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CASE REPORT

A Rare Suspected Case Of Congenital Dyserythropoietic Anaemia Type II

SHAH V N, MEHTA M N, SANTWANI P M

ABSTRACT

A young 18 year old Hindu boy presented with anaemia, joint pain and features of growth retardation. There was hepato-splenomegaly and features suggestive of haemochromatosis. As it was a classical bone-marrow picture with markedly elevated S.ferritin level and evidence of increase iron overload, we suspected it as a case of Congenital Dyserythropoietic anaemia type II.

Key Words : : Congenital Dyserythropoietic anaemia type II, Haemochromatosis

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Introduction

The term Congenital Dyserythropoietic anaemias (CDAs), was first used by Crookston et al[1]. CDAs comprise a group of rare hereditary disorders of erythropoiesis that is characterized by ineffective erythropoiesis as the predominant cause of anaemia, and by distinct morphological abnormalities of erythroblasts in the bone marrow. Three major subgroups, designated types I, II, and III, and several minor subgroups have been identified, based on morphological and serological characteristics. CDA type II is frequently encountered among all CDAs [2]. We report a similar rare case of congenital Dyserythropoietic anaemia type I in an 18 year old boy.

Case report:

A male Hindu patient aged 18 years old, visited our hospital with complaints of easy fatiguability and joint pain involving bilateral knee, ankle and wrist since 23 days.

On examination, there was stunted growth (121cm); secondary sexual characteristics like axillary and pubic hair were not developed. Skin texture was gray/black, and there was mild pallor. Systemic examination was unremarkable, except for non-tender hepato-splenomegaly. There was no joint swelling, tenderness, or redness, but mobility was partially restricted due to the pain.

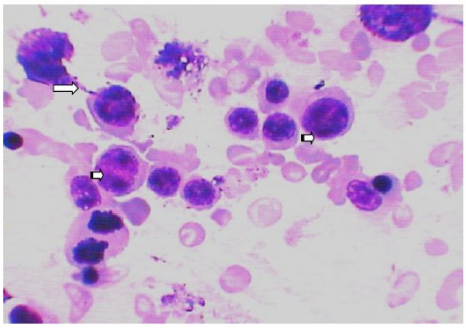
The patient was diagnosed previously as a case of HbE/B thalassaemia based on electrophoresis in the year 2000, and was receiving blood transfusion of one or two units, once in every four to six months.

He had a past history of pain in the knee and ankle joints, anaemia and splenomegaly. He was complaining of on and off joint pains, with no other complaints in between.

Investigations during admission in our hospital were as follows; Haemoglobin (Hb) was 6.8gm%, total count was 6600/cumm, with a differential count of P64/L30/E02/M04/B00, the platelet count was 1.8 lakhs, the RBC count was 3.2 millions/cumm, the Retic count was 0.8%, PCV was 22.6%, MCV was 64.2fl, MCH was 17.8pg, MCHC was 30.1gm%, RDW was 43.1% and ESR was 04 mm in the 1st hour. Peripheral smear examination was suggestive of hypochromic microcytic anaemia, with few macrocytes and spherocytes with moderate anisopoikilocytosis, and with unaffected WBC and platelet series. Smear examination of the parents were normal.

Bone-marrow examination revealed erythroid hyperplasia and megaloblastoid features with binucleated and multinucleated late normoblasts in the erythroid series. There was presence of an internuclear bridge connecting two erythroblasts, the classical features of CDA type II (Table/Fig1). Prussian blue stain was positive for iron, suggestive of iron overload (Table/Fig-2). Renal function and Liver function tests were within the

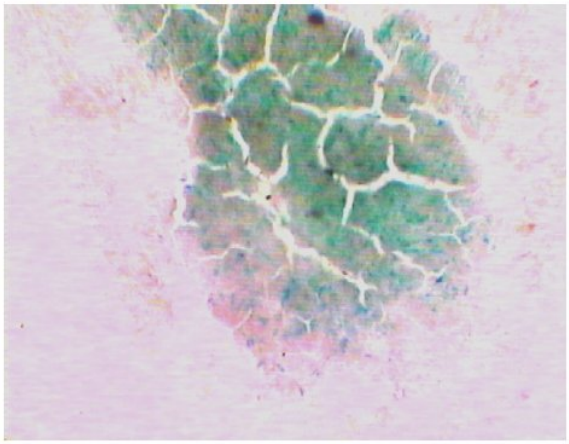
Table/Fig 1



Bone-marrow examination reveals erythroid hyperplasia and *megaloblastoid feature* with *binucleated* (smallarrows head) and multinucleated late normoblasts in erythroid series. The classical features of CDA type II is presence of *internuclear bridge* connecting two erythroblasts (large arrow head)

normal range. Serum.HIV, HBsAg, and HCV were non-reactive. ECG was normal, CXR was suggestive of mild cardiomegaly, ECHO was normal with an EF of 60% and normal LV size and function. Ultrasonogrphy was suggestive of hepatomegaly of 15 cm and splenomegaly of 24 cm in the long axis, with altered echo texture in liver and spleen. There were changes of portal hypertension, probably secondary to huge spleen. There was no ascites, and the barium bolus was negative for the oesophageal varices. Both testes were underdeveloped. CT scan of abdomen was suggestive of hepatomegaly and splenomegaly with increased density, and this raises the possibility of iron overload (Table/Fig-3). CT scan of brain revealed increased density in the pituitary gland. Fundus examination was unremarkable.

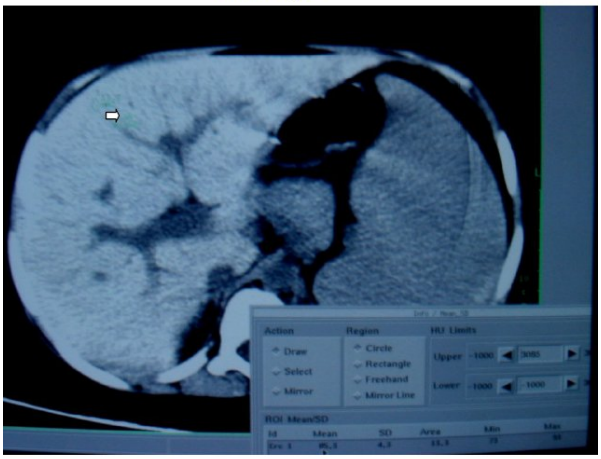
Table/Fig 2



Bone marrow exanimation stained with Prussian blue suggestive of iron overload.

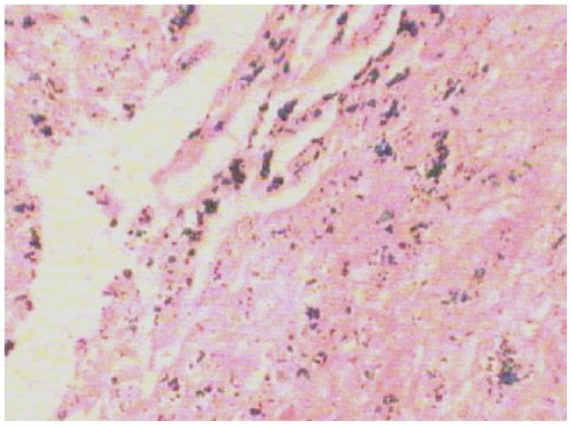
Liver biopsy revealed increased iron deposition in the parenchymal cells, sparing the kupffer cells, suggestive of primary haemochromatosis, and therefore, the possibility of iron overload due to blood transfusion was the least possibility (Table /Fig 4). S.ferritin levels in year 2000 was 246 ng/ml, and during our admission (year 2006), it was 933.6 ng/ml, suggestive of increase in S.ferritin levels gradually, as age advances. S.ceruloplasmin was within normal range.

Table/Fig 3



CT scan abdomen was suggestive of hepatomegaly and spleenomegaly with increased density suggestive of iron overload (arrow).

Table/Fig 4



Liver biopsy reveals increase iron deposition in parenchymal cells sparing kupffer cells suggestive of primary haemochromatosis.

Discussion

The congenital dyserythropoietic anaemias (CDA) comprise a group of rare hereditary disorders of erythropoiesis. The term was first coined by Crookston et al[1], and later by Wendt and Heimpel[3]. Congenital dyserythropoietic anaemias are classified into three varieties, based on distinct differences in the morphology of the bone marrow erythroblasts[4]. As clinical and laboratory findings are not distinctive, it is believed that CDA are often under diagnosed.[5] CDA type II is more common than other varieties.

A large study carried out by Hermann Heimpel et al.[6] revealed clinical features and investigation in 48 patients with CDA type II as follows; Anaemia and/or jaundice was usually recognized in childhood or in young adults. Age at

first diagnosis of CDA II ranged from 0.1 to 78 years (median, 18.2 years). Previous incorrect diagnoses included haemolytic anaemia, thalassemia, hereditary spherocytosis, iron deficiency, and hepatitis. Some patients had been treated with iron, a variety of vitamins, or prednisone. This also happened with our case which was diagnosed as haemoglobinopathy, and was never investigated further. Splenomegaly was documented on follow-up, in almost all patients.
A study by Heimpel et al observed that haemoglobin concentrations were below the age-specific reference intervals in children and adolescents. Relative reticulocyte counts were normal or moderately increased. There were always distinct anisocytosis and poikilocytosis without specific types of poikilocytes, with basophilic stippling of cells and few, occasionally binucleated, mature erythroblasts. This picture of peripheral examination is almost same in our case, as observed by Heimpel et al. Reticulocyte production index was 0.85, which favours ineffective erythropoiesis rather than a haemolytic cause for anaemia.

The only finding that contradicts with the Hermann's observation is the level of serum bilirubin. He found that bilirubin at the time of diagnosis was moderately increased in 90% of all cases.

The bone marrow picture described by us (Table/Fig 1) is the same as observed by Hermann Heimpel et al. These characteristic finding were also noted by others.[7]

The main problem encountered by patients after the first year of life is iron loading, which is also seen in patients without the ongoing need for transfusion. The fact that patients with both CDA I and CDA II load iron in a manner similar to those with other chronic states of ineffective erythropoiesis, has been known since the early observation[8] .

Therapy for chelation should be started when the S.ferritin level reaches 1000 µg/mL. Interferon alfa is also one of the treatment modality in CDA. We explained all consequences to the parents of the patient. However, due to financial constraints we were unable to start any treatment.

Conclusion

Typical skin texture, hypogonadism and increasing S.ferritin levels as the patient grows, with classical changes in bone-marrow and increased iron deposition in various organs like liver, spleen, pituitary and bone-marrow, makes us to believe that it was a case of congenital Dyserythropoietic anaemia type-II. There are case reports to suggest that haemoglobinopathies and CDA can coexist together.

Limitations

1) Electron microscopy (EM) is the diagnostic for CDA type II, but unavailability of electron microscopy in our institute was the limiting factor for us. 2) We didn't test patients for HPCL and acidified ham test. 3) We lost the follow up of the patient (a common problem in India!), and hence were unable to re-review the case.

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