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Case Report

Concurrent Presence of Haemoglobin S and Hemoglobin D in Pregnancy: A Case Report

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I N F O

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A B S T R A C T

Introduction: Haemoglobinopathy is the clinical condition that arises from genetically abnormal structure or synthesis of the haemoglobin molecule. Among the inherited disorders of the blood, haemoglobinopathies and thalassemia constitute a major bulk of non-communicable genetic diseases in India. Heterozygous Haemoglobin Sickle Cell Disease (HbSC) is the second most frequent Haemoglobinopathy Behind Sickle Cell Anaemia (SCA). Compound heterozygous HbSD-Punjab is an uncommon haemoglobinopathy encountered in Indians. Hereby we have presented a case with clinical and laboratory findings of HbSD-Punjab accidentally diagnosed when a primigravida female came to the hospital with severe anaemia.

Case Report: A 34-year-old primigravida came to the hospital with complaints of breathlessness. On a complete haemogram with a peripheral smear (CH with PS), it was revealed that haemoglobin was 7.6% and RBCs were normocytic normochromic with many nucleated RBCs (nRBCs). High-Performance Liquid Chromatography (HPLC) showed double heterozygosity for HbS and HbD.

Conclusion: Double heterozygosity for HbSD is a rare disorder. Genetic Counselling is recommended.

Keywords: Double Heterozygous, HbSD, Pregnancy

Introduction

Haemoglobinopathies are a group of clinical disorders caused by genetic defects that cause either an abnormal structure of haemoglobin or insufficient production.[1] In general, haemoglobinopathies can be classified broadly as disorders that result from structurally altered haemoglobin molecules (e.g., SCA) or disorders that arise from a numerical imbalance of otherwise normal globin chain synthesis (e.g., b-thalassemia).[2] Prevalence of abnormal haemoglobins varies considerably with geographic location and racial groups. Regarding the four haemoglobin variants, HbS, HbE, HbC, and HbD, each, affects millions worldwide.[3] SCA is a hereditary haemoglobinopathy characterized by the presence of abnormal haemoglobin, specifically HbS, which leads to the formation of sickle-shaped red blood cells (RBCs).[4] Haemoglobin D (Hb D) has more than a dozen variants among which Hb D-Punjab is most common. The variants differ at the molecular level, but genetic tests are often unavailable in premarital screening. Some uncertainty might exist about other Hb D-Punjab double heterozygotes due to marked geographic variations in the frequency of the HbD and other major haemoglobinopathies, a small number of reports, evolving methodology of analysis of haemoglobinopathies, and sometimes confusing terminology.[5] HbD Punjab also known as HbD Los Angeles is a β-chain variant and is characterized by a Glu→Gln substitution at codon 121 with a GAA→CAA change at the DNA level and the electrophoretic mobility at alkaline pH

is similar to HbS (β6, Glu→Val). HbD-Punjab is an uncommon structural Hb variant seen in Punjabis and a higher frequency in Muslims in consanguineous marriages.[6] Heterozygous and homozygous states are usually clinically asymptomatic. Compound heterozygous states with another haemoglobin variant, such as HbS, HbE and b-thalassemia are uncommon and present with a chronic haemolytic disorder.[7] Hereby we are presenting a case with double heterozygous HbSD as a rare presentation in pregnant females.

Case Report

A 34-year-old primigravida with precious pregnancy, a known case of severe preeclampsia and severe oligohydramnios was referred to KIMS, HUBLI with complaints of breathlessness. On general examination, pallor and oedema were found. A systemic examination revealed that air entry was decreased on the left side, which on chest X-ray, was confirmed to be having left lower lobar pneumonia. On CH with PS, Hb was found to be 7.6% and revealed RBCs were normocytic normochromic with anisopoikilocytosis showing many nRBCs-, a few sickle cells, schistocytes and fragmented RBCs (Figure 1). WBCs were increased in number with a corrected WBC count of 20,247 cells/mm^3. Platelets were adequate with no haemoparasites suggesting haemolytic anaemia. The Reticulocyte Count (RC) was 15%.

In view of sickle cells, a sickling test was done which turned out to be positive (Figure 2). On further workup, HPLC was performed, and HPLC analysis revealed the presence of both HbS and HbD (HbS-30.6%, HbD-35.2%, HbA-26.4% and HbF-5.1%). The patient was advised parental screening for abnormal haemoglobin and DNA analysis for a definitive diagnosis. Haematological tests including haemoglobin, haematocrit, and cell indices are shown in Table 1.

Table 1.Haematological Parameters of Patient Investigation

Parameters	Result	Unit	Reference Range
Haemoglobin	7.6	g/dl	11.5_14.5
RBC	3.08	10*6 /uL	4.0_5.3
PCV	30	%	33_43
MCV	88.3	fl	76_90
MCH	28.8	pg	25_31
MCHC	32.5	g/dl	32-36
RDW (CV)	21.2	%	11.5_15.0
WBC	34,330	10*3 /uL	4000_11000
Corrected WBC count	20.247	10*3 /uL	-
Platelet count	260	10*3 /uL	140_440

PCV: Packed Cell Volume, MCV: Mean Corpuscular Volume, MCHC: Mean Corpuscular Haemoglobin Concentration, MCH: Mean Corpuscular Haemoglobin, RDW: Red Cell Distribution Width

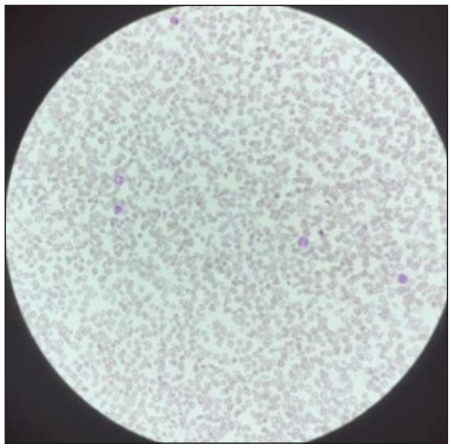

Figure 1.Peripheral Blood Film (MGG, 100x) Showing Severe Anisopoikilocytosis with a Few Sickle Cells, Schistiocytes and Fragmented RBCs

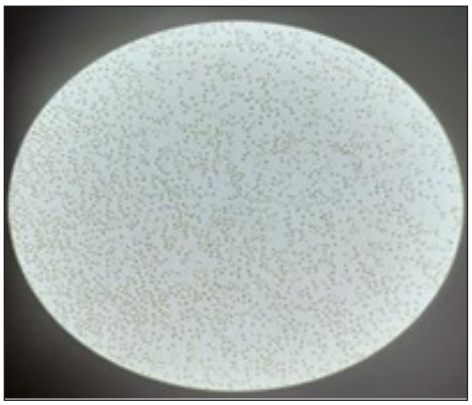

Figure 2.Positive Sickling Test (Using 2% Sodium Metabisulphite)

High-performance liquid chromatography (HPLC) was done for patients to know the type of haemoglobinopathies (Figure 3). It showed two abnormal Hb peaks, one within the D-window (as unknown) with a retention time (RT) of 3.82 min comprising 35.2% of the total Hb and the other peak within the S-window with an RT of 4.03 min comprising 30.6% of the total Hb.

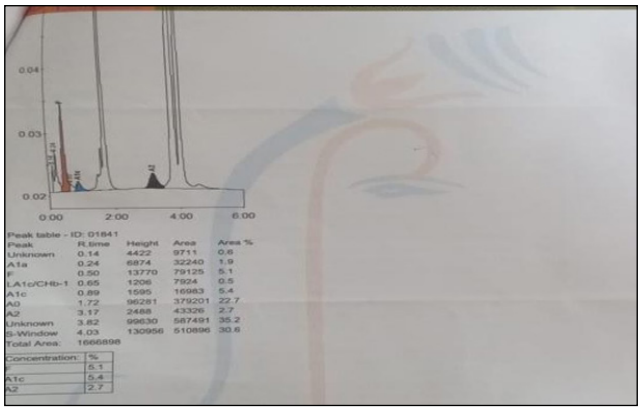

Figure 3. High-Performance Liquid Chromatography Analysis

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As shown above, HbD elutes as an unknown window at 3.82 min (35.2%) and HbS elutes at 4.03 min window (30.6%).

The results of abnormal Hb studies by HPLC were as follows:

1. Unknown window - 35.2% Hb at RT 3.82, where HbD elutes
2. S window - 30.6% Hb at RT 4.03, where HbS elutes

Discussion

Haemoglobin-D-Punjab (HbDP), also known as HbDLos Angeles, is an uncommon structural haemoglobin variant reported to be prevalent in northwestern India with the highest frequency (2%) found in the Sikh population.[8] The patients with Hb D-Punjab/ S genotype/ phenotype have a diversity of clinical presentations, ranging from asymptomatic to severe anaemia.[1,9,10] There are several variants of haemoglobin D such as HbD Punjab (Los Angeles), HbD Iran, and HbD Ibadan. Of these variants, HbD Punjab only interacts with HbS, however, the nature of this interaction is not known.[9] HbD molecules don't sickle and have normal solubility but Hbs have sickling properties and are not soluble. So, on citrate or acid agarose gel electrophoresis, it allows the separation of HbS and HbD giving clues about heterozygous conditions. Both electrophoresis and CE-HPLC are complementary in making an accurate diagnosis.

Conclusion

All Hb D-Punjab double heterozygotes are clinically insignificant except Hb D-Punjab/ S. Patients with double heterozygous for HbSD present with anaemia and sickle crisis. As pregnancy itself is a stressful condition, the patient may present with vaso-occlusive crisis. The fraction of Hb-D in HbD-Punjab homozygotes is higher than in Hb D-Punjab/ β double heterozygotes and a value of 92% could be used as the diagnostic cutoff. Automated HPLC is nowadays widely used for screening patients with suspected haemoglobinopathies based on clinical features and peripheral smear pictures. As these haemoglobinopathies are genetically inherited conditions, parental screening with DNA analysis and genetic counselling plays an important tool preventing further cases.

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