

A case of erythroleukaemia in an eight year old boy

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Introduction

Erythroleukaemia was first recognized by Giovanni DiGuglielmo¹ from Italy in 1917 as a malignant condition and has been rarely reported in children². It accounts for less than 1% of all childhood leukaemias and 2-7% of all acute myelogenous leukaemias³ with very few of them from India³⁻⁶. It is still referred to as acute Di Guglielmo syndrome and classified as M6 subtype of acute myelogenous leukaemia (AML) in French American British (FAB) classification. Its rarity has prompted us to report this case.

Case report

An eight year old boy presented with complaints of progressive pallor and fever off and on for one month. There was nothing contributory in the past or family history. Child was fairly nourished but had severe pallor. There was no lymphadenopathy, icterus, petechiae or bruises. No bony tenderness was present. Signs of congestive cardiac failure (raised jugular venous pressure and pedal oedema) were present. Abdomen was soft and liver as well as the spleen were not palpable. Respiratory, nervous and musculoskeletal systems were normal.

Haemoglobin was 3.3g/dl and the packed cell volume (PCV) was 11%. The total leucocyte count was 3,200/cu mm with 17% polymorphs, 63% lymphocytes and 20% blast cells. Peripheral blood smear had 23 nucleated red blood cells (RBC) per 100 leucocytes (Figure 1).

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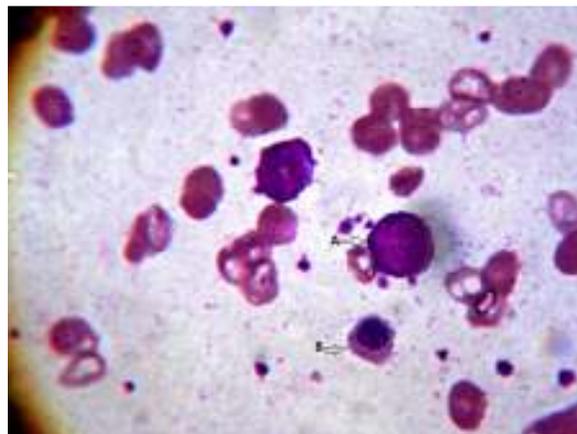


Figure 1: Peripheral blood smear. Leishman stain (x 1000) showing erythroblast (A) and nucleated red blood cell (B)

Reticulocyte count was 3% and the RBC count was 89,000/ cu mm. The mean corpuscular volume (MCV) was 107.6fl, the mean corpuscular haemoglobin (MCH) 37pg, the mean corpuscular hemoglobin concentration (MCHC) 31.4g/dl and the red cell distribution width (RDW) 17.4%. The platelet count was 545,000/cu mm. The prothrombin time (PT) was 15 seconds (control 17 seconds), and augmented partial thromboplastin time (aPTT) 40 seconds (control 40 seconds). No haemoparasites were seen. Serum creatinine, liver function tests and serum proteins were all normal and so were the serum B₁₂ and folate levels. Blood and urine cultures were sterile. Hepatitis B surface antigen (HBsAg) and antibodies to hepatitis C virus (anti HCV) were negative. Chest X ray was normal.

Bone marrow aspirated from the posterior superior iliac spine showed erythroid hyperplasia, suppression of myeloid series and reversal of M: E ratio (3:1). Early immature cells with megaloblastic features were increased with 68% proerythroblasts. Megakaryocytes showed dysplastic features like hypolobation with presence of pawn ball megakaryocytes (Figure 2).

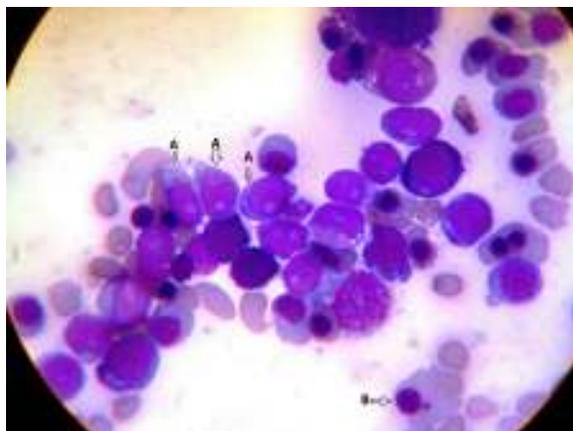


Figure 2: Bone marrow. Giemsa stain (x1000) showing proerythroblasts (A) and pawn ball megakaryocyte (B)

Periodic acid Schiff (PAS) staining was positive (Figure 3).

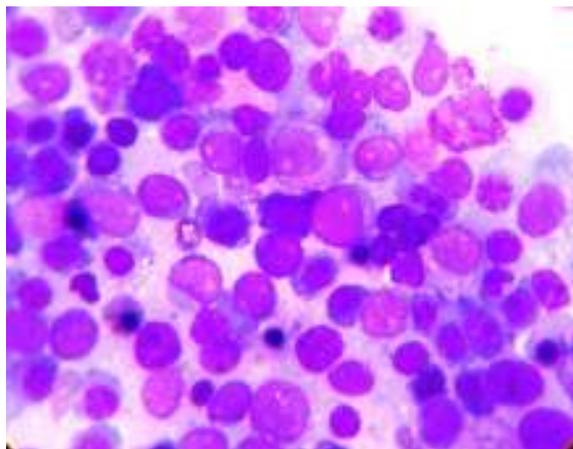


Figure 3: PAS staining of bone marrow

Flow-cytometry and genetic studies could not be done. On the basis of haematological and bone marrow features, a diagnosis of acute erythroleukaemia (AML-M6) was made. Treatment options were discussed and parents opted for supportive treatment only. Patient was discharged after packed RBC transfusions.

Discussion

Erythroleukaemia is a rare haematopoietic malignancy with predominant proliferation of pan-myelotic precursors, erythroblasts as well as myeloblasts. It was first reported by Copelli in 1912 but recognized and described as a leukaemia by Di Guglielmo¹ in 1917. Only small numbers of cases, mostly as single case reports, have been reported in the paediatric population worldwide³. Even in adults there is paucity of data, there being only a single case

in 10 years follow up from Tata Memorial Hospital, Mumbai².

Three stages consisting of a primary erythroid phase (chronic erythraemic myelosis), a transient phase involving erythroid and myeloid precursors (erythroleukaemia) and a terminal pure myeloblastic phase (AML) have been described. Further, depending on the numbers of various blast cells M6 leukaemia has been classified into M6A, M6B and M6C. But, classification of EL depending on the numbers of types of blast cells is difficult as blasts are very dysplastic⁷. Common clinical presentations reported in children consist of male preponderance and marked pallor^{3,4}. Hepatosplenomegaly and lymphadenopathy have been reported but are not common³⁻⁶. Bleeding manifestations and rheumatic complaints are found to be more common in erythroleukaemia in comparison to other acute non lymphocytic leukaemia (ANLL)⁴. Pancytopenia as well as isolated thrombocytopenia have been commonly reported^{3,4}. Batra *et al*⁴ reported thrombocytopenia in all of a series of four cases, the only multi-case paediatric series reported from India. Leucocytosis has been reported in a child⁶ as well as in adults⁷. It is important to differentiate erythroleukaemia from myelodysplastic syndrome, reactive erythroid hyperplasia sometimes following viral infections, other leukaemias and also from nutritional deficiency of vitamin B₁₂ and folic acid⁶.

Megakaryocytes in erythroleukaemia are very often dysplastic with abnormalities of segmentation of the nucleus or abnormalities of size (micro-megakaryocytes)⁸. Pawn ball megakaryocytes seen in our case are probably a feature of severe myelodysplasia

Management of AML (including M6 subtype) constitutes induction chemotherapy and post-induction/consolidation chemotherapy. Cytarabine is the most active agent and various regimens are designed around it. Induction therapy is "7 + 3" regimen: Cytarabine at 100 mg/m²/d intravenously (IV) by continuous infusion on days 1-7 plus an anthracycline (idarubicin 12 mg/m² or daunorubicin 45-60 mg/m²) or anthracenedione (mitoxantrone 12 mg/m²) (IV) push on days 1-3⁸. Consolidation therapy includes 2 options. The high-dose ara-C (HiDAC) regimen includes cytarabine at 3 g/m² IV q12h on days 1, 3, and 5 for 4 cycles. The "5+2" regimen includes cytarabine at 100 mg/m²/d IV continuously infused on days 1-5 plus daunorubicin at 45 mg/m² IV on days 1 and 2 for a total of 2 cycles. A bone marrow biopsy should be performed 14 days after induction therapy to assess remission

status. If persistent blasts are noted, a second course (with dose-reduced "5 +2" regimen) is recommended

Patients with acute erythroleukaemia have a poor prognosis often due to primary induction failure, relapse, and toxicity of chemotherapeutic agents. In a study of 91 patients with newly diagnosed erythroleukaemia, Santos et al⁹, after a multivariate analysis, concluded that erythroleukaemia is not an independent risk factor in disease-free and overall survival and standard AML prognostic factors should guide treatment. Median disease-free survival reported was 32 weeks and median period of overall survival was 36 weeks. Others have reported a median survival from 3.5 to 77 months⁸.

In our case, the duration of illness was one month which is similar to 4 of the seven paediatric cases^{3,4,6} from India while in 3 cases it was more than 6 months^{3,5}. Our case had an unusual feature of thrombocytosis in spite of depressed red as well as white blood cell lines. Thrombocytosis has been reported in acute lymphocytic leukaemia (ALL) and chronic granulocytic leukaemia (CGL), but we could not find any report of thrombocytosis in erythroleukaemia. A low leucocyte count with pro-erythroblast predominance in the bone marrow as well as peripheral blood smear suggests that case was probably still in Stage I only.

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