Mucopolysaccharidosis Type VI: Case Report

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ABSTRACT

Mucopolysaccharidosis type VI, also known as Maroteaux-Lamy syndrome, is caused by a deficiency of the arylsulfatase B enzyme, which causes intracellular accumulation of dermatan sulfate. The risk of spinal cord compression is particularly high and frequent at the occipitocervical junction. Enzyme replacement therapy has been essential for patients with this disease; however, it has no effect on skeletal abnormalities, and its impact on spinal stability is still under study. An annual examination (neurological evaluation, radiography, magnetic resonance imaging, and somatosensory evoked potentials) is recommended. In case of anomalies, it should be repeated every 6 months. Despite the high anesthetic risk, myelopathy and progressive symptoms indicate the need for surgical decompression. We present the case of a 12-year-old girl with mucopolysaccharidosis type VI treated with enzyme replacement therapy since the age of 7, who came to the consultation with symptoms compatible with progressive high cervical myelopathy. She underwent occipitocervical decompression and fusion with enlargement of the foramen magnum. This disease is rare; therefore, multidisciplinary patient follow-up is imperative, as well as knowing the risk of spinal cord compression and its timely surgical treatment by spinal surgeons.

Keywords: Mucopolysaccharidosis; Maroteaux-Lamy syndrome; spinal cord compression; myelopathy.
Level of Evidence: IV

Mucopolisacaridosis tipo VI: a propósito de un caso

RESUMEN

La mucopolisacaridosis tipo VI o síndrome de Maroteaux-Lamy se produce por la deficiencia de la enzima arilsulfatasa B que ocasiona la acumulación intracelular de dermatán sulfato. El riesgo de compresión medular es particularmente elevado y muy frecuente en la unión occipito-cervical. La terapia de reemplazo enzimático ha sido esencial para los pacientes con esta enfermedad; sin embargo, no tiene efecto sobre las alteraciones esqueléticas, y su impacto sobre la estabilidad espinal está aún en estudio. Se sugiere un examen anual (evaluación neurológica, radiografías, resonancia magnética y potenciales provocados somatosensitivos) y, en caso de anomalías, cada 6 meses. Pese al alto riesgo anestésico, la mielopatía y los síntomas progresivos indican la necesidad de una descompresión quirúrgica. Presentamos a una niña de 12 años con mucopolisacaridosis tipoVI tratada con terapia de reemplazo enzimático desde los 7 años, que acude a la consulta con síntomas compatibles con mielopatía cervical alta progresiva. Fue sometida a una descompresión y artrodesis occipito-cervical con ampliación del foramen magno. Esta enfermedad es infrecuente; por lo tanto, es imperativo el seguimiento multidisciplinario del paciente, así como conocer el riesgo de compresión medular y su oportuno tratamiento quirúrgico a cargo de cirujanos espinales.

Palabras clave: Mucopolisacaridosis; síndrome de Maroteaux-Lamy; compresión medular; mielopatía.
Nivel de Evidencia: IV

INTRODUCTION

Mucopolysaccharidoses (MPS) are a group of hereditary diseases, mostly autosomal recessive, characterized by the accumulation of glycosaminoglycans caused by the deficiency of lysosomal enzymes. The intracellular accumulation of metabolites in different tissues leads to systemic compromise, which reduces life expectancy and quality of life. The clinical and skeletal manifestations depend on the deficient enzyme. Systemic involve-

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ment includes: liver, cardiac, visual, cardiovascular, central nervous system, and airway disorders. It affects both the formation and growth of the skeletal system.[1-3] Typical spinal manifestations are: atlantoaxial instability (with or without odontoid hypoplasia), thoracolumbar kyphosis, scoliosis, canal stenosis, and spinal cord compression.[23]

MPS VI or "Maroteaux-Lamy syndrome" was first described in 1963 by Maroteaux and Lamy, and is caused by an autosomal recessive hereditary deficiency of the enzyme arylsulfatase B (also called N-acetylgalactosamine-4 -sulfatase), which causes intracellular accumulation of dermatan sulfate. It is characterized by organomegaly, hearing disorders, bone dysplasia, cardiorespiratory and neurological problems. There are more than 100 types of mutations of this enzyme that cause different phenotypes categorized as slowly or rapidly progressive. Patients with a slowly progressive phenotype often present late; however, they are at risk of serious and sometimes fatal neurologic complications as a result of spinal cord compressions.[1,4-10]

Some manifestations of osteoarticular compromise are: short stature, joint stiffness, vertebral anomalies, coxa valga, and lack of ossification of the femoral head.[11] The risk of spinal cord compression is particularly high and, although it can occur at any spinal level, it is very frequent at the occipito-cervical junction. Compression is produced by retro- or periodontoid tissue that is thickened by deposition of glycosaminoglycans, ligament hypertrophy, and bone stenosis.[8-11]

The advantages of new enzyme replacement therapies and stem cell transplantation for the management of this disease have been demonstrated, especially at the visceral level; however, it is ineffective in bone deformities, including the spine.

The objective of this study is to present this disease, its main manifestations and treatment, through the presentation of a case and a literature review.

CLINICAL CASE

In March 2021, a 12-year-old girl presented to our office with non-specific neck pain associated with claudication when walking at 200 m, diffuse and progressive paresthesias in all four limbs, of approximately two years of evolution, which had increased in the last six months, and a delay in consultation due to the COVID-19 pandemic.

She suffered from type VI MPS (monitoring and enzyme replacement treatment at another institution) and minor heart disease (mild involvement of the mitral and aortic valves).

Physical examination revealed a short overall height, a short neck, overweight, no observable distal weakness, symmetrical hyporeflexia, Babinsky and Lhermitte signs, and negative clonus. The Japanese Orthopedic Association scale score was 15. Laboratory parameters, including those related to inflammation but excluding those related to the underlying disease, were all normal.

Initial radiographs showed a decrease in height of the C3-4-5 vertebral bodies. In addition, there was an impressive hypoplasia of the odontoid process, with no signs of instability on dynamic radiographs (Figures 1 and 2).

Computed tomography and magnetic resonance imaging (MRI), performed in the supine position, showed morphological varieties from C1 to C5, with decreased height of the vertebral bodies (hypoplasia), mainly in C3-4-5, hypoplasia of odontoids and periodontoid tissue that caused a decrease in the diameter of the cervical canal at that level; and myelomalacia in C0-1-2 (Figures 3-5).

Furthermore, a posterior displacement of the nucleus pulposus of the thoracic discs was observed, as well as an anatomical variation of the vertebral foramen in C2 that placed it slightly medial. No other congenital abnormalities were detected. The electromyogram was normal; however, she had abnormal conduction of the posterior cord in the upper cervical sector suggestive of high cervical myelopathy on somatosensory evoked potentials.

Given her progressive condition and irreversible spinal cord damage, as well as the underlying disease, the case was presented to a specialized surgical center, and surgery for decompression and posterior occipito-cervical fixation was proposed.

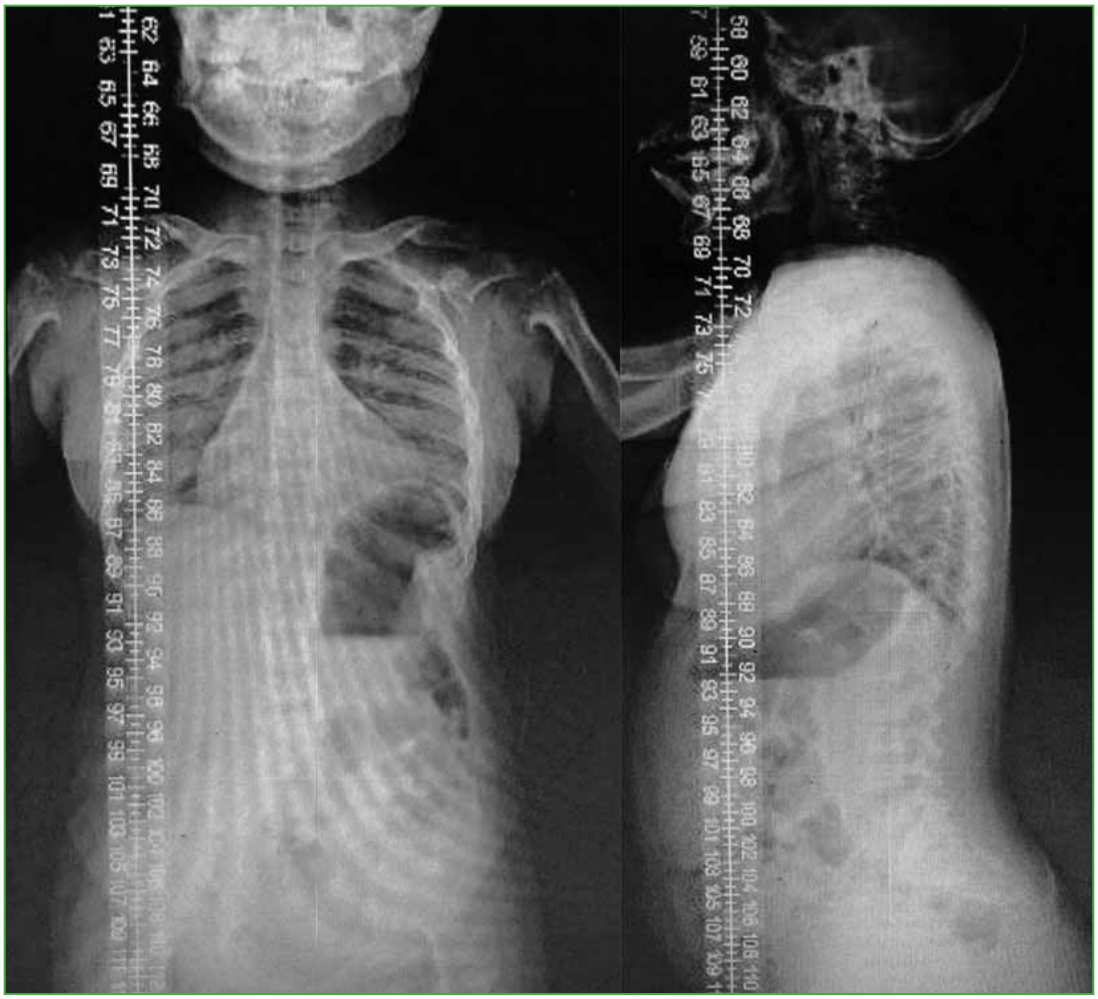

Figure 1. Anteroposterior and lateral spinogram. Note the overweight and short stature, the flat back, and the decreased height of the C3-4-5 vertebral bodies.

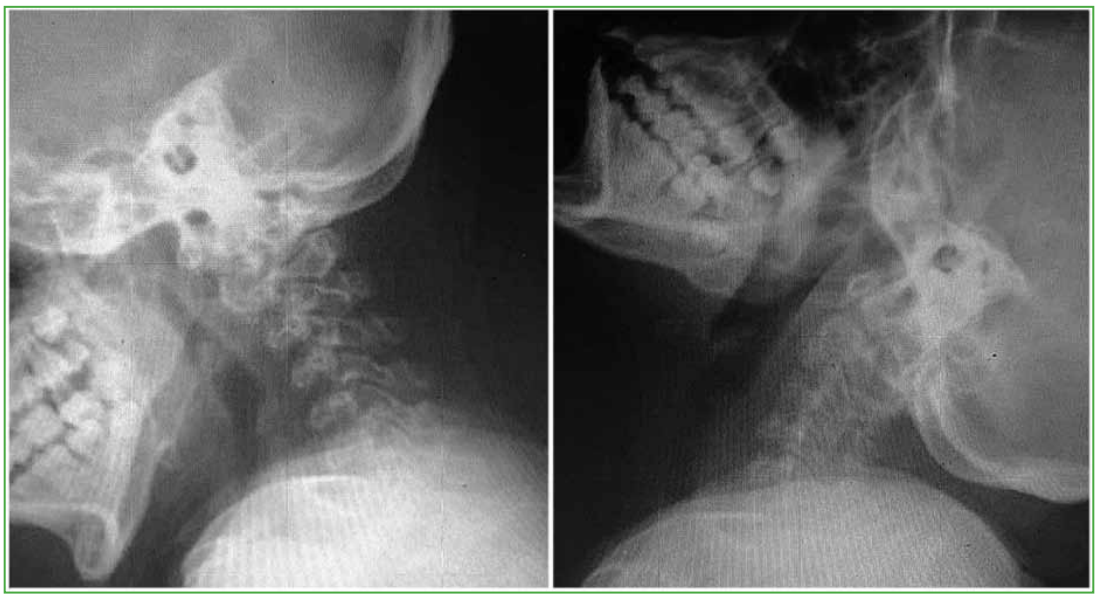

Figure 2. Dynamic cervical radiographs (flexion/extension). Decreased height of the C3-4-5 vertebral bodies, with apparent hypoplasia of the odontoid process, without signs of instability.

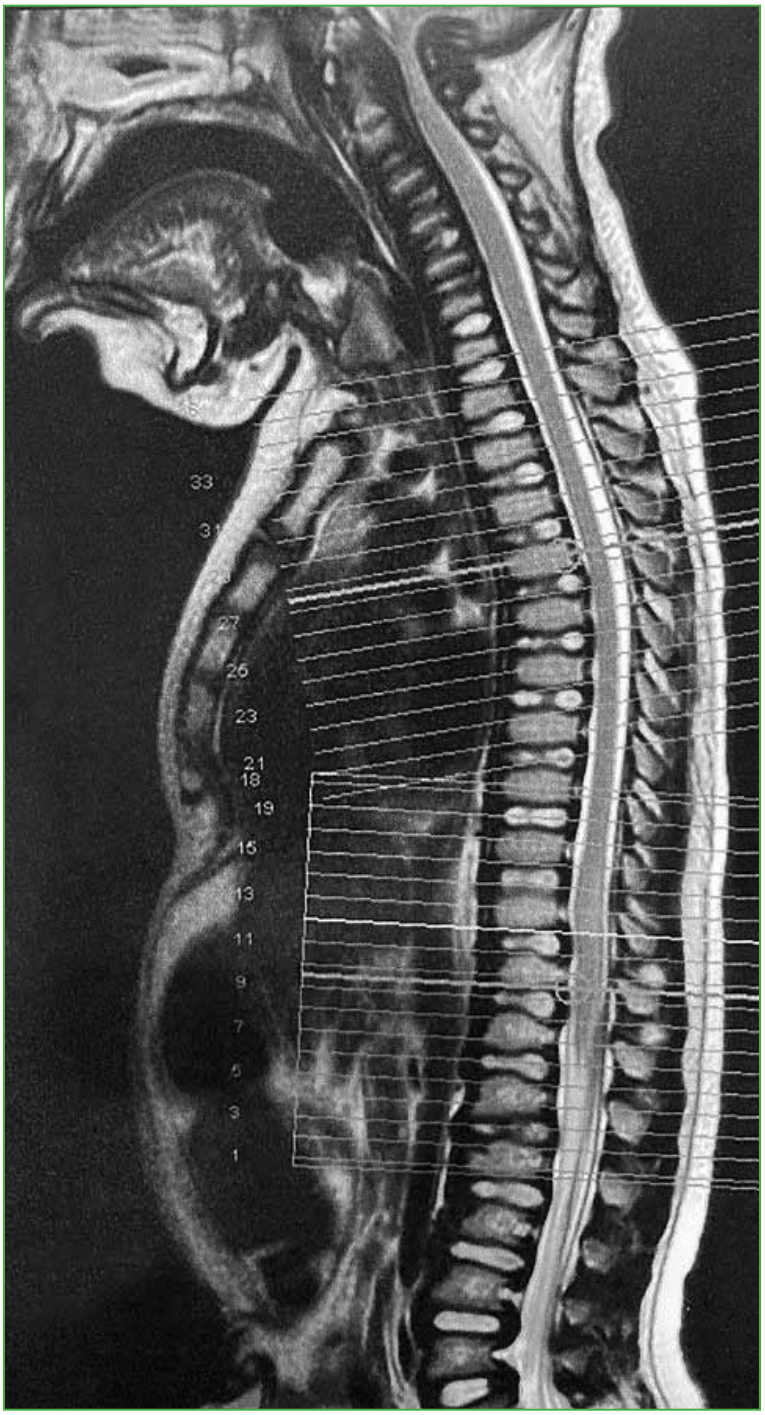

Figure 3. Magnetic resonance imaging of the complete spine, sagittal section. Posterior displacement of the nucleus pulposus, dysplasia of the vertebral bodies, and a decrease in spinal diameter at C0-2 are observed.

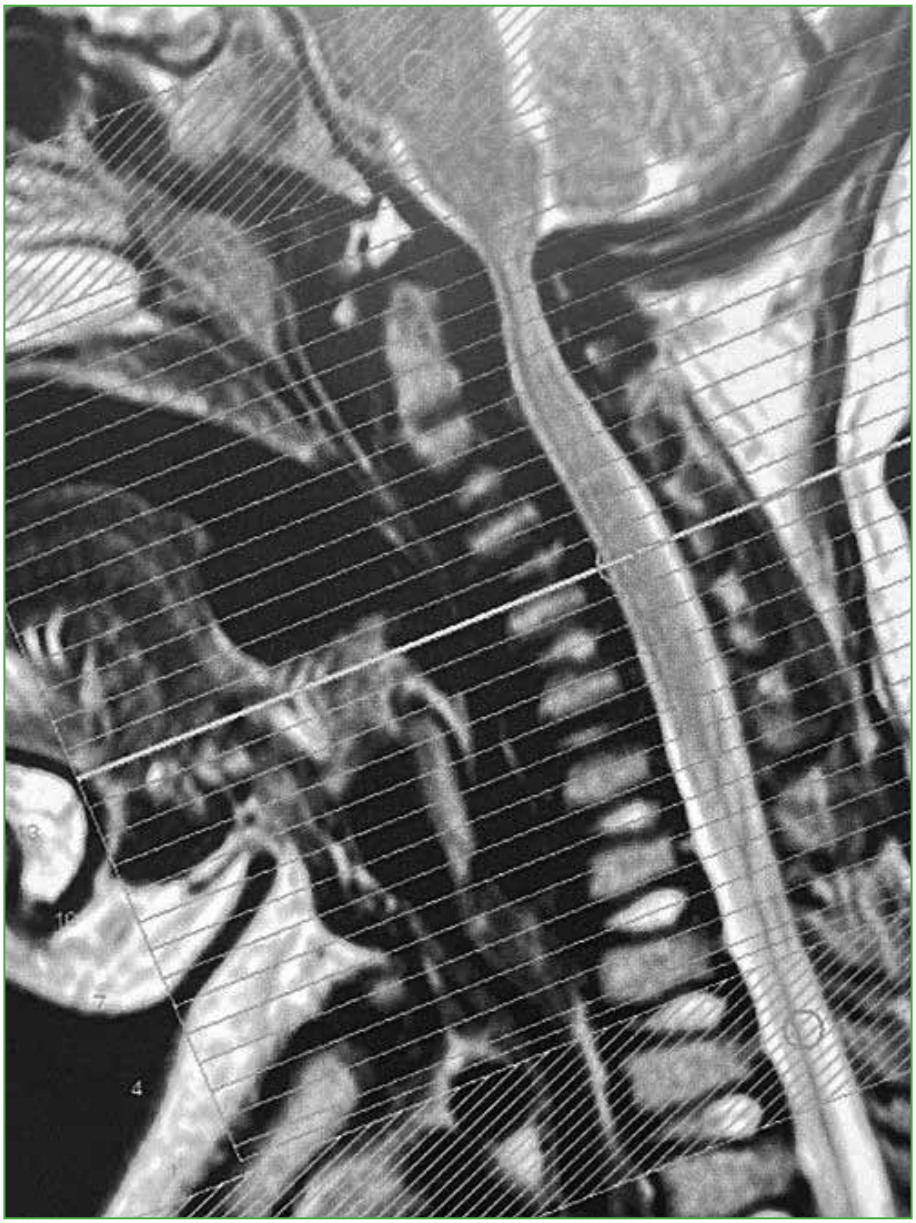

Figure 4. Cervical magnetic resonance, sagittal section. There is dysplasia of the vertebral bodies, hypoplasia of the odontoid process, and periodontoid tissue that causes a decrease in the diameter of the spinal canal, as well as myelomalacia in C0-1-2.

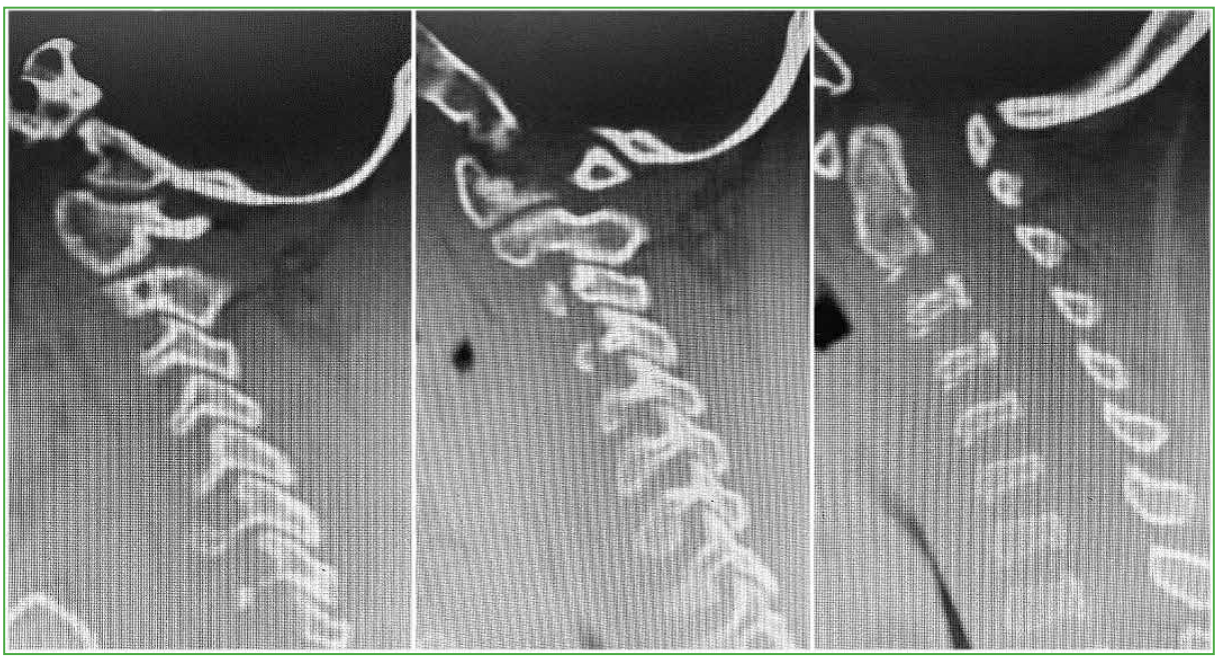

Figure 5. Cervical computed tomography, sagittal section. A decrease in the height of the C3-4-5 vertebral bodies is visualized, with no other bone anomalies.

Our center does not have an established protocol for this type of patient, but based on previous publications, preoperative check-ups were requested with the cardiology, neurology, pediatrics, anesthesiology, and pulmonology services, and the pediatric intensive care unit.

In June 2021, an arthrodesis of C0-C4 was performed with laminectomy of C1 and C2, and enlargement of the foramen magnum (in charge of the neurosurgery service). A protective halo brace was placed (Figure 6).

In this type of patients, intubation is a challenge, because they have a short neck, with a difficult airway associated with tracheal anatomical variations, so they must be evaluated by a specific team to define the need for a preoperative tracheotomy. In our case, it was not initially considered necessary.

Another concern is surgical positioning. Neuromonitoring should begin with the sedated patient in the supine position to avoid injury during intubation (controlling hyperextension of the neck) and rotation (it must be performed en bloc with head protection). The surgical position must be prone, with the head in a neutral position. If possible, it is preferred to place the halo brace for correct positioning.

The approach must be performed without any sudden movements and with careful bleeding control, because the pressure applied to the vertebral bodies to release or place the screws increases intracanal pressure and can cause neurological disorders. During the procedure, we found hypoplastic C1 and C2 posterior arches. During the decompression maneuvers (both at the level of C1 and the foramen magnum), the patient had episodes of extreme bradycardia with a drop in potentials and partial recovery at the end of the decompression. After the procedure, the patient was admitted intubated to the pediatric intensive care unit.

She was kept intubated and sedated for a month due to the difficult airway, short neck, and neutral position of the neck maintained by the halo brace, until it was decided to perform a tracheotomy. The patient suffered a lung infection associated with mechanical ventilation and a urinary infection, both conditions were treated with intravenous antibiotics, without complications at the surgical site.

Postoperatively, a control CT scan was performed and decompression was observed with the material in the correct position (Figures 7 and 8).

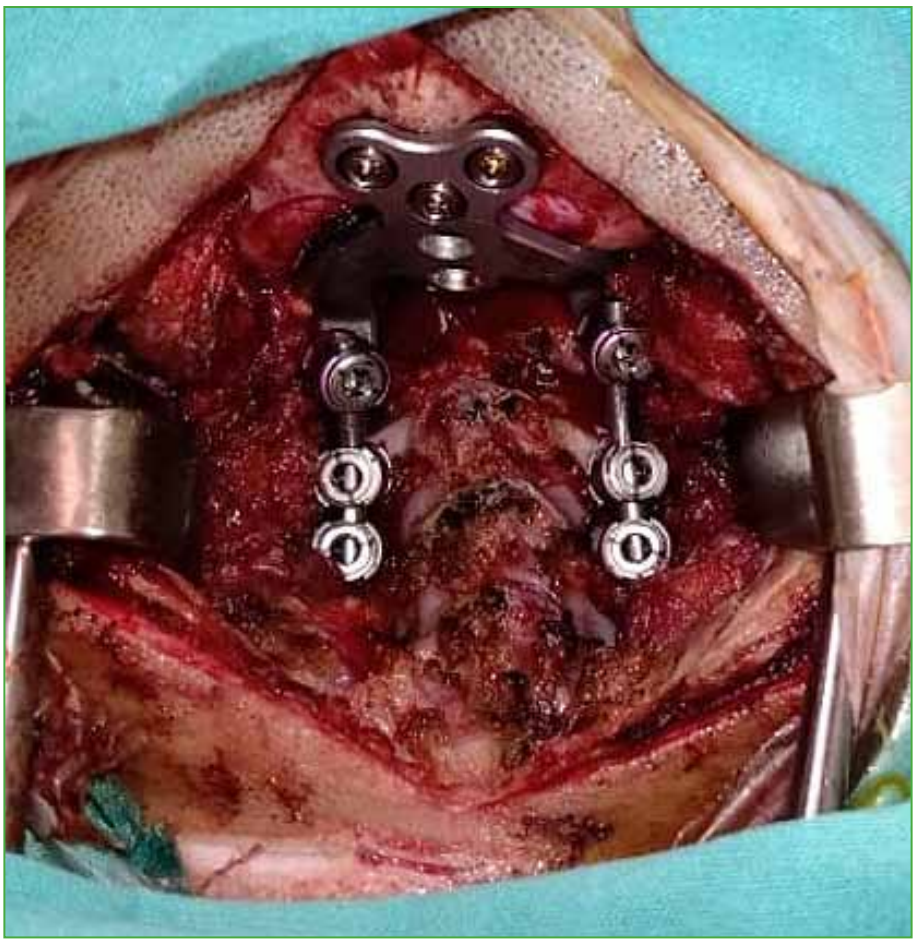

Figure 6. Intraoperative image. Decompression of C1-2. Occipito-cervical instrumentation.

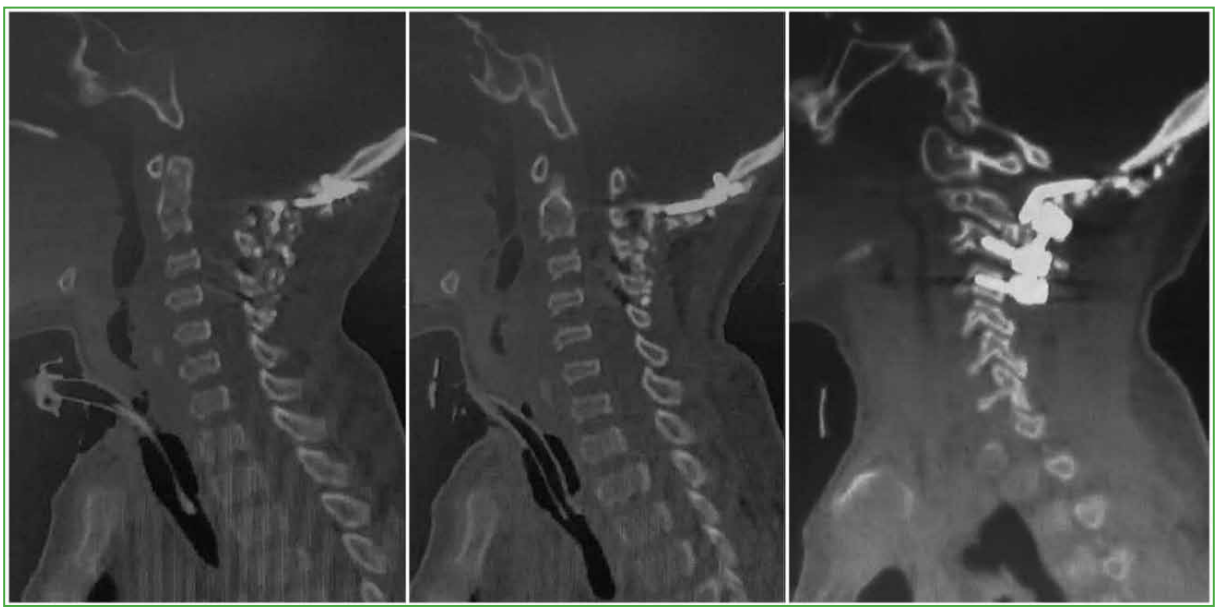

Figure 7. Postoperative cervical computed tomography, sagittal section. Instrumentation is appreciated, with occipital plate and cervical screws.

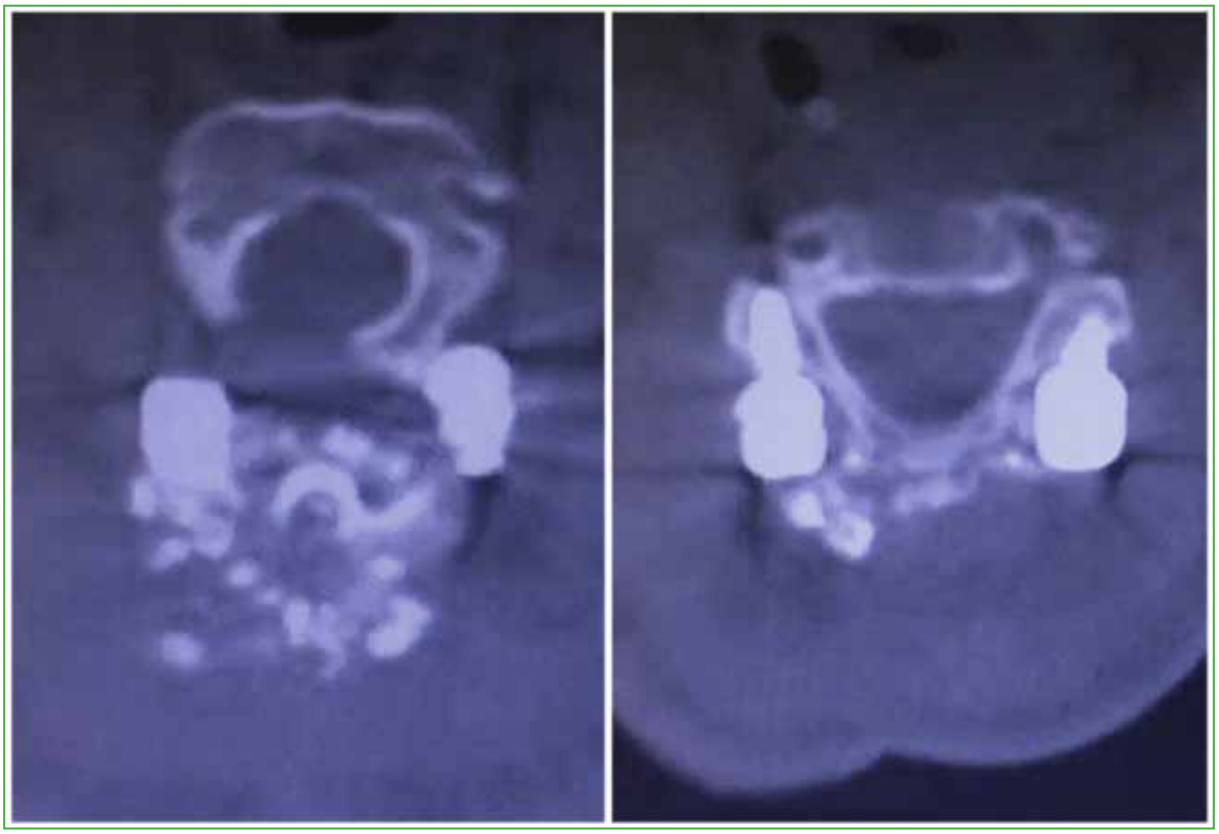

Figure 8. Postoperative cervical computed tomography, axial section. Note the decompression and the position of the screws.

When this article was written (18 months after surgery), the patient still had a tracheotomy, was walking unaided at home and with assistance outside the home, her paresthesias and neck pain had improved (Figure 9), and her preclaudication walking distance had increased. No signs of loosening were observed on the last radiographs (Figure 10).

DISCUSSION

The international literature on this disease mainly includes case reports or series of few patients. The preparation of treatment guidelines is complex.

In 2016, Solanki et al. published the findings of the Clinical Surveillance Program for MPS VI where 75% of patients with MRI had signs of spinal cord compression, demonstrating its high prevalence.[6] In agreement with the observations of Horovitz et al., they observed that spinal cord involvement can occur at very early ages, even in children <2 years of age.[4,6] They highlight an association between the severity of the baseline condition and abnormal findings of the cervical spine on MRI (dysmorphic vertebrae, stenosis, odontoid hypoplasia, periodontoid tissue) and conclude that it is essential to perform an MRI of the entire spine since the diagnosis of MPS VI.

Spinal cord compression can occur in both phenotypes (rapidly and slowly progressive forms) of patients with MPS VI. When the phenotype is rapidly progressive, compression occurs as early as 2 years of age, and patients typically require surgical decompression at a median age of 12 years, compared to those with the slowly progressive forms, which may require the procedure in the second or third decades of life. Despite the fact that there are no specific guidelines and given the high incidence of spinal cord compression, some follow-up rules have been established:[6,8-12]

Figure 9. Clinical image 17 months after surgery.

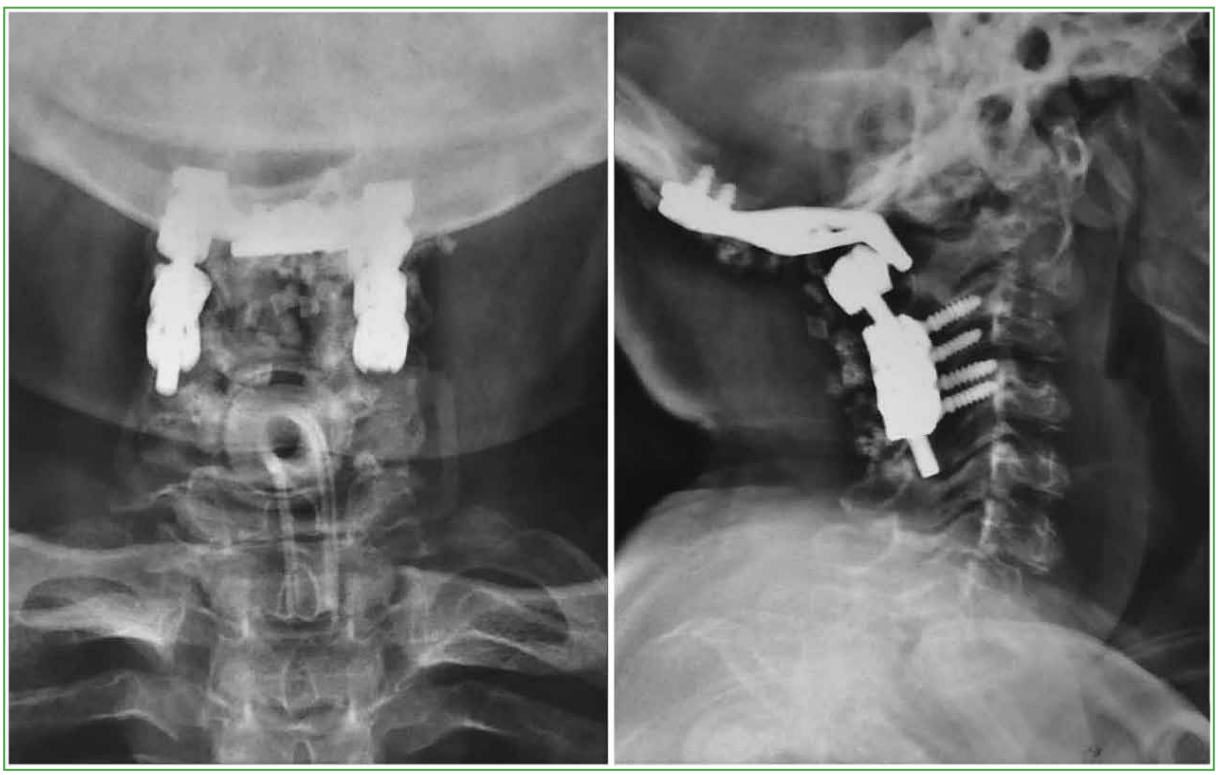

Figure 10. Anteroposterior and lateral cervical radiographs, after 9 months. Occipito-cervical instruments (C0-4) without signs of loosening.

- MRI of the entire spine, with sedation, before starting the enzymatic treatment. Despite the anesthetic risks posed by young patients, different groups suggest this study to establish a baseline risk and guide potential risks.[4,6]

- Routine neurological evaluation every 6 months to look for upper motor neuron signs, impaired proprioception, gait disturbances, reduced gait tolerance, bladder or rectal dysfunction. The search for impaired deep tendon reflexes, clonus, Babinsky, and Hoffman signs is especially important.

- Somatosensory evoked potentials every six months or yearly.[5,8]

- Cervical spine radiographs (static and dynamic), MRI or, if necessary, cervical computed tomography at least once a year, or every six months if the findings are abnormal.

MRI is considered the reference study in these patients, it is important to include the entire spine and the cerebellar fossa. It should be noted that, in specialized centers, flexion-extension MRIs are being performed to assess instability; however, to date, the risk of spinal cord injury in sedated patients is unknown.[6,9,11]

Since 2005, galsulfase enzyme replacement therapy has been available to treat patients with MPS VI, which has proven beneficial effects on some of the conditions of this disease, such as visceromegaly, respiratory infections, and quality of life. However, it has no effect on skeletal abnormalities and its effect on spinal stability is controversial. According to various studies,[4,5,9,11] enzyme replacement therapy can promote spinal cord damage by improving cervical mobility, and in cases of instability, even a few millimeters of movement can be clinically problematic, because the canal stenosis prevents any movement. As a result, regular neurological examinations and MRI follow-up are advised.

Lins et al.[11] analyzed the MRI findings of 12 patients and correlated them with the clinical manifestations. They evaluated the presence of odontoid process dysplasia, periodontoid tissue thickening, the space available for the medullary cord, the presence or absence of myelopathy, the presence of basilar intussusception and flattened vertebral bodies, disc signal alterations or disc disease, and nasopharyngeal airway narrowing. They found that all patients had cervical stenosis and periodontoid tissue. 50% had spinal cord compression, which was severe in 33%. Solanki et al.[6] reported a prevalence of spinal cord compression of 75% with 10% myelopathy. These authors emphasize that even asymptomatic patients with a normal neurological examination can have spinal cord compression.

Bullut et al.[9] analyzed the role of MRI and their findings were similar. They pointed out that age has a statistically significant relationship with the presence of periodontoid tissue, and reported a prevalence of myelopathy of 79% (the age range was higher than that of the Lins group). The authors concluded that MRI changes may precede the appearance of neurological examination abnormalities, so it is essential to perform neuroimaging studies before the changes become irreversible.

Not only was our patient symptomatic, but she also had unusual imaging findings: myelopathy, occipitocervical junction compression, vertebral body dysplasia, thoracic disc changes, and odontoid hypoplasia.

Regarding treatment, although there are no defined guidelines that guide when to operate and whether to opt for decompression or arthrodesis, there is consensus that surgery is indicated when symptoms or myelomalacia appear.[9-13]

When deciding on a treatment, the high anesthetic risk and potential benefit of decompressive surgery must be carefully considered. Multidisciplinary management of these patients is essential, as is preparation for the treatment of intraoperative (emergency tracheostomy, paraplegia) and postoperative complications (complex extubation, respiratory or urinary infections, cardiac complications). It would be useful to establish pre-surgical protocols for these patients in order to reduce complications, for example, tracheotomy planning could reduce complications associated with prolonged ventilation, as in this case.[2,6,12]

In 2013, Lampe et al.[13] developed a scale to indicate surgical treatment and predict outcomes, analyzing data from 31 patients. It contains three areas: the clinical-neurological examination, the somatosensory evoked potentials, and the MRI findings. Each is scored from 0 to 3 based on the findings. They recommend surgery in patients with a score of 4 or more; score 3 represents a relative indication for surgery and requires close monitoring of these patients. Our patient had 7 points on this scale (myelomalacia, increased latency in somatosensory evoked potentials, and weakness of the lower limbs); according to Lampe, surgery was imperative.

Although there are no specific recommendations, we opted for C0-1-2 decompression and C0-4 arthrodesis, due to the instability generated by the large release.

CONCLUSIONS

We present a patient with a rare disease who underwent surgery and discuss the factors to consider when making a therapeutic decision as well as the precautions to take during the operation.

It is critical to understand this disease in order to provide adequate follow-up, a multidisciplinary evaluation for proper management, and the appropriate choice of surgery.

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