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HBE BETA THALASSEMIA- A CASE REPORT HIGHLIGHTING THE NEED TO EXPECT THE UNEXPECTED

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ABSTRACT Hemoglobin E (HbE) is common structural hemoglobin variant that occurs throughout many Asian countries at high frequencies. Its coinheritance with beta thalassemia is called as haemoglobin E β thalassemia. They are expected to have a moderately severe disease. Due to migration of people across the globe these inherited diseases are diagnosed in areas without documented disease prevalence. Hemoglobin (Hb) electrophoresis and High- performance Liquid Chromoatography (HPLC) are required in the diagnosis of HbE beta thalassemia. But definite diagnosis will require DNA testing. We report a case of 13 year old migrant female child suspected to have a hemoglobinopathy by peripheral smear findings and diagnosed as HbE βthalassemia by Hb electrophoresis and HPLC.

KEYWORDS : Hemoglobin(Hb) E, Hb electrophoresis, thalassemia.

INTODUCTION:

HbE beta thalassemia is the most common form of severe thalassemia in south-east Asian countries[1]. HbE carriers are found in Burma, Thailand, Laos, Cambodia, Malaysia and Indonesia [2]. In north-eastern regions of India the prevalence is 7-50% and in west Bengal it is 1-2%.[3] HbE beta thalassemia may presents as refractory anemia, hepatosplenomegaly, unexplained jaundice, growth retardation and regular transfusion requirement.

We present a case of HbE Beta thalassemia in a female child from the north-eastern state of Assam in India.

CASE HISTORY:

A 13 year old girl from Assam presented with fever, weakness of 1 week duration. She was malnourished, pale, had bilateral cervical lymphadenopathy, a leg ulcer and elevated JVP. Per abdomen there was hepatosplenomegaly.Chest was clear and there were no neurological deficits. Her hemoglobin was 2gm/dl and was in the state of congestive heart failure at the time of admission. She was transfused one unit of packed red cells and further investigations were done.

Investigations: Hb 4.7 g/dl, TC- 8100/mm^3, DC- P50% L37% Mix13%, Hematocrit- 13.1%, MCV- 64.9fl, MCH-23.3pg, MCHC-35.9g/dl, RDW-35%, Platelet count- 2.52 lakhs/mm^3. Urine examination- sugar nil, albumin trace, 3-5 pus cells/HPF. Urine tests for bilirubin, bile salts, urobilinogen and blood were negative.

Reticulocyte count= 1.7%, Corrected reticulocyte count= 0.6%, RPI= 0.3. Her total bilirubin- 1.8mg/dl (0.2-1.0), direct bilirubin 0.6mg/dl (0.4); all other liver function tests and renal function tests were within normal limits. Serum LDH was mildly elevated 590.9 U/L (120-330). Iron studies showed normal serum iron, total iron binding capacity and transferrin saturation but her serum ferritin was increased 328.7ng/ml (20-200). Serum vitamin B12 was 180ng/ml (211-946) and serum folic acid was 2.3ng/ml (4.6-18.7) Investigations were suggestive of possible nutritional deficiency and compensated hemolysis.

Peripheral smear shows marked anisopoikilocytosis with hypochromic microcytic RBCs, target cells, tear drop cells, spherocytes, nRBCs and occasional Howel jolly bodies. Neutrophils predominate with some hypersegmented neutrophils. Platelets were adequate. Sickling test was negative. In the view of hemoglobinopathy, family members were screened. She had a symptomatic brother who was pale. We proceeded with Hemoglobin(Hb) electrophoresis and High- performance Liquid Chromoatography(HPLC) for her family members. Hb electrophoresis of the patient and symptomatic brother on Alkaline electrophoresis showed bands in the regions of A, F, A2/C/E and on Acid electrophoresis no band in the C region excluding HbC . HPLC of the patient and symptomatic brother showed elevated HbF and HbA2 consistent with β thalassemia. (Table:1)

Table 1: HPLC values of the patient and her family members.

	HbA2	HbA	Hb F
Patient	21.1%	56.4%	13.9%
Symptomatic brother	20.6%	51.6%	19.8%
Asymptomatic brother	3.7%	84.4%	0%
Mother	6.4%	82.6%	<0.8%

Since HbA2 window was >7% possibility of an additional Hb structural variant was considered, the most common variant being HbE. In HbE β thalassemia usual HbA2 fraction is >39% but in our case it was only 21% which may be due to the post transfusion sample tested. Hence we finally came to a diagnosis of HbE β thalassemia.

HPLC of the mother showed elevated HbF and HbA2 which is <7%, and was diagnosed to be β thalassemia trait. Another brother was normal. Since the patient's father expired during her early age details were not available.

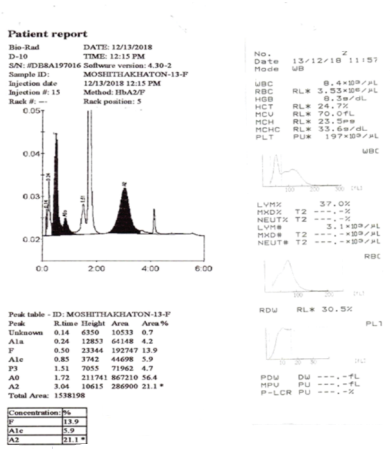

Fig 1: HPLC of the patient showing % of Hb F, A and A2.

DISCUSSION:

β-thalassemias are caused by mutations that diminish the synthesis of β-globin chain. β^0 mutations are associated with absent β-globin synthesis and β^+ mutations are associated with reduced β-globin synthesis. HbE is a β-hemoglobin variant which is formed by a substitution of glutamic acid by lysine at codon 26 of the β-globin gene. This mutation leads to reduced beta chain production and thalassemia phenotype[4]. HbE alone does not cause any significant clinical problems but its interactions with alpha / beta thalassemia produce a wide range of clinical syndromes of varying severity.

An overview of the global distribution of thalassemia shows that thalassemias are frequent in Asia and Far East countries in addition to Mediterranean countries where they were first recognised. Due to continual migration of populations from one area to another, there is virtually no country in the world in which thalassemia does not affect some percentage of the inhabitants[5]

Hemoglobin in HbE β thalassemia ranges from 3 g/dl or less to as high as 11 g/dl. HbE, β0 thalassemia is characterized by the production of HbE and HbF without detectable HbA. In HbE, β+ thalassemia variable amounts of HbA are produced in addition to HbE and HbF. [6]

Ineffective erythropoiesis, apoptosis and oxidative damage are the main components of the disease. The interaction between Hb E and β-thalassemia alleles is the main determinant in the pathophysiology.[7]

Marked expansion of erythropoiesis is responsible for hepatosplenomegaly, growth retardation, delayed sexual maturation, extramedullary haematopoietic masses and bone deformities[8]. Cardiopulmonary disease is the most common cause of death in Hb E β-thalassemia[9]. Our case presented with features of congestive cardiac failure.

The diagnosis is made by doing hemoglobin electrophoresis as soon as anemia is detected. In alkaline electrophoresis, HbE migrates with C, O Arab, and A2. In acid electrophoresis, it migrates with HbA2. High-pressure liquid chromatography (HPLC) is a rapid, automated method that is capable of identifying most hemoglobin variants and provides precise measurement of HbA2 and HbF in various haemoglobin genotypes [10]. However, it cannot separate HbE from HbA2

The percentage of the variant haemoglobin will be lower and the percentage of HbA will be higher if the patient is recently transfused. Multiple transfusions will show significant difference in haemoglobin electrophoreis pattern than single transfusion[11]. In our case transfusion was given, hence the value of HbA was higher than expected and HbA2 value was lower at 21%.

Family studies in HbE- β-thalassemia reveal the carrier state for HbE in one parent and β-thalassemia trait in the other. The mother of this child was a β-thalassemia carrier. Details of her father was not available. Quantitation of HbF seems to be more important than HbA2 in β-thalassemia major as HbF plays an important role in diagnostic and prognostic purposes.[11]

To conclude, hereditary hemoglobinopathy is becoming more prevalent in areas where it was uncommon due to the continuous migration of the people. A high index of suspicion is necessary to diagnose correctly. The diagnosis is made by doing Hb electrophoresis and HPLC before any blood transfusion is given as it may interfere with diagnosis.

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