A Case of Hemoglobin Sickle-D Punjab

Wahid Ali¹ · Mili Jain¹ · Sarita Agarwal² · Ashutosh Kumar¹

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Introduction

Itano initially described hemoglobin D Punjab (Hb DP) as hemoglobin D-Los Angeles in 1951. It is a structural variant derived from point mutation in the beta globin gene in the first base of the codon 121 (GAA to CAA) resulting in substitution of glutamine for glutamic acid (Glu > Gln). The otherwise asymptomatic Hb DP is important for its interaction with HbS in double heterozygous state. The highest frequency of Hb DP been reported from Punjab ($\approx 2\%$). In a report of structural hemoglobin variants Hb DP constituted 0.55% (38/6889) of all screened samples. Of these double heterozygous Hb Sickle D Punjab (Hb SD) constituted 0.03% (3/6889) [1]. We report a case of heterozygous Hb SD from the state of Uttar Pradesh, India.

Case Report

A 29-year-old male was referred for HPLC analysis with history of recurrent episodes of jaundice since the age of 9 years. He also had history of episodic severe backache radiating to chest associated with fever. He had no history

of blood transfusion. His mother had died at the age of 43 years with complaint of severe chest pain. He was a resident of village Sarsawa, district Lakhimpur Khiri, Uttar Pradesh. On examination he had pallor. No hemolytic facies or organomegaly was seen. His complete blood count findings are shown in Table 1. The peripheral blood smear showed mild aniso-poikilocytosis with presence of target cells, occasional sickle shaped cells and mild polychromasia. Occasional nucleated red cells were also seen. Sickling test was positive. The HPLC done on Biorad D10 instrument (Dual β thalassemia program) is shown in Fig. 1a. In addition to S window (32.0%), an additional unknown peak (retention time 3.80) of 43.3% was seen. The sample was also run on sebia capillary electrophoresis system, which showed a fusion peak at the border of Hb S and Hb D zone. (Fig. 1b). In view of these results suggesting a double heterozygous Hb SD the sample was subjected to molecular analysis for confirmation. The amplification refractory mutation system PCR (ARMS-PCR) for Sickle cell mutation was positive. Hemoglobin D mutation was confirmed by sequencing.

Discussion

Compound Heterozygous Hb SD is an uncommon hemoglobinopathy with a variable clinical expression. Our patient was from a village along Nepal border and belonged to Yadav community. His parents were not related and belonged to the same area, residing there for past two generations. Any positive migration history was not known. Out of the total 2200 patients screened for HPLC this is our first case contributing 0.04%. The glutamine residue in Hb DP facilitates the polymerization of Hb S resulting in a moderately severe clinical phenotype. Our

✉ Mili Jain
milijain@kgmcindia.edu; milijain786@gmail.com

¹ Department of Pathology, King George's Medical University, Lucknow 226003, India

² Department of Medical Genetics, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Table 1 Complete blood count parameters

CBC parameter	Value
Hemoglobin (g/dl)	7.0
RBC count ($\times 10^{12}/L$)	1.91
HCT (%)	19.1
MCV (fl)	99.9
MCH (pg)	37.1
MCHC (g/dl)	37.1
RDW%	17.4

patient was diagnosed in adulthood (29 years) despite onset of symptoms in childhood (9 years). The age of presentation correlates with previous reports, but highlights the lack of awareness to hemoglobin disorders in remote parts of our state. The clinical presentation has been reported to heterogeneous. Recurrent jaundice and splenomegaly have been reported in approximately 50% cases of HbSD [2, 3].

Our case had history of recurrent jaundice but no organomegaly. Transfusion requirement has been reported to vary from 0 to 80% in different studies [1–3]. Our case did not receive any transfusion. He had severe anemia with presence of target cells and sickle cells on peripheral blood smear similar to previous reports [1–4]. The proportion of Hb S and Hb D in our patient is coherent with the mean values in previous reports [1, 3]. Hb F (7.8%) is lower in our patient as compared to the previous reports [3, 4]. A higher Hb F has been reported to play a protective role in these patients.

The compound heterozygous hemoglobin D syndromes are not common but clinically relevant. A clinical suspicion and evaluation of hemoglobin fractions by cation exchange HPLC or electrophoresis can yield timely results. Antenatal screening can prevent the occurrence of these cases.

Fig. 1 **a** Cation exchange HPLC chromatogram showing peak in Hb S region (retention time 4.10) along with a unknown peak (retention time 3.80), **b** Hemoglobin electrophoresis showing a fusion peak at border of HbD and HbS zone

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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