (AML), along with >50% of erythroid precursors, there should be additional >20% of myeloblasts in nonerythroid population and in case of AML-M6b, erythroid precursors represents ≥80% of bone marrow cells with no evidence of a significant myeloblastic component.[1]

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CASE REPORT

A 2-year-old female child born out of consanguineous marriage, presented with history of fever for last 2 months and one episode of malena and gum bleeding 2 weeks back for which child required packed cell and platelet transfusions. On examination, child had characteristic facies with mongoloid slanting of eyes, hypertelorism, blackish pigmentation of right half of forehead and pallor, liver 1.5 cm enlarged, spleen 2.5 cm enlarged, few lymphnodes (maximum size 2 cm) were palpable in right cervical region. Her complete hemogram showed - hemoglobin 5.4gm/dl, white blood cell (WBC) - 2.9 × 10^3/μL, platelet - 24 × 10^3/μL, neutrophil - 31, lymphocyte - 54, blasts - 5% and nucleated RBCs - 8/100 WBCs. Liver function test and renal function test were within normal limits. Serum lactate dehydrogenase - 2667 U/L. Echocardiography findings were normal. Bone marrow examination [Figure 1] revealed 26% blasts (54% of nonerythroid nucleated marrow cells) of moderate to large size, high N: C ratio, opened up

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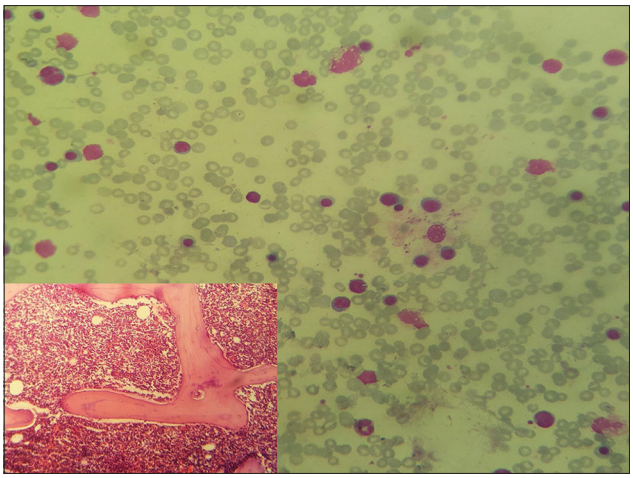

Figure 1: Bone marrow smear revealed population of erythroid precursors at varying stages of maturation with dyserythropoietic features and myeloblasts. The dual lineage proliferation was confirmed immunophenotypically by flow cytometry. Inset: Trephine biopsy shows grossly hypercellular marrow with many erythroid precursors and immature myeloid cells

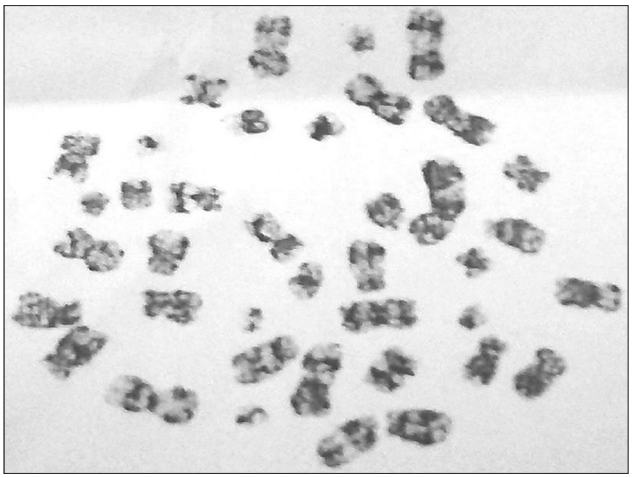

Figure 2: Conventional cytogenetic analysis revealed extremely complex rearrangements with 38–39 chromosomes involving with almost all chromosomes in all the cells

chromatin, prominent 1–2 nucleoli and scant to moderate amount of basophilic cytoplasm, occasionally showing cytoplasmic blebbing. Erythroid precursors comprised 52% of all nucleated marrow cells. Megakaryocytes not seen in the smear examined. Immunophenotyping by flow cytometry for CD45/side scatter (SSC) plot shows two population of cells - one population (29%) with intermediate scatter and moderate CD45 expression, moderate expression of cytoplasmic myeloperoxidase and moderate expression of CD117, CD13, CD33 and negative for B- and T-lymphoid markers. The other population of cells (28%) with low to intermediate SSC and negative CD45 expression, revealed dim expression of CD235a (64%) indicating lysis resistant abnormal erythroid progenitors.

Cytogenetic analysis following unstimulated culture of the bone marrow sample revealed extremely complex rearrangements with 38–39 chromosomes involving with almost all chromosomes in all the cells. Karyotypic classification was not possible due to complexity [Figure 2].

DISCUSSION

Erythroleukemia is a rare disorder characterized by uncontrolled proliferation of erythroblasts and myeloblasts comprising 2–7% of all AMLs.[2,3] The FAB group proposed the classification of these leukemias as AML-M6.[4] They are generally seen in old age.[5] Very few cases of pediatric erythro-leukemia have been reported in the literature, comprising <1% of pediatric leukemias. A 16-year-old study at Memorial Sloan-Kettering Cancer Center, New York reported only one case of pediatric erythroleukemia.[6] Similarly, Day *et al*.[7] published a report of two cases of erythroleukemia in infancy. Batra *et al*. published a clinic-hematological review of four erythroleukemia cases in children.[8]

AEL can occur *de novo* in 1% of all *de novo* AML. Secondary AEL are described associated with previous diseases such as myelodysplastic syndrome, AML with recurrent genetic abnormalities, chronic myelogenous leukemia blast phase, and previous cytotoxic treatment.[1,9]

A thorough clinical history, laboratory data, immunophenotypic analysis, genetic, and molecular studies are necessary for the correct diagnosis. Additional cytogenetic and molecular studies are required to elaborate our understanding of this disease.

The two subgroups (AML-M6a, M6b) differ clinically with M6b having a worse prognosis. Recent studies showed that the group of erythroid/myeloid leukemia (AML-M6a) is also heterogeneous and has different prognosis depending on the cytogenetics results. The most important adverse prognostic factor is the type of cytogenetic abnormalities. The prognosis is poorer with unfavorable and complex karyotypes.[6]

CONCLUSION

AEL in childhood is a very rare entity. A thorough clinical history, laboratory data, immunophenotypic analysis, genetic and molecular studies are necessary for the correct diagnosis. The prognosis is worst with unfavorable and complex karyotypes.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Mihova D, Zhang L. Acute erythroid leukemia: A review. North Am J Med Sci 2012;5:110-8.
2. Olopade OI, Thangavelu M, Larson RA, Mick R, Kowal-Vern A, Schumacher HR, *et al.* Clinical, morphologic, and cytogenetic characteristics of 26 patients with acute erythroblastic leukemia. Blood 1992;80:2873-82.
3. Domingo-Claros A, Larriba I, Rozman M, Irriguible D, Vallespí T, Aventin A, *et al.* Acute erythroid neoplastic proliferations. A biological study based on 62 patients. Haematologica 2002;87:148-53.
4. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, *et al.* Proposals for the classification of the acute leukaemias. French-American-British (FAB) co-operative group. Br J Haematol 1976;33:451-8.
5. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, *et al.* Proposed revised criteria for the classification of acute myeloid leukemia. A report of the French-American-British Cooperative Group. Ann Intern Med 1985;103:620-5.
6. Hetzel P, Gee TS. A new observation in the clinical spectrums of erythroleukemia. A report of 46 cases. Am J Med 1978;64:765-72.
7. Day DS, Gay JN, Kraus JS, Sabio H, Satya-Prakash KL, Russell B, *et al.* Erythroleukemia of childhood and infancy: A report of two cases. Ann Clin Lab Sci 1997;27:142-50.
8. Batra VV, Karan AS, Saxena R. Erythroleukemia: A clinco-hematological review of four cases. Indian Pediatr 2004;41:587-90.
9. Malkin D, Freedman MH. Childhood erythroleukemia: Review of clinical and biological features. Am J Pediatr Hematol Oncol 1989;11:348-59.