Errores innatos del metabolismo. Reporte de cuatro casos con mucopolisacaridosis tipo I, II y VI en tres familias

Inborn errors of metabolism. Report of four cases with type I, II and VI mucopolysaccharidosis in three families

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Resumen

Se reportan cuatro casos de mucopolisacaridosis (**MPS**) en tres familias. Una de las familias presenta dos hijas afectadas con la variante de síndrome de Hurler, otra familia con el síndrome de Hunter y la ultima familia con un hijo con síndrome de Maroteaux-Lamy.

Las **MPS** son un grupo de trastornos hereditarios causados por la degradación y acumulación de mucopolisacáridos ácidos. Las manifestaciones clínicas son consecuencia del depósito de mucopolisacáridos en varios órganos. En todas las mucopolisacáridosis se han identificado el déficit de la enzima lisosómica degenerativa específica.

Las mucopolisacáridosis (**MPS**) se heredan de forma autosómica recesiva, a excepción del síndrome de Hunter que se hereda como rasgo recesivo ligado al cromosoma X. Estos procesos se sospechan por sus manifestaciones clínicas y radiológicas, y el pronóstico se confirma mediante el hallazgo de un aumento de la excreción urinaria de mucopolisacáridos y el déficit de la enzima específica, asi como las complicaciones clínicas

inherentes a la patología de base del tipo de mucopolisacaridosis que se trate y los órganos que se encuentren afectados por este padecimiento. Este tipo de alteraciones lisosomales son progresivas. Sin embargo el tratamiento nutrimental es muy importante para el control y disminución en la acumulación lisosomal de **MPS**. También importante mencionar que ya existe tratamiento médico enzimático para algunas de las **MPS** y se encuentran dentro de las enfermedades que el gobierno apoya para los pacientes que manifiestan este tipo de enfermedades lisosomales.

Palabras clave: Mucopolisacaridosis, tamiz metabólico, genética, errores innatos del metabolismo.

Abstract

Four cases of mucopolysaccharidosis (MPS) are reported in three families. One family has two daughters affected with variant of Hurler's syndrome, another family with Hunter syndrome and the last family with a child with Maroteaux-Lamy syndrome.

The MPS are a group of inherited disorders caused by degradation and accumulation of acid mucopolysaccharides. Clinical manifestations result from the deposition of mucopolysaccharides in various organs. All MPS has identified specific deficit degenerative lysosomal enzyme.

Key Words: Mucopolysaccharidosis, metabolic screening, genetic, inborn errors of metabolism.

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Introduction

Mucopolysaccharidoses (MPS) belong to the family of hereditary disorders caused by deficiency of lysosomal enzymes necessary for the degradation of glycosaminoglycosans, also called mucopolysaccharides, which are stored in lysosomes and/or excreted in the urine (table 1). (Spranger J. 1972, Sly WS 1980, Hurtado H et al, 2009).

Since the first clinical description by Maroteaux (Maroteaux et al, 1963, 1982), Hunter (Young ID et al 1982a, 1982b, 1983) and Hurler (Donaldson MDC et al 1989, Stephan MJ et al 1989), this genetic disorder is It is evident that different anomalies can be recognized that reflect metabolism disorders, which produce a visceral storage of dermatansulfate and heparinsulfate, respectively; there is also an excessive storage of gangliosides Gm1, Gm2 and Gm3 in the brain (Kytzia HJ and Sandhoff K 1985, Constantopoulos G and Dekaban AS 1978, Constantopoulos G et al 1978).

The general clinical features of this group of disorders are short stature, skeletal deformities, restriction of joint movement, deafness, abdominal hernias, hepatosplenomegaly, cardiac anomalies, and usually mental retardation.

The amount of mucopolysaccharides excreted in the urine may be increased or within the normal limit depending on the type of mucopolysaccharidosis.

Based on clinical, genetic and biochemical studies, 6 types and a classification developed by McKusick in 1972 have been outlined (table No 1)

TYPE I. HURLER SYNDROME.

This autosomal recessive disorder was described in 1919. The primary defect is a lack of L-iduronidase in all tissues.

It is associated with mental and physical deterioration in the neonatal period, the diagnosis is usually made in the first year of life, and the clinical features include:

Gargoloid facies, with coarse features, lumbar hump, hydrocephalus, joint stiffness, claw hands, excessive hair, early and progressive clouding of the cornea, and mental retardation. Dermatan sulfate and heparan sulfate are found in excessive amounts in the urine. Development and growth are markedly impaired, leading to death in childhood.

Cardiomyopathy associated with endocardial fibroelastosis has been observed (Donaldson MDC et al 1989, Stephan MJ et al 1989).

TYPE II. HUNTER'S SYNDROME.

This X-linked recessive disorder is generally less severe than Type I. Clinical features include joint stiffness, dwarfism, hepatosplenomegaly, and macrofacial appearance. Similarly, dermatan sulfate and heparan sulfate are increased in the urine. The features that distinguish Type II are: absence of hump, clear corneas, deafness and mental retardation are not as deep as in the previous one, but progressive. (Young ID et al 1982, Young ID et al 1982, Young ID 1983) and affected males usually live to adulthood and die of respiratory infection or cardiovascular complication.

TYPE VI. MAROTEAUX-LAMY SYNDROME.

Growth retardation is the dominant feature of this autosomal recessive disorder, first described in 1963 as a deficiency of a lysosomal enzyme called N-acetylgalactosamine 4-sulfatase (Maroteaux et al, 1963, 1982).

The clinical manifestations described are dwarfism with decreased trunk and stroke, genu valgum, lumbar kyphosis, anterior sternal protrusion and corneal cloudiness. Although other general features are manifested, the distinguishing features are: Normal intelligence and severe bone abnormalities. Increased amount of dermatan sulfate is found in urine. Metachromatic inclusions are seen in all types of white blood cells in peripheral blood. Life span is shortened due to progressive cardiovascular impairment.

Methods

There are three families, one of them has two sisters one year apart affected with Hurler syndrome or MPS type I (patient No 1 and 2, respectively), another with a son affected with Hunter syndrome or MPS type II (patient No 3) and a last family with a son affected with the variant of Maroteaux-Lamy syndrome or MPS type VI (patient No 4). The patients

were treated at the Hospital in a multidisciplinary manner by the different pediatric subspecialties.

GENETICS SERVICE

QUANTIFICATION OF MUCOPOLYSACCHARIDES IN URINE. (CETYL-PYRIDIUM CHLORIDE METHOD)

SAMPLE COLLECTION: Post-prandial urine was collected from the four patients 1 or 2 hours after ingestion of a protein-rich meal that includes milk, in order to overload the patient's metabolism and make the urine clearer and more evident. biochemical test.

REAGENTS:

1-Sodium citrate buffer pH 4.8

2-Cetyl Pyridium Chloride Reagent

3-Chondroitin sulfate standard solution

PROCESS:

1. Filter problem urine on No. 40 Watman paper.
2. Determine the creatinine concentration by making a 1:10 dilution
3. Label the tubes as Blank and Problem
4. In the white tube add 1ml. of filtered urine plus 1ml. of sodium citrate buffer.
5. In the problem tube 1ml. of filtered urine plus 1ml. of the cetyl pyridium chloride reagent.
6. Mix and wait 5 minutes.
7. Read in transmittance at 680nm.
8. Express the result in CCP units (cetyl-pyridium chloride), or in CCP units per gram of crestinine.

INTERPRETATION:

The concentration of urinary mucopolysaccharides is related to age:

EDAD	***VALORES DE REFERENCIA.***

MENOS DE 1 AÑO DE EDAD	HASTA 375 unidades
MENORES DE 9 AÑOS	HASTA 175 unidades
MAYORES DE 9 AÑOS	HASTA 85 unidades
ADULTO	

INTRODUCTION

In 1900, the first case of mucopolysaccharidosis (MPS) was described by John Thompson, in Edinburgh, and work was done on genetic counseling in MPS. The first publication was made by Charles Hunter in 1917: he described two patients with short stature, coarse facies, inguinal hernia, noisy breathing, no corneal opacity. In 1946, Nja clarified that this description corresponded to an X-linked MPS and was called Hunter syndrome.

In 1919, Gertrud Hurler published the clinical history of patients with findings similar to those of Hunter who additionally had corneal opacity and mental retardation. In 1952, Brante isolated the mucopolysaccharide dermatan sulfate from the liver of two patients with Hurler syndrome, receiving these diseases the name of MPS. Dorman and Meyer discovered mucopolysaccharidiuria and established that it corresponded to a defect in the metabolism of glycosaminoglycans. Van Hoof and Hers in Belgium, using electron microscopy studies, found lysosomal abnormalities.

In the 1960s, the glycosaminoglycans dermatan and heparan sulfate were identified in the urine of patients with Hurler, Scheie, and Hunter syndromes; heparan sulfate in Sanfilippo syndrome; keratan sulfate and chondroitin sulfate in Morquio syndrome and dermatan sulfate in Marotaux-Lamy syndrome.

Mc Kusick et al in 1971 proposed the numerical classification based on the type of glycosaminoglycan excreted in the urine and the predominant clinical features.

Subsequently, this classification has been modified due to the identification of deficient enzymes in each disease.

EPIDEMIOLOGY AND INHERITANCE

MPS are a group of inherited disorders caused by the degradation and accumulation of acidic mucopolysaccharides. The clinical manifestations are a consequence of the deposition of mucopolysaccharides in various organs. Deficiency of the specific degenerative lysosomal enzyme has been identified in all MPS.

MPS are inherited in an autosomal recessive manner, with the exception of Hunter syndrome, which is inherited as an X-linked recessive trait. These processes are suspected by their clinical and radiological manifestations, and the prognosis is confirmed by the finding of an increased urinary excretion of mucopolysaccharides and the deficit of the specific enzyme, as well as the clinical complications inherent to the underlying pathology of the type of MPS in question and the organs that are affected by this condition

MPS therefore belong to the family of hereditary disorders caused by deficiency of lysosomal enzymes necessary for the degradation of glycosaminoglycosans, also called mucopolysaccharides, which are stored in lysosomes and/or excreted in the urine (Table 1). (Spranger J. 1972, Sly WS 1980).

Since the first clinical description by Maroteaux (Maroteaux et al, 1963, 1982), Hunter (Young ID et al 1982a, 1982b, 1983) and Hurler (Donaldson MDC et al 1989, Stephan MJ et al 1989), this genetic disorder is It is evident that different anomalies can be recognized that reflect metabolism disorders, which produce a visceral storage of dermatansulfate and heparinsulfate, respectively; there is also an excessive storage of gangliosides Gm1, Gm2 and Gm3 in the brain (Kytzia HJ and Sandhoff K 1985, Constantopoulos G and Dekaban AS 1978, Constantopoulos G et al 1978).

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PHYSIOPATHY OF THE GLYCOSAMICA.

Glycosamicans (GAGs) are products of cellular degradation of proteoglycans, which constitute the macromolecular forms of GAGs in the extracellular matrix. The main proteoglycans degraded in cellular lysosomes are dermatan sulfate, heparan sulfate, keratan sulfate and chondroitin sulfate, in whose catabolic pathways the enzymes whose deficiency gives rise to the different MPS participate

DEGRADATION OF DERMATAN SULFATE

Dermatan sulfate is formed by sulfated N-acetylgalactosamide with uronic and glucuronic acid residues. The degradation of this proteoglycan is due to the action of 5 enzymes, 3 glycosidases and 2 sulfatases.

Alpha-L-iduronidase, deficient in MPS I, is a monomeric glycosidase of 653 amino acids with a molecular weight of 74 KDa that hydrolyzes the terminal residues of alpha-L-iduronic acid. Its gene is located on chromosomal region 4p 16.3 and has 14 exons. MPS 7 deficient beta-glucuronidase is a glycosidase of 651 amino acids and 75 KDa that in active form is made up of 4 subunits (tetramer). Participates in the elimination of glucuronic acid residues present in dermatan sulfate. It was the first enzyme to be located at the chromosomal level; its gene is in the 7q 21.11 region and its complete sequence is known. The third glycosidase is beta-hexosaminidase, whose deficiency does not lead to MPS but to glanguiosidosis, SANDHOFF's disease.

The first sulfatase in this chain is the MPS II deficient iduronate sulfatase, which has 550 amino acids and is involved in removing the sulfate group at position II of iduronic acid. The gene that encodes this enzyme is located in the distal region of chromosome X (XQ28), has 9 exons and 8 introns and is 24 Kb long. The other sulfatase is arylsulfatase B, deficient in MPS 6, which is made up of 533 amino acids. and participates in the hydrolysis of sulfate groups in position 4 of N-acetylgalactosamine that forms dermatan sulfate. Its gene is located in the 5Q region 11-13.

DEGRADATION OF HEPARAN SULFATE.

Heparan sulfate is composed of glucuronic L-hyduronic acids, some sulfated, and alpha-glucosamine, sulfated or acetylated. In its degradation, 3 glycosidases, 4 sulfatases, and an acetyl transferase participate. 2 glycosidase also participate in the degradation of dermatan sulfate, alpha-L-idurodinase and beta-glucuronidase. The third is the MPS II-deficient alpha-acetyl glucosaminidase and participates in the elimination of N-acetylglucosamine from heparan sulfate. It is a protein of 743 amino acids whose gene is located in the 17 Q21 region, occupying an extension of about 9kb.

Of the sulfatases, iduronate sulfatase (MPS II) has already been mentioned in the degradation of dermatan sulfate. Heparan N-sulfatase, deficient in MPS III–A, removes sulfate (sulfamate) groups from glucosamine. Its gene is located in the 17q25.3 region. N-acetylglucosamine 6-sulfatase, deficient in MPS III-D, removes sulfate groups from N-acetylglucosamine and its gene is located on chromosomal region 12q14.

KERATAN SULFATE DEGRADATION.

Keratan sulfate is the only GAG that does not contain uronic acid. It is made up of galactose and N-acetylglucosamine, mostly sulfated. Its degradation is also by glycosidases and sulfatases. The inability to degrade keratan sulfate gives rise to MPS IV which, depending on the type of enzyme, will give rise to different subtypes of disease.

B-galactosidase removes galactose from keratan sulfate.

It is made up of 677 aa and in its multimeric form has a molecular weight of about 600 kDa. Its gene is located on chromosomal region 3p21.33. Partial deficiency of B-galactosidase gives rise to MPS IVB, while its total absence causes GM1-type gangliosidosis. N-acetylglactosamine 6-sulfatase (galactose 6-sulfatase) removes the galactose sulfate groups from keratan sulfate. It is a 522 aa protein encoded by a gene located in the 16q24.3 region that is about 50 kb long and contains 14 exons. Its deficiency gives rise to MPS IV-A.

HURLER'S SYNDROME

This autosomal recessive disorder was described in 1919. The primary defect is a lack of L-iduronidase in all tissues Figure 1.

It is associated with mental and physical deterioration in the neonatal period, the diagnosis is usually made in the first year of life, and the clinical features include: Gargoloid facies, with coarse features, lumbar hump, hydrocephalus, joint stiffness, claw hands, excessive hair, early and progressive clouding of the cornea, and mental retardation. Dermatan sulfate and heparan sulfate are found in excessive amounts in the urine. Development and growth are markedly impaired, leading to death in childhood. Cardiomyopathy associated with endocardial fibroelastosis has been observed (Donaldson MDC et al 1989, Stephan MJ 1989).

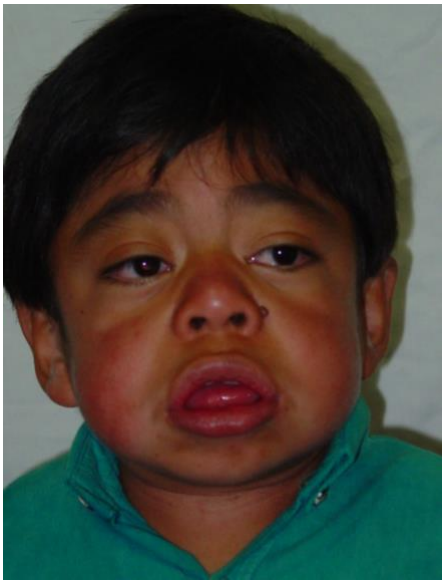

Figure 1

SCHEIE'S SYNDROME

It can be considered the mild form of MPS I. It is characterized by joint stiffness, aortic valve disease, and corneal opacity. Facies are coarse but height is normal, as is intelligence. Figure 2 A, B.

The onset of symptoms usually occurs after 5 years of age, although the diagnosis does not occur until the second decade of life.

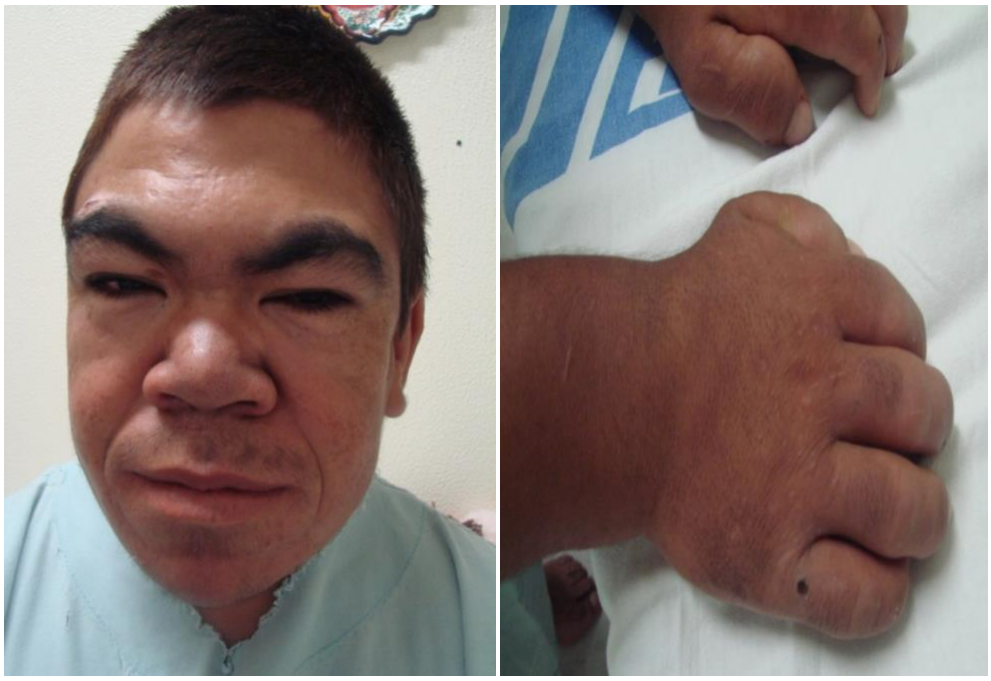

Figure 2 A **B**

HURLER-SCHEIE SYNDROME

Intermediate form between MPS IH and MPS IS. The symptomatology is highly variable in pure forms (stiffness, corneal opacity, deafness, valvular heart disease) and usually appears in the first decade of life. From the phenotypic point of view, the presence of micrognathia is characteristic, which gives a peculiar appearance to the patient's face. Intelligence is normal and symptoms usually occur after 3 years of age, with survival to adulthood being common.

HUNTER'S SYNDROME

This X-linked recessive disorder is generally less severe than Type I. Clinical features are joint stiffness, dwarfism, hepatosplenomegaly, and macrofacial appearance Figure 3. Similarly, dermatan sulfate and heparin sulfate are increased in the urine. The features that distinguish Type II are: absence of hump, clear corneas, deafness and mental retardation are not as deep as in the previous one, but progressive. (Young ID et al 1982, Young ID et al 1982, Young ID 1983) and affected males usually live to adulthood and die of respiratory infection or cardiovascular complication.

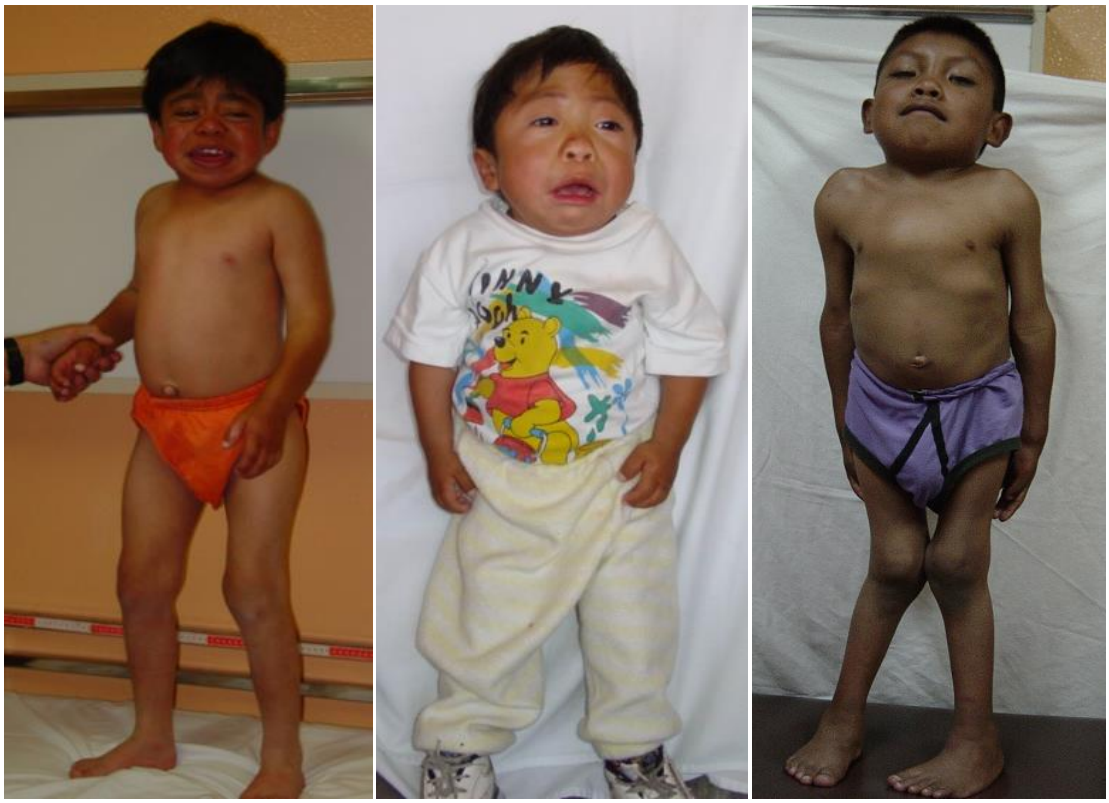

Figure 3 **4** **5**

SANFILIPPO SYNDROME.

Although 4 enzyme subtypes are known in this disease, the clinical picture is quite similar in all of them, being especially difficult to diagnose the mildest form.

The main characteristic of MPS III is the severe involvement of the central nervous system, which contrasts with mild somatic involvement Figure 4. The age of presentation is between 2 and 6 years, although they can be variable and the symptoms are behavioral changes , which may consist of hyperactivity, attention deficit, episodes of aggressiveness or destructive behavior. Sleep disturbances and seizures are common. Mental retardation becomes more evident with age, highlighting difficulties with language, which can sometimes be absent. With age, these patients lose contact with their environment and suffer a process of progressive dementia.

The somatic findings common to MPS are here less marked, and patients are usually of normal size with mild skeletal abnormalities. Deafness is common in patients with moderate and severe form.

In the MPS III-A subtype, the onset of the disease is earlier, its progression is faster, and survival is shorter. MPS III-B is the most heterogeneous with mild and severe cases. MPS III-C is an intermediate subtype between A and the mild form of B. Finally, MPS III-D is very rare and very heterogeneous.

MORQUIO SYNDROME.

There are two subtypes, the most common MPS IV-A, due to deficiency of the enzyme N-acetylgalactosamine 6-sulfatase (galactose 6 sulfatase), and MPS IV-B due to beta-galactosidase deficiency. The clinical findings of both forms overlap and consist of short stature due to a short trunk, severe spondylo-episisal dysplasia, something different from MPS and which can give rise to an important neurological picture due to spinal cord compression. Intelligence is normal Figure 5.

Skeletal anomalies predominate in the clinical picture and although they are not apparent at birth, they manifest throughout the first two years of life (MPS IV-A), with spinal deformity (kyphosis), genu valgus and flat feet , giving rise to a characteristic posture and ambulation that produces frequent falls. Height is increasingly affected and it is rare for patients to exceed 100 cm in height in adulthood. The radiological study shows flat feet, giving rise to a characteristic posture and ambulation that produces frequent falls.

MAROTEAUX-LAMY SYNDROME

Growth retardation is the dominant feature of this autosomal recessive disorder, first described in 1963 for deficiency of a lysosomal enzyme called N-acetylgalactosamine 4-sulfatase (Maroteaux 1963, 1982).

The clinical manifestations described are dwarfism with decreased trunk and stroke, genu valgum, lumbar kyphosis, anterior sternal protrusion and corneal cloudiness. Although other general features are manifested, the distinctive characteristics are: Normal intelligence and severe bone abnormalities Figure 6. Increased amount of dermatan sulfate is found in urine. Metachromatic inclusions are seen in all types of white blood

cells in peripheral blood. Life span is shortened due to progressive cardiovascular impairment.

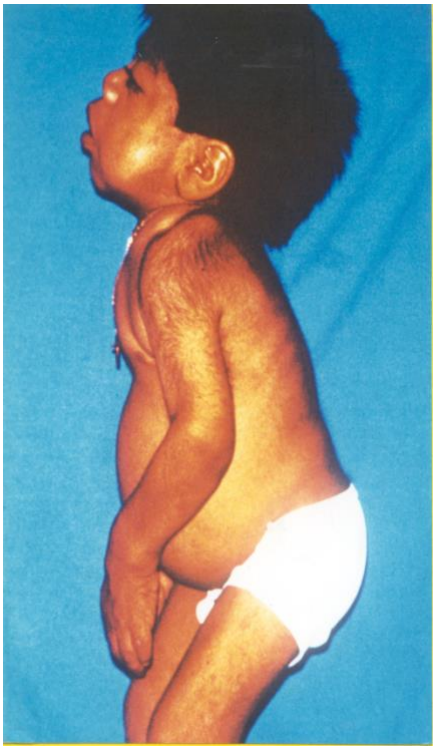

Figure 6

DIAGNOSIS

Initially, the clinical diagnosis of MPS was confirmed with the quantitative analysis of the GAGs in the patient's urine, which allowed each patient to be included in some of the groups within the main classification, although it did not allow differentiation of the different subgroups within each disease.

Subsequently, rapid drop tests (of urine) were developed, which are cheap and very useful as an initial analysis, but are subject to the appearance of false negatives and false positives depending on the experience of each laboratory.

There is also a semi-quantitative analysis based on the presence of metachromasia in glycosaminoglycan-chromogen complexes in solution. Currently, the study of GAGs in urine has been displaced by the specific enzymatic study in each form of MPS, although it

can be used for the diagnosis of new forms of disease and for monitoring the results of experimental treatment.

Definitive diagnosis of each form of MPS is made with enzyme assays. Different tissues are used, such as skin (fibroblasts), or blood (with leukocytes or serum or plasma). Quantification of the specific enzyme in cultured fibroblasts is useful in all known forms of MPS and in blood leukocytes in most.

PRENATAL DIAGNOSIS

Prenatal diagnosis is possible in all forms of MPS. The method applied to amniotic fluid cells is similar to that used with fibroblasts. The long time spent culturing and analyzing amniotic cells has prompted researchers to develop more rapid diagnostic techniques, for example, quantification of iduronate sulfatase enzyme activity in cell-free amniotic fluid is used in prenatal diagnosis of Hunter's disease. The study of the chorionic villi also allows prenatal diagnosis, although this is more complicated, because some enzymes have normal or very low levels in the chorion.

In the case of Hunter's disease, with X-linked recessive inheritance, there is the problem of mosaicism in heterozygous women, who will have cells with normal or mutated IDS. As a result of the process of biased inactivation or selection, in the female fetus the activity of the iduronate sulfatase enzyme may in some cases be as low as in male fetuses. Therefore, prenatal diagnosis of Hunter's disease requires prior determination of fetal sex.

Conclusions

Mucopolysaccharidoses are a family hereditary disorder caused by the deficiency of lysosomal enzymes necessary for the degradation of glycosaminoglycans or also called mucopolysaccharides. This group of storage diseases has recently been observed to have the clinical and radiological features of mucopolysaccharidoses and mucopolysaccharidoses. (McKusick VA 1972, Spranger J 1972, Sly WS 1980). The mode of inheritance for all mucopolysaccharidosis types described so far is autosomal recessive, except for Type II (Hunter Syndrome), which is inherited in an X-linked recessive manner.

The frequency for all types is very rare, except 1 in every 100,000 newborns; all types are widely distributed among the major ethnic groups.

MPS type II appears to be only one-fifth as frequent as MPS types I and VI (Hurler and Maroteaux Lamy syndromes, respectively). In the case of an X-linked recessive type II, which is passed on to the affected son by her mother, two-thirds of the X-chromosome mutation occurs in earlier generations.

Cytogenetic studies have been carried out, of which karyotype analyzes have shown that they are normal in number and morphology.

Heterozygous detection has been possible through cell culture studies. Cellular metachromasia of cell culture intracellular mucopolysaccharide content is increased in fibroblasts and peripheral cultures of heterozygous-derived white blood cells.

RESPIRATORY CONDITIONS

Alterations in the respiratory system of patients with this disease are frequent and represent, together with cardiac complications, the most frequent causes of death in these children.

The pathophysiology of respiratory symptoms is caused both by deformities of the thoracic cage at the level of the sternum, ribs and spine, as well as by the deposition of mucopolysaccharides in the tissues that modify the structures of the connective tissue, altering by both mechanisms the pulmonary mechanics and resulting in a mixed alteration in the pulmonary functional pattern; restrictive due to the low mobility of the bony thorax and the pulmonary parenchyma due to collagen and elastin affection, and on the other hand a chronic obstructive disease conditioned by the accumulation of the same and a high predisposition to become infected and present recurrent infections. The natural evolution of these complications is cor. Pulmonary, respiratory failure, heart failure and finally death occurs at an early age. The management of these pulmonary complications is generally symptomatic, they respond well to bronchodilators in their initial phases, and recurrent infections must be treated correctly.

Early initiation of a pulmonary physiotherapy and inhalation therapy program is suggested, aimed at improving pulmonary vital capacity, improving bronchial hygiene, and preventing the onset of infections.

PATHOGENESIS.

Since the identification of the storage material as acidic mucopolysaccharides, some explanations for the metabolic defect have been suggested but not experimentally proven:

1) DEFECT IN BINDING WITH PROTEINS. Dorfman observed that mucopolysaccharides were easily extracted from the tissues of patients with Huler's Syndrome and that there was a deficiency in serine suggesting a defect in protein binding in these patients.

2) DEGRADATIVE ENZYME DEFICIENCIES. Van Hoof and Hers found that intracellular mucopolysaccharides stored in inclusion bodies, probably derived from lysosomes, reflect a deficiency of a degradative enzyme in the tissue. Fibroblast culture studies have shown intracellular mucopolysaccharide storage in types I, II, and VI. Enzyme studies in various types I, II, and VI patients have shown a specific deficiency of lysosomal beta-galactose and excess activity of a number of other lysosomal enzymes. The relationship of bategalactose deficiency to the fundamental defect remains obscure.

Regardless of the different types of MPS presented, they belong to a group of diseases that have in common a disorder of the metabolism of mucopolysaccharides (MPS) or glycoamonoglycans (GAGS), due to a deficiency or alteration in some lysosomal enzymes, causing an accumulation of the same in cells and tissues, more specifically in cartilage and bone, as well as an excessive excretion of these in urine. These mucopolysaccharides are macromolecules that contain numerous positive charges on their surface that are precipitated by molecules that contain negative charges, so for their quantification in this laboratory, Cetyl Pyridium Chloride (CCP) is used, which gives the clinical characteristics found in the four patients in This studio.

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