Thalassemia and bone changes

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ABSTRACT

In Beta-Thalassemia Major or Cooley's Anemia, the accelerated rate of destruction of erythroid cells both in the medulla and in the periphery, strongly stimulating the proliferation and maturation of erythroblasts through renal erythropoietin. Therefore, there is a great expansion of the bone marrow, more than in any other anemia, leading to the classic thalassemic bone deformities, such as: prominence of the jaws (thalassemic face or squirrel face), enlargement of the upper dental arch, with separation of the teeth and frontal bossing. Patients also present with other bone manifestations, such as: pain, growth retardation and bone age, scoliosis, spinal cord compressions, papathological fractures, osteopenia, and osteoporosis. However, osteopenia and osteoporosis seem to be caused by hormonal issues such as hypothyroidism, hypoparathyroidism, diabetes mellitus and hypogonadism, which cause an imbalance in bone remodeling. Objective: To address how thalassemia major acts on bone changes. Method: This is a systematic review of the literature. It was prepared from a bibliographic survey, covering national scientific articles and books, in the last ten years. The databases used were SciELO, Google Scholar, Journal of Pediatrics and pathology books. Discussion: Thus, thalassemia can be correlated with bone loss in children, in addition to chronic anemia and hypoxia associated with pubertal and weight delay, making it lethal in this age group. Conclusion: this study confirms that there is severe bone loss in children with thalassemia major, which reinforces the importance of efficient diagnosis and treatment to improve the quality of life of these patients.

Keywords: Anemia, Thalassemia, Betathalassemia, Osteopenia.

1 INTRODUCTION

Thalassemias are hereditary disorders that have as their basic characteristic a deficiency in the synthesis of globin chains. They have a broad clinical spectrum of presentation, ranging from completely asymptomatic individuals to children with severe anemia, bone deformities, and accelerated destruction of red blood cells. The periods of childhood and adolescence are fundamental for mineral acquisition and bone growth, since the peak of bone mass occurs at the end of the second decade of life. In Betathalassemia Major, there is expansion of the hematopoietic cord, which leads to erosion of the surrounding bone tissue and trabecular resorption.

2 LITERATURE REVIEW

A variety of a and b-globin mutations underlie the development of thalassemias, which are autosomal codominant conditions (ROBBINS, 2013). Adult hemoglobin, or HbA, consists of a tetrameter made up of two a-chains and two b-chains. The a-chains are encoded by two α-globin genes located on chromosome 11, while the b-chains are encoded by a single b-globin gene located on chromosome 16. Clinical features vary greatly depending on the specific combination of mutated alleles inherited by the patient. (ROBBINS, 2013). B0 associated with the total absence of b-globin chains; and B+ characterized by reduced (but detectable) synthesis of b-globin. (ROBBINS, 2013).

Individuals who inherit an abnormal allele have b-thalassemia minor (also called b-thalassemic character), which is either asymptomatic or mildly symptomatic. Most people who inherit b0 and b+ alleles have b-thalassemia major; Occasionally, individuals who inherit two B+ alleles have a milder form of the disease called B-thalassemia intermedia. As opposed to a-thalassemias, gene deletions are uncommon in b-thalassemia. (ROBBINS, 2013).

Beta thalassemia minor/beta-thalassemia trait, carriers are usually asymptomatic but may have mild microcytic anemia and hypochromic anemia, heterozygous beta-thalassemia of the β++ mutation (β++/β) are silent carriers of beta-thalassemia 11 (POLAINAS, 2017). As the name suggests, this type is intermediate between thalassemia minor (not at all severe) and thalassemia major (more severe), with mutations inherited from either the father or the mother, never both. Carriers may present with less pronounced anemia in some cases and more severe anemia in other cases (TRENTO, 2019). Heterozygous (β/β0) or homozygous (β/β) doubles may occur, and symptoms range from asymptomatic to patients with severe clinical conditions, with delayed growth and development. These patients have decreased HbA1c and a 40-70% increase in fetal Hb (JESUS, 2021). Double heterozygosity (β0/β) or homozygosity (β0/β0) occurs when both genes are damaged, this means that they carry the thalassemia gene of each parent. Patients with beta-thalassemia major have the most severe disease and usually require blood transfusions (JESUS, 2021).

Unlike b-thalassemia, a-thalassemia is primarily caused by deletions involving one or more α-globin genes. (ROBBINS, 2013). Two mechanisms contribute to the development of anemia in b-thalassemia. Reduced synthesis of b-globin results in abnormal HbA formation and the production of erythrocytes with a lower amount of hemoglobin, producing pale (hypochromic) and small (microcytic) cells. Even more important is the imbalance between the synthesis of chains a and b; The creation of an excess of A chains without complementary B chains leads to the formation of aggregates of A chains and subsequently insoluble precipitates, which bind to and severely damage the membranes of both erythrocytes and erythrocyte precursors. Most erythrocyte precursors die by apoptosis, a phenomenon called ineffective erythropoiesis; The few remaining erythrocytes produced have a reduced lifespan due to extravascular hemolysis. (ROBBINS, 2013).

The anatomical changes in b-thalassemia major are similar to those observed in other hemolytic anemias, but profound in degree. Ineffective erythropoiesis and hemolysis lead to marked hyperplasia of the erythrocyte parents, with deviation towards the primitive forms. The expanded erythropoietic medulla can completely fill the intramedullary space of the skeleton, invade the bony cortex, impair bone growth, and produce skeletal deformities. (ROBBINS, 2013).

Severe deficiency or deficiency of beta-chain production causes severe anemia, severe microcytosis, and hypochromia associated with some degree of hemolysis, jaundice, progressive hepatosplenomegaly, and general bone changes. These changes result from intense erythroid hyperplasia in the bone marrow in response to intramedullary hemolytic processes 12 (particularly in the spleen) and strong and ineffective erythropoiesis (DOMINGOS, SHIMAUTI and SILVA, 2016).

Ineffective haematopoiesis has another disastrous effect: it is associated with an inappropriate increase in the absorption of iron from the diet, leading to an inevitable iron overload when no medical interventions are carried out. Increased iron absorption is caused by inappropriately low levels of hepcidin, which is a negative regulator of iron absorption. tag. (ROBBINS, 2013).

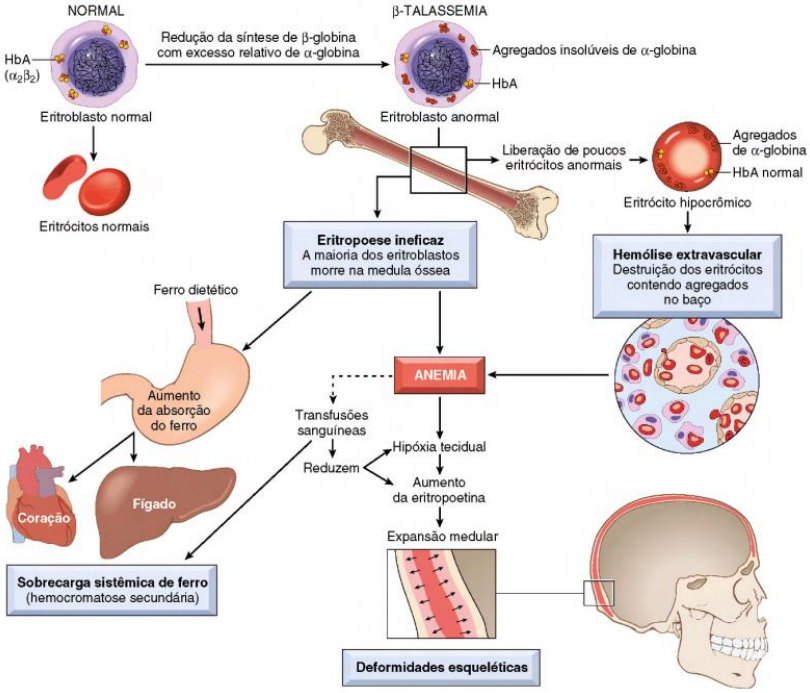
Clinical and Genetic Classification of Thalassemias.

Síndrome Clínica	Genótipo	Características Clínicas	Genética Molecular
β-Talassemias			
β-talassemia maior	β-talassemia homozigota (β^0/β^0, β^+/β^+, β^0/β^+)	Anemia severa; requer transfusões sanguíneas regulares	Principalmente mutações puntiformes que induzem defeitos na transcrição, processamento ou tradução do mRNA da β-globina
β-talassemia intermediária	Variável (β^0/β^+, β^+/β^+, β^0/β, β^+, β)	Anemia severa, porém não exige transfusões sanguíneas regulares	
β-talassemia menor	β-talassemia heterozigota (β^0/β, β^+/β)	Assintomática com anemia leve ou ausente; ocorrência de anormalidades eritrocitárias	
α-Talassemias			
Portador silencioso	$-/\alpha, \alpha/\alpha$	Assintomática; ausência de anormalidade eritrocitária	Principalmente deleções de genes
Caráter α-talassêmico	$-/-, \alpha/\alpha$ (asiáticos) $-/\alpha, -/\alpha$ (negros africanos, asiáticos)	Assintomática, semelhante à β-talassemia menor	
Doença da HbH	$-/-, -/\alpha$	Severa, assemelha-se à β-talassemia intermediária	
Hidropisia fetal	$-/-, -/-$	Letal *in utero* quando na ausência de transfusões	

HgH, hemoglobina H; mRNA, ácido ribonucleico mensageiro.

(ROBBINS, 2013).

Pathogenesis of b-thalassemia major.



(ROBBINS, 2013).

3 FINAL THOUGHTS

After analyzing data and case reports, it is possible to confirm that there is severe bone loss in children with thalassemia major. Expansion of the hematopoietic marrow leads to erosion of the surrounding bone tissue and trabecular resorption. This reinforces the importance of efficient diagnosis and treatment with transfusion and iron chelation to reduce fracture rates and increase bone mass. In order to improve the quality of life of these patients.

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