

Haemoglobin E β +-Thalassaemia. A case report from Bijapur, South India.

Quais Mujawar^{*}, Sadashiva Ukkali, N N Malagi, and AN Thobbi

Department of Pediatrics, Al Ameen Medical College, Bijapur-586108, Karnataka, India

Abstract: Haemoglobin E β -thalassaemia is the commonest form of severe thalassaemia in many Asian countries, but little is known about its natural history, the reasons for its clinical diversity, or its optimal management. In India; it is prevalent in North-Eastern region, but relatively rare in the rest of the country. Identification of this Hb variant thalassaemia is important, because doubly heterozygous state for HbE and β -thalassaemia is characterized clinically by thalassaemia major. Manifestations of E-beta thalassaemia include refractory anemia, splenomegaly and sometimes, unexplained Jaundice. In addition these patients have additional complications like iron overload, hypercoagulable states (post-splenectomy), pulmonary hypertension and cardiopulmonary disease. Thus the affected individual may be symptomatic and transfusion dependent at an early age. Recent studies indicate 40% of patients will clinically improve with hydroxyurea. This paper reports a case with Hb E β + thalassaemia from Bijapur in South India.

Case History

A 5 yr old female with apparently normal parents, only child born out of non consanguineous union presented with history of repeated transfusions (3 total) and intermittent jaundice since birth. On examination the child was found to have growth retardation, thalassaemic facies, splenomegaly and hepatomegaly with pallor. First transfusion was at 18mths of life. Investigations showed a Hb of 5.9, MCH of 21.5, MCV of 50.3 MCHC of 43 & RDW of 26. PS showed anisopoikilocytic RBCs, target cells with few nucleated RBCs and occasional fragmented cells. Hb Electrophoresis showed HbA 28%, HbF 37.3 %, HbA₂ 3.5% and Hb E 31.3%. Considering her history, clinical examination and investigations she was diagnosed as HbE β + thalassaemia. The parents have been advised Electrophoresis and follow up with a Geneticist including option of Antenatal Diagnosis for subsequent pregnancies. We plan to give a trial of Hydroxyurea to the patient.

Discussion

HbE is a variant haemoglobin with a mutation in beta globin gene causing substitution of glutamic acid for lysine at position 26 in beta globin chain. HbE Disease presents in 3 forms namely Heterozygous State (Genotype AE or HbE trait), Homozygous State (Genotype EE or Hb E disease) and Compound Heterozygous States [1 Hb E Beta Thalassaemia (E β Thalassaemia) 2. Sickle Cell / HbE Disease (SE Genotype)]. [1-3]

Pathophysiology is complex which involves ineffective erythropoiesis, apoptosis, oxidative damage and shortened red cell survival. Interaction between Hb E and β -thalassaemia alleles is main determinant in pathophysiology. HbF level is strongest predictor of morbidity. HbE Trait may be co-inherited with either β 0-thalassaemia or β + thalassaemia. [4]

The compound heterozygous state is quite common in Thailand and occurs throughout a large part of SouthEast Asia stretching from Indonesia to Sri Lanka, NorthEast India and Bangladesh with prevalence rate of 30-40%, with very few pediatric cases being reported from India [5-7]

Clinical features range from that of β thalassemia minor through thalassemia intermedia to thalassemia major. Most severely affected individuals are transfusion dependent and have hepatosplenomegaly, intermittent jaundice, growth retardation and overexpansion of bone marrow cavity leading to facial deformity and defective tooth implantation.[1-3]

Less severely affected individuals may have splenomegaly and facial deformity but don't require regular transfusion to maintain life. Hypersplenism may be seen and splenectomy reduces transfusion requirements. Extramedullary hematopoiesis has sometimes led to compression of spinal cord and brain by tumor like masses of hemopoietic tissue leading to paraplegia. Even in non transfused patients iron overload results from increased gastrointestinal absorption of iron Splenectomy can lead to hypercoagulability, thrombocytosis, thromboembolism and pulmonary hypertension. Hemolysis induced nitric oxide deficiency can also occur. Haemoglobin is lower than in HbE disease .Hb Electrophoresis and HPLC show presence of HbE ,HbA₂ and Hb F in HbE/ β 0-thalassemia and HbE ,HbA,HbA₂ and HbF in HbE/ β +thalassemia. HbA when present represents about 10% of total Haemoglobin. It is possible to make diagnosis of E β -thalassemia even in neonates by Haemoglobin Electrophoresis. Prenatal Diagnosis can be done by Chorionic Villous Sampling at 10-12 weeks gestation in couples with identified β -thalassemia and HbE mutations. Special DNA testing can also be done to identify mutation/disease. [8]

Management of HbE β -thalassemia is similar to homozygous β -thalassemia.In those patients with Hb > 7gm% without complications, long term folic acid is recommended. Many may benefit from hydroxyurea therapy which decreases ineffective erythropoiesis and increases Hb with or without increase in HbF .During childhood regular follow of growth and facial deformities, hemoglobin level, prophylaxis of infections causing worsening of anemia with vaccines, treatment of potential infectious sites are essential .Daily oral penicillin is recommended.[9-10]

Indications for regular transfusion are persistently low hemoglobin(Hb <7gm/dl),significant skeletal abnormalities and marked extramedullary hematopoiesis.Complications are usually due to iron overload hence regular iron chelation is recommended.Endocrinopathy secondary to hemosiderosis may require exogenous hormonal therapy .Splenectomy is indicated when there is high transfusion requirement, huge spleen and evidence of hypersplenism. Bone marrow transplantation has very rare indications and high morbidity and mortality.Recombinant erythropoietin alone or associated with hydroxyurea may be useful in reducing transfusion requirements, in improving quality of life and in diminishing hemopoietic ectopic extramedullary masses. Periodic assessment of serum ferritin , calcium, T4, TSH, RBS, LFT etc. aids in proper management .In those with hypogonadism serum testosterone or estradiol levels and bone mineral

density may be required. Complications are mainly due to iron overload causing hemosiderosis, hepatopathy, endocrinopathy and cardiomyopathy leading to right heart failure.[10]

Acknowledgments

The authors wish to thank Dr Mahammad Safi Bagawan and Dr Syed Adnan Anwar, Junior Residents in Department of Paediatrics, Al Ameen Hospital and Dr Mohammed Zakiuddin, Intern, Al Ameen Medical College for their valuable help in preparation of this manuscript.

Consent:

Written informed consent was obtained from the patient for publication of this case report.

Author's contributions:

QMM and SU analyzed and interpreted the patient data regarding the diagnosis and patient management. RN, HP, ANT, and NM were major contributors in writing the manuscript and made substantial contributions to conception and design, and acquisition of data. QMM and SU were involved in drafting the manuscript and revising it critically for important intellectual content and in writing the manuscript. All authors read and approved the final manuscript.

References

1. Weatherall DJ. Introduction to the problem of hemoglobin EB thalassemia. *J Pediatr Hematol Oncol.* 2000;22:551.
2. Fucharoen S, Winichagoon P. Clinical and hematologic aspects of hemoglobin E beta-thalassemia. *Curr Opin Hematol.* 2000;7:106-112.
3. Olivieri, Nancy F.; Muraca, Giulia M.; O'Donnell, Angela; Premawardhena, Anuja; Fisher, Christopher; Weatherall, David J. Studies in haemoglobin E beta thalassaemia. *British Journal of Haematology*, Volume 141, Number 3, May 2008 , pp. 388-397(10)
4. Vichinsky E. Hemoglobin E Syndromes. *Hematology Am Soc Hematol Educ Program.* 2007;2007:79-83
5. Krishnamurti L. Few reports of hemoglobin E/beta-thalassemia in Northeast India: underdiagnosis or complete exclusion of beta-thalassemia by hemoglobin E. *J Pediatr Hematol Oncol.* 2000 Nov-Dec;22(6):558-63.
6. Premawardhena A, De Silver S, Arambepola M, Olivieri NF, Vichinsky EP, Merson L, Muraco G, Allen A, Fisher C, Peto T, Weatherall DJ. Hemoglobin E-beta-thalassemia: Progress report from the International Study Group. *Ann N Y Acad Sci.* 2005;1054:33-9.
7. Agarwal S, Gulati R, Singh K. Hemoglobin E beta thalassemia in Uttar Pradesh. *Indian Pediatr* 1997; 34: 287-292.
8. Phadke S, Agarwal SS. Prenatal diagnosis in beta-thalassemia: an Indian experience. *Fetal Diagn Ther* 2003; 18: 328-332.
9. Kishore B, Khare P, Gupta RJ, Bisht S, Majumdar K. Hemoglobin E disease in North Indian population: a report of 11 cases. *Hematology.* 2007 Aug;12(4):343-7.
10. Doctor Dora Bachir, Professor Frédéric Galacteros, Professor Gilbert Tcherna. Hemoglobin E. <http://www.orpha.net/data/patho/GB/uk-HbE.pdf> (1 Jan 2009)

All correspondence to: Dr. Quais Mujawar, Assistant Professor of Pediatrics, Al Ameen Medical College, Bijapur-586108, Karnataka, India. Email: quais_mujawar@yahoo.com