Case Report

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Hemoglobin D-Punjab Trait of Non-Punjabi Heritage in Karnataka, South India: An Exceptionally Rare Occurrence

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Abstract

Hemoglobin-D (Hb-D) is an uncommon and abnormal structural Hb variant. The present case study is an eye opener that though Hb-D Punjab trait is one of the important differential diagnoses to be considered in the areas where Hb-D is known to be prevalent, its possibility however cannot be ignored even in the areas where its prevalence has not been identified or documented. We report one such extremely rare case of Hb-D Punjab trait in a 1-year old child of South Indian heritage hailing from Karnataka. To the best of our knowledge, this is probably the first case to be reported and documented from the Southern part of our country since extensive literature search did not reveal any documented case till date from South India.

Key words: Hemoglobin variant, Heterozygous, High performance liquid chromatography

INTRODUCTION

Hemoglobin-D (Hb-D) is an uncommon and abnormal structural Hb variant. Its prevalence has been reported in North eastern part of India and Iran. A small number of cases of this entity have been reported and documented in literature. Hb-D is due to amino acid substitution for glutamic acid at codon 121 of the β globin gene. The heterozygous form of Hb-D is clinically silent, but its co-inheritance either with HB-S or Hb-F produces clinically significant conditions with moderate severity. Hb-D Punjab which is synonymous with Hb-D Los Angeles has an incidence of 2-3% among Sikhs in Punjab, 1% in Gujaratis and 0.37% in Bengalis in India and has been found all over the world with a variable incidence rate. Extensive literature search did not yield any reported incidence of Hb-D Punjab in Southern parts of India.[1,2]

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CASE REPORT

A 1-year old south Indian male child was admitted to the pediatric ward with history of fever for 1 week. There was no significant past or family history. There was no history of consanguinity. Both the parents and the sibling brother were clinically healthy. There was no history of previous blood transfusion or medication.

General physical examination revealed depressed nasal bridge, severe pallor and icterus.

Systemic examination revealed abdominal distension, hepatomegaly (3 cm), and splenomegaly (6 cm).

Routine hematological investigations were carried out using an automated cell counter. The results showed a very low Hb value of 4.4 g/dl, reduced packed cell volume at 12.2%, reduced red blood cell (RBC) count at 1.28 million/cumm. The absolute indices were decreased with mean corpuscular volume at 64.2 fl, mean corpuscular Hb (MCH) at 20 pg and MCH concentration at 36.1%. The reticulocyte count and red cell distribution width were increased being 5% and 49.6%, respectively. The white blood cell (WBC) and platelet counts were within

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normal limits. Peripheral blood smear examination showed marked anisopoikilocytosis and dimorphic blood picture with a near equal population of microcytic hypochromic and macrocytic RBCs. A few target cells, spherocytes, and tear drop cells were seen. Occasional intermediate normoblasts (8/100 WBCs) and fragmented RBCs were seen. A few macropolycytes were also seen. Occasional red cells showed basophilic stippling and Howell–Jolly bodies. WBCs showed a mild shift to the left by the presence of band neutrophils, metamyelocytes, and myelocytes. A few hyper segmented neutrophils were also seen (Figure 1).

The impression was found to be leukoerythroblastic/dimorphic blood picture associated with features of hemolysis.

In view of the clinical and hematological pictures suggesting hemolytic anemia, high performance liquid chromatography (HPLC) was undertaken to investigate for abnormal Hb. HPLC revealed near normal fetal Hb (Hb-F) and Hb-A2. Hb-D was markedly abnormal at 36.7% (normal value - 0%) and Hb-A was markedly reduced to 55.1% (normal value - 94.3-98.5%).

Osmotic fragility test was within normal limits.

Biochemical assays revealed markedly elevated lactate dehydrogenase levels at 4500 IU/L (normal reference range 225-450 IU/L). Serum bilirubin level was within normal limits.

Hematological screening of parents and sibling did not reveal significant abnormalities. The final diagnosis was given to be Hb-D Punjab trait.

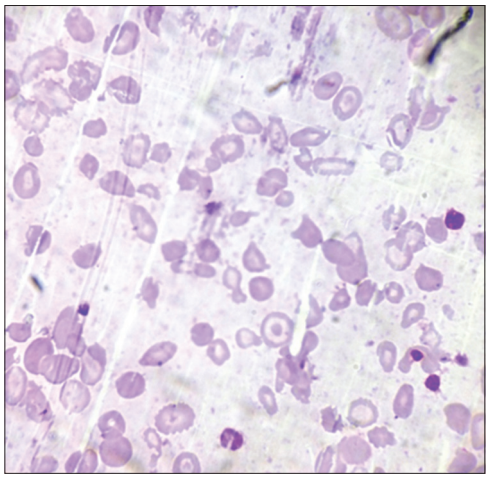

Figure 1: Hemolytic blood picture in hemoglobin D Punjab disease (Leishman stain, ×100)

DISCUSSION

Hb-D is an abnormal variant of Hb being the fourth most common variant discovered and described till date.

Hb-D has a wider distribution among the various races of the world than any other type of abnormal Hb.[1]

Areas of Hb-D prevalence have been encountered in Algerian Muslims and Indians of North central India which is the Punjab belt of Sikh origin.[2,3] In the Punjab region of India, the heterozygosity is reported at 3%.[4]

Four clinical stages of Hb-D syndromes have been reported namely heterozygous Hb-D trait, mixed heterozygous state in combination with Hb-S (Sickle cell - HB-D disease), homozygous Hb-D disease[5] and Hb-D in combination with thalassemia.[6]

There are several variants of Hb-D Punjab which is also known as Hb-D Los Angeles named after the city where it was first discovered. The abnormal Hb-D Punjab/Los Angeles has glycine substituting for glutamic acid at codon 121 of β chain.[7] It has been suggested that genetic mutation responsible for Hb-D may have arisen from several ethnic groups rather than from a single one.[1] Studies among affected families prove that Hb-D is an allele of Hb-A, S and C.

No specific abnormalities related to presence of abnormal Hb are associated with Hb trait and no well-defined hematological criteria have been formulated for diagnosis Hb trait.

The hematological picture in patients with Hb-D trait may range from entirely normal with absent hemolytic picture to mild hemolytic anemia associated with moderate splenomegaly[8] similar hematological findings have been reported in the other heterozygous forms of Hb-D.[1] The patients with mixed co-inheritance of Hb-D along with either Hb-S or Hb-F may show a certain degree of clinical variability.[8] Parab *et al.* observed in their study that homozygous state of HB-D presents with mild hemolytic anemia and mild to moderate splenomegaly. They opined that Hb-D Punjab trait is a harmless condition showing normal Hb and RBC indicies.[9] In contrast to this, though our case belonged to the heterozygous Hb-D Punjab trait as diagnosed by HPLC, its clinical and hematological features like jaundice, hepatosplenomegaly, and mild hemolytic anemia were deviant from the usual presentation.

Dolai *et al*. opined that hypochromia rather than microcytosis was a consistent finding in their study on Hb-D trait.[10] They also observed that anisocytosis was consistently absent in Hb-D trait. Chernoff reported microcytosis in their cases of Hb-syndromes.[1] In striking contrast, we observed severe anisocytosis in our case. The other exceptional feature in the present case was the hemolytic blood picture which has almost never been reported in heterozygous Hb-D trait.

The clinical and hematological profiles of Hb-D have not been specifically described anywhere, except in a few published case reports.[11] The data available in these case reports suggest that the hematological profile in Hb-D trait may be variable.

Some of the studies conducted have concluded that Hb-A is always more than 50% in Hb-D trait but Hb-D is within 40% of total Hb.[10] Similar was the observation in our case.

In a study from West Bengal, the authors have concluded that hypochromia is a consistent feature in Hb-D disease. These authors also opined that red cell indices and Hb electrophoresis were sufficient in screening for Hb-D Punjab trait in a resource-poor setting.[10]

Pandey *et al*. opined that HPLC may not be the gold standard for diagnosing Hb-D Punjab trait and that the confirmation should be by molecular analysis.[8]

CONCLUSION

The present case study is an eye opener that though Hb-D Punjab trait is one of the important differential diagnoses to be considered in the areas where Hb-D is known to be prevalent, its possibility however cannot be ignored even in the areas where its prevalence has not been identified or documented.

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