

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.elsevier.com/locate/radcr](http://www.elsevier.com/locate/radcr)

## Case Report

# Mucopolysaccharidosis type IV: report of 5 cases of Morquio Syndrome ☆,☆☆

Jorge Alejandro Cadena Arteaga, MD. MSP.<sup>a</sup>, Fabricio Andres Lasso Andrade, MD. MSP.<sup>b,\*</sup>, Denny Marcela Achicanoy Puchana, MD<sup>c</sup>, Diana Fernanda Achicanoy Puchana, MD.<sup>c</sup>, Gina Natalia Caicedo Morillo, MD. MSP.<sup>d</sup>, Paola Andrea Medina Bravo, MD<sup>e</sup>, William Fernando Juez Neira, MD<sup>f</sup>, Cristian Ricardo Vanegas Bastidas, MD<sup>g</sup>, Diana Carolina Montoya Ríos, MD<sup>h</sup>, Karen Julieth Vasquez Correa, MD<sup>i</sup>, Laura Catalina Suárez Cuéllar, MD<sup>j</sup>, Lady Johana Osorio Segura, MD<sup>k</sup>

<sup>a</sup>Especialista en Radiología. Universidad del Valle. Cali, Valle del Cauca- Colombia

<sup>b</sup>Universidad del Cauca. Especialista Epidemiología, Universidad Autónoma de Bucaramanga. Residente Anestesiología y Reanimación, Universidad Nacional de Colombia.

<sup>c</sup>Universidad de Nariño. Residente de Imagenología diagnóstica y terapéutica, Universidad Nacional Autónoma de México.

<sup>d</sup>Universidad de Antioquia. MSP. Gerencia de la Seguridad y Salud en el Trabajo, Universidad Iberoamericana.

<sup>e</sup>Universidad El Bosque.

<sup>f</sup>Universidad del Valle.

<sup>g</sup>Universidad Tecnológica de Pereira

<sup>h</sup>Universidad de Manizales.

<sup>i</sup>Universidad de Antioquia.

<sup>j</sup>Universidad Cooperativa de Colombia.

<sup>k</sup>Universidad del Valle.

## ARTICLE INFO

## Article history:

Received 26 October 2021

Revised 2 November 2021

Accepted 2 November 2021

## Keywords:

Morquio syndrome

Mucopolysaccharidosis

Short stature

Glycosaminoglycans

## ABSTRACT

Mucopolysaccharidosis type IV or Morquio Syndrome, is a lysosomal deposit disease, of autosomal recessive inheritance with a similar incidence in men and women. The clinical picture is of variable expressiveness, its phenotype is characterized by skeletal dysplasia that includes neck and short trunk, short stature, keel thorax, kyphosis, scoliosis, genu valgus, flat foot, coxa valga, gait disorders, instability of the cervical spine and wedge or ovoid vertebrae. The treatment is symptomatic, with enzyme replacement. We present a series of 5 cases, the product of 2 couples, with a confirmed diagnosis of Mucopolysaccharidosis type IV, and different clinical presentation.

© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

☆ Competing Interests: We declare that the patient described in this study gave informed consent prior to inclusion in this study. We also declare that we have no conflicts of interest.

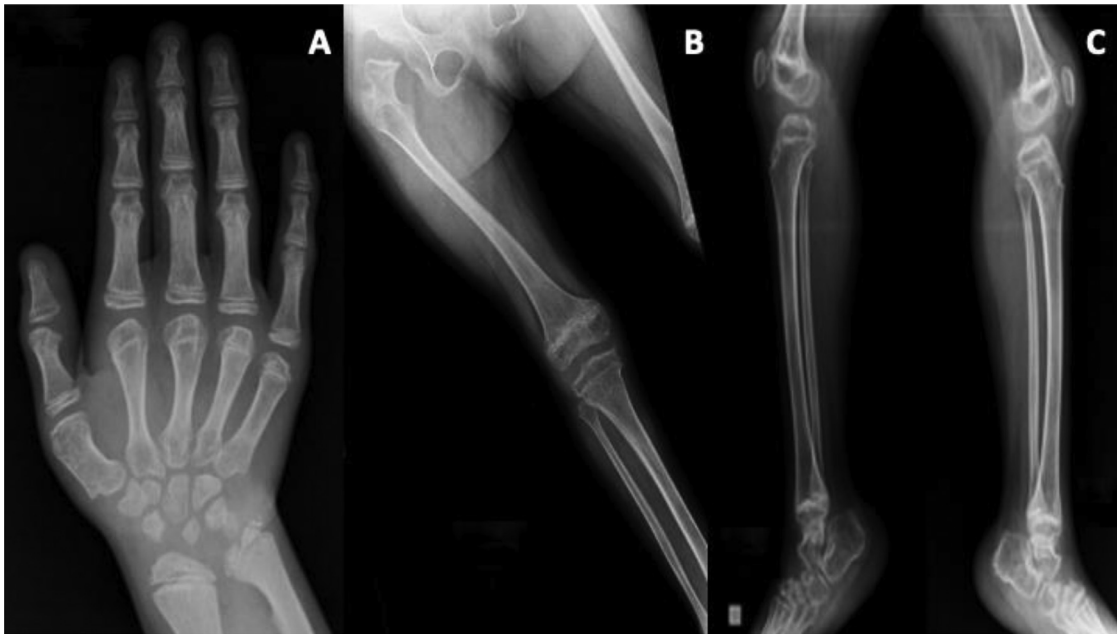
☆☆ Patient consent: We declare that the patient described in this study gave informed consent prior to inclusion in this study.

\* Corresponding author.

E-mail address: [fabriciolasso@gmail.com](mailto:fabriciolasso@gmail.com) (F.A. Lasso Andrade).

<https://doi.org/10.1016/j.radcr.2021.11.012>

1930-0433/© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)



**Fig. 1 – (A).** Hand X-Ray: diaphyseal thickening with short and wide metacarpals and dysplasia in the formation of the carpal bones with increased scapho-lunar distance suggesting instability. **(B).** Flattened acetabulum, coxa valga deformity, femoro-acetabular joint dysplasia. **(C).** Bilateral tibial antecurvature

## Introduction

Mucopolysaccharidosis (MPS) is a skeletal dysplasia that is characterized by a group of inherited disorders caused by a deficiency of mucopolysaccharide degrading enzymes or also called glycosaminoglycans (GAGs) [1]. This disease is characterized by excessive lysosomal storage of partially degraded GAG in connective tissue and elevation of GAG fragments in urine, blood, and cerebrospinal fluid [1–3]. Eleven different types of enzyme deficiencies have been identified that have been associated with seven different types of MPS (MPS I to IV, VI, VII and IX) [1] whose clinical manifestations and severity vary from one MPS to another, but also within the same type of MPS [2].

We present a series of 5 cases. The cases 1,2 and 3 are sons of the first couple, and cases 4 and 5 are sons of a second couple. The cases are product of 2 couples, with a confirmed diagnosis of Mucopolysaccharidosis type IV. The couples were not related to each other.

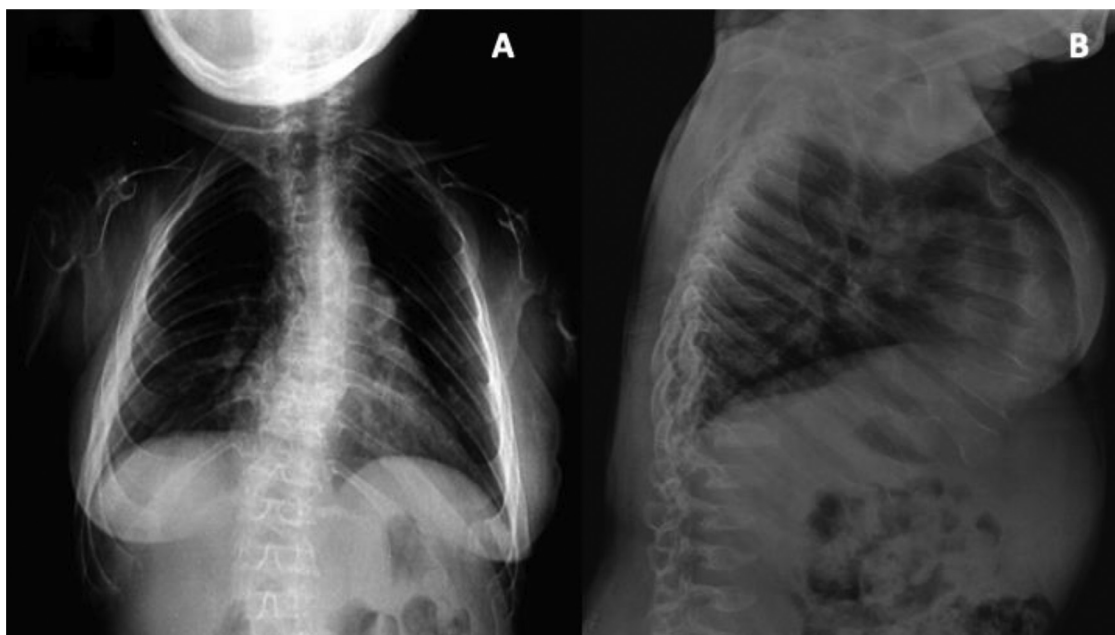
### Case 1

A 15-year-old female patient, diagnosed with MPS type IV, consulted for paresthesia in the upper limbs, lameness and recurrent pneumonia. Physical examination revealed a flat nasal bridge, thick lips and macroglossia, short stature and a short trunk, without neurological focus. X-rays of the upper limbs were performed, showing diaphyseal thickening of the phalanges with short and wide metacarpals, in addition to dys-

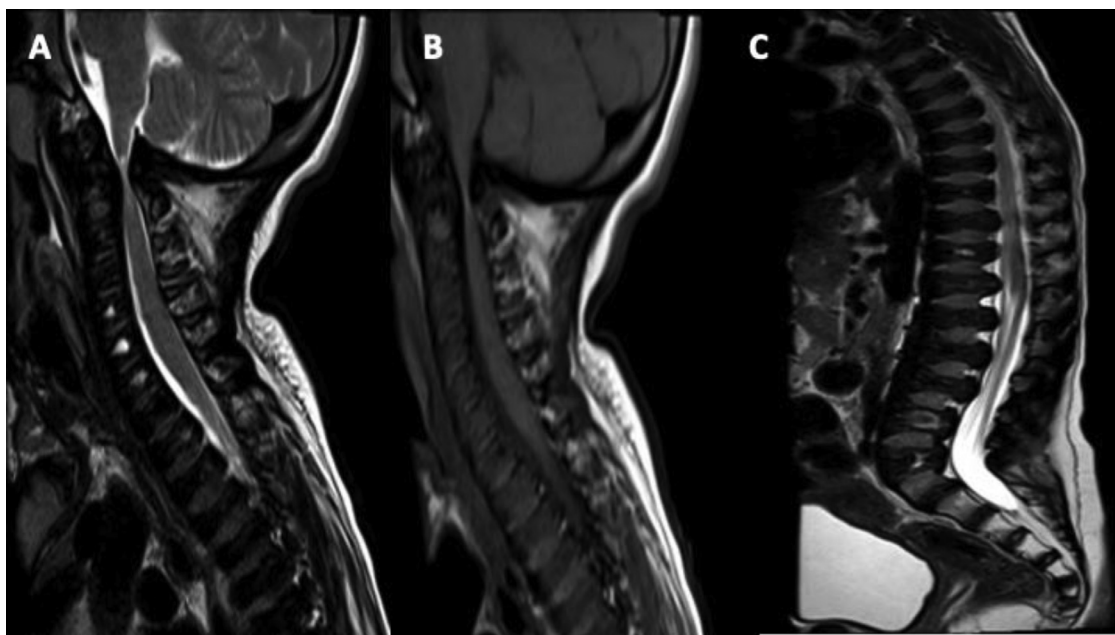
plasia of the carpal bones (Fig. 1A). X-rays of the hip and lower limbs showed dysplasia of the femoro-acetabular joint and antecurvature and bilateral tibial (Fig. 1). The chest X-ray revealed widening of the costal arches with flattening of the vertebral bodies with a pointed edge and formation of pectus carinatum, without findings compatible with a pneumonia (Fig. 2). Due to the presence of paresthesias, she was taken to nuclear magnetic resonance imaging (MRI) of the spine, showing spinal compression at the C2-C3 level, without spinal involvement in the rest of the spine (Fig. 3). Finally, she was taken to spinal decompression, with resolution of symptoms. At the 1-year follow-up, she did not present new symptoms of pneumonia.

### Case 2

A 17-year-old male patient diagnosed with MPS type IV attended the consultation due to persistent dyspeptic symptoms. On physical examination, he presented a typical phenotype with short stature, flat nasal bridge, thick lips, macroglossia, but no organomegaly or pain on palpation of the abdomen. A magnetic resonance imaging study of the spine and thorax was performed, showing platyspondyly, dorso-lumbar kyphosis without spinal cord compression; furthermore, hepatomegaly and an elongated aorta were evidenced, considering the cause of gastroesophageal reflux (Fig. 4). Medical treatment was given with a high-dose proton pump inhibitor, the patient had resolution of symptoms at one year of follow-up.



**Fig. 2 – Anteroposterior and lateral chest X-ray. (A). Widening of the costal arches. (B). Platyspondyly: planar vertebral bodies with pointed anterior border. Pectus carinatum (anterior sternal protrusion). Progressive widening of the costal arches from posterior to anterior "paddle-shaped"**

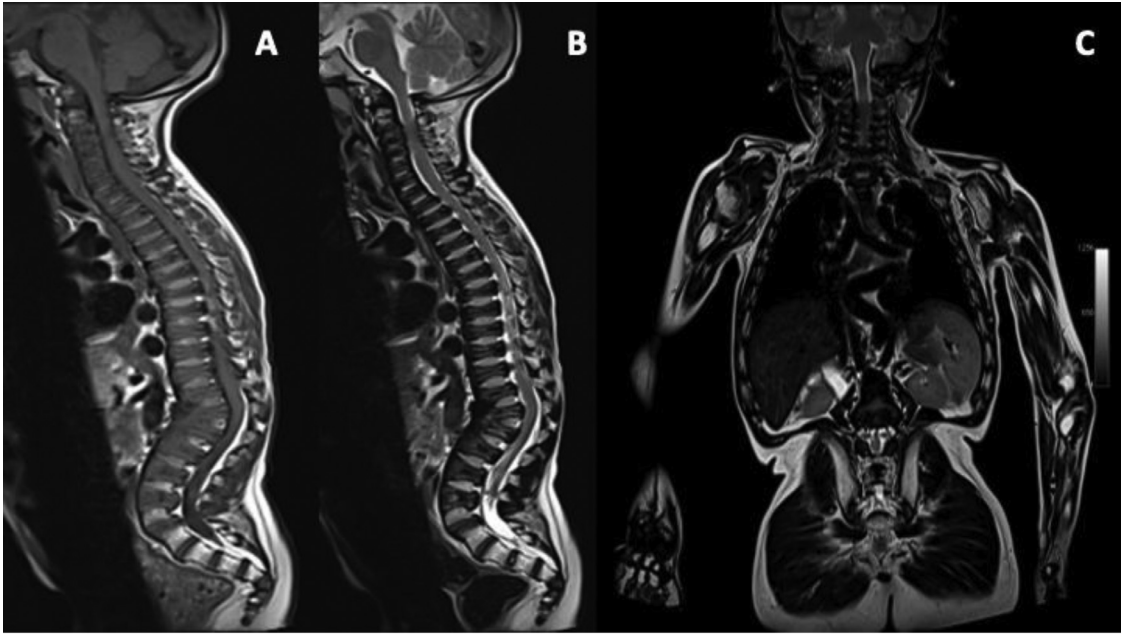


**Fig. 3 – (A and B). Decrease in the amplitude of the medullary canal at the C2-C3 level, with compression of the medullary cord generating changes in myelopathy. (C). Platyspondyly: Decrease in the height of the vertebral body with an increase in the AP diameter**

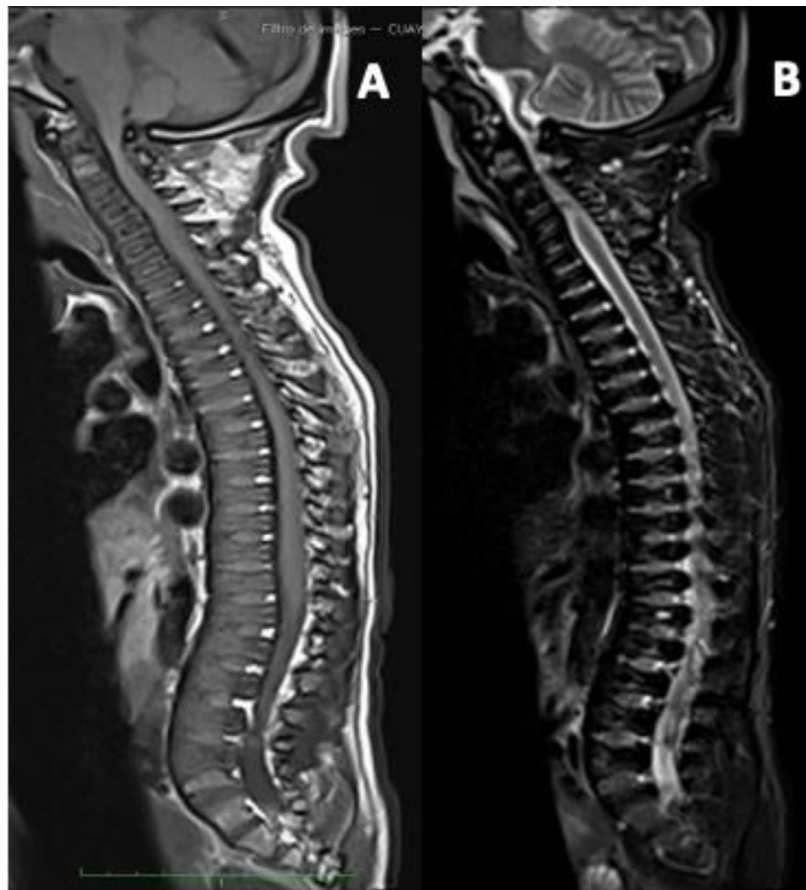
### Case 3

A 22-year-old male patient diagnosed with MPS type IV, consulted for presentation of upper limb paresthesia. On physical examination, with short stature, hypertrichosis and

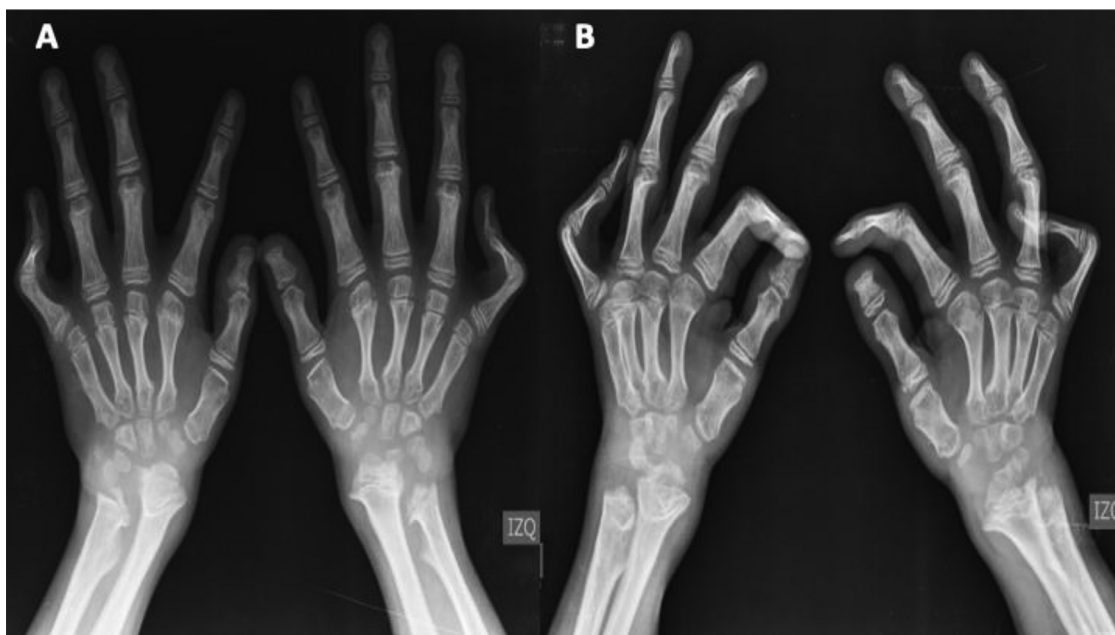
short claw-shaped hands, without other neurological findings. A spinal magnetic resonance study was performed, which showed spinal compression at the C2 level, without spinal involvement in the rest of the spine (Fig. 5). He was taken to spinal cord decompression in two surgical moments, with resolution of symptoms after 6 months of follow-up.



**Fig. 4 – (A and B).** Decreased amplitude of the medullary canal at C2 level without signs of myelopathy, with decreased anterior and posterior subarachnoid space. **(C).** Platyspondyly: Decrease in the height of the vertebral body with an increase in the AP diameter



**Fig. 5 – MRI without contrast. (A).** Decreased width of the medullary canal at C2 level without signs of myelopathy. **(B).** Reduced anterior and posterior subarachnoid space



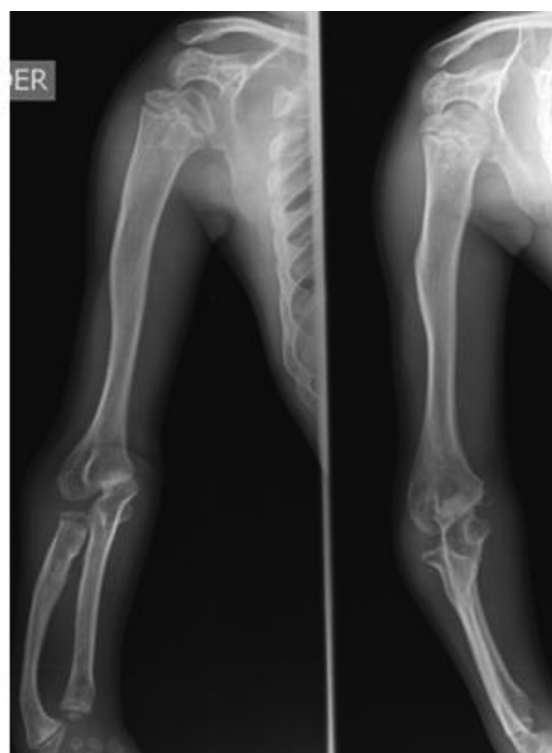
**Fig. 6 – (A and B). Boutonniere deformity with proximal narrow metacarpals and distal widening**

#### Case 4

A 15-year-old male patient, the product of twin pregnancy, diagnosed with MPS type IV, presented with deformity in the forearms and hands, associated with paresthesia in the fingers of the right hand with hypotrophy in the thenar area. Physical examination revealed short stature, claw hands, hypertrichosis and a bilateral dorsal curvature deformity at the radius and a distal level, with no previous history of trauma. X-rays of the upper limbs showing boutonniere deformity, with narrow metacarpals, shortening of the nail with epiphyseal dysplasia of the radius, configuring Madelung deformity (Fig. 6 and Fig. 7). The patient is considered to have carpal tunnel syndrome due to Madelung's deformity, is undergo surgical decompression and osteotomy, with resolution of symptoms at 1 year of follow-up.

#### Case 5

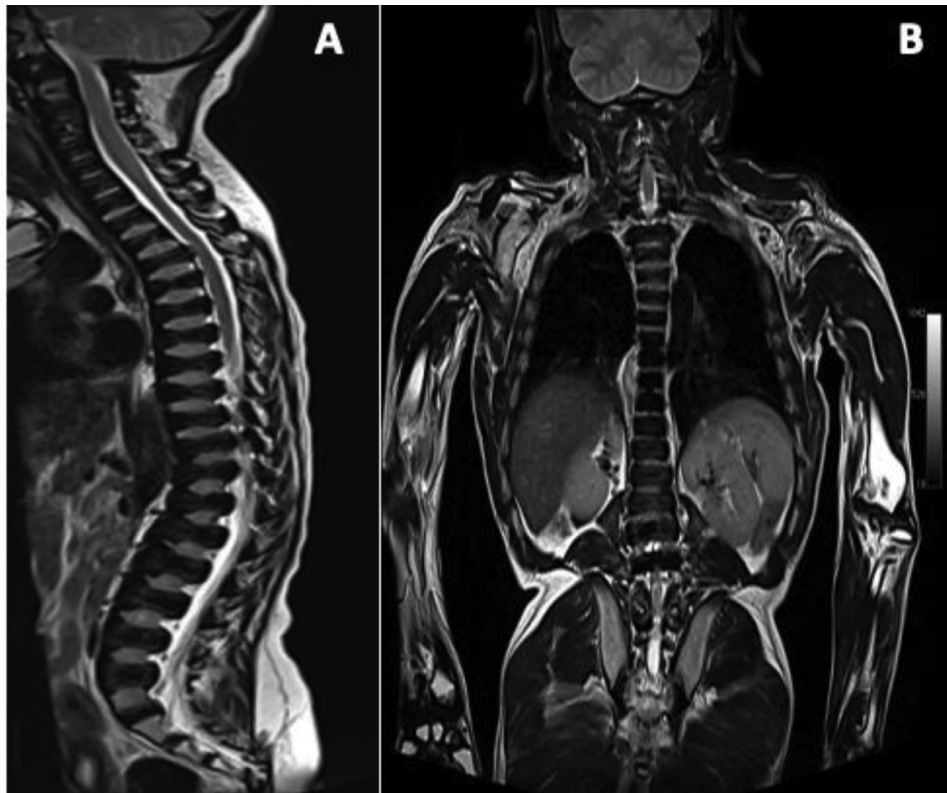
A 15-year-old male patient, the product of a twin pregnancy, diagnosed with MPS type IV, consulted for chronic cough. On physical examination with normal vital signs, without kyphoscoliosis or abnormal findings on auscultation. A spinal MRI was performed, accentuation of kyphosis with platyspondyly without evidence of spinal cord compression, however, in chest and abdominal MRI, splenomegaly and hepatomegaly were evident (Fig. 8). A mechanical cause of chronic cough was considered, which is why conservative treatment is performed, without complications at one year of follow-up.



**Fig. 7 – Epiphyseal dysplasia of the radius and shortening of the ulna, configuring Madelung's deformity**

#### Discussion

MPS type IV or Morquio Syndrome is a lysosomal storage disease, of autosomal recessive inheritance with a similar inci-



**Fig. 8 – (A). Platyspondilia. (B). Decrease in the height of the vertebral body with an increase in the AP diameter, with accentuation of the dorso-lumbar kyphosis**

dence in men and women, the incidence is 1 in every 75,000 to 1 in 200,000 births [4].

It was first described in 1929 by the Uruguayan pediatrician Luis Morquio and almost simultaneously by the radiologist James Brailsford in England, which is why it is also known as Morquio Brailsford syndrome. Representations of people with this syndrome have been described in 2,000-year-old ceramics in pre-Hispanic cultures of southwestern Colombia [5,6].

It is classified into three subtypes according to the enzymatic involvement present, MPS type IVa, IVb and IVc [1,4]. The clinical picture of type IVa and IVb MPS is indistinguishable, and both have wide clinical heterogeneity. Affected children appear normal at birth because they do not show impairment of the intellectual coefficient or psychomotor development, more than 70% have initial clinical manifestations within the first 2-3 years of life [5–8].

Although the clinical picture is of variable expressiveness, its phenotype is characterized by skeletal dysplasia that includes neck and short trunk, short stature, keel thorax, kyphosis, scoliosis, genu valgus, flat foot, coxa valga, gait disorders, instability of the cervical spine and wedge or ovoid vertebrae [4,6]; At the craniofacial level, they present coarse facies, prognathism, wide mouth, flat nasal bridge, corneal opacities, odontoid hypoplasia, dental caries, hearing loss and joint hypermobility at the hip and lower extremities. (7.8). Growth is highly compromised from before 5 years of age and the average height is between 85 and 100 cm (4.9).

Disharmonious short stature guides the differential diagnosis of skeletal dysplasias, and the absence of intellectual commitment throughout life helps to differentiate MPS type IV from other types of MPS, thus the phenotypic findings of these patients indicate the need for biochemical studies and genetics for diagnostic orientation [4].

The diagnosis is confirmed by direct enzyme assay on leukocytes or fibroblasts, either in heparinized blood or fibroblasts cultured from a small skin biopsy; the detection of mutations in the GALNS or GLB1 genes helps to distinguish between a type A or type B Morquio syndrome [4]. The five patients that we present had a direct enzyme assay study on leukocytes 7 years prior to the time of consultation.

In the spinal X-ray, the deviation of the spine secondary to the presence of abnormal vertebral bodies such as wedge or ovoid, hypoplasia of the odontoid process and platyspondyly can be observed, mainly in T11, T12 and L5 [4,10]; as evidenced in almost all the cases that we present, with the exception of case 4.

In the x-ray of the hip and lower limb, short and wide metacarpals, coxa valga, as well as small femoral heads or flattening of the same, flattening of the femoral head [7,10], as evidenced in case 1 (Fig. 1) can be observed. )

Imaging is beneficial for airway assessment, particularly in patients with obstructive symptoms and before intubation [11]. Three-dimensional tomographic reconstructions of the trachea and spine can be of great value in planning intubation

in this population of patients or evaluating respiratory symptoms (14), this usefulness was evidenced in case 5 to demonstrate a mechanical cause of respiratory symptoms of the patient.

Treatment depends on the age group in which the diagnosis or follow-up is made [4], and is clearly symptomatic. From 1 to 6 years, the consequences of thoracic and spinal deformity become more frequent, for which the more active participation of the orthopedist, pulmonologist and otolaryngologist is required [7]. Cardiovascular manifestations can appear after one year of age, so a cardiological evaluation should be carried out in the usual controls [4,11].

Complications in patients over 6 years of age are mainly secondary to skeletal abnormalities, for which surgical fusion of the cervical spine is recommended in order to avoid myelopathy; Orthopedic management of scoliosis and osteotomy are also recommended for genu valgus correction in addition to rehabilitation [4,11].

In 2014, the FDA approved elosulfase alfa which is a recombinant form of the human lysosomal enzyme N-acetylgalactosamine-6-sulfatase for the treatment of Mucopolysaccharidosis type IVA, with which improvement has been seen in patients, however, there is no enzyme replacement treatment for Mucopolysaccharidosis type IVb [9,11].

Finally, patients with mild phenotypes that can survive until the seventh decade of life [4,9] and can continue their growth in adolescence and even have a normal height [5,11]. Severe forms such as MPS IVA, do not usually exceed 25 years with death occurring due to cardiac or respiratory complications [5].

## REFERENCES

- [1] Palmucci S, Attinà G, Lanza ML, Belfiore G, Cappello G, Foti PV, et al. Imaging findings of mucopolysaccharidoses: A pictorial review. *Insights Imag* 2013;4:443–59.
- [2] Michaud M, Belmatoug N, Catros F, Ancellin S, Touati G, Levade T, et al. Mucopolysaccharidosis: A review. *Rev Med Interne* [Internet] 2020;41(3):180.
- [3] Muenzer J. Overview of the mucopolysaccharidoses. *Rheumatology* 2011;50(SUPPL. 5):4–12.
- [4] Hung S, Hernández G, Briceño Y, Silvestre R, Barrios MC. Morquio syndrome as a rare cause of disproportionate short stature . pathophysiological , diagnostic and therapeutic approach . about a case. *Rev venez Endocrinol Metab* 2016;5(P 90):217–25.
- [5] Syndrome M. Presentación de un caso Clínico de Mucopolisacaridosis Tipo IV, Síndrome de Morquio. 55(1):40–6.
- [6] Pachajoa H, Ruiz-Botero F, Hernández-Amariz MF, Eichler S, Castillo-Giraldo AO. Síndrome de Morquio: nueva mutación del gen GALNS en dos hermanos del sur-occidente colombiano. Análisis clínico, molecular y bioinformático. *Rev Mex Pediatr* 2016;83(3):85–92.
- [7] Suárez-Guerrero JL, Suárez AKB, Santos MCV, Contreras-García GA. Caracterización clínica, estudios genéticos, y manejo de la Mucopolisacaridosis tipo IV A. *Medicas UIS* 2013;26(2):43–50.
- [8] Nicolas-Jilwan M. Imaging features of mucopolysaccharidoses in the head and neck. *Int J Pediatr Otorhinolaryngol* [Internet] 2020;134(January):110022 Available from: doi:10.1016/j.ijporl.2020.110022.
- [9] Julien DC, Woolgar K, Pollard L, Miller H, Desai A, Lindstrom K, et al. Immune Modulation for Enzyme Replacement Therapy in A. Female Patient Hunter Syndrome. *Front Immunol*. 2020;11(May):1–8.
- [10] González Gámez S, Yambay Paucar N, del P, Ramírez Teope K. Enfermedad de Morquio en un niño TT - Morquio disease in a child. *Medisan* [Internet]. 2017;21(11):3267–71. Available from: [http://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S1029-30192017001100017&lang=es](http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192017001100017&lang=es) .
- [11] Giughiani R, Gutierrez Carvalho C, Herber S. Lapagesse de camargo pinto l. recent advances in treatment approaches of mucopolysaccharidosis VI. *Curr Pharm Biotechnol* 2011;12(6):956–72.