

A Young Male with Progressive Pallor

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Abstract:

Dyserythropoiesis occurs in a variety of congenital and acquired haematological disorders. The term congenital dyserythropoietic anaemia was first used by Crookston et al. CDA comprises a group of rare hereditary disorders of erythropoiesis which are characterized by distinct morphological abnormalities of erythroblasts in the bone marrow. CDA is classified into three classical types (type I, II and III). Most cases of CDA are diagnosed early in life. Our patient was diagnosed at the age of 22 years with clinical presentation of anaemia, hepatomegaly and bone marrow morphology compatible with CDA type III. We report this case for rarity.

Keyword: *Dyserythropoiesis, Congenital Dyserythropoietic Anaemia (CDA), Bone marrow*

Introduction:

Dyserythropoiesis occurs in a variety of congenital and acquired haematological disorders. The term congenital dyserythropoietic anaemia (CDAs) was first used by Crookston et al¹. These disorders are defined by their bizarre red cell precursor morphology and associated serological finding. CDAs comprise a group of rare hereditary disorders of erythropoiesis which are characterized by ineffective erythropoiesis as the predominant cause of anemia and by distinct morphological abnormalities of erythroblasts in the bone marrow. Three major subgroups, designated type I, type II and type III and several minor subgroups have been identified, based on morphological and serological characteristics. CDA type II is frequently encountered among all CDAs². More than 210 cases of CDAs are found.¹⁻³

Case Summary:

A 22 years old nonsmoker, and unmarried farmer presented with progressive pallor and generalized weakness for 1 year which was associated with headache, vertigo, and palpitation. It was not associated with anorexia, loss of appetite, weight loss, any bleeding manifestations and fever. During the course of illness, he developed mild intermittent jaundice which was not associated with any prodromal symptoms, vomiting, itching, pale stool and abdominal pain & fever. He had no significant past illness. None of his family members has similar type of illness.

Examination revealed that patient was severely anaemic, non icteric and non oedematous. His pulse was 98 beats/min, temp-normal, JVP-was not raised. No lymphadenopathy was present. He had hepatosplenomegaly which was nontender.

Investigation revealed, Hb-2.6g/dl, Hct-11%, WBC- $2.64 \times 10^9/L$ (N-64%, L-29%, M-5%) & platelet- $118 \times 10^9/L$. PBF revealed severe hypochromia, with anisopoikilocytosis and microcytes and schistocytes and nucleated RBCs were seen. Bone

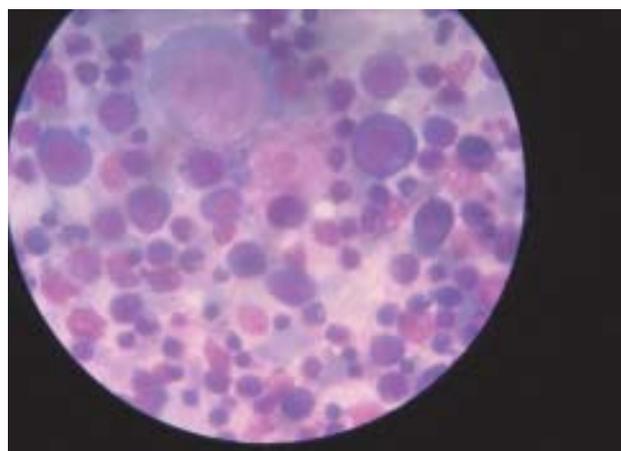


Fig-1: *Bone marrow showed hyper cellular marrow with M/E ratio decreased & erythropoiesis was grossly hyperactive with marked dyserythropoiesis with megaloid changes, intercellular connection of erythroblasts with significant number of giant erythroblasts.*

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marrow showed hyper cellular marrow with M/E ratio decreased & erythropoiesis was grossly hyperactive with marked dyserythropoiesis with megaloid changes, intercellular connection of erythroblasts with significant number of giant erythroblasts. Granulopoiesis was active & megakaryocytes were increased. Reticulocytes-01%, bilirubin (direct- .21mg/dl, indirect- .49 mg/dl), serum ferritin- 8 ng/ml, Hams test-negative, Hb electrophoresis-normal, MP-not found, ICT for kala-azar-negative, Endoscopy of upper GIT-normal study.

Discussion:

CDAs are classified into 3 varieties based on distinct differences in morphology of the bone marrow erythroblasts.⁴ CDA type I is a well defined entity within the heterogenous group of the CDAs.⁵ Patients of type I usually present with Jaundice, mild to moderate anaemia and moderate splenomegaly. Ineffective erythropoiesis is the predominant mechanism of anaemia and diagnosis is based on characteristic dysplasias of the majority of polychromatic & oxyphilic erythroblasts, with internuclear chromatin bridges being a morphological hallmark of the disorder.^{6,7} Patients of type II usually present with mild to severe anaemia, jaundice & splenomegaly. Bone marrow examination shows normocytosis, bi and multinuclearity, pleuripolar mitoses with karyorrhexis. Hams test is positive, sucrose lysis test is negative and reticulocytes are low (4%) in type II CDA. CDA type III usually present with moderate to severe anaemia and hepatosplenomegaly. Bone marrow shows macrocytoses, multinuclearity up to 12 nuclei and giantoblasts. In 1977 David and Van Dorpe described that many cases with variable clinical features among these 3 types had subsequently occurred.⁸

As clinical & laboratory findings were not distinctive, it was believed that CDAs were often underdiagnosed.⁹

From above case summery, this patient is consistent with CDA type III due to following reasons. First, mean age of type I & II is 15 years but type III is 22 years with male : female = 1.9 : 1, which is consistent with our patient . Severe anaemia & hepatosplenomegaly was present in our patient which is consistent with type III. Typical features of PBF (macrocytosis), normal unconjugated bilirubin, low reticulocytes consistent with type III. Subsequent typical bone marrow findings and negative Hams test strengthen our diagnosis. The gene responsible for CDA type III, which has been mapped to chromosome 15_q 21-25, is expressed not only in erythroblasts but also in B-cells and in cells of the retina¹⁰, but there was no associated B-cell lymphoma or retinal disorder in our patient. Serum ferritin was not raised in our patient.

We know that CDA type III is autosomal dominant disease. None of his parents has been suffering from this type of illness. So patient had developed CDA type III due to spontaneous mutation of the gene responsible (15q 21-25). We treated our patient with blood transfusion & vitamins and the patient was improved.

Other typical causes of hepatosplenomegaly were excluded both by clinically and biochemically. As for example, there was absence of fever and generalized lymphadenopathy. Test for MP and ICT for kala-azar was also negative. Hb electrophoresis and endoscopy of upper GIT revealed no abnormality and HBsAg was negative.

Evaluation of anaemia in any patient requires meticulous history taking, clinical examination and diagnosis is reached after adequate investigations. Our patient was provided with supportive treatment and adequate counseling.

Conflict of Interest: None

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