

ACUTE ERYTHRO-LEUKEMIA (DI GUGLIELMO SYNDROME) IN A YOUNG ADULT IN BASRAH CITY**Zuhair Al-Barazanchi* & Thya Al-Saadi#.**

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Introduction

Giovanni Di Guglielmo first described erythroleukemia, a leukemia composed of purely erythrocytic precursors in 1926, and the disorder is often still referred to as acute Di Guglielmo syndrome. It is classified as an M6 subtype of acute myelogenous leukemia (AML) in the French-American-British (FAB) classification system based on morphologic and cytochemical criteria^{1a}. Acute erythroleukemia accounts for 3-5% of all de novo AMLs and 20-30% of secondary leukemias. It is very rare in children. The incidence of erythroleukemia increases in people older than 50 years² Mazzella et al (2000) described 2 peaks, one in the seventh decade of life and a second, smaller peak in the fourth decade of life. Although rare in children, M6 AML has been reported in children from the newborn period through age 7 years.³ Clinically, upon presentation, signs and symptoms of erythroleukemia are usually nonspecific and result from decreased hematopoiesis from the replacement of bone marrow by leukemic cells. This results in anemia, thrombocytopenia, and 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. The most common presenting symptoms are as follows: fatigue or malaise, minimal-to-modest weight

loss, easy bruising, fever, bone or abdominal pain, dyspnea, meningeal signs and symptoms (very rare, only if leukemic involvement of CNS is present), diffuse joint pain (nonspecific in one third of patients).⁴

Physical signs include: pallor, hemorrhages, ecchymoses or petechiae, gum bleeding, epistaxis, retinal hemorrhage, fever and infection: Common sites include the respiratory tract, urinary tract, sinuses, perirectal area, and skin. hepatosplenomegaly (<25% cases)lymphadenopathy⁵. It can be primary or secondary. De novo (primary) cases have no identifiable risk factors. The most common predisposing factors in secondary acute erythroleukemia are as follows: myelodysplastic syndrome (MDS), ionizing radiation, thorotrast, a radiographic contrast medium used in the 1940s, is associated with increased risk of erythroleukemia (latent period of 10-30 years after exposure), prior chemotherapy, such as with alkylating agents. Rare cases of familial erythroleukemia (autosomal dominant with variable penetrance) have been described, which manifest in the sixth decade of life.⁶

It had been classified, using both peripheral blood smear & bone marrow aspirate smears and touch preparations from biopsy, stained with Wright-Giemsa and other histochemical stains and according to the FAB classification as acute myeloid leukemia(AML), M6 subtype¹.

Peripheral blood smear: Findings may vary and include blasts (may not be present in as many as 50% of cases), macrocytosis, nucleated erythrocytes, schistocytes, and thrombocytopenia.

FAB criteria require ¹ a 50% or more erythroid component in all nucleated cells and ² at least one of the following: 30% or more nonerythroid blasts, excluding erythroblasts, or less than 30% blasts in all nucleated cells. Nonerythroid blast cells are blast I (ie, myeloblast with no cytoplasmic granules, distinct nucleoli) or blast II (ie, granules, centrally placed nucleus) and monoblast.¹ But nowadays, and using the WHO classification, it had been categorized with the group: acute myeloid leukemia, not otherwise categorized. The World Health Organization (WHO) proposed a new subclassification that recognizes 2 subtypes of acute erythroid leukemia:

M6a erythroleukemia is 50% or more erythroid precursors in the nucleated cells population and 20% or more nonerythroid elements (ie, myeloblasts I, myeloblasts II, monoblasts), and M6b, a pure erythroid leukemia, the erythroid component seems to be singularly involved. The erythroid component is 80% or more of bone marrow. The myeloblast count is usually less than 30%, and distinguishing the myeloblasts from primitive erythroblasts is difficult. For this reason, Auer rods are never observed in this subtype. Periodic acid-Schiff (PAS) stain findings are usually positive in erythroblasts and abnormal erythroid precursors and negative in normal erythroid precursors of all stages of maturation.⁷⁻⁹ However, a third subset, M6c had been characterized by the mixed, (myeloblast- and proerythroblast-rich mixed variant with M6C with >30% myeloblasts and >30% proerythroblasts)¹⁰.

It should be differentiated from acute Lymphoblastic Leukemia, acute, acute

myelogenous Leukemia(M2 subtype), myelodysplastic syndrome, pernicious anemia, and besides, some cases of erythropoietin therapy (which may induce increased erythroblasts in bone marrow and, in some situations, may complicate the interpretation of bone marrow morphology)¹¹

Lactate dehydrogenase (LDH) and uric acid elevated levels may be present. Rheumatoid factor, antinuclear antibody, Coombs test, and immunoglobulins should be evaluated. Autoantibodies and hypergammaglobulinemia have been reported in patients with erythroleukemia who have joint or bone pain. Vitamin B-12 and folate levels should be measured because severe pernicious anemia sometimes mimics acute erythroleukemia. Using flow cytometry, the leukemic cells often express both erythroid and myeloid markers. They are often positive for myeloid markers, such as CD117, CD13, CD33, and MOP, while the expression of HLA-DR and CD34 is often decreased or absent. The megakaryocytes antigens CD41 and CD61 can be positive in some cases.

Erythroid markers such as glycophorin A and transferrin receptor (CD71 and CD45) may be increased, but they are negative in many patients with erythroleukemia. Therefore, while the expression of glycophorin A and/or transferrin receptor may be helpful, the absence of erythroid antigens does not exclude erythroleukemia. The assessment of chromosomal abnormalities in patients with erythroleukemia is critical in the diagnosis and prognosis of disease. Multiple chromosomal abnormalities have been described, but none of them is specific for M6 AML.

Results from many studies demonstrate that certain chromosomal abnormalities are associated with different prognoses in all AMLs, including acute

erythroleukemia, as follows: Prognosis is favorable with t(8;21), inv16/t(16;16), and +14. Prognosis is unfavorable with -5/5q, -7/7q-, inv3, 11q, 17p, del20q, +13, t(9;22), or more than 2 cytogenetic abnormalities.

Prognosis is intermediate with normal karyotype and all other cytogenetic abnormalities¹²⁻¹⁴. It's a rare and heterogeneous disease with a poor prognosis¹⁰.

CASE DESCRIPTION

A young adult male, 29 yrs old, from Basra City presented with fever of 2 months duration with night sweating, progressive pallor, generalized weakness & exertional dyspnea. The condition did progress rapidly during the last 10 days with bone pains, blurring of vision, multiple ecchymotic patches all over the body, pyrexia, bleeding hypertrophied gums (figure 1) & bleeding from the nose.

Fig.1



On examination, the patient was extremely pale, with multiple bruises & ecchymotic spots all over the body. He was feverish, yet he was conscious. He had bilateral leg edema, gum hyperplasia. He had generalized lymphadenopathy & hepatosplenomegaly (Fig.2).

His chest X-ray showed a pleural effusion.

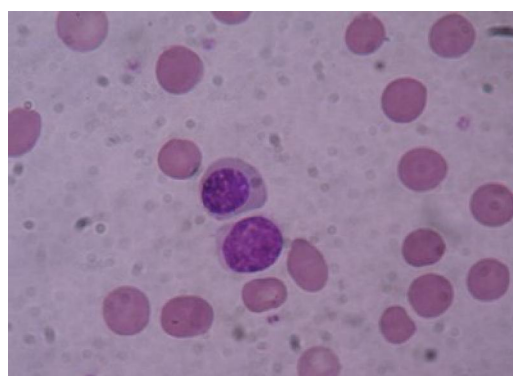
His complete blood count showed a hemoglobin concentration of 42 g/L, HCT 0.12, total WBCs $14.3 \times 10^9/L$, platelets $3.0 \times 10^9/L$, ESR 125 mm/1st

hr. Peripheral blood film shows a leuco-erythroblastic blood picture with

Fig.2



Fig.3



abnormal nasty malignant mononuclear cells of both erythroid & myeloid origin seen (Figure-3).

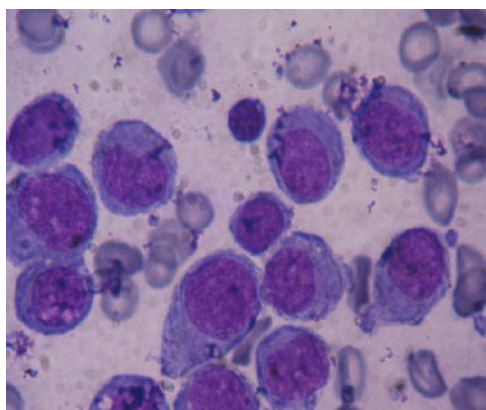
He was blood group O Rh(D) positive, Direct & indirect Coombs, tests were both negative, C-reactive protein was positive in dilution of 192 IU/L. His pleural fluid LDH was 324 IU/L, sugar 11.4 mmol/L, proteins 101 g/L, Gram stain was negative, Zeihl Nelsen stain for Acid fast bacilli was negative too.

Bone marrow aspirate & trephine biopsy were done to the patient using Salah BM aspiration needle & Jamshidi trephine biopsy needle, from right posterior iliac crest. Marrow aspirate was extremely hypercellular with almost total suppression of all normal cellular marrow elements with replacement by a mixed malignant population of cells, both of erythroid & myeloid components constituting >90%

of TMNCs. Erythroid blasts showed an abnormal morphology with binuclearity, abnormal mitosis & gigantism in many, constituting, collectively > 50 % of TMNCs. The diagnosis was proven to be of acute erythroleukemia Di Guglielmo syndrome (Fig.4,5&6).

Bone marrow trephine biopsy showed an extremely hypercellular marrow with almost total suppression of normal

Fig.4



cellular elements by malignant erythroid & myeloid precursors with open chromatin, vesicular nuclei & frequent mitoses (Fig.6).

Fig.5

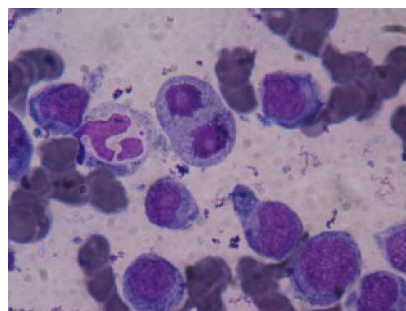
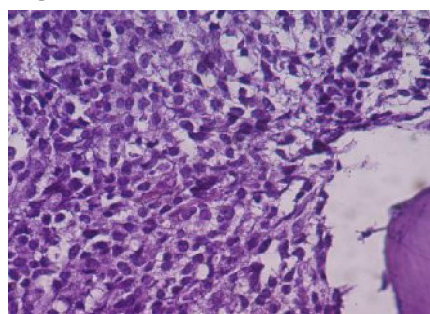


Fig.6



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