Case Report

Acute Erythroid Leukemia (AML-M6a) of protracted onset in a child: Evolution from pre-existing MDS or de novo entity

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Abstract :

Acute erythroid leukemia is a heterogenous disease, which may arise de novo, secondary to MDS (myelodysplastic syndrome) or after cytotoxic therapy. Pediatric erythroleukemia is an acute onset leukemia which is usually diagnosed within 1-2 months after the onset of symptoms. Patients very rarely present with symptoms lasting longer than 6 months. Here is a case of erythroleukemiain a child of age 10 years, who presented with low grade fever, severe pallor and hepatosplenomegaly for 12 months duration. Peripheral smear examination showed anemia, thrombocytopenia,nucleated red blood cells and circulating blasts. The bone marrow displayed erythroid hyperplasia with dysplasiaand presence of myeloid blasts which showed auer rods and myeloperoxidase positivity. Immunophenotypic characterization by flow cytometryrevealed myeloid and erythroidprecursors. Hence a diagnosis of erythroleukemia was made. The case is being discussed here because of its rarity and unusual presentation with such long clinical history and its probable evolution from pre-existing MDS.

Key words:

Erytholeukemia, Myelodysplasia, Bone marrow examination, Immunophenotyping

Introduction:

Leukemia purely comprising erythrocytic precursors was first described by Di Guglielmo in 1928.1Until recently, this fulminant acute leukemia was alternately classified as a myeloproliferative disorder or a myelodysplastic syndrome. At presentation, the signs and symptoms of erythroleukemia (EL) are usually nonspecific and are attributable to the decreased hematopoiesis resulting from the replacement of bone marrow by leukemic cells. 2 This decrease results in anemia, thrombocytopenia and/or leukopenia. Patients rarely present with symptoms lasting longer than 6 months, and they are usually diagnosed within 1-3 months after the onset of symptoms. Myelodysplasiamay precede the onset of EL especially in adults, and myelodysplastic features involving multiple haemopoietic lineages are observed at the time of leukemia presentation. Herein we discuss a rare case of pediatric EL with protracted course, in whom bone marrow (BM) examination was requested with clinical possibility of leishmaniasis/hemolytic anemia.

Case history

A ten-year-old male presented with complaints of low-grade fever, jaundice and severe pallor since twelve months. On examination, he had pallor with icterus and periobitaloedema. Multiple cervical and inguinal lymph nodesmeasuring 1-2 cm, were palpable. On per abdominal examination, there was hepatomegaly of 9 cm and splenomegaly of 10 cm below the right and left costal margin respectively. There were multiple purpuric spots present all over the body. Serology for HIV was negative. Mantoux and widal were also negative. Serum vitamin B12, folic acid and iron profile were normal. The complete

blodd counts showed anemia (hemoglobin 50 g/L), thrombocytopenia (platelet count 5x109/L) and a raised total leucocyte count (total leucocyte count 19.6x109/L) with circulating blasts and nucleated red cells.Bone marrow (BM) examination was requested with clinical possibility of hemolytic anemia/leishmaniasis.Peripheral blood film at the time of bone marrow examination revealed moderate anisopoikilocytosis with macrocytes, microcytes, spherocytesand polychromatophilic cells. There were 48 nucleated RBCs/100 WBCs seen. Corrected reticulocyte count was 5.6%. Total leukocyte count was 6.9x109/L with differential count of polymorphs 21%, lymphocytes 61%, monocyte 03%, eosinophil 01%, blasts 12%, myelocytes 02%(Figure 1a). Platelets were reducedon smear. BMaspirate wasaparticulate, however showed predominantly erythroid population with marked megaloblastic change and dyserythropoiesis. Myeloid blasts containing auer rods were seen (Figure 1b). Occasional megakaryocyte was seen showing dysmegakaryopoiesis in the form of hypolobation and lobe separation(Figure 1c). Differential count done on trephine touch imprint smears showed 25 % blasts, 01% promyelocyte,05% myelocytes, 03% metamyelocytes, 04% polymorphs, 08% lymphocytes, and erythroid 54%. Bilateral trephine biopsies showed hypercellular marrow spaces with sheets and interstitial excess of immature cells witherythroid colonies. Scattered megakaryocytes were seen showing dysplasia in the form of hypolobation and lobe separation(Figure 1d). Other hematopoietic elements were reduced. There were no ring sideroblasts on Perl's stain. Multiparametric flow cytometery was performed on bone marrow sample. The cells present in precursor region on side scatter versus CD45 plot showed expression of erythroid markers only i.e. CD71 and CD235a. Myeloid markers (CD33, CD13 and CD117) were seen only in a small population of cells with dim expression.Other markers for B and T-lineage (CD19, CD10, CD22, HLADR, CD3, CD4, CD5,CD7, CD8) and monocytic markers (CD14, CD64, CD11c) were negative. Thus, based on peripheral smear findings, BM examination and immunophenotyping, a diagnosis of erythroleukemia was made.

Discussion

Acute erythroid leukemia accounts for <5% of all acute myeloid leukemias, mainly affecting adult population, mostly people above 50 years.3 The male to female ratio varies from 2.4:1 to 4:1.4 Clinical presentation is non-specific including weakness, pallor, fever and hemorrhages, rarely intracranial hemorrhages.4 Patients may also present with hepatosplenomegaly or isolated hepatomegaly or splenomegaly. 5 Anemia (mean hemoglobin Hb 75 g/L reported in 1 study) and thrombocytopenia are present in all the cases, while the neutrophil count varies from normal to low.

The time course is variable. Some patients, particularly younger ones, present with acute symptoms over a few days to 1-2 weeks. Others have a longer course, with fatigue or other symptoms lasting from weeks to months. Mean duration from symptoms presentation to the diagnosis is 5.75 months in children <12 years of age.6 A longer course as happened in the present case, may suggest an antecedent hematologic disorder, such as myelodysplastic syndrome (MDS).

Our patient presented with pallor, fever and hepatosplenomegaly of long duation. Severe anemia was noted associated with thrombocytopenia in the peripheral smear with circulating blasts and nucleated red blood cells. The bone marrow showed erythroid hyperplasia with features of megaloblastosis and dyserythropoiesis. Although megakarypoiesis was significantly reduced but morphological features of dysplasia were seen in the few scattered megakaryocytes.Dysplasia in erythroid and megakaryocytic lineage, although known to occur in acute erythroleukemia, an unusually long history of duration of symptoms for almost one year, without any specific treatment, suggest a possibility of an evolution from MDS.

The important differential diagnoses include, childhood MDS, acute myeloid leukemia with myelodysplasia related change (AML-MRC), acute megakaryoblastic leukemia, reactive erythroid hyperplasia following immunosuppressive therapy or following viral infections or nutritional deficiencies. Thus, BM differential count of all nucleated cells should be performed, if the overall percentage of blasts is >20% and multilineage dysplasia is present in >50% of the cells of two or more lineages; diagnosis of AML-MRC should be made. If blasts are <20%, diagnosis is usually MDS. Acute megakaryoblastic leukemia can be diagnosed by expression of CD41 and CD61 in megakaryoblasts.

A confirmation of acute leukemia evolving from MDS would require either prior documentation of MDS in the BM examination, which was not the case in present case. A cytogenetic abnormality classical of MDS might also compliment the diagnosis, however the patient left against the medical advice and no further evaluation could be done. The diagnosis in the present case was offered based on a combination of history, physical examination, BM examination and immunophenotyping.

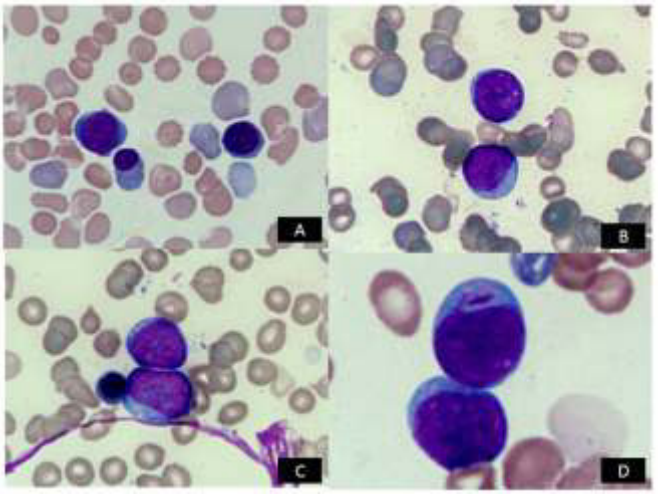

Figure 1. (A)Peripheral smear showing severe aniospoikiocytosismicocytes, macrocytes, polychromasia (B) & (C) High power view showing circulation Myleoid blasts and nucleated red cells (D) Myeloid blast showing Auer rods. (40X, MGG)

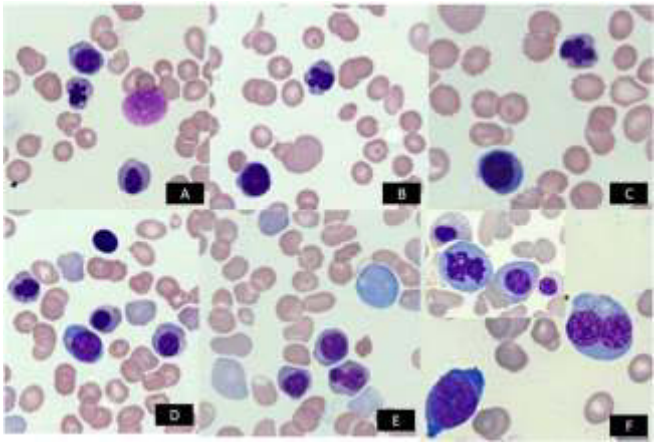

Figure 2. Panel of photographs showing erythroid dysplasia in the form of (A, B & C) multinuclearity; (D, E) nuclear budding and irregular nuclear membrane; (F) binuclearity, karyrrhoxis and megaloblastosis (40X, MGG)

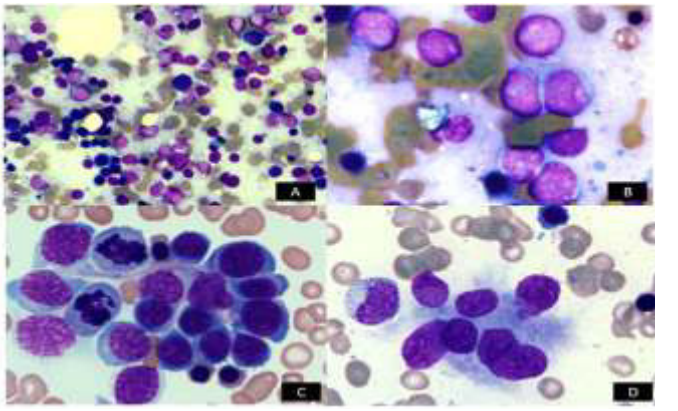

Figure 3. (A)Trephine imprint smears showing mixed population of erythroid and myeloid blasts (20X, MGG); (B) Large myeloid blasts; (C) Dysplastic erythroid precursors showing megaloblastosis and karyorrhexis (arrow) (D) Dysmegakaryopoiesis in the form of lobe separation (40X, MGG)

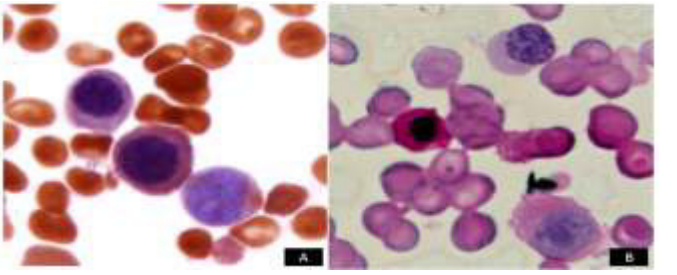

Figure 4.(A) MPO positive myeloid blast (arrow); (B) Erythroid precursor showing diffuse PAS-positivity (arrow) (40X).

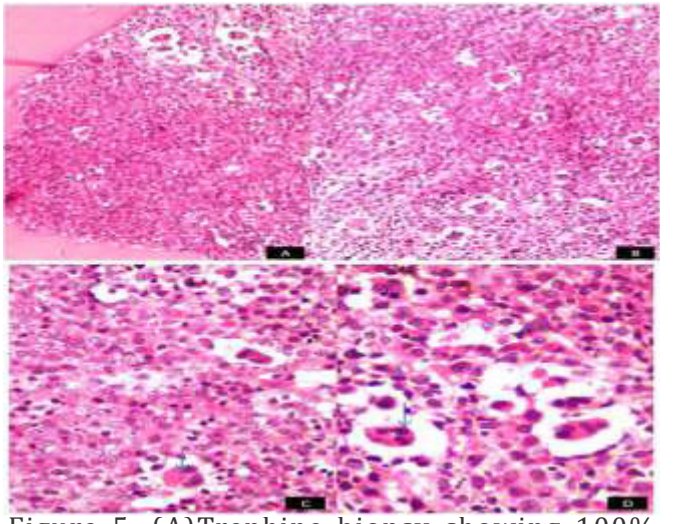

Figure 5. (A)Trephine biopsy showing 100% cellularity (B) Sheets and interstitial excess of immature cells admixed with erythroid colonies. (C) Dysplastic megakaryocytes showing hypolobationand (D) lobe separation (H & E, 40X)

Conclusion

Acute erythroid leukemia is a heterogenous disease, which may arise de novo, secondary to MDS or after cytotoxic therapy. A thorough clinical history, laboratory data, cytochemical and immunophenotypic analysis, genetic and molecular studies are necessary for the diagnosis of this rare neoplasm with a very poor prognosis.

References

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