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Case Report

Homozygous delta beta-thalassemia: A rare case report

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ABSTRACT

Delta Beta (δβ) thalassemia is a rare autosomal recessive hemoglobinopathy. This is caused by either reduced production of δ and β genes (heterozygous state) or complete absence (homozygous state). High-performance liquid chromatography (HPLC) is an important screening and diagnostic tool, to be supported by molecular data and parental studies. A 40-year-old male (propositus), with mild anemia presented in the outpatient department. There were no other definitive causes of anemia with adequate nutritional status and no response after the treatment with nutritional supplements. HPLC was advised to look for any qualitative/quantitative defects. HPLC findings reveal 96% fetal hemoglobin (HbF), a very small quantity of adult hemoglobin (HbA), and an absent HbA2. In view of this data, followed up with parental studies. Both parents had elevated HbF and similar grades of anemia. These supported the presence of a heterozygous state of δβ-thalassemia in parents and homozygous δβ thalassemia in propositus. In δβ-thalassemia, there is a deletion of the δ and β genes on Chromosome 11. Expression of the gamma gene increases to compensate, causing increased production of gamma globulin for HbF (α2 β2). On HPLC or electrophoresis, heterozygosity shows as normal HbA2 and elevated HbF, and as absent HbA2 with almost 100% HbF for homozygous individuals. Screening of hemoglobinopathies by HPLC is that can be further subjected to parental screening for a more definitive diagnosis and narrow down the differentials as compared to molecular testing considering the cost, limited availability, and higher turnaround time.

Keywords: Homozygous delta beta-thalassemia, High-performance liquid chromatography, Parental

INTRODUCTION

High-performance liquid chromatography (HPLC) is routinely performed as a screening procedure for the diagnosis of hemoglobinopathy in anemia workup. However, it is not commonly available in all places in India, and lack of awareness leads to incidental detection of hemoglobinopathies most of the time. This method separates different forms of hemoglobin based on their composition and elution properties. It detects fetal hemoglobin (HbF [alpha 2; gamma 2]), adult hemoglobin (HbA [alpha 2; beta 2]), and hemoglobin A2 (HbA2 [beta 2; delta 2]).

The percentage of these subtypes of hemoglobin is variable as per the age of the patient and based on their percentage different types of hemoglobinopathies are diagnosed. In addition to this, other abnormal hemoglobin such as hemoglobin D, E, and S is also separated based on their retention times and diagnosis.[1]

Delta beta (δβ) thalassemia is generally associated with elevated HbF. In the case of the heterozygous state, it shows mildly elevated hemoglobin F with slightly reduced/normal hemoglobin A2. Complete blood count (CBC) data show mild anemia with microcytic

hypochromia indices. Generally do not require transfusion. The close differential diagnosis is hereditary persistence of fetal hemoglobin (HPFH) with normal hemoglobin A2 and normal CBC indices.[2]

Homozygous δβ-thalassemia is characterized by markedly elevated hemoglobin F with an absence of hemoglobin A2. Clinically, there is mild anemia but not much improvement after nutritional supplements.[3]

CASE REPORT

A 40-year-old male (propositus) with mild anemia presented in the outpatient department. There were no other definitive causes of anemia with adequate nutritional status and no response after the treatment with nutritional supplements. HPLC was advised to look for any qualitative/quantitative defects. HPLC findings reveal 96% HbF, a very small quantity of HbA, and an absent HbA2 [Figure 1]. The possible differential diagnosis of markedly elevated HbF includes beta-thalassemia major, HPFH, and homozygous δβ-thalassemia. In view of clinical presentation, graphical, and CBC data, the possibility of homozygous δβ thalassemia was favored and a parental sample was requested. HPLC findings of the father and mother suggest mildly elevated hemoglobin F [Figure 2] with similar grades of anemia [Table 1]. Considering all together, the possibility of the presence of a heterozygous state of δβ thalassemia in parents and homozygous δβ-thalassemia in propositus is confirmed. In view of financial constraints, molecular testing was not done.

DISCUSSION

Homozygous δβ-thalassemia is a rare autosomal recessive disorder. Genetically, either a complete absence of delta and beta genes or mutation on chromosome 11 can be detected leading to an absence of hemoglobin A2 and increased HbF due to excess production of gamma chains on the HPLC study.[3]

In the case of δβ-thalassemia heterozygous clinically show mild anemia with microcytic, hypo chromic indices, and a mild increase in red cell count resembling beta-thalassemia

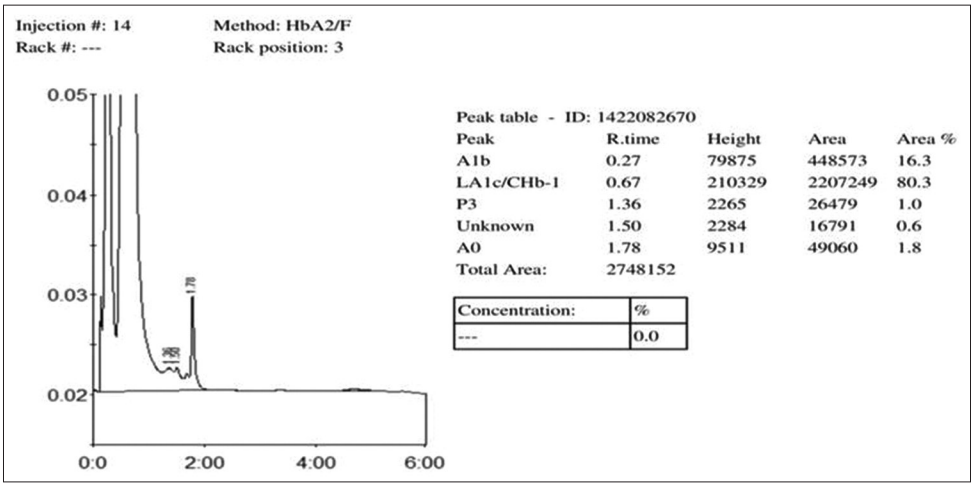

Figure 1: High-performance liquid chromatography shows markedly elevated hemoglobin F with absent hemoglobin A2.

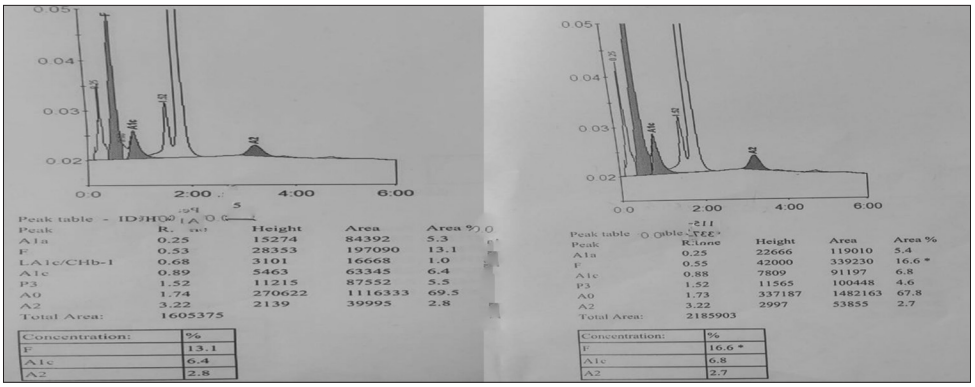

Figure 2: High-performance liquid chromatography from father to mother show elevated fetal hemoglobin (left and right), respectively.

Table 1: Complete blood count and high-performance liquid chromatography findings.

Laboratory data	Index Case	Father	Mother
Hemoglobin(g/dL)	11.7	11.1	11.6
Red cell Count(Millions /ul)	6.08	5.06	4.68
MCV (fL)	64.2	71.8	81.2
MCH(pg)	19.3	22.0	24.8
MCHC(g/dL)	30.0	30.6	30.5
RDW (%)	23.2	18.0	19.1
HbF (%)	96.6	13.1	16.6
HbA(%)	3.4	84.1	80.7
HbA2(%)	0.0	2.8	2.7

trait. On the other hand, homozygous δβ-thalassemia may present variably mild-to-moderate anemia mimicking thalassemia intermedia.[4]

Very high hemoglobin F is normally observed in newborns and slowly it reduces to <2% at the age of 1 year.[5] High HbF beyond that can be seen in pregnancy and stressed marrow condition and in juvenile myelomonocytic leukemia but the values will not be more than 10%. Significant high HbF with absence or <10% adult hemoglobin can be seen in beta-thalassemia major and homozygous HPFH. However, the clinical and hematological parameters are very characteristic in both groups, and also hemoglobin A2 is preserved in both conditions.[6] In our case, laboratory data suggest mild anemia with no transfusion requirement and hemoglobin A2 was completely absent. Hence, the possibility of homozygous δβ-thalassemia is favored.

In the literature, very few cases were reported as homozygous δβ-thalassemia from the Indian region.

CONCLUSION

Molecular studies as compared to the HPLC have a higher cost, limited availability, and higher turnaround time. Hence, our emphasis is on parental studies to help to narrow down the differential. Implementation of premarital counseling, awareness programs for schools, and newborn screening will definitely help to prevent or intervene early in the management of hemoglobinopathies.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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