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Hunter's Syndrome and Oral Manifestations

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Abstract

Hunter's syndrome is a mucopolysaccharidosis that compromises cell function and generates tissue accumulations of glycosaminoglycans, which can lead to death, especially in severe forms. However, patients generally reach adulthood, in a way that emphasizes the need for medical and dental care in this period in the face of changes, which commonly include: progressive cognitive limitation, breathing difficulties due to pulmonary and airway disorders, and cardiac and skeletal disorders. It is noticed mainly difficulty in mouth opening, dental positioning, and bone configuration alteration in dental practice. Enzyme replacement therapy effectively reduces urinary glycosaminoglycans and the volume of the liver and spleen. In contrast, cardiac and joint results are variable and are generally unsatisfactory about the heart valves, trachea and bronchi, hearing, and eyes. The follow-up is multidisciplinary, and in dental practice, the concern is with breathing difficulties and limited mouth opening, which can make it difficult to treat oral needs that are not necessarily related to the syndrome..

Keywords: Hunter's Syndrome; Mouth Opening; Respiratory Disorder; Heart Disorder

Introduction

Mucopolysaccharidosis type II or Hunter syndrome (HS) is a multisystemic, progressive, X-linked disorder caused by deficiency of the lysosomal enzyme urinate-2-sulfatase [1]. This deficiency results in the accumulation of glycosaminoglycans in most cells, tissues, and organs, causing the volumetric increase and cellular physiological changes [2].

Its incidence is 1:100,000 but varies greatly between populations, it mostly affects men and is characterized by great clinical variety concerning phenotypes and genotypes. Signs and symptoms include facial dimorphism, joint stiffness, skeletal abnormalities, hepatosplenomegaly, cardiac and cardiovascular disorders, developmental delay, and deterioration of intellectual function, with treatment being palliative or supportive [2,3].

Characteristics of the Syndrome

HS can present itself in two forms, severe or mild. Approximately two-thirds of affected individuals present the severe form characterized by progressive clinical deterioration with neurological involvement, multiple dysostosis including joint stiffness, coarse facial features

with a wide nose, and macroglossia with involvement of the cardiac, pulmonary, and central nervous systems; These patients also present varying degrees of behavioral disorders, such as hyperactivity, aggression, impulsivity, anxiety, and sleep disorders. Patients with milder forms of the disease may or may not present neurological involvement, being minimal when present, and are characterized by joint stiffness and mild somatic changes [1,4,5]. Death usually occurs in the second decade of life for patients with the severe form, while patients with the mild form usually survive into adulthood [6].

Respiratory organ involvement is the leading cause of death in Hunter syndrome, particularly in younger patients, but the contribution of cardiac causes may be substantialan X-linked metabolic disorder caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase.\nSTUDY DESIGN: The Hunter Outcome Survey was established to characterize the natural history of Hunter syndrome and to assess the response to enzyme replacement therapy. Echocardiographic and electrocardiographic examination results were available for 102 patients who were enzyme replacement therapy-naïve in the Hunter Outcome Survey (median age at examination, approximately 8 years. Respiratory problems are a consequence of the progressive deposition of glycosaminoglycans in the soft tissue of the throat and trachea, and abnormalities in the shape and structure of the ribs, enlargement of the abdominal organs, short neck, and immobile jaw also contribute to the condition [7]which characterize the syndrome. Other physical characteristics, including abnormalities in the shape and structure of the ribs, abdominal organ enlargement, short neck and immobile jaw, further contribute to the respiratory problems. New measurement systems specifically tailored to paediatric patients now allow clinicians to follow the progressive deterioration of lung function, which was previously challenging in this population. Sleep apnoea is another common feature of Hunter syndrome, which can lead to a reduction in oxygen saturation of the blood and severely disrupts sleep. In our clinic, continuous positive airway pressure (CPAP.

Hunter Syndrome, also known as Mucopolysaccharidosis type II (MPS II), is a rare genetic disease that mainly affects boys. It manifests itself due to a deficiency of the enzyme iduronate-2-sulfatase, resulting in the accumulation of glycosaminoglycans in body tissues.

Age Ranges of Manifestation

Early Childhood

Onset of symptoms: Symptoms generally begin to appear between 2 and 4 years of age. However, in some cases, signs can be observed even earlier, during the first year of life.

Severity of Symptoms

Severe Form (Severe Hunter Syndrome)

- Neurological Development: Progressive mental retardation, with deterioration of cognitive and behavioral skills.
- Growth: Short stature, with growth interrupted after the first few years.
- Respiratory System: Frequent respiratory infections, sleep apnea.
- Skeletal System: Skeletal deformities, such as bone dysplasia, and joint stiffness.
- Cardiac System: Cardiomyopathy, valvulopathy, arterial hypertension.
- Life Expectancy: Reduced, often not exceeding the second or third decade of life.

Mild Form (Mild Hunter Syndrome)

Neurological Development: Intelligence is generally normal or slightly affected.

Growth: Delayed growth, but less severe than in the severe form.

Respiratory System: Less susceptible to respiratory infections, sleep apnea may be present.

Skeletal System: Skeletal deformities may be present but are less severe.

Cardiac System: Heart problems may be present, but tend to be less serious.

Life Expectancy: Can reach adulthood, although with varying quality of life depending on the severity of the symptoms.

The presentation and progression of Hunter Syndrome can vary significantly from one individual to another, even within the classifications of mild and severe forms.

Dental Features

Among the oral changes present in patients with HS are: diastema, open bite, posterior crossbite, narrow and deep palate, wide and flat palate, malocclusion, impacted teeth, ectopic teeth, and thick lips [8]. Late eruption of dental elements is associated with areas of bone involvement that resemble dentigenous cysts and are present mainly in the first permanent molars [9]. X-linked disorder caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase. In the absence of sufficient enzyme activity, glycosaminoglycans accumulate in the lysosomes of many tissues and organs and contribute to the multisystem, progressive pathologies seen in Hunter syndrome. The nervous, cardiovascular, respiratory, and musculoskeletal systems can be involved in individuals with Hunter syndrome. Although the management of some clinical problems associated with the disease may seem routine, the management is typically complex and requires the physician to be aware of the special issues surrounding the patient with Hunter syndrome, and a multidisciplinary approach should be taken. Subspecialties such as

otorhinolaryngology, neurosurgery, orthopedics, cardiology, anesthesiology, pulmonology, and neurodevelopment will all have a role in management, as will specialty areas such as physiotherapy, audiology, and others. The important management topics are discussed in this review, and the use of enzyme-replacement therapy with recombinant human iduronate-2-sulfatase as a specific treatment for Hunter syndrome is presented.

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Furthermore, according to the study of Khan, et al. [10] SH possibly causes disturbances in the organization of enamel crystallites, making the tooth structure weak and subject to fractures.

On radiographic examinations, a short mandibular ramus, condylar defect, wide coronoid process, wide mandibular base, and malformed glenoid cavity are usually present.

Diagnosis

The diagnosis is made based on the patient's clinical manifestations and on the quantitative and qualitative biochemical analysis of the concentration of glycosaminoglycans in the urine, for confirmation, the IDS enzyme activity is measured. The IDS gene genetic test is used in prenatal diagnosis of families with a history.

Treatment

Treatment of SH mainly involves developmental, occupational, and physical therapy; maneuvers for hydrocephalus; tonsillectomy and adenoidectomy; continuous positive ventilation or continuous tracheostomy; carpal tunnel release; heart valve replacement; inguinal hernia repair; and hip relocation, when symptoms manifest [11]; in addition to hematopoietic stem cell transplantation and enzyme replacement therapy (ERT).

Unfortunately, the enzyme used in ERT is not able to cross the blood-brain barrier, therefore it does not affect cognitive decline. ERT is effective in reducing urinary glycosaminoglycans and liver and spleen volume, while cardiac and joint results are variable; its effectiveness on heart valves, trachea and bronchi, hearing and eyes is not satisfactory. In the end, all patients end up developing antibodies against the drug, but their role in the tolerance and effectiveness of ERT is not yet well defined [12].

As a consequence of anatomical and pathological changes in the upper airways, every general anesthesia procedure, especially intubation, is a difficult and high-risk procedure, therefore such procedures must be performed by an anesthetist, preferably accompanied by a pediatric pulmonologist/intensivist with experience in treating patients with HS.

Medications such as antipsychotics, benzodiazepines, and anticonvulsants have been tried to control behavioral disorders, with varying degrees of improvement.

Dental Treatment

Dental care for patients with HS is complicated even when carrying out simple procedures, the limited maximum opening of the jaw worsens visualization, making it difficult to apply anesthesia and use dental instruments. In patients with a severe form of the disease, it may be necessary to use general anesthesia, which in itself already presents a risk in these cases. Surgical procedures are even more complex because of the short neck, bone density, and inelasticity of soft tissues.

The confirmatory diagnosis of Hunter Syndrome (Mucopolysaccharidosis type II) involves a combination of clinical, laboratory, and genetic tests.

- **Analysis of Glycosaminoglycans (GAGs) in Urine:**
  Initial test that measures levels of GAGs in urine.
  Elevated levels of dermatan sulfate and heparan sulfate are indicative of MPS II.

Objective: Identify the excessive presence of GAGs that accumulate due to enzyme deficiency.

- **Enzyme Activity Test:**

Description: Measurement of the activity of the enzyme iduronate-2-sulfatase in leukocytes, fibroblasts or plasma.
Objective: To confirm the deficiency of the enzyme

iduronate-2-sulfatase, characteristic of Hunter Syndrome.

- **Genetic Analysis:**

Description: Sequencing of the IDS gene (iduronate-2-sulfatase) to identify specific mutations.
Objective: Confirm the diagnosis by identifying disease-causing mutations. This test is particularly useful for prenatal diagnosis or in familial cases.

- **Imaging Exams (optional):**

Description: X-rays, magnetic resonance imaging (MRI), or computed tomography (CT) to evaluate skeletal abnormalities and other complications.
Objective: To assess the degree of involvement of organs and systems, although not confirmatory, they can support the clinical diagnosis.

These combined tests help confirm the diagnosis of Hunter Syndrome and differentiate it from other mucopolysaccharidoses and similar diseases.

Discussion

The difficulties encountered in the treatment given to patients with HS will be directly influenced by its form. Patients with the mild form of the disease are characterized by joint stiffness and mild somatic changes, which associated with the short mandibular ramus, condylar defect, wide coronoid process, wide mandibular base and malformed glenoid cavity limits the maximum opening of the mandible, making it difficult to perform any procedure. in mouth.

A severe form has a progressive clinical deterioration with neurological involvement, which leads to varying degrees of behavioral disturbances, and impairment of the cardiac, pulmonary, and central nervous systems. Controlling behavioral disorders can be attempted with the use of antipsychotic medications, benzodiazepines and also the use of behavioral management strategies, although their efficiency is not yet clear in the literature for these cases. Due to the association of these disorders and the aforementioned limitation of mouth opening, it may be necessary to use general anesthesia which, due to the anatomical changes in the respiratory system, needs to be performed by at least one anesthetist with experience in this group of patients, making it even more laborious to carry out the procedures [13].

Conclusion

Patients with Hunter syndrome experience various systemic changes, which can be more severe in their severe form or milder in their mild form. Understanding the characteristics of each manifestation is extremely important because this knowledge allows for the development of an appropriate plan that considers all the limitations present in these cases, enabling adequate treatment of oral changes.

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