INTRODUCTION

Thalassemia and other structural hemoglobinopathies are the major Red cell genetic disorders prevalent in certain parts of the world including Pakistan. 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. Beta Thalassemia is more common in Pakistan compared to Alpha Thalassemia. There are 5% carriers of beta thalassemia trait, thus posing a major risk of thalassemia major progeny if consanguinous marriages keep on occurring at the same pace. There are a number of mutations that can cause beta thalassemia, some will result in severe disease, others a moderate one. Compound heterozygotes of B thalassemia can either worsen the symptoms or lessen these. Whereas thalassemia 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. Compound heterozygosity for thalassemic gene and structural variant gene is not very uncommon in Pakistan where one of the parents is a carrier of 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.

CASE HISTORY

A 10 years old male child presented to the department of Haematology, Children’s Hospital with H/O 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, Thalassemia, Compound Heterozygote, Autoimmune Hemolytic anemia

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.

Thalassemia consists of two main classes, alpha and beta thalassemia, in which the respective globin genes are involved. The 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.

One such modifier is a combination of thalassemia 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 one 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.

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, whereas autoimmune hemolytic anemias where there is marked reticulocytosis is a macrocytic anemia, the resultant indices were in the upper limit of normal range and having both these in our case the peripheral picture gave severely dimorphic picture with both microcytic and macrocytic RBCs.

After the hemolytic anemia 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

Hb D/B+ Thalassemia is 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.

REFERENCES


CONFLICT OF INTEREST

Authors declare no conflict of interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

None declared.