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DOUBLE HETEROZYGOSITY OF HBS AND HBD PUNJAB IN TWO SIBLINGS WITH COVID-19 INFECTION: A CASE REPORT

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Abstract:

Introduction : HbD Punjab is also known as HbD Los Angeles was first described by Itano in 1951. In HbD point mutation in beta globin chain occurs . HbD associated with HbS in which one gene carries HbD while other gene carries HbS mutation . Infants are at increased risk of life threatening complications like severe anaemia , splenic sequestration , overwhelming septicaemia .

Method: Two siblings one 9 year old male and other 4 year old male patients were presented with covid 19 infection in the hospital . Both were known case of sickle cell disease . There blood samples were taken and cbc , retic and HPLC was done . Both were diagnosed as HbSD Heterozygosity by HPLC method .Their mother was a know case of sickle cell trait and father was known case of HbD Punjab trait.

RESULT : In above study diagnosis of HbSD in both siblings was confirmed by HPLC. Since both their parents were carriers of sickle cell trait(mother) and HbD trait(father) . HbSD is a heterozygous state beta 121 glutamine residues stabilise the polymer and increases intracellular polymerization of HbS and increase sickling phenomenon .

CONCLUSION : HbSD is a rare but very serious disorder with high prevalence in northern part of India . It is a genetically inherited disorder occurs when either of one parent is HbD trait and other one being HbS trait.

Keywords: HbD Punjab, HbS trait, Heterozygous

Introduction:

HbD Punjab, also known as HbD Los Angeles was first described by Itano in 1951[3]. In HbD point mutation in β globin chain occurs. In β chain Glu→Gln substitution at codon 121 with a GAA→CAA change at the DNA level occurs. Its electrophoresis mobility at alkaline pH is similar to HbS (β6, Glu→Val) HbD can be inherited as heterozygosis with HbA causing no clinical or hematological alteration or in homozygosis state which is rare and commonly not related to clinical symptomatology [1]. Moreover, it can also be associated in combination with HbS or β-thalassemia. HbD associated with β -thalassemia is almost asymptomatic. However, HbSD disease may manifest with variable clinical features. One gene carries the HbD mutation while other gene carries HbS mutation - β^D β^S Infants with HbSD are at increased risk of life-threatening complications like moderate to severe anemia, spleen sequestration and overwhelming septicemia. HbD Punjab is one of the most common hemoglobin variants worldwide after HbS and HbC. Its prevalence is 1-3% in northwest India, especially in Punjab and 2nd most commonly in Gujarat. In India prevalence of HbS gene varies from 0-34% mainly seen in tribal groups of Madhya Pradesh, Orissa, Andhra Pradesh, Chatty tribe of Kerala and Tamil Nadu. Also common in Muslims consanguineous marriage [2].

CASE HISTORY

Two siblings, a 9-year-old male (Patient A) and a 4-year-old male (Patient B) were presented to the hospital as suspected cases of COVID-19 infection.

PATIENT A: At 5 months of age, the patient was diagnosed as a case of sickle cell anemia by sickling solubility test. Patient presented us with fever and on examination had non-tender hepatosplenomegaly and globular abdomen. He had been given 11 blood transfusions from April 2019 to Nov 2020.

PATIENT B: At 1 year of age, the patient was diagnosed as a case of sickle cell anemia by sickling solubility test. Patient presented us with fever, mild cough and abdominal pain in the last 3 days. On examination, there was hepatosplenomegaly and abdominal distension. He has received multiple blood transfusions (1-2/month) since age of 1 year.
The brothers have 2 sisters, aged 6 years and 2 years who are asymptomatic.

INVESTIGATIONS:

TEST/PATIENT	PATIENT A	PATIENT B	MOTHER	FATHER
Hb	7.3g/dL	3.4 g / dL	NA	NA
Retic count	3%	7.0 %	NA	NA
Sickling solubility test	Positive	Positive	Positive	Negative

Hb electrophoresis Findings	PATIENT A	PATIENT B	MOTHER	FATHER
HbA	53%	59.3%	60.3%	58.5%
HbF	1.3%	1.2%	-	-
HbA2	3.4%	3.1%	4.6%	3.1%
HbS	14.9%	12.2%	26.1%	2.5%
HbA1C	6.1%	5.6%	5.2%	5.0%

Other/Unknown	17.9%	14.1%	-	26.8%
Retention time	3.93	3.92	-	3.91
DIAGNOSIS	Sickle cell disease heterozygous with combination of unknown window with possibility of HbD Punjab heterozygous hemoglobinopathy	Sickle cell disease heterozygous with combination of unknown window with possibility of HbD Punjab heterozygous hemoglobinopathy	Sickle cell Trait	Hb D Punjab Trait

DISCUSSION:

About 7% of world's populations have mutation in genes encoding hemoglobin chain. Most common being HbS, HbD being 3rd most common [5]. HbSD is double heterozygous state. The β121 glutamine residue stabilizes the polymer and increases intracellular polymerization of HbS and enhances sickling phenomenon. There are several variants of hemoglobin D such as HbD Punjab (Los Angeles), HbD Iran, HbD Ibadan. Of these variants, HbD Punjab only interacts with HbS. HbD has also been reported with other hemoglobin apathies' like β-thalassemia without any additional clinical or hematological abnormalities. Few studies from Pakistan, Iran, and UAE have shown that the clinical presentation of HbSD disease cases is similar to that of patients with the severe form of sickle cell anemia, while reports from India have shown variable clinical manifestations of HbSD disease. Since there is considerable variability in presentation of HbSD patient's early detection and appropriate follow up can help specific treatment strategies to be consider. Repeated episodes of spleen sequestration and painful crises requiring regular blood transfusion. Recurrent abdominal pain due to gall stones requiring cholecystectomy. Hypersplenism necessities splenectomy. In HbSD disease, HbD does not take part in the sickling process. Although HbD itself does not polymerize, it facilitates the polymerization of HbS, thus enhancing the severity of the disease. At the same time, the co-inheritance of α-thalassemia and enhanced HbF levels also has an inhibitory effect on the clinical expression of sickle cell disease. Earlier, it has been observed that the inheritance of α-thalassemia with sickle cell anemia and high HbF levels often results in milder clinical manifestations. On the other hand, normal or excess α-globin's genes could increase the severity of sickle cell disease [1].

CONCLUSION:

HbSD is a rare but very serious disorder with high prevalence in northern part of India Although there is great variation in disease phenotype. HbF levels do not affect disease severity. Patients show significant sickling. Further studies are required to identify other genetic and environmental modifiers that influence the clinical and hematological profile of patients with this disease. Diagnosis is based on HPLC since electrophoresis cannot separate HbS and HbD. Since this disease is not curable, prenatal testing is important in community where HbSD β heterozygosity is more common and shows severe manifestation.

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