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OSTEOPETROSIS: CLINICAL AND PHYSIOOGICAL FEATURES

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ABSTRACT

Introduction. Osteopetrosis (Albers-Schonberg disease) is an inherited bone disease characterized by the occurrence of osteoclast dysfunction, this causes bone density to increase, making it dense, hard and brittle. Goal. This is an integrative review in order to answer the following research question: what factors lead the individual to develop osteopothesis. **Methodology**. The search was performed in the following databases and online libraries: Pubmed, Medline and SciELO. **Results** and discussion. Osteopetrosis is a disease caused by gene mutations, which manifests itself mainly in two classifications: of recessive (malignant) and dominant (benign) type, its main diagnostic methods are radiographic analysis and histopathological exams. In both disease classifications some biochemical and physiological characteristics are altered as bone matrix components, genes, hormones and cells in the blood tissue causing both abnormal proliferation and the malfunctioning of cell members responsible for bone maintenance. **Conclusion**. Since it is a condition that has serious health consequences, osteopetrosis is still little known in the medical and social spheres. Thus, it is of fundamental importance that there is greater dissemination of research on this disease so that there is an increasingly early diagnosis and, thus, minimize its consequences and to establish an increasingly concise and efficient treatment plan.

Keywords: Osteopetrosis, osteosclerotic fragility, Diagnosis, Osteoclasts.

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INTRODUCTION

Osteopetrosis (Albers-Schonberg disease) is a rare hereditary bone disorder characterized by the occurrence of osteoclast dysfunction, which causes an increase in bone density, making them hard and brittle[1]. This abnormal development of bone tissue occurs mostly in white male individuals. Individuals with the disease may present clinical complications that interfere with the patient's well-being, because osteopetrosis leads to disorders such as anemia development, decreased platelet count, increased lymph and liver ganglion, low immunity and mainly neuropsychomotor problems[2].

Osteosclerotic frailty has several classifications, one of them being early osteopetrosis, of autosomal recessive character, which can be diagnosed even during the intrauterine and postnatal period. It is the most lethal and recurrent form of this disease, since it demonstrates among its main clinical features hearing loss and optic atrophy (loss of optic nerve fibers) due to compression in the nerves related to these functionalities. In addition to these complications, bone marrow problems, balance, tooth eruption delay, facial paralysis, pathological fractures can also arise and affect the patient's well-being[3].

Other classifications that characterize this condition are: late autosomal dominant osteopetrosis, caused by defects in the chloride channel 7 gene (CLCN7), which manifests itself as the milder case of the disease, may appear in different age groups, but has a predominance in older individuals. Its diagnosis is made through a genetic mapping that will detect the presence or absence of genes that characterize this abnormal development of bone tissue. In addition to this diagnostic method, it is also detected from radiographic images, which show the typical bone characteristics of the disease, such as the appearance of bone within the bone caused by increased bone density in these individuals[1]. Likewise, other possible classifications of the disease occur with intermediate recessive ospetrosis and tubular acidosis osteopetrosis. In these cases, the individual has frequent bone fractures and a moderate case of anemia, and there may or may not be an increase in hepatosplenomegaly[1.4]

Bone tissue is a highly living tissue that is formed by numerous cell types, among which osteoblasts and osteoclasts can be highlighted. Osteoblasts are cells responsible for the production and deposition of organic components of the bone matrix, while osteoclasts are important bone tissue cells in tissue resorption and remodeling. In individuals with osteopetrosis, osteoclast cells do not function optimally, which is significantly reduced, resulting in increased Ca^{2+} (Calcium) deposition inside the bones, causing biochemical and structural modifications of this bone. which become more disorganized and thus more susceptible to fractures[8]. Albers-Schonberg disease is a disease directly related to the bone marrow, because this bone dysplasia is characterized by the permanence of the primary cartilage that becomes calcified, which causes the filling of the medullary cavity, making it impossible to accommodate the bone marrow in this space. Thus, individuals with this genetic condition tend to have cases of severe anemia and thrombocytopenia, as there is a malfunction of the production of hematopoietic lineage cells produced in the red bone marrow[10]

Because it is a rare disease with low information dissemination in society, it is worth highlighting the importance of diagnosis, and disseminating the causes and consequences of this pathology in children by making an informational survey about the differences in biochemistry and physiology between children with and without those who do not have the disease. Thus, the aim of this paper is an integrative review in order to answer the following research question: What factors lead the individual to have osteopetrosis, highlighting its diagnosis and the biochemical

and physiological characteristics that a patient with disease.

METHODOLOGY:

The data search was performed in the following databases and online libraries: Pubmed, Medline and SciELO. For this, the following health descriptors were listed: Osteopetrosis, frailty osteosclerosis, diagnosis and osteoclasts in Portuguese and English. The inclusion criteria were: complete articles published in the last 17 years, in the Portuguese and English languages and that answered to the research question. We found 34 articles. After applying the inclusion criteria, 14 were selected, which made up the study sample and then proceeded to the exploratory reading of all material.

RESULTS AND DISCUSSION

Osteopetrosis is a disease caused by gene mutations that manifests itself mainly in two classifications: recessive (malignant) and dominant (benign) diagnostic analyzes by radiographic characteristics and histopathological exams. In both disease classifications some biochemical and physiological characteristics are altered as bone matrix components, genes, hormone and blood tissue cells causing both abnormal proliferation as well as the malfunction of cellular members responsible for the bone maintenance[1]. Given this, it is possible that individuals with this genetic condition develop systemic abnormalities such as: anemia, psychomotor problems of visual relationship, hearing and balance, restriction of range of motion, among others[10,2,12].

Genes

Most of the problems related to osteopetrosis alter the development of structural and biochemical modification of osteoblasts. Osteopetrosis is directly related to some genes, because when they are changed they end up developing situations in which the individual is affected by the disease, expressing, therefore, the characteristics of this disease. Beyond Mutation in genes such as CLCN7, TCIRG1 and CA2, hormonal alteration is also shown to be a factor that leverages osteopetrosis. The CA2 gene encodes the carbonic anhydrase enzyme 2, thus a mutation in this gene causes the proton pump to fail, this gene is essential for activating cells osteoclasts, leading to bone resorption and osteoclasts. The absence of CA2 results in the inhibition of acidification of the resorption bone gap. As well as in the process of dissolving hydroxyapatite from osteoclasts causing osteopetrosis occurs. Thus, there is kidney and urine impairment, where the kidney has its affected capacity and acidified urine, leading to kidney damage and calcification in the brain[1,4]. Also, alteration of the CLCN7 gene also causes modification in the proton pump, as the mutation it causes the lack of chloride channel 7 protein, causing it not to work. The interference in this gene causes damage to the central nervous system and consequently leads to problems of intellectual disability. Another gene that is altered and causes osteopetrosis is TCIRG1, which encodes a proton pump component as a result of this mutation the individual with have hypogammaglobulinemia, a change in humoral immunity- immunity subdivision in which the immune response is carried out by antibodies - which causes the carrier of this problem has a susceptibility to bacterial infections mainly in the respiratory tract[1,4].

Osteoblasts and Osteoclasts

Osteoblasts are cladding cells and are located in the Bone surfaces, these cells synthesize, transport and organize various matrix proteins. While osteoclasts are cells responsible for bone resorption, they are derived from same hematopoietic progenitor cells, which also give rise to monocytes and macrophages. In individuals with osteopetrosis, it is noted that the function of osteoblastic cells occurs normally, but a process of osteoclast deficiency is noticed, which results in inability of the organism in bone resorption and remodeling. This situation changes the

composition biochemistry of bone tissue leading to calcium (Ca^{+2}) accumulation in tissue excessive mineralized steroidal material as well as poor bone structure modeling. Of that Thus, bones become dense, sclerotic and radiopaque and more susceptible to the development of multiple fractures[5,6,7].

Anemia

Anemia is a disease characterized by the amount of red blood cells below the level

normal or inefficient hemoglobin oxygen transport to meet Physiological In individuals with osteopetrosis, anemia is one of the consequences biophysiological diseases that cause more problems for the health of lead the patient to develop other problems such as: thrombocytopenia - decreased amount of platelets in the blood - hepatosplenomegaly, that's why the compartments that produce the cells of blood lose their erythropoietic spaces by invasion of osteoid substance, with this there is a difficulty in optimal production of blood cells as well as blood. Thus, the Individuals with osteopetrosis who have anemia should have a nutritional education based on ingestion of foods rich in substances that help in the treatment of this disease. Foods rich in vitamins and iron such as meat, fruits and vegetables are of crucial importance to the health evolution of patients with this physiological condition. (11)

Neuropsychomotor problems

The nervous system is one of the main functional systems of the organism and has the function of capturing information, messages and other external stimuli to promote an interpretation and response of the stimuli to which the individual is exposed. This anatomical system is one of the main components affected by osteopetrosis, because this dysplasia has the characteristic of in the patient who has the disease, a relative increase in bone thickness and density. This increase in bone density, especially of the skull, causes compression of the optic nerves, and hearing that have a sensitive character. Thus, the increase in bone thickness generates a gradual pressure on these nerve structures, which generate problems related to vision and hearing, which are irreversible[13,14].

In addition, neuropsychomotor impasses also characterize this bone dysplasia, which occurs when the individual is not developing or does not reach skills according to a data sequence predetermined. People with osteopetrosis have learning difficulties and delays maturatives, which results in a delay in the intellectual development of this person. That failure in psychomotor development is lacking and causes problems, especially for patients with child age, as the consequences will be carried to future years of this child's life. The patient with neuropsychomotor problems is dependent on professionals and caregivers to assist in everyday situations that a healthy person could handle without difficulty. Some activities they are used for neuropsychomotor development such as motor, body games, communication stimuli and personal contact with the use of words, etc[13,14].

Bone marrow transplant

As presenting as a typical characteristic of the disease the difficulty of some cells of bone tissue, the bone structures, especially those linked to the development of cells and blood lineage components - hematopoietic marrow - suffer from intense repressions regarding its performance and cellular function. That way it becomes It is common to observe that individuals with this type of bone dysplasia have high chances of develop complications related to the blood system, such as presenting with anemia, thrombocytopenia, among others. In such cases, the use of measures aimed at ensure the minimization of this problem, such as the adoption of bone marrow transplantation compatible individuals in order to have a quantitative increase in red blood cells, white blood cells and platelets to develop bone remodeling in the bone from the generation of functional osteoclasts[9]

CONCLUSION

Osteoetrosis is a genetic modification that is associated with numerous factors and brings with it physical, biochemical, social and physiological sequelae to the individual with this disease. Although as a condition that has serious health consequences, osteopetrosis disseminated in the medical and social sphere. thus, it is of fundamental importance that there is a greater dissemination of research on this disease so that there is an increasing diagnosis minimize its consequences and to establish a treatment plan each year more concise and efficient.

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