CASE REPORT

HEMOGLOBIN D/B+ COMPOUND HETEROZYGOTE WITH AUTOIMMUNE HEMOLYTIC ANEMIA.

Unaiza Qamar, Nisar Ahmed
Department of Haematology, Children's Hospital and Institute of Child's Health, Lahore, Pakistan

ABSTRACT:

A 10 years old child presented with progressive pallor since birth and history of jaundice and abdominal distension since 4 months.Investigations revealed a positive Direct antiglobulin test and a diagnosis of Autoimmune hemolytic anemia was made.Steroids were given and patient responded to it as evidenced by laboratory investigations returning to normals and alleviation of jaundice,but clinically pallor persisted. Hemoglobin Electrophoresis performed by HPLC(high performance liquid chromatography) revealed a significant percentage of Hb D and A2, suggestive of HbD/B+ trait that was later confirmed by parents' screening.Sickling test was performed that turned out to be negative.

KEY WORDS: Hemoglobin D, Thalssemia, Compond Heterozygote, Autoimmune Hemolytic anemia

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INTRODUCTION

Thalassemia and other structural hemoglobinopathies are the major Red cell genetic disorders prevalent in certain parts of the world including Pakistan[1]. They place a large burden on the patients, their families and even their communities. They are generally not curable but can be prevented by population screening and genetic counseling[2]. Beta Thalassemia is more common in Pakistan as compared to Alpha Thalassemia. There are 5% carriers of beta thalssemia trait[3], thus posing a major risk of thalassemia major progeny if consanginous marriages keep on occurring at the same pace[4]. There are a number of mutations that can cause beta thalssemia,some will result in severe disease, others a moderate one. Compuond heterozygotes of B thalassemia can either worsen the symptoms or lessen these[5]. Whereas thalssemia results from decreased production of globin chains, the structural variants produce normal amount of globin chains but these are structurally different, thus not performing the function as efficiently as normal globin chains would[4]. Compound heterozygosity for thalssemic gene and structural variant gene is not very uncommon in Pakistan where one of the parent is athalssemia trait and other is a carrier of structural variants[3]. HbD is one such structural variant,not very commonly found and that too with beta trait is even rarer. One of the consideration to be taken into account in making a diagnosis of HbD is to rule out Hb S as both share same band positions when cellulose acetate electrophoresis at alkaline pH is done, so sickling test becomes mandatory, but with HPLC both the bands can be differentiated. We present a case of 10 years old male child who other than having compound heterozygosity for HbD and Beta trait had had autoimmune hemolytic anemia, the combination is something not very commonly witnessed[5].

Corresponding author:
Dr. Unaiza Qamar
Assistant Professor
Department of Haematology Children Hospital and Institute of Child Health, Lahore, Pakistan.
e-mail: unaiza.qamar@gmail.com

CASE HISTORY

A 10 years old male child presented to the department of Haematology, Children's Hospital with H/O pallor since birth, jaundice since 4 months, lethargy, poor apetite for last 4 months. He was transfused with 4 Red cell concentrate transfusions during these last 4 months. On examination the patient was pale, jaundiced and abdominal examination revealed mild splenomegaly.CBC showed Hb=4 G/dl, TLC =12.9 x 10 3 /ul, Platelete count= 560,000/ul,MCV of 81.1 fl, MCH of 25.6 pg and MCHC of 30.1%. LFTS showed Bilirubin =5.6 mg/dl. Direct Bilirubin of 0.9 mg/dland Indirect of 4.5mg/dl. Peripheral smear showed severe anisocytosis, macrocytosis with microcytic RBC population and spherocytes, Nucleated RBCs= 3/ 100 WBCs, neutrophilia with hypersegmented neutrophils, metamyelocytes and myelocytes. Direct antiglobu-

lin test was ordered and it turned out to be positive. Patient was put on Steroids with proton pump inhibitor cover and folic acid. His Transfusion requirements completely diminished, Hemoglobin started to improve and jaundice subsided. Direct antiglobulin test also became negative. Patient was put on follow up, but hemoglobin did not rise above 9G/dL, also the peripheral smear kept on showing Nucleated RBCs. Parents CBC showed mother's RBC indices suggestive of thalssemia trait and father's indices were normocytic normochromic. Hemoglobin electrophoresis performed by HPLC (as last transfusion was given 6 months back)that showed Hb A= 35%,Hb D=51%,Hb A2=5.4% and Hb F=9.6%, that was suggestive of compound heterozygosity for HBD/B+. Mother's Hb electrophoresis showed Hb A2 of 5.1% suggestive of beta thalassemia trait and Father's Hb electrophoresis revealed Hb D to be 38 % suggestive of Hb D trait.Sickling test for both the child and father was done and it turned out to be negative. The child's pallor since birth was because of compound heterozygosity for HbD/B+ ,although he never required transfusions previously, as the mutation for B thalassemia trait might be a mild one.This is ,to our knowledge the first ever reported case of Hb D/B+ trait presented with Autoimmune hemolytic anemia.

DISCUSSION

Autoimmune hemolytic anemia (AHA) is characterized by shortened red blood cell (RBC) survival and the presence of autoantibodies directed against autologous RBCs. A positive direct antiglobulin test (DAT, also known as the Coombs test) is essential for diagnosis. About half of patients with AHA have no underlying associated disease; these cases are termed primary or idiopathic. Secondary cases are associated with underlying autoimmune, malignant, or infectious diseases or with ingestion of certain drugs.Patients present with anemia, jaundice and splenomegaly. CBC shows either normocytic normochromic anemia or macrocytic anemia, with Nucleated RBCs and high reticulocyte count. Although autoimmune hemolytic anemia is fairly seen in our population but its presentation can overlap with other RBC disorders like membrane, enzyme and hemoglobin disorders. Direct antiglobulin test can help in delineating autoimmune hemolytic anemia, but cannot exclude the co existence of the former[5]. The present case is one such example where despite the treatment for autoimmune hemolytic anemia and subsequently achieving a negative DAT (suggestive of alleviation of immune phenomenon), the patients symptoms were not resolved, that prompted us to look for some other underlying condition. A proper work up and family studies revealed presence of underlying Hb D/B+ condition. The thalassemias are the most common monogenic diseases in man. They occur at a high gene frequency throughout the Mediterranean populations, the Middle East, the Indian subcontinent, Myanmar, and in a line stretching from southern China through Thailand and the Malay peninsula into the island populations of the Pacific. They are seen commonly in countries to which these high-frequency populations immigrate[2].

Thalassemia consists of two main classes, alpha and beta thalassemia, in which the the respective globin genes are involvedThe pathophysiology of the thalassemias can be traced to the deleterious effects of the excessively produced globin-chain subunits that damage the red cell precursors and red cells, leading to profound anemia. The clinical pictures of thalassemia vary widely. Knowledge is gradually accumulating about the genetic and environmental factors that modify these phenotypes[3].

One such modifier is a combination of thalssemia trait with a structural variant. Depending on the type of structural variant the thalassemic presentation can fare better or poorly,One example where the presentation can range from mild to thalassemia intermedia like picture is a combination of B gene mutation on none chromosome and gene for Hb D on the other. hemoglobin D_{Punjab}, results from a substitution of glutamate for lysine at the 121st position in the beta-chain. The heterozygous state for hemoglobin D is entirely asymptomatic. The abnormal hemoglobin constitutes between 35 and 50 percent of the total hemoglobin. Homozygous hemoglobin D disease is very rare, and the clinical consequences are very mild.Diagnosis of compound heterozygosity for Hb D/B+ can be confirmed either by PCR or by family studies like we did[6].

Our patient did not have any prior history of transfusion, so the possibility of underlying alloimmune hemolytic anemia was a remote possibility that could also give a positive DAT. Thalassemia with or without structural variant inheritance are microcytic hypochromic anemias[3],whereas autoiimune hemolytic anemias where there is marked reticulocytosis is a macrocytic anemia,the resultant indices were in the upper limit of normal range[7] and having both these in our case the peripheral picture gave severely dimorphic picture with both microcytic and macrocytic RBCs.

After the hemolytic aanemia settled the indices reverted to microcytic hypochromic type. Uptil now HbD/B+ case with autoimmune hemolytic anemia being presented with autoimmune hemolytic anemia and later confirmation of underlying disease per se has not been reported. Having a suspicion for concomitant pathologies can help in alleviation of patients morbidity and an accurate and targeted treatment.

CONCLUSION

HbD/B+ Thalassemia is a a common cause of Anemia but if the anemia is aggravating or the transfusion requirements increase some other underlying pathology should be ruled out, in our case it was autoimmune hemolytic anemia .

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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