

Acute DiGuglielmo's Syndrome in a 2 Month Old Boy - A Very Rare Case Report

Dr Mirza Asif Baig¹, Dr Anil K. Sirasagi²

¹ Former Asst. professor BLDUs Shri B.M.Patil medical college Bijapure, Karnataka, India

² Associate professor ESI medical college Gulbarga, Karnataka, India

Abstract: Acute erythroid leukemia (AEL) was first described by coppelli in 1912 as eritromatosis in a patient with hepatosplenomegaly, foci of erythroblast in liver, spleen, lymph node and bone marrow. Giovanni Di Guglielmo's first described Erythroleukemia in the 20th century and the disorder is often still referred to as Acute Di Guglielmo's syndrome. It is classified as Acute Myeloid leukemia (AML) M6 in FAB Classification system. It includes 2 subtypes AML M6a (erythroid/ Myeloid) Leukemia and rare Subtype AML M6b (Pure Erythroid Leukemia). Erythroleukemia comprises 1% of all AML cases. It usually occurs in adult Males. A 2 month old boy presented with hepatosplenomegaly, Ascitis and fever. Preliminary investigation shows bicytopenia elevated liver enzymes and increased serum ferritin. Periperal smear Shows Leucoerythroblastic picture. Bone marrow aspirate shows 85 % of cells comprising predominantly of Erythroblasts with few proerythroblasts. Mild dyserythropoises and Pawn bowl Megakaryocytes noted. Diagnosis - ACUTE MYELOID LEUKEMIA - M6b. Immunophenotyping by flow cytometry shows about 35% of cells are blasts positive for CD 13, 33, 4, 7, 71, 38, glycophorine, CD 11. Acute erythroleukemia is a rare form of AML accounts for less than 5% of all AML. AML M6b also known as acute pure erythroid leukemia is a very rare entity especially in 2 month old. Due to its rarity the frequency and incidence cannot be determined exactly. In this case 85% Erythroblasts were noted favouring a diagnosis of pure Erythroid leukemia which is very rare in this age group. AML M6 is a rare entity and its subtype M6B in 2 months old is rarest of rare case. The very rare nature of this subtype and dismal prognosis merits its reporting

Keywords: Myelodysplastic syndrome, Acute Erythroid leukemia, Pure erythroid leukemia, AML-M6, Leucoerythroblasts.

1. Introduction

Acute erythroid leukemia (AEL) was first described by coppelli in 1912 as eritromatosis in a patient with hepatosplenomegaly, foci of erythroblast in liver, spleen, lymph node and bone marrow ¹ In 1917 Giovanni Di Guglielmo's published first scientific significant original observation on Erythroleukemia. In 1923 he published first case of pure erythroid leukemia (Eritremia Acuta) ¹ . PEL is characterised by neoplastic erythroid proliferation and maturation arrest.

1958 Dameshek described the equivalent to erythroid/ myeloid leukemia as an evolution from erythemic proliferation through erythroleukemia to myeloblastic leukemia and he named it Di Guglielmo's Syndrome ²

Giovanni Di Guglielmo's first described Erythroleukemia in the 20 th century and the disorder is often still referred to as Acute Di Guglielmo's syndrome. It is classified as Acute Myeloid leukemia (AML) M6 in FAB Classification system¹. It includes 2 subtypes AML M6a (erythroid/ Myeloid) Leukemia and rare Subtype AML M6b (Pure Erythroid Leukemia)¹. Erythroleukemia comprises 1% of all AML cases. It usually occurs in adult Males.

2. Case History

A 2 month old boy presented with hepatosplenomegaly, Ascitis and fever. Preliminary investigation shows bicytopenia elevated liver enzymes and increased serum ferritin levels. Family history shows Patient's brother and paternal brother were diagnosed with hemophagocytic syndrome. A provisional clinical diagnosis of hemophagocytic syndrome/ leukemia was made.

Laboratory investigations

WBC- 15.79 (10³/ul) RBC- 2.16(10⁶/uL) HGB- 5.6 g/dl
HCT- 17.9%. MCV-82.9(fl) MCH- 25.9pg MCHC-33 (g/dl)
PLT - 25(10³/ul) RDW-CV- 19(%)

Manual differential:

BLAST-03% Neutro-29% Band foms – 05% Meta-3%
Myelo-2% monoytes- 07% Reactive + atypical
lymphocytes- 10%

Peripheral smear shows Polychromasia, few fragmented RBCs , Basophilic stippling, Few NRBC (5-6/100WBC) , Retic Count- 5.2%

WBC - shows 3% blasts + 10% atypical lymphocytes and PLT - Reduced

The peripheral blood smear was reported as **Leukoerythroblastic Reaction**

Bone marrow aspirate from left tibia is partially diluted with blood and shows 85 % of cells comprising predominantly of Erythroblasts with few proerythroblasts and early basophilic normoblasts .The Erythroblasts are large with moderate amount of bluish cytoplasm , multiple prominent nucleoli and many shows cytoplasmic buddings. Mild dyserythropoises with few binucleated and multinucleated erythroid cells noted.

MYELOID Series is severely reduced. Few Megakaryocytes shows multiple separate nucleir lobes (pawn bowl) megakaryocytes. **Diagnosis: ACUTE MYELOID LEUKEMIA - M6**

Flow cytometry: Immunophenotyping by flow cytometry is

consistent with Acute Myeloid Leukemia (AML M6).
Markers performed – CD 2, 3,4,5, 7,8,10, 11c, 11b, 13, 14, 15, 19, 20, 22, 56, 38, 34, 71, 41, 61, tDT, MPO, glycophorine, kappa, lambda and CD 117. Immunophenotyping by flow cytometry shows about 35% of cells are blasts positive for CD 13, 33, 4, 7, 71, 38, glycophorine, CD 117.

Coagulation profiles
PT= 31.5 sec and aPTT= 48.

Serum biochemistry result

RBS – 3 mmol/l (4 to 7 mmol/l)
NA- 144.9 mmol/L (139-146) K- 3.97 mmol/L (4 - 5.5)
CL – 112 mmol/L (98 – 107)
BUN – 4.82 mmol/L (1.8 – 6.4)
Sr creatinine - 56.4umol/l (18- 35) uric acid- 341umol/L (120 – 320)
AST - 928 U/L (15- 60) bilirubin total - 29.4umol/l (0- 17)
Direct bilirubin 14.4 umol/L(0- 5)
ALP –131 U/L (50 – 350)
Ca – 1.97 mmol/L (2.2 – 2.7)
Cholestrol – 1.3 mmol/L (2.9 – 5.2) Triglycerides – 0.58 mmol/L (.3- 1.8)
Total proteins and albumin were low

3. Discussion

Acute erythroid leukemia (AEL) was first described by coppelli in 1912 as eritromatosis in a patient with hepatosplenomegaly, foci of erythroblast in liver, spleen, lymph node and bone marrow¹ In 1917 Giovanni Di Guglielmo's published first scientific significant original observation on Erythroleukemia. In 1923 he published first case of **pure erythroid leukemia (Eritremia Acuta)**¹ PEL is characterised by neoplastic erythroid proliferation and maturation arrest.

In 1958 Dameshek described the equivalent to erythroid/myeloid leukemia as an evolution from erythemic proliferation through erythroleukemia to myeloblastic leukemia and he named it **Di Guglielmo's Syndrome**²

In 1976 FAB classified AEL or AML M6 but doesnot take into account acute erythroid leukemia³ According to WHO classification AEL (2008)¹ it falls into AML NOS type. It further divided into **Acute erythroid leukemia(erythroid/myeloid) AML M6a and Pure erythroid leukemia AML M6b**. It depends upon erythroblast and myeloblast count.

Table

AEL, Classifications comparisons changes¹
Classification year subtype B.M Findings
Dyserythropoiesis Erythroid pr. Blast % of NEP

FAB 1976 AML-M6 > 30 % NA > 10 %

1985 AML- M6 >50 % > 30 % Prominent

WHO 2001 Erythroid/myeloid > 50 % > 20 % Prominent
Pure Erythroid > 80 % Prominent

WHO 2008 Erythroid/myeloid > 50 % > 20 % Prominent
{ Dysplasia
Pure Erythroid > 80 % Prominent < 50% }

Dyserythropoiesis is prominent in FAB and WHO Classification. In WHO 2008 Classification dysplasia in < 50% of less than 2 cell lines and AML MRC are excluded

Acute erythroleukemia is a rare form of AML accounts for less than 5% of all AML. AML M6b (acute pure erythroid leukemia) is a very rare entity especially in 2 month old. Due to its rarity the frequency and incidence cannot be determined exactly⁵
The Age range of survival is 1 – 7 months⁵

It is a disease of adulthood accounting for 90 % of all acute leukemia of the adult⁴ AML M6 is common in older with mean age of diagnosis of 50 years¹

In this case patient presented with hepatosplenomegaly, fever ascites with anaemia and thrombocytopenia with 3 % Blasts and few atypical cells in peripheral blood smear.

B. M Findings are:

WHO(2008) defined AML M6 as

Acute erythro leukemia (M6a) = Erythroid precursors > 50% and > 20% of NEC as myeloblasts

Pure Erythroid leukemia (M6b) = > 80 % of Erythroid precursors Dyserythropoiesis being prominent

Bone marrow aspirate from left tibia is partially diluted with blood and shows 85 % of cells comprising predominantly of Erythroblasts with few proerythroblasts and early basophilic normoblasts. The Erythroblasts are large with moderate amount of bluish cytoplasm, multiple prominent nucleoli and many shows cytoplasmic buddings. Mild dyserythropoiesis with few binucleated and multinucleated erythroid cells noted. **MYELOID** Series is severely reduced. Few Megakaryocyte shows multiple separate nuclear lobes (pawn bowl) megakaryocytes

The Differential diagnosis includes

MDS (RAEB) = < 20 % Blasts , Dyserythropoiesis

AML – MRC = > 20 % Blasts and > 50 % dysplastic cells , cytogenetic abnormalities and prior history of MDS

t-AML - history of cytotoxic drugs and radiation

AML – NOS = < 50 % Erythroid cells, Immunohistochemistry

AML with recurrent genetic abnormalities - genetic / molecular abnormalities

The patient also had elevated uric acid, creatinine levels and BUN. In AEL, hepatosplenomegaly accounts for 25 % of all cases and lymphadenopathy is very rare. Hyperuricemia is the most common biochemical abnormality associated with AML due to increased turnover of leukemic cells.

In this case the patient's serum calcium, albumin, total protein, magnesium all are low. Hypocalcemia is due to impaired release of PTH hormone.

Other biochemical abnormalities noted in this case is low cholesterol levels and serum glucose levels which is due to utilisation of these substances by tumor cells.

4. Conclusion

AML M6 is a rare entity and its subtype M6B in 2 months old is rarest of rare case. The very rare nature of this subtype and dismal prognosis merits its reporting.

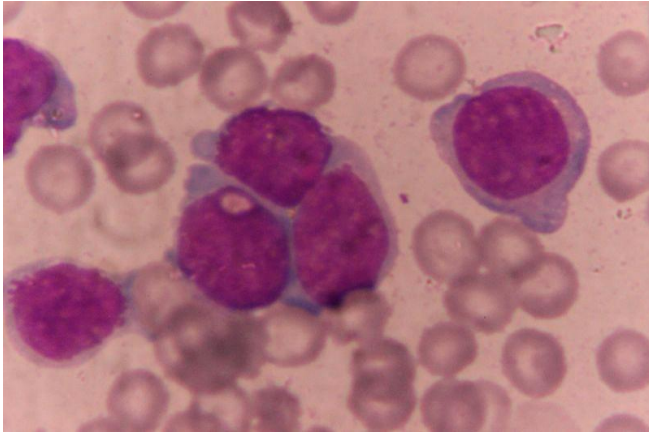


Figure 1: BM HP (100 X 10) - SHOWING TRINUCLEATED ERYTHROBLASTS WITH PROMINENT NUCLEOLI

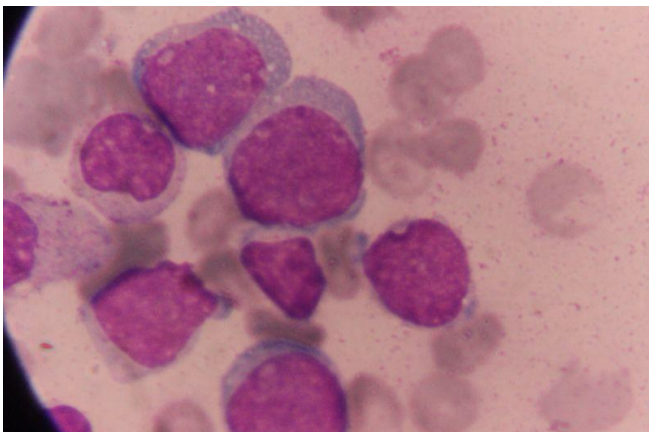


Figure 2: BM: HP(100X 10)- ERYTHROBLASTS WITH PROMINENT NUCLEOLI

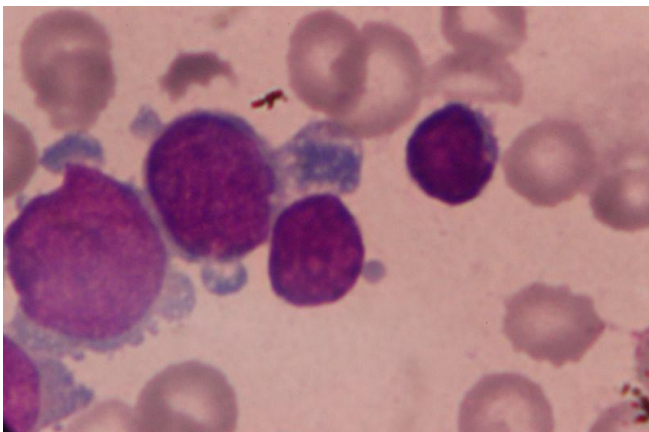


Figure 3: BM: HP(100X 10)- ERYTHROBLASTS WITH CYTOPLASMIC FRAGMENTS

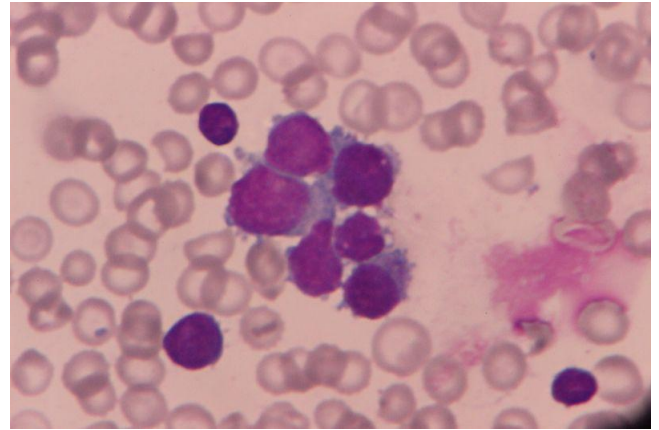


Figure 4: BM: HP (40 X 10) - MILD DYSERYTHROPOISES

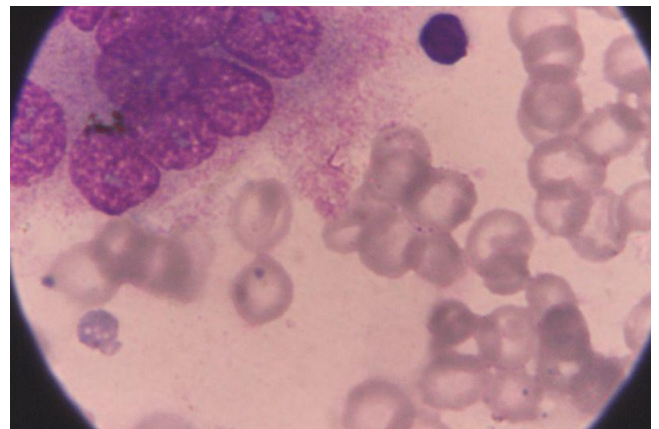


Figure 5: BM: HP(100X 10)-MEGAKARYOCYTES SHOWING MULTIPLE SEPERATE NUCLEI (PAWN BALL)

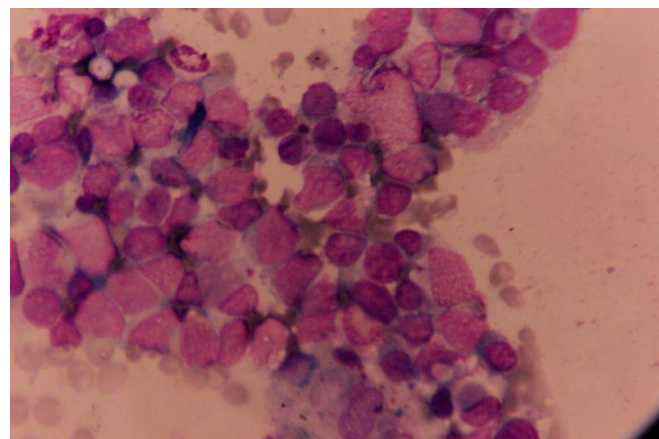


Figure 6: BM: LP (10X 10) - ERYTHROBLASTS

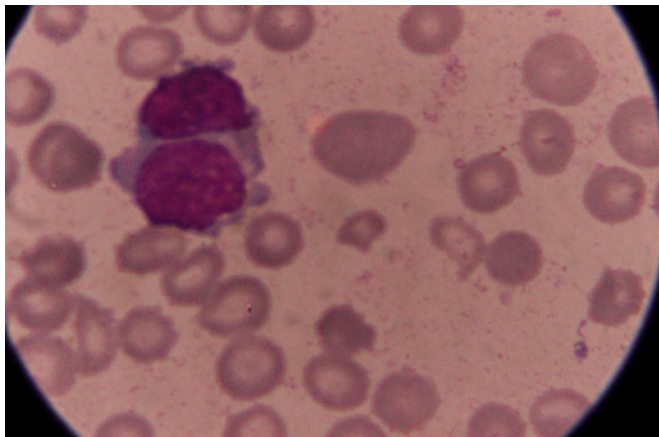


Figure 7: BM HP (100 X 10) - SHOWING BINUCLEATED ERYTHROBLASTS

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