

A clinicopathological study of a case of Hemoglobin E-beta Thalassemia

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Abstract

A 11-year-old male was seen with complaints of general weakness and growth delay with no previous history of blood transfusion and jaundice. On examination the child was pale with thalassemic facies with mild liver and spleen enlargement. His blood picture showed microcytic hypochromic anaemia. Hemoglobin electrophoresis showed no HbA, with raised HbE and HbF. HPLC showed rise in HbE more than HbF. All these findings were consistent with the diagnosis of HBE- α thalassemia. This case is reported here because of its late presentation and phenotypic diversity that poses a diagnostic and management dilemma.

Keywords: Thalassemia; Hemoglobin E; Phenotypic diversity.

Introduction

Hemoglobin E-beta thalassemia is a common hemolytic anaemia in South East Asia. In India, hemoglobin E [α -26 glutamine – lysine] has a prevalence of 7-50% in Northeastern region and 1-2% in West Bengal[1]. Interaction of thalassemia and hemoglobin produces its remarkable variable clinical phenotype[2] which presents a major challenge in determining its most appropriate management. In particular it is not clear why some patients with this condition can develop

and function well at very low hemoglobin levels. The doubly heterozygous state of hemoglobin E-beta thalassemia results in chronic hemolytic anemia with clinical picture similar to that in beta thalassemia intermedia or major. Other manifestations include splenomegaly, unexplained jaundice, iron overload, hypercoagulable states, pulmonary hypertension and cardiopulmonary disease. Despite its frequency, hemoglobin E-beta thalassemia is often managed in an ill-defined and haphazard way, usually by demand transfusion. Age-related changes in the pattern of adaptation to anaemia suggest that more cost effective approaches to management should be explored. Recent studies indicate 40% of patients will clinically improve with hydroxyurea and that in many patients hemoglobin E α thalassemia can be managed without transfusion, even with low hemoglobin levels. It is important to diagnose

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early to ensure adequate prevention and management of complications. This also facilitates proper counseling of families for future pregnancies, prevent recurrences and reduce burden of diseases. This paper reports a case of hemoglobin E-beta thalassemia from Ghaziabad, North India.

Case report

An 11-year-old male with apparently normal parents presented with complaints of general weakness, lethargy and growth delay.

The child showed distinct pallor, mild hepatosplenomegaly, thalassemic facies and growth retardation.

Investigations

Revealed his hemoglobin to be 5.4g/dl, MCV 58.5fl, RDW of 25.9% and slightly increased reticulocyte count. A blood smear revealed microcytic hypochromic red cells of distinct variable size and shape [anisopoikilocytosis] and density [polychromasia] His hemoglobin electrophoresis pattern showed predominantly HbE and F [E greater than F] with no hemoglobin A. High performance liquid chromatography [HPLC] found 72.6% HbE and 18.1% HbF, rest 9.3% being HbA₂. These findings along with the clinical presentation were consistent with a diagnosis of HbE- $\hat{\alpha}$ thalassemia.

The parents were advised electrophoresis and option of antenatal diagnosis for subsequent pregnancies. The patient was given blood transfusion and a trial of hydroxyurea planned.

The patient was on follow up for one year. During this period, no further complications were reported and he was doing well.

Discussion

Worldwide, hemoglobin E thalassemia is one of the most important varieties of

thalassemia[3,4]. The condition results from co-inheritance of $\hat{\alpha}$ thalassemic allele [either $\hat{\alpha}^-$ or $\hat{\alpha}^+$] from one parent and the structural variant hemoglobin E from the other[4]. The disease presents in three forms, mainly heterozygous state [Genotype AE or HbE trait], homozygous state [Genotype EE or HbE disease] and compound heterozygous state [a/ $\hat{\alpha}^-$, hemoglobin E beta thalassemia {E $\hat{\alpha}$ thalassemia}, b/ Sickle cell /HbE disease {SE genotype}[5,6,7]. HbE trait may be coinherited with either $\hat{\alpha}^-$ or $\hat{\alpha}^+$ thalassemia. Although, in general, severity of the disease is greater with $\hat{\alpha}^-$ thalassemia mutations, the mutation type is not a reliable predictor of clinical course, and predicting clinical course is notoriously difficult.

About half of the individuals who have hemoglobin E-beta thalassemia have severe manifestations that resemble thalassemia major, requiring regular blood transfusions to treat severe anaemia. Without treatment, this condition can result in lethargy, pallor, growth delay, hepatosplenomegaly and ineffective erythropoiesis leading to distortion of bones and characteristic facial facies[5,6,7]. Heart failure and infection are leading causes of death in untreated thalassemia major, usually before the third decade. About half of the individuals who have hemoglobin E- $\hat{\alpha}$ thalassemia have symptoms similar to thalassemia intermedia, including pallor, jaundice, mild to moderate anaemia and hepatosplenomegaly. Blood transfusions are rarely needed. Other complications can include folic acid deficiency secondary to high rate of erythropoiesis, leg ulcers, gall stones and thrombosis. Chronic anaemia causes increased iron absorption from gastrointestinal tract leading to complications of iron overload. Hemoglobin E- $\hat{\alpha}$ thalassemia can also occur in mild form in which affected individuals usually do not develop clinically significant problems and require no treatment. The management of hemoglobin E- $\hat{\alpha}$ thalassemia is similar to that of homozygous $\hat{\alpha}$ thalassemia[8]. In those maintaining hemoglobin of $>7g\%$, long term folic acid is advocated. Hydroxyurea is beneficial as it decreases ineffective erythropoiesis and increases hemoglobin with or without HbF[9]. Periodic follow up of

growth and skeletal deformities, hemoglobin level, prophylactic vaccination against infections which may worsen anaemia is important. Indications for regular transfusions are persistently low hemoglobin [hemoglobin <7g%], significant skeletal abnormalities and marked extramedullary hematopoiesis. Hypersplenism warrants splenomegaly. Iron overload requires regular iron chelation therapy. Periodic assessment of serum ferritin, calcium, T4, TSH, blood sugar, LFT etc aids in proper management. In case of hypogonadism, serum testosterone/estradiol levels and bone mineral density have to be done. Recombinant erythropoietin alone or associated with hydroxyurea may be useful in reducing transfusion requirements and in improving quality of life.

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