CASE REPORT

A Benign form of HbE/ Beta-Thalassemia

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Abstract

HbE/ β-thalassemia has a variable presentation with symptoms varying from a mild to severe form of thalassemia. We present a case of incidentally discovered HbE/β-thalassemia in a twenty eight year old male. He had splenomegaly, hemoglobin of 14.9 gm/dL and microcytic red cell indices. He had an HbE of 39.4%, HbF of 57.5% and HbA formed 3% of the total hemoglobin.

Key words

HbE/β- thalassemia, Xmn1 polymorphism, Fetal haemoglobin, Haemoglobin E

Introduction

HbE/β-thalassemia has a variable clinical presentation with symptoms varying from a mild form of thalassemia to thalassemia major [1-5]. The hemoglobin at presentation varies from 3-13gm/dL with an average of 7.7gm/dL [1]. Patients with a mild form have normal development with no blood transfusions and are discovered by chance. However, half of the patients present with moderate to severe anemia, growth retardation, hepatosplenomegaly requiring regular or occasional blood transfusions. Bone pain, pericarditis, neurological complications, infections, iron overload leading to endocrinopathies are other causes of morbidity in these patients [1]. The factors leading to variability of this clinical presentation are uncertain. The clinical course and severity of anemia is influenced by both genetic and environmental factors. The presence of β + thalassemia mutation, coexistent α thalassemia, and Xmn1 polymorphisms in the γ globin gene are believed to ameliorate the symptoms [2, 6, 10]. Thai investigators have suggested that patients who have co-inherited severe β + or β0 alleles might be more severely affected than those who co-inherited a mild β-thalassemia allele [6]. Studies from India and Srilanka have however, suggested a limited role for β-thalassemia mutation on the clinical severity [4, 7]. Co-inheritance of α-thalassemia is a major genetic factor affecting clinical phenotype and considerable number of patients who have a co-existent α-thalassemia may be diagnosed later in life [8]. Polymorphisms in Xmn1 and BCL11A gene may be associated with increased synthesis of foetal hemoglobin and a milder clinical phenotype [8]. Alpha-hemoglobin stabilising protein gene, a chaperone of α-globin has also been suggested as a modifying factor of the clinical severity, though its role is uncertain [9]. Chronic hyperbilirubinemia, gall bladder disease, and co-inheritance of other hematologic disorders may worsen the clinical phenotype of HbE/β-thalassemia [8]. High levels of erythropoietin in thalassemia cause expansion of the erythroid mass with resultant hepatosplenomegaly and bone deformity. In Sri Lankan patients it was

found that serum erythropoietin concentrations correlated with steady state hemoglobin concentration, while a significant decline in serum erythropoietin in the face of anemia was observed with advancing age [7]. Other environmental factors such as high frequency of malaria (*Plasmodium vivax*) could contribute to the clinical phenotype. *P.vivax* infects young red cells and these patients have hemolysis and reticulocytosis with a resultant younger red cell population and are hence more susceptible to infection [8]. The mean HbE is around 58% and HbF varies from 5%-85 % (mean of 42%). HbA is not present in untransfused patients with HbE/β0-thalassemia [11].

Case report

A twenty eight year old male was evaluated for the possibility of an underlying thalassemia syndrome. He was a healthy male leading a normal active life. There was no abnormality detected on general examination. The only significant finding was an enlarged spleen which was 5cm below the costal margin.

He had hemoglobin of 14.9 gm/dL, mean corpuscular volume (MCV) OF 77fl, mean corpuscular hemoglobin (MCH) of 26pg and mean corpuscular hemoglobin concentration (MCHC) of 34gm/dL. His peripheral smear showed microcytic hypochromic RBCs with a few target cells and polychromasia. On high performance liquid chromatography (HPLC) he had an HbA of 3%, HbF of 57.5% and HbE of 39.4% with the minor hemoglobin HbA1a contributing to the rest (figure 1). He had led a normal life with no blood transfusion requirements. His growth and development had been normal and he denied any history of jaundice.

He had a five year old son with growth retardation and history of repeated hospitalisations for blood transfusions starting at the age of seven months. This boy had hepatosplenomegaly, hemoglobin of 9.3gm/dL, HbF of 86% and HbA of 4% and no HbE. This was the only reason which prompted the boy's father to undergo a haematological evaluation.

The boy's mother was also evaluated and found to have an HbA2 of 5.7 % (Table 1).

Table 1. Comparison of red cell indices, anemia, organomegaly and hemoglobin percentages

Parameters compared	Father	Mother	Child
clinical	Healthy	Healthy	Anemic with stunted growth
Hepatosplenomegaly	Only splenomegaly	None	Hepatosplenomegaly
Hemoglobin(gm/dL)	14.9	10.7	9.3
MCV(fl)	77	66	68
MCH(pg)	26	21	19
MCHC(gm/dL)	34	31	29
RDW (cv)	16	14.9	23.3
Reticulocyte count (%)	7	5	20
Blood picture	Microcytic hypochromic	Hypochromia basophilic stippling	Microcytic hypochromic, many nRBCs
HbE(%)	39.4	Nil	Nil
HbF(%)	57.5	1.7	86
HbA(%)	3	82	4

DNA analysis of the samples was not done as we did not have the facility for testing in our setup.

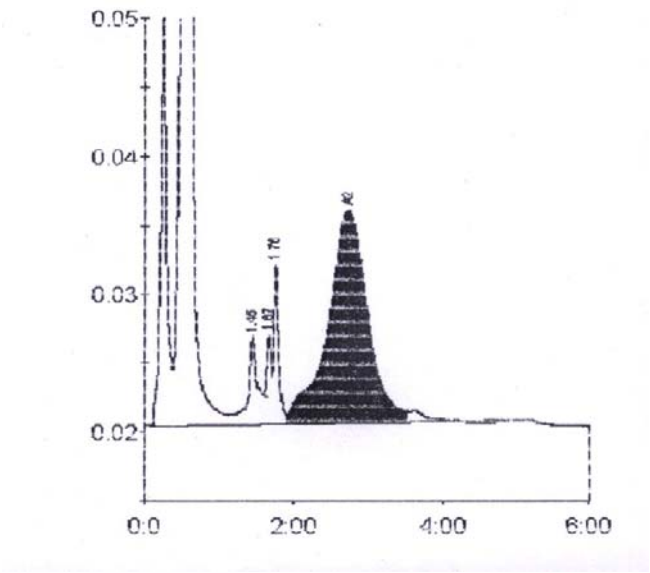

Figure 1. Chromatogram of the father showing both HbE and increased HbF. (Time in minutes on the x-axis and hemoglobin concentration on the y-axis)

Discussion

HbE/β-thalassemia has a variable clinical phenotype with half the patients presenting as thalassemia intermedia needing occasional blood transfusions. The anemia is due to ineffective erythropoieseis, globin chain imbalance leading to apoptosis and instability of HbE. This leads to extramedullary hematopoiesis with organomegaly. Repeated blood transfusions cause iron overload leading to endocrinopathy, recurrent infections and congestive cardiac failure.

Here, we have a patient with HbE/β- thalassemia presenting as thalassemia minor which was incidentally diagnosed when his son was undergoing evaluation for bone marrow transplantation for thalassemia major. He was clinically healthy with normal growth and near normal hemoglobin and living an active life. He never received any blood transfusions and the only positive finding clinically was an enlarged spleen. His family history was unremarkable except for his mother who had hemoglobin of around 9gm/dL. Hemoglobin varying from 3-13gm/dL has been described in HbE/β- thalassemia [1]. Our patient had higher hemoglobin of 14.9gm/dL.

Panigrahi I et al. [4] studied the factors affecting the phenotype of HbE/β-Thalassemia in thirty cases from North India. They found that the hemoglobin varied from 4.3-9.4 gm/dL, HbE 21-67.6% and HbF 16.1-69%. Krishnamurti et al. [12] reported a case of hemoglobinE/β0-thalassemia occurring in a father and son. The son was symptomatic whereas, the father was symptom free due to the coinheritance of α- thalassemia-1.

Presence of β + thalassemia mutations or a concomitant α thalassemia or Xmn 1 polymorphisms with a high level of HbF reduces the severity of anemia in HbE/β thalassemia. The amount of alternately spliced β E may also have a role in manifestation of disease severity [13]. Our patient′s HbA was only 3% which is less likely in HbE/β + thalassemia. The possibility of Xmn 1 polymorphism in the γ chain leading to elevation of HbF may be a possibility in this patient. We cannot rule out the possibility of α thalassemia as there was no molecular analysis.

This case is significant for the incidental discovery of HbE/β thalassemia in a healthy and active person. This presentation of HbE/β thalassemia is rare; rather its presentation is usually similar to like thalassemia intermedia or thalassemia major.

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