Haemoglobin-D A Rare Case Report

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Abstract: Hemoglobin D a hemoglobin variant occurs in a group of asian population particularly from India, Pakistan, Iran, Iraq. In India, it is mainly reported in northwestern states of Haryana, Punjab and Gujarat. In heterozygous form, Hb D disease is mild and causes subclinical jaundice. In heterozygous form, it can cause severe hemolytic anemia. Here we present a similar case of Hb D with hemolytic jaundice after a physiological stress of twin delivery.

Key words: Hb D · Stress · Hemolytic Anemia · Jaundice

INTRODUCTION

Human haemoglobin is formed from two pairs of globin chains each with a haem group attached. Seven different globin chains are synthesised in normal subjects. Four are transient embryonic haemoglobins, Hb F in fetal life. Hb A and A2 and Hbf attained by 6-12 months of age[1].

Each hemoglobin chain has a molecular weight of 16000. Four of them in turn bind together loosely to form the whole hemoglobin molecule. There are several slight variations in different subunit hemoglobin chains, depending on the amino acid composition of polypeptidal portion. The nature of hemoglobin chains determine the binding affinity of the hemoglobin for oxygen. Abnormalities of the chains can alter the physical characteristics of hemoglobin molecule [2].

There are many naturally occurring genetically determined variants of haemoglobin (>1000) and although many are harmless, some have serious clinical effects. Collectively, the clinical syndromes resulting from disorders of haemoglobin synthesis are referred to as haemoglobinopathies [1].

Hemoglobin D (Hb D) is not very uncommon in India, its homozygous form is very rare. Hemoglobin D, a hemoglobin variant, occurs mainly in north-west India, Pakistan and Iran. Hemoglobin D-Punjab occurs with greatest prevalence (2%) in Sikhs in Punjab, India, whereas Gujarat, the province in the west from where the case was reported, has a prevalence rate of 1%. It is also found sporadically in Blacks and Europeans, the latter usually coming from countries that have had close associations with India in the past [3]. Hemoglobin D is the fourth most common hemoglobin variant, which developed as a response to the selective pressure of malaria. 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 [4].

Case Report: A 24 years old primi with twin gestation was admitted to hospital for safe confinement. Patient developed immediate post partum hemorrhage after the delivery and was treated for the same. Patient developed jaundice in the immediate post partum period and was referred for diagnostic workup. On clinical examination the patient was icteric, no organomegaly.

Peripheral smear showed severe erythropaenia accompanied by a severe anaemia, RBC morphology displayed macrocytic RBC’s with giant macrocytic forms, marked polychromasia, numerous nucleated red cells, few appearing dyserythropoietic. Few helmet cells and occasional RBC fragments noted. WBC shows
leucocytosis with marked myeloid left shift and reactive lymphocytes. Osmotic fragility test was negative. Coombs test both direct and indirect was negative. Sickling was negative. Urine & Blood culture sensitivity was negative. G6PD levels were normal and serum LDH level was 5308 IU.

**Peripheral Smear:**

Electrophoresis done to rule out hemoglobinopathies which showed Hb D Punjab / Los Angeles heterozygous pattern.

**Hemoglobin Electrophoresis:**
In our case, hersolubility test for sickling was negative. Electrophoreticalllyhemoglobins showed mobility at the position of Hb D. The red cell Hb A2 and Hb F levels were not in the thalassemic range. RBC G6PD levels were normal.

**DISCUSSION**

The geographical distribution of the heriditary disorders of hemoglobin are world wide. The thalasaemias are wide spread with maximum pervelance around the Mediterranean and in south East Asia. The common abnormal hemoglobin’s Hb-s and Hb-c are prevalent in tropical Africa and among black population in new world. Hb-E is common in south East Asia and Hb-D Punjab in Indian subcontinent Heriditary disorders of hemoglobin are less common among people of northern European origin but no ethnic group is totally spread [3].

Hb-D Punjab arises from the substitution of glutamine for glutamic acid in the 121st position of Beta chain. The electrophoretic mobility of Hb-D on cellulose acetate is identical to that of Hb-S. on agar gel electrophoresis, Hb-D migrates with Hb-A, Hb-D does not sickle. The Hb-D disorders were first documented by vella and lehman [5].

The carriers of Hb D and homozygous cases for Hb D are not anemic and had normal red blood cell morphology, as they are not usually detected. If Hb D was inherited in combination with thalassemia, the subjects had mild anemia and in some of them, the spleen was palpable (1-2 cm). Co-inheritance of alpha thalassemia and Hb D resulted in the slightly higher Hb level and lower Hb D level as compared to Hb D/ beta thalassemia cases (Hb D 24-37% vs 57-88%). Co inheritance of Hb D and sickle cell results was moderate to severe hemolytic anemia [5].

Extravascular hemolysis takes place whenever red cells are rendered less deformable. with extravascular hemolysis, hemoglobinemia and hemoglobinurea are not observed and the principal clinical features are anemia and jaundice. There is often splenomegaly.

Intravascular hemolysis of red cell is caused by mechanical injury, complement fixation, infection with malaria or exogenous toxic factors. There is hemoglobinemia, hemoglobinuria, jaundice and hemosiderinemia. The urine is red brown in colour due to presence of methemoglobin. There is jaundice with unconjugated hyperbilirubinemia [6].

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. Hb D has been reported in association with hematological malignancy such as leukemia and Hodgkin’s lymphoma [7] two cases of hematological malignancies were reported by sumithra dash et al. one case was acute myeloid leukemia (M3 FAB) in a 27 yr old male, heterozygous for Hb D Punjab another case was Hodgkin’s disease, lymphocytic predominance in stage 4b in a 14 yr old boy who was found homozygous for Hb D Punjab. these 2 cases were from 95 analysed for hematological malignancies with abnormal hemoglobins [8]. In a case of 13-year-old Indian girl from the state of Gujarat, presented with the complaint of a gradually increasing painless lump in the left upper quadrant of abdomen. Hb electrophoresis on cellulose acetate at pH 8.4 showing hemoglobin mobility of samples from patient, father, mother and a control from a known case of sickle cell trait. Following the patient's tests, her parents were investigated. Both of them showed the heterozygote state for HbD [9]. A four year old girl presented with microcytic, hypochromic anemia. The girl, her mother and sisters were of the HbD Punjab trait and they, with the exception of one, demonstrated measurable Hb A2. On the other hand, Hb A was seen in the father's specimen [7]. Apart from hemoglobin electrophoresis, there are other methods to identify abnormal hemoglobins.

A 10 yr old boy was admitted in jaipur who was admitted with weakness and marked pallor was found to have HbDD in electrophoresis. one sibling and mother were found to have Hb D disease [10]. A turkish man whose offspring had Hb S-D disease was found to have hemoglobin D punjab (los angels). He incidentally also had G6PD deficiency. there was no evidence of present or past hemolysis in the patient [11].

An infant with hemoglobin D Ibadan-beta zero thalassemia with hemoglobinopathy was initially detected by neonatal screening. This previously undescribed condition was confirmed by family studies and by globin chain analysis by mass spectrometric techniques [12].

**REFERENCES**


