The Effect of Globalization on Hemoglobinopathies and its Genetic Inheritance: The Booster Effect of Genetic Combinations

O Efeito da Globalização no Paradigma das Hemoglobinopatias e a sua Herança Genética: Combinações Genéticas Potenciadoras

Keywords: beta-Thalassemia; Hemoglobinopathies/epidemiology; Transients and Migrants
Palavras-chave: Hemoglobinopatias/epidemiologia; Migrantes; Talassemia beta

Hemoglobin E (HbE) is a structural β-hemoglobin variant that presents as asymptomatic or mild disease, similar to β-thalassemia minor.[1] The association between HbE and β-thalassemia (HbE/β-thalassemia) has a variable phenotype that can go from asymptomatic or mild anemia to a life-threatening disorder requiring transfusions from an early age.[2] Worldwide, it is more common in Southeast Asia, but it is rarely described in Europe, representing approximately 50% of the clinically severe β-thalassemia disorders.[1] The pathophysiology is similar to other forms of β-thalassemia.[1] Disease severity depends on the type of mutation, the co-inheritance of α-thalassemia and polymorphisms in genes involved in HbF production.[3]

Children are asymptomatic until six to 12 months when HbF is replaced by HbE. Clinical features include anemia, jaundice, hepatosplenomegaly, growth retardation and thalassemic facies.[1] Severe forms manifest as a β-thalassemia major.[1]

We present the case of an 8-year-old girl (Fig. 1) from Bangladesh with microcytic and hypochromic anemia requiring on-demand transfusions since the age of three. Having migrated to Portugal with her family at the age of seven, she was referred by the family physician to our hospital with the diagnosis of a transfusion-dependent hemoglobinopathy without any written medical information. Electrophoresis showed HbA2 4.2% (N: 2 - 3.5), HbF 23% (N: < 2), HbE 31% and HbA 41.8% (N: 95 - 98) (post-transfusion). Gene analysis showed a compound heterozygote for Hb E/β^0-thalassemia (c.79G>A; p.Glu27Lys(HbE)/c.93-1G>C). Because of disease severity (requiring monthly transfusions) and iron overload (liver iron concentration at 91 µmol/g dry weight), she was started on iron chelation therapy and proposed for stem cell transplantation.

Hemoglobin E/β-thalassemia leads to significant clinical heterogeneity, which makes its management particularly challenging. A study in Sri Lanka found a median survival of 49 years.[4] Poor survival was associated with lower hemoglobin, higher serum ferritin and liver iron levels.[4] To our knowledge there are no survival studies in Europe. Studies of β-thalassemia major show 30 year-overall survival ranging from 83.6% to 93.3%, with improved survival in recent years because of regular transfusions, iron chelation therapy, close monitoring of complications, and stem cell transplantation.[5] We can extrapolate that in developed countries these patients might have a similar evolution as β-thalassemia major, if proper treatment is initiated.

The increase in migration has changed the geographic distribution of hemoglobinopathies. The arrival of immigrants to Europe increases the public health burden.[6] In immigrants with severe disease, it is crucial to be aware of hemoglobinopathy associations for an accurate diagnosis and follow-up, including genetic counseling.

AUTHOR CONTRIBUTIONS

CGF, AFL, AS: Literature search and writing of the manuscript.

AF, ER: Critical review of the manuscript.

All authors approved the final version to be published.

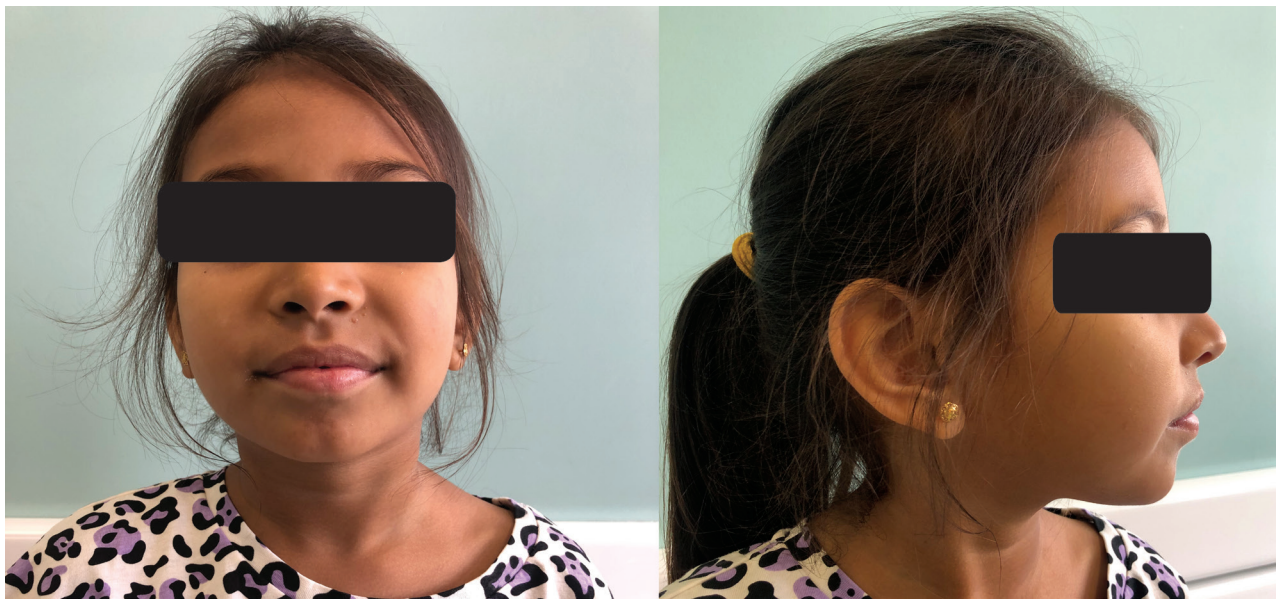

Figure 1 – Patient with HbE/β-thalassemia (characteristic facial features)

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PARENTAL CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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