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HbE-Beta-Thalassemia- a case report

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Abstract:
A 21 year old male with a past h/o one blood transfusion presented with complaints of fever for 4 days. On physical examination, the patient had pallor, icterus, and splenomegaly. Routine investigations revealed normal values except for Hb-8g/dl, serum bilirubin-3.0, and plt-95000/mm^3(mild thrombocytopenia). This made us suspect chronic malaria and dengue for which we did a peripheral smear, USG abdomen, and IgM dengue. The peripheral smear revealed microcytic hypochromic anemia with mild thrombocytopenia, RBC target cells, and USG abdomen showed massive splenomegaly. This made us suspicious of thalassemia and autoimmune hemolytic anemia for which hemoglobin electrophoresis and DCT were done. The investigations revealed serum ferritin of 3596ng/ml and hbA of 35.7% hbA2-11.1%, hbE-53.2%, and positive IgM dengue. hence, a diagnosis of Beta-Thalassemia hbE disease with Dengue was suggested. The patient was advised genetic mutation study for a beta-thalassemia/hbE heterozygous state. Beta-Thalassemia/hbE is a very rare disease in which patients present with severe anemia in the early stages or with features of iron overload in the later stages due to repeated transfusions. The patient's blood picture and presence of splenomegaly could have been explained by tropical fevers such as malaria or dengue. The patient also had evidence of hemolytic anemia and the presence of target cells in peripheral blood led to further probing by doing hemoglobin electrophoresis which revealed an underlying rare thalassemic syndrome. Hence, despite the clinical presentation and endemicity of tropical fevers, one must keep in mind the possibility of such rare causes of anemia since it affects patient management. In view of possible iron overload in the future, the patient was started on deferasirox. The patient's platelet count improved from 95000mmcube to 1,50,000mm^3 during the course of treatment. Periodic monitoring of iron levels, hemoglobin, glycemic status, thyroid function was also advised on discharge.

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I. Introduction

In a tropical country like India when a patient presents with fever for more than 4 days with anemia, splenomegaly, and thrombocytopenia, we most likely think of infectious etiology. If we do not probe into anemia properly, then we might think that the anemia might be due to an infectious etiology and transfuse blood which might lead to, endocrine complications, Cardiac complications, gastroenterological complications; allergic complications; infectious complications, and thrombosis. The endocrine complications are osteoporosis, growth retardation, developmental delay, short stature, hypothyroidism, delayed puberty, hypogonadism, and diabetes mellitus. The cardiac complications are left ventricular wall hypertrophy, diastolic dysfunction, systolic dysfunction, heart failure, pericardial effusion, dilated cardiomyopathy, left ventricular dilatation, left atrial dilatation, and fatal arrhythmias[1].

II. Case Report

A 21 year old male came to the outpatient clinic with complaints of fever for the past 4 days with .yellowish discoloration of the sclera. Past history revealed that he had a history of one blood transfusion.

Upon general examination, he was icteric and pallor was present. Abdomen examination revealed massive splenomegaly. Routine investigations were done and findings are listed below.

Complete blood count:

Hemoglobin	8.0 g/dl
RBC	2.58 million/cu.mm
WBC	3800 cells/cu.mm
HCT	25.5%
MCV	75.6fL
MCHC	25.4 g/dl
Platelet count	95,000/cu.mm

Renal function test

Random blood sugar	90mg/dl
Urea	40mg/dl
Creatinine	0.8mg/dl
Sodium	139meq/l
Potassium	3.7 meq/l

Liver function test

Total serum bilirubin Serum bilirubin Direct Indirect	3mg/dl 1.3mg/dl 1.7mg/dl
sSGOT	86U/L
SGPT	17U/L
Serum ALP	44U/L
Total protein	6.2g/dl
Albumin	3.7g/dl
Globulin	3.5g/dl

Other investigations

Peripheral blood smear	Microcytic hypochromic anemia with mild thrombocytopenia and RBC target cells
IgM Dengue Malarial parasite by QBC	Positive Negative
Reticulocyte count	1.4%
Direct Coombs test	Negative
Serum LDH	345U/l
USG Abdomen	Massive splenomegaly measuring 18 cm

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The presence of RBC target cells in the peripheral smear and splenomegaly made us suspect thalassemia and autoimmune hemolytic anemia. Since DCT was negative we ruled out autoimmune hemolytic anemia. After obtaining hematologist opinion, Hemoglobin electrophoresis was done [HbA – 53.7% (96.8 – 97.8) HbA2 – 11.1% (2.2 – 3.2)] HbE – 53.2%(0.0-0.0). Hemoglobin electrophoresis, IgM Dengue, a negative DCT, along with hemolytic anemia with target cells in the peripheral smear and splenomegaly, suggest a diagnosis of Dengue co-existing with HbE/Beta-Thalassemia. Supportive management with fluids helped improve the platelet count from 95,000/mm^3 to 1,50,000/mm^3. One unit of PRBC was transfused to correct the anemia. Deferasirox was added to prevent future iron overload. Periodic monitoring of iron levels, hemoglobin, glycemic status, thyroid function was also advised on discharge.

III. Discussion

hemoglobinE-beta-thalassemia (Hb E/β-thalassaemia) is the genotype responsible for approximately one-half of all severe beta-thalassemia worldwide. The disorder is characterized by marked clinical variability, ranging from mild and asymptomatic anemia to a life-threatening disorder requiring transfusions from infancy[2].

Compound heterozygotes for HbE and a β thalassemia gene can have β thalassemia intermedia or β thalassemia major, depending on the severity of the coinherited thalassemia genes.

Beta thalassemia is usually due to a point mutation in chromosome 11 which can occur in any step of the beta globin chain expression, transcription, translation. Common forms occur due to mutations that arise from the splicing of mRNA[3]. Due to the decrease in the beta globin the alpha globin chain precipitates forming inclusion bodies. These inclusion bodies are then identified by the spleen leading to hemolytic anemia. Individuals with thalassemia major usually present within the first two years of life with severe anemia, requiring regular red blood cell (RBC) transfusions. Findings in untreated or poorly transfused individuals with thalassemia major, as seen in some developing countries, are growth retardation, pallor, jaundice, poor musculature, hepatosplenomegaly, leg ulcers, development of masses from extramedullary hematopoiesis, and skeletal changes that result from the expansion of the bone marrow[5]. This is due to the deletion of both the genes of the beta globin chain. A milder variant is the beta-thalassemia intermedia in which patients present later in life still requiring blood transfusions. The third type of beta-thalassemia is called beta-thalassemia minor in which the patients maybe asymptomatic or rarely require blood transfusions. Peripheral smear in all forms of thalassemias shows RBC target cells.

HemoglobinE or hbE is due to a single base change in codon 26 that causes the amino acid substitution of glutamic acid to lysine[4]. Heterozygotes resemble individuals with a mild beta-thalassemia trait. Homozygotes have somewhat more marked abnormalities but are asymptomatic. The whole-blood oxygen dissociation curves of homozygotes for HbE appear to be normal or very slightly right-shifted[6]. HemoglobinE is unstable in the setting of increased oxidative stress such as infections[7]. So the patient might present with hemolytic anemia. If we do not evaluate the hemolytic anemia properly, we might endanger the patient's life from the complications of iron overload such as hypogonadism, hypothyroidism, Diabetes Mellitus resulting from deposition of iron in the testis thyroid, and pancreas respectively. Iron overload in the liver may lead to liver cirrhosis. Iron overload in the heart may lead to dilated cardiomyopathy leading to systolic heart failure endangering the patient's life. Therefore, timely diagnosis and management with iron chelators help improve the quality of life in these patients.

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