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Case Report

HbE Beta - Thalassemia: A Case Report

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ABSTRACT

HbE beta thalassemia is the most common form of severe thalassemia in south-east Asian countries. [1] HbE carrier rates of up to 30% are found in Burma, Thailand, Laos, Cambodia, Malaysia, and Indonesia. [2] In India it is more common in north-eastern regions with prevalence of 7-50% and 1-2% in west Bengal. [3] It is rare in other parts of country. The gene frequency of HbE is 10.9% in the northeastern region of India. [4] It has a variable picture of presentation from mild to severe form of thalassemia. Heterozygous of HbE are normal clinically. HbE beta thalassemia manifests as refractory anemia, hepatosplenomegaly, unexplained jaundice, growth retardation and regular or occasional transfusion requirement. [4]

Keywords: HbE, thalassemia.

INTRODUCTION

HbE/β-thalassemia has a variable clinical presentation with symptoms varying from a mild form of thalassemia to thalassemia major. [5] The hemoglobin at presentation varies from 3-13gm/dL with an average of 7.7gm/dL. [5] Patients with a mild form do not require blood transfusions and are discovered by chance. Many patients present with moderate to severe anemia, hepatosplenomegaly, growth retardation, 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. [5] 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. [6,7] Polymorphisms in Xmn1 and BCL11A gene may be associated with increased synthesis of foetal hemoglobin and a milder clinical phenotype. [8] Chronic hyperbilirubinemia, gall bladder disease, and co-inheritance of other hematologic disorders may worsen the clinical phenotype of HbE/β-thalassemia. [8] 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 resultant younger red cell destruction and are hence more susceptible to infection. [8]

CASE HISTORY

A 45 year old male presented to medicine outpatient with chief complaints of nausea and vomiting for 3 weeks. He also complained of headache & dizziness. He was otherwise a healthy male, leading a normal active life. His BP was recorded to be 180/100mm Hg & FBS was 140mg/dl

and PPBS was 228mg/dl. On per abdomen examination there was hepatosplenomegaly.

Past history revealed that there was history of jaundice & malaria on & off since 1996 and history of fever on & off since 2003. Patient had taken treatment for severe anemia and chronic malena at various hospitals

Family history revealed one of his younger brother expired due to fever, weakness, and anemia at the age of 22years

Present Investigation Reports

CBC report showed Hb-8.7gm/dl, MCV-46.8fl, MCH- 14.5pg, MCHC-31.1gm/dl, RDW-CV-25.4%, Reticulocyte count-0.5%, Sickling- Negative.

Peripheral Smear showed

RBC - microcytic and hypochromic, moderate anisopoikilocytosis, occasional normoblasts, marked hypochromasia, some target cells were also seen.

WBC was normal in number and morphology and platelets were adequate in number.

Impression was given as microcytic hypochromic anemia, suggestive of hemolytic anemia, & patient was advised for HPLC.

HPLC report showed HbA-15.9%, HbA_2/E-66.3%, HbF-5.59%, S-window-2.7%.

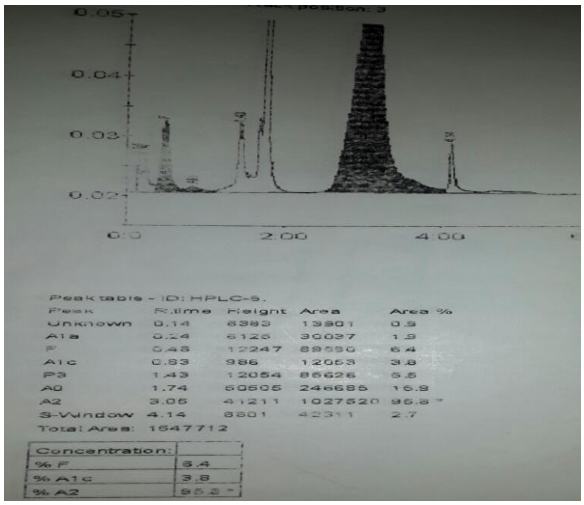

Figure 1: HPLC

Impression was given as HPLC suggestive of HbE-Beta thalassemia & patient was advised for Capillary zone electrophoresis

Capillary Zone Electrophoresis showed HbA-7.3%, HbA_2-7.3%, HbE-77.8%, HbF-7.70%, HbS-0%, Impression was suggestive of HbE-Beta thalassemia

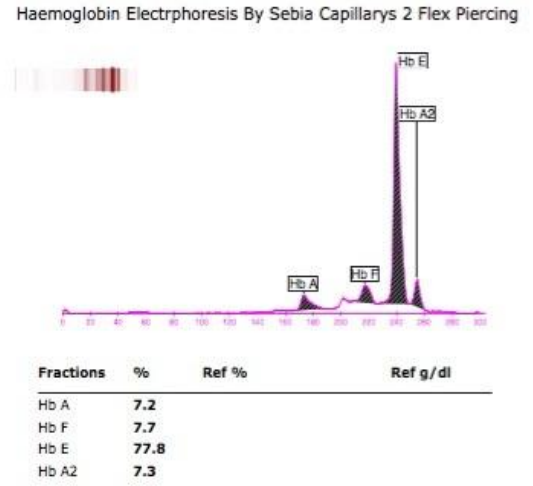

Figure 2: Capillary Zone Electrophoresis

Previous Investigation Reports

Patient had been evaluated for the above-mentioned complaints at various centers and his reports were mentioned here in chronological order

1. PS report in 2003 showed- RBC-Microcytic++, Marked Hypochromic, anisopoikilocytosis
2. HPLC report on 21.01.04 showed- HbA-7.7%, HbA2-78.6%, HbF-13.7%
3. HPLC report on 17.12.2006 showed- HbA-7.90%, HbA2+E- 91.60%, HbF-6.50%, Others-3.30%
4. BM Aspiration report on 3.7.12 showed - possibility of myelodysplasia - subtype refractory anemia, however immune-hemolytic anemia to be ruled out.
5. CBC report on 26-04-13 showed - MCV-56.6fl, MCH -17.2pg, MCHC-30.3gm/dl, RDW CV- 27.1%
6. HPLC report on 26.04.13 showed- HbA-19.2%, HbA_2-78.5%, HbF-8.2%
7. USG whole abdomen report on 25.02.14 showed- liver -enlarged (16.0 cm), spleen- enlarged (15.1cm)

DISCUSSION

HbE is a variant of haemoglobin having mutation in β globin gene causing substitution of glutamic acid residue for

lysine at 26th position of β-globin chain. The presentation varies from heterozygous state (AE/HE trait), homozygous state (EE/HbE disease) to compound heterozygous state. Compound heterozygous can be of 2 types (a) HbE Beta Thalassemia (Eβ thalassemia) (b) Sickle cell /HbE disease (SE genotype). [9-11] The HPLC and HB-electrophoresis pattern reveals HbE, HbA2, HbF i.e. HbE/β0 or HbE, HbA, HbA2, HbF i.e. HbE/β+. Pathophysiology is complicated and characterized by ineffective erythropoiesis, due to globin chain production imbalance there is apoptosis and instability of HbE, oxidative damage, shortened RBC life span, extramedullary hematopoiesis leading to organomegaly, facial deformity. Repeated blood transfusion leads to iron overload, which eventually causes endocrinopathy, recurrent infections, and congestive cardiac failure. Here we have a case, which was diagnosed as HbE/β thalassemia by HPLC and further confirmed by capillary zone electrophoresis presenting as thalassemia minor. There was no previous history of blood transfusion. In HbE/β thalassemia Hb level varies between 3-13gm/dl. [5] Our patient had Hb level of 8.7gm/dl, which was within the above-mentioned range. Study done by Panigrahi et al [12] on thirty patients from North India on the factors affecting the phenotype of HbE/β-thalassemia showed, Hb level varies between 4.3-9.4gm/dl, HbE 21-67%, HbF 16.1-69%. Our patient had HbA-7.3%, HbA_2-7.3%, HbE-77.8%, HbF-7.70%, as HbE> HbA, with increased HbF, it's a case of HbE/β^+ thalassemia. This case is significant for the fact that patient had been suffering from the similar complains for a long period of time without definite diagnosis, hence we confirmed the diagnosis by performing Capillary Zone electrophoresis, this will definitely be helpful for the further management of this case.

Table 1: Hemoglobin E and Hemoglobin E/Beta - Thalassemia

Genotype	Clinical Manifestations	Hemoglobin Electrophoresis
Hb E carrier (A/E)	None	Hb A and Hb E (with amount of Hb A > Hb E)
Hb E homozygous (E/E)	Mild anemia, may have no clinical manifestations	Hb E
Hb E/beta+-thalassemia (E/beta+)	Mild to moderate anemia	Hb E and Hb A (with amount of Hb E > Hb A), usually increased Hb F
Hb E/beta $^{0-}$ thalassemia (E/beta^0)	Moderate to severe anemia, may be transfusion dependent	Hb E and increased Hb F

CONCLUSION

HbE/β^+ thalassemia are an incidental discovery in a healthy and active person. Most of the patients fails to have a proper diagnosis. It has a heterogeneous clinical presentation and variable clinical course. Also the HbE phenotype is unstable. All this factors make it difficult to develop broad treatment protocols. Evidence suggests that steady state haemoglobin concentration is of limited value for regular transfusion. It is now generally appreciated that no patient with Hb E/β-thalassaemia should be placed on a regimen of regular transfusions without an extended period (of at least 3-6 months without intercurrent illness) in which growth, pubertal development if applicable, quality of life, symptoms and signs of anaemia including changes in spleen size, are monitored. [11] Hence, consideration of general guidelines for management, including careful consideration of maintaining such patients off transfusions, has been suggested for the management of Hb E/β-thalassaemia. [13]

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