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Sickle Cell E Disease: A Case Report

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Abstract: ***HbE is a variant haemoglobin that results from substitution of lysine for glutamic acid at 26th position in β globin chain. It can present as homozygous state or in heterozygous state associated with other haemoglobin chain disorders or haemoglobinopathies like sickle cell anemia or thalassemia. A case of a 23 year old female who presented with signs and symptoms of anemia was investigated and was found to be a compound heterozygous case of HbSE.***

Keywords: Anaemia, Haemoglobin E, β globin gene, Sickle cell/Haemoglobin E disease (HbSE)

1. Introduction

Normal haemoglobin (HbA) consists of 2 α-globin chains and 2 β-globin chains. The normal β-globin chain, located on the short arm of chromosome 11, has a glutamic acid in the β-6 position (codon). HbE results from substitution of lysine for glutamic acid at β-26 (glu→lys). The formation of HbS occurs from substitution of valine for glutamic acid (glu→val). Both HbS and HbE are inherited as autosomal recessive variations of the β-globin chain.

Sickle cell haemoglobin E disease results when an infant has inherited one copy of the Hb S variant gene from one parent and one copy of the HbE variant gene from the other parent. There is a 25 percent chance of inheritance of compound heterozygous HbSE disease with each pregnancy. The coinheritance of HbS and HbE (HbSE), may result in a clinically significant sickling disorder similar to sickle cell disease (homozygous HbSS) in contrast to the benign nature of the homozygous form (HbEE) disease, which is usually clinically silent. HbSE is accompanied by vaso occlusion and hemolysis, producing moderately severe anemia and painful episodes, although usually milder than sickle cell anemia (HbSS).

2. Case Report

A case of 23 year old female who presented with weakness, moderate pallor and vague abdominal pain. She was of average built and stature. On examination the spleen was measured two fingers below the left costal margin. Laboratory investigations showed RBC count 3,200,000/cumm, haemoglobin 8.4 gm/dl, WBC count 9200/cumm (59 percent neutrophils, 3 percent band forms, 2 percent eosinophils, 4 percent monocytes and 32 percent lymphocytes). Reticulocytes 4 percent, Platelets 3,80,000/cumm, Hematocrit 31 percent, MCV 90 , MCH 26

Erythrocytes on the peripheral blood film showed mild anisocytosis, polychromatophilia, numerous target cells and few sickle cells. Sickling test was positive. Total Bilirubin was 1.3mg/dl. HPLC showed Hb F concentration 7.9%, A2 concentration 30.1% with S-window area of 57.6% (Figure 1)

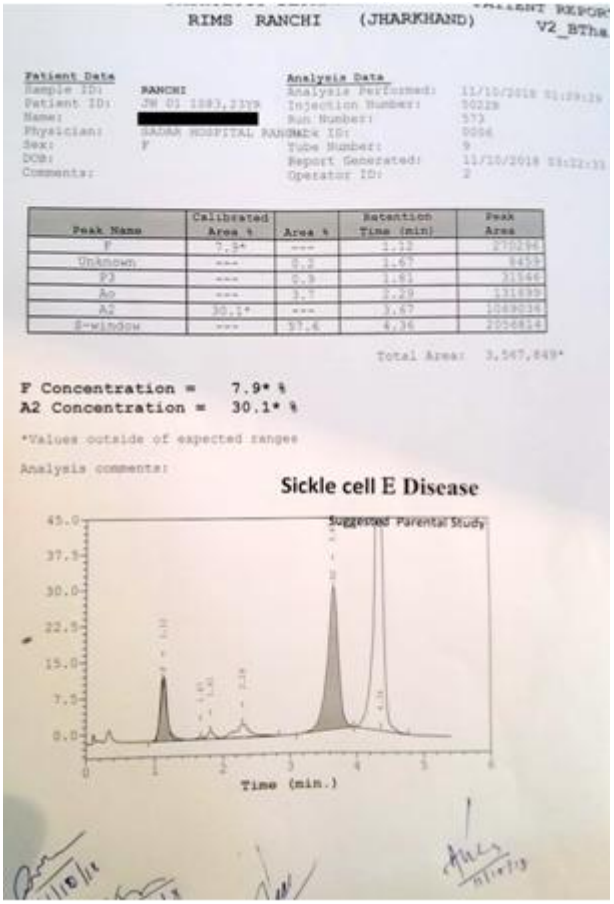

Figure 2 shows the electrophoretic finding which corresponds with the HPLC

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The patient was advised for genetic studies but could not be followed up.

3. Discussion

Hb E may be present in the heterozygous state (genotype AE or haemoglobin E trait), the homozygous state (EE or haemoglobin E disease) and a variety of compound heterozygous states such as haemoglobin E/β thalassemia (E/βthal)[5], sickle cell/haemoglobin E disease (SE genotype)[2, 6].The β chain of HbE(βE) is synthesised at a reduced rate compared with that of normal adult haemoglobin (Hb A) because of the mutation which creates an alternate splicing site within an exon.

HbE trait is defined by the heterozygous condition associated with one normal adult haemoglobin β gene and one variant haemoglobin E β gene. It is an asymptomatic condition with no clinical relevance, except for the risk of compound heterozygous states with either β thalassemia or sickle cell anemia. On HPLC, HbE is easily separated from HbA and usually comprises 33% or less of total HbA. Patients with less than 30% of HbE almost always have co existing a thalassemia trait.

Hemoglobin E disease is defined by the coexistence of two β E alleles (homozygous state EE). Study of both parents (in case of homozygous EE child) is mandatory.Patients are usually asymptomatic with HPLC showing major haemoglobin to be HbE with HbE and HbA_2 constituting 95-99% of total haemoglobin,

Haemoglobin E trait may be co inherited with either β0 or β* thalassemia. The severity of compound heterozygotes is variable with clinical picture ranging from β thalassemia minor to thalassemia major.Most patients have moderately severe disease. HPLC shows the presence of HbE. HbA2 and HbF in case of HbE/β0 thalassemia and HbE, HbA, HbA2 and HbF in HbE/β* thalassemia .If HbA is present, it is about 10% of total haemoglobin.

Compound heterozygotes SE- occurs due to co inheritance of βS and βE gene leading to sickling disorder. It usually presents with features of mild chronic haemolytic anemia with rare episodes of vaso occlusive crises or recurrent splenic infarctions, On HPLC HbS represents a larger proportion of total haemoglobin than HbE(about 65%). HbF may be normal or slightly elevated . The disorder was first reported in Eti-Turks by Aksoy and Lehmann[2]. The gene mutations for HbS and HbE are present in all racial and ethnic groups affecting males and females equally. HbE is one of the most common mutations. It is very high among persons from Southeast Asia, especially Cambodia, Laos and Thailand, whose borders are considered the "HbE Triangle". HbE is also found in Vietnam, Malyasia, northeastern India, Bangladesh, Pakistan, Nepal and Sri Lanka. . HbS is more prevalent in people of African, Caribbean, Southeast Asian, Central and South American descendants and in much less frequency in Mediterranean and Middle Eastern people. Both HbS and E hemoglobin traits have evolved as "positive" genetic mutations in areas where malaria is endemic impairing malarial parasite growth and development.

The clinical manifestations and hematologic findings of sickle cell-haemoglobin E disease may vary greatly. All spectrum between completely asymptomatic state to a moderate or severe anaemia, comparable to sickle cell anaemia in severity, can be found. Most of the abnormal haemoglobins are controlled by genes which are alleles of haemoglobin A. Studies have data which are sufficient to suggest that the genes responsible for hemoglobins E, S and A are alleles which are linked.

4. Conclusion

HbE is a variant haemoglobin with a mutation in β globin gene. It may present in heterozygous state (AE or Haemoglobin E trait) and variety of compound heterozygous state such as E/βthal, SE genotype.

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