Research Paper Medical Science

Case Report: A Rare Presentation of Haemoglobin D Disease

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ABSTRACT

Haemoglobin D (Hb D) is the fourth most common haemoglobin variant. With the exact chemical analysis of hemoglobin variants, it became apparent that hemoglobin $D_{Los\ Angeles}$ was identical to hemoglobin D_{Punjab}, both manifesting a substitution of glutamate for lysine at the 121st position in the β -chain. Another "D" hemoglobin, $G_{Philadelphia}$, is, on the other hand, an β-chain variant with a substitution of asparagine for lysine at the 68th position. Like the other structural mutations of hemoglobin, hemoglobin D trait is the heterozygous state for hemoglobin D and hemoglobin A, whereas the homozygous state for hemoglobin D is designated hemoglobin D disease. Hb D disease is usually clinically silent with no special treatment required. Homozygous Hb DD is rare and a relatively mild disease. Though Hemoglobin D is not very uncommon in India, its homozygous form is very rare and very few case reports have been reported. I hereby present a case of symptomatic Hb D homozygous, who presented with hemolytic anemia and hepatospleenomegaly from Turvekere, Karnataka which is a rare phenomenon.

KEYWORDS Haemoglobin D disease, Homozygous HbD, Haemoglobin D trait.

Introduction:

In 1951, Itano[1] encountered a new haemoglobin variant, which co-migrated with haemoglobin S (Hb S) at alkaline pH, but failed to sickle. It was labeled as haemoglobin D (Hb D). The substitution in Hb D is a glutamic acid to glutamine at the 121st amino acid of the beta -globin chain (121Glu-Gln). Hb D has an S-like mobility on alkaline electrophoresis but co-migrates with HbA on acid pH. Osmotic fragility may be decreased. Blood films may show target cells. It was found that the Hb D gene can be detected by DNA amplification and globin chain analysis[2-4]. 2 - 3 % of the population of Punjab carries the Hb D gene. Several cases of Hb D have been reported and were labeled as Hb D Punjab or Hb D Los Angeles.[5-9] Hemoglobin D Punjab was first discovered in the early fifties in a mixed British and American family of Indian origin from the Los Angeles area; hence it is also sometimes called as "D Los Angeles". Hemoglobin D is the 4th common haemoglobin variance. Biochemically, Hb D occurs in four forms: heterozygous Hb D trait, Hb D-thalassemia, Hb S-D disease, and the rare homozygous Hb D disease, which is associated with a clinical disorder similar to, but less severe than, sickle cell anemia.[10] Hb D heterozygotes (Hb D trait) are usually asymptomatic, not anaemic, and have normal red cell Indices. Hb D homozygotes (Hb D disease) manifests as mild hemolytic anemia and spleenomegaly.

Case Report:

1 year old male child, 2nd in order born of a 3rd degree consanguineous marriage, presented with history of 6 days fever, not responding to medication, with anemia identified clinically and referred for blood transfusion. With no history of focus of fever. No past history of repeated infections, bleeding tendencies and repeated transfusion. Birth history was uneventful, faulty feeding habits and global development delay. No history of similar complaints in sibling or in family. Hemolytic facies with knuckle pigmentation is present with severe pallor and icterus. Anthropometry revealed height and weight <3rd percentile and head circumference 5th-10th percentile. Per abdomen examination revealed Splenohepatomegaly. CNS examination being normal.

Investigations showed Hb: 4.4gm%, Total count 7600 cells/cumm, ESR 91mm/1st hr, platelet count of 91,000cells/cumm, Haematocrit of 12 and Reticulocyte count 8.4%.

Peripheral blood smear: RBCs- show moderate anisopoikilocytosis, macrocytic normochromic with macroovalocytes, microcytes, polychromatic cells. Few target cells, nucleated RBCs. Occasional binucleated RBCs seen. Occasional howell jolly bodies and basophilic stippling, spherocytes, tear drop cells seen. WBCs- normal in number, occasional reactive lymphocytes. Occasional metamyelocytes, myelocytes are seen. Occasional large cell with fine chromatin and inconcpicous nucleoli seen. Few hyper segmented neutrophils and macropolycytes seen. Platelets - reduced in number

Impression: Leucoerythroblastic blood picture with features of haemolysis (dimorphic predominantly macrocytic type blood picture).

MCV-95.3fl, MCH-34.4pg, MCHC- 36.1g/dl. In view of clinical history and lab investigations, provisonal diagnoisis of haemolytic anemia was made and Hb electrophoresis was done which revealed HbF : 5.2%, HbA2 : 3%, HbD : 36.7%. In view of Hb electrophoresis report, diagnosis of HbD (Homozygous)disease was made.

Discussion :

Hemoglobin D is the fourth most common hemoglobin variant, which developed as a response to the selective pressure of malaria. It is most often found in people living in India, Pakistan, England, Ireland, Holland, Australia, China, Iran, Turkey and their descendants.

With the exact chemical analysis of hemoglobin variants, it became apparent that hemoglobin $D_{Los\ Angeles}$ was identical to hemoglobin D_{Punjab}, both manifesting a substitution of glutamate for lysine at the 121st position in the β -chain. Another "D" hemoglobin, $G_{Philadelphia}$, is, on the other hand, an β-chain variant with a substitution of asparagine for lysine at the 68th position.

Like the other structural mutations of hemoglobin, hemoglobin D trait is the heterozygous state for hemoglobin D and hemoglobin A, whereas the homozygous state for hemoglobin D is designated hemoglobin D disease.

The heterozygous state for hemoglobin D is entirely asymptomatic. The abnormal hemoglobin constitutes between 35 and 50 percent of the total haemoglobin. Homozygous hemoglobin D disease is very rare, and some patients originally believed to be homozygous for hemoglobin D subsequently were

found to be heterozygous for hemoglobin D and β-thalassemia. A small number of true homozygotes have been described, however, and the clinical consequences are very mild. Hemoglobin $S/D_{Punjab/Los\ Angeles}$ disease is a relatively severe sickle cell disease.

Homozygous Hb DD is rare and a relatively mild disease. Heterozygous Hb D/β-thal is more common and more serious. Most people with hemoglobin D disease have mild anemia, which may be associated with a slightly enlarged spleen. Hemoglobin DD red blood cells look like a bull's eye target with a dark center . Though Hemoglobin D is not very uncommon in India, its homozygous form is very rare [10,11] and very few case reports have been reported[12]. Heterozygous state of Hb D does not produce any clinical or hematological symptoms, but its association with Hb S produces clinically significant, but less severe condition mimicking sickle cell anemia[13]. Even the different Hb D variants seem to produce different severity of disease with Hb S. Hb D-Punjab produces clinically significant condition like sickle cell disease, whereas Hb D Iran and Hb D Ibadan are non-interacting and produce benign conditions like sickle cell trait[14]. A Saudi family reported in the HbD trait with alpha thalassemia that showed mild phenotypic behaviour[15]. Hemoglobin D disease is usually clinically silent with no special treatment required. A mild hemolytic anemia usually develops in the first few months of life as the amount of fetal hemoglobin decreases. The presented case of HbD disease showed mild phenotypic nature. It assumed the homozygous conditions of HbD disease does not produce serious complications to the patients.

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