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CASE REPORT

# Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome): 15 years follow-up after enzyme replacement therapy

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## Abstract

Type VI mucopolysaccharidosis, known as Maroteaux-Lamy syndrome, is an autosomal recessive genetic disease caused by deficiency of the lysosomal arylsulfatase B enzyme, leading to the accumulation of glycosaminoglycans in the lysosomes of all cell from an affected patient. This accumulation can lead to several clinical manifestations (growth retardation, dysmorphic facial features, motor impairment, audiovisual deficiencies, osteoarticular contractures and cardiorespiratory problems) that reduce the quality of life of an individual affected by such disorder. Symptom progression can lead to premature death. The only therapeutic possibilities for Maroteaux-Lamy syndrome were multiprofessional team care and bone marrow transplant (that has a high morbidity and mortality rate). Recently, clinical studies have demonstrated the safety and positive impact of enzyme replacement therapy (ERT) with rhASB (galsulfase, Naglazyme®) in MPS VI patients, especially when early initiated, halting the progressive involvement of many systems affected by this disease. Here we report the a Maroteaux-Lamy patient under ERT, drawing a parallel with his elder brother, also affected by the same disorder, who passed away before initiating ERT, pointing out the impact of the specific therapy in the management of multisystemic genetic disease and the challenges in the clinical follow-up of such patients.

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## INTRODUCTION

Maroteaux -Lamy syndrome , also known as mucopolysaccharidosis type VI (MPS VI) is an inherited lysosomal storage disorder in which there is accumulation of undegraded mucopolysaccharides due to deficiency of the enzyme arylsulfatase B (ASB)[1,2]. The origin of its name comes from two French doctors, Dr. Marateaux and Dr. Lamy, who were the pioneers to describe the exact biochemical deficiency of this syndrome in 1965. MPS VI, although it is a rare syndrome in the world, seems to be frequent in Brazil, for example in the city of Monte Santo, in the state of Bahia, the prevalence disease, is estimated at around 1:5,000 live births[3]. Its global incidence is estimated at 1.3-4.5: 100,000 births[4]. However, the true incidence of the disease may be higher, mainly due to the absence of mandatory screening for MPS VI in newborns[5].

Mucopolysaccharidoses were classified into types: I, II III, IV, VI, VII and IX. Type VI is a rare disease inherited in an autosomal recessive manner, caused by a mutation in the gene for the enzyme N - acetylgalactosamine 4-sulfatase ( arylsulfatase B) that leads to a deficiency or elimination of the function of this enzyme[6]. Arylsulfatase B is important because it breaks down glycosaminoglycans ( GAGs ), in this case dermatan sulfate. Its deficiency leads to the progressive accumulation of this GAG in lysosomes, causing osteoarticular, audiovisual and cardiovascular changes[1].

The clinical presentation of the disease varies greatly depending on the age of onset of clinical manifestations, the forms of disease progression are: slow, moderate and advanced[7,8]. MPS VI can have a wide spectrum of clinical phenotypes: there is an increase in the anteroposterior diameter of the skull, coarse facies, thick eyebrows, ocular proptosis, saddle nose, hypertrophy of the lips, high palate, dental dysplasia, macroglossia, neck short, narrow shoulders, globular abdomen, fingers and toes in semi-flexion position, single palmar crease, generalized hypertrichosis, valgus knees, flat feet and thick and less elastic skin.

These characteristics are not always present in their entirety, as there are severe forms that appear before the age of two and have rapid progression, and there are also intermediate to mild forms, in which the disease is diagnosed later in adolescence or even in adulthood, having a milder phenotype[5]. Despite the appearance changes, the disease does not cause intellectual disability, unlike types I, II, III, and VII, which may present cognitive deterioration[9].

For many years, MPS VI was progressive and, unfortunately, fatal in most patients due to the absence of specific treatment. Bone marrow transplantation represented an advance in the therapy of this disease, but was associated with a high risk of morbidity and mortality. Recently, however, the advent of enzyme replacement therapy has constituted a significant advance in the treatment of this disease, changing the natural history of this disease.

The objective of this work is to report the clinical history of a patient with Maroteaux - Lamy syndrome treated about 15 years ago and to draw a parallel with the brother also affected by this disease, but who died before having access to enzyme replacement therapy (ERT). ). In this report, data were obtained by reviewing the medical records with the authorization of the hospital ethics committee and the patient, obtained by signing the informed consent form, in addition to written authorization for the use of photos of the patient and his brother. by the family.

## CASE REPORT

Patient, male, son of a young and non-consanguineous couple, started the investigation for lysosomal storage disease because he had physical characteristics similar to those of his older brother, who was already being investigated for mucopolysaccharidosis

Her gestational history did not reveal intercurrences, the mother performed prenatal exams that showed no abnormalities.

Neuropsychomotor developmental history did not reveal significant delay in motor milestones. There is no report of other hereditary pathologies, parents were young at the time of conception and not consanguineous. There was no maternal exposure to teratogenic agents during pregnancy.

At the time, the patient had few findings for the disease (figure 1), but, due to the affected older brother, radiographic examinations were performed and biochemical tests were collected aimed at the hypothesis of Maroteaux - Lamy syndrome (table 1).

Biochemical tests confirmed the diagnosis of MPS VI at 2 years and 6 months of age, in September 1994. Brother, however, died due to respiratory complications associated with the disease in 1995. Patient continued to be followed up with several specialties and progressively showed somatic signs of the disease (figures 2 and 3).

Height deficit , joint contractures, valvulopathy , conductive hearing loss and, due to chronic cranial hypertension, developed bilateral optic atrophy, irreversibly losing vision.

Patient started enzyme replacement therapy (ERT) as part of a phase 3 clinical trial (double-blind 24-week duration) that was carried out in Brazil from October 20, 2003. After completion of the study phase, the patient continued with the use of ERT in the extension phase of



**Figure 1.** On the left, the patient in the report and, on the right, his deceased older brother. Source: The Authors.

the study and, later, began to use it regularly as part of its therapeutic management without participating in a clinical study.

In about 15 years of treatment with ERT, stability of the clinical picture was observed, with improvement of some parameters such as hearing loss, although others remained with irreversible sequelae (such as visual loss).

Her current clinical-genetic examination, aged 28 years, revealed: height below the 3rd percentile; weight between the 75th and 90th percentiles; head circumference between the 50th and 97th percentiles, infiltrated facies, short nasal dorsum, flat nasal root, thick lips, joint contracture and stiffness, claw hands, thick skull hair, umbilical hernia, grade 3 osteotendinous reflexes in lower limbs and grade 3 in upper limbs, exhaustible clonus in lower limbs, cutaneous-plantar reflex in extension.

At the moment, the patient has a regular job, managed to complete higher education and is currently back in college.

Regarding complementary exams, a radiographic study showed signs of *multiplex dysostosis* ; echocardiogram showed mitral valve with anterior leaflet thickened to a marked degree, double mitral lesion; electroneuromyography demonstrated the presence of multiple sites of nerve compression, compatible with carpal tunnel syndrome; audiometry revealed conductive hearing loss.

## DISCUSSION

Maroteaux -Lamy syndrome is caused by a deficiency of the enzyme arylsulfatase B, leading to the accumulation of glycosaminoglycans in the lysosomes of the cells of the affected individual[11]. This accumulation can lead to several clinical manifestations (growth retardation, facial dysmorphia, motor alterations, audiovisual deficiencies, osteoarticular deformities and cardiorespiratory problems) that reduce the quality of life of the individual without altering their intellectual capacity, which is preserved in this disease. Cardiovascular injuries are frequent in MPS VI and constitute an important cause of morbidity and mortality[11,12]. They result from the deposition of proteoglycans, dermatan sulfate and chondroitin sulfate in the interstitium of the myocardium and blood vessels. There may be an accumulation of glycosaminoglycans in the aortic and/or mitral valves, which leads to progressive valve degeneration, resulting in stenosis and/or insufficiency. Consequently, with the progression of valvular degeneration, hypertrophy of the left ventricle may occur, its dilation and later leading to pulmonary congestion and heart failure[12].

The first signs of involvement of the osteoarticular system are: deficit in stature and joint stiffness. These changes are progressive and may limit movements, due to metaphyseal involvement and the thickening and fibrosis of the joint capsule. The greater the progression of the disease, the worse the mobility of the joints, thus, the evaluation of the mobility of the knee, hip and elbow, can be considered a good marker of evolution of MPS VI. The vertebral column presents alterations in the vertebrae and ribs, which can be evidenced: thoracolumbar kyphosis, oval vertebral bodies with inferior bone protrusion. In the wrists and hands, there may be widening and shortening of the metacarpals and phalanges. Altogether, these findings are generically called *dysostosis multiplex* , a finding presented by the patient in the report. There may also be flexural contractures of the fingers (claw-hand appearance), knees, or shoulders. Another alteration found is the carpal tunnel syndrome (also observed in our patient), as the deposit of GAG leads to compression of the median nerve[1,12].

Patients with MPS VI are more likely to have glaucoma in up to 50% of cases in addition to progressive corneal opacification present in about 95% of patients. Optic nerve abnormalities may occur due to accumulation of glycosaminoglycans in ganglion cells, compression of the optic nerve due to thickening of the dura mater. and

**Table 1.** Laboratory tests.

| Glycosaminoglycans | 235 micro GAGs /mg (VN 13-45) |
|---|---|
| Plasma beta- glucuronidase enzyme assay | 125 nanomoles /hour/mg prot (VN=30-300) |
| Arylsulfatase B enzyme assay in leukocytes | 6 nanomoles /hour/mg prot (VN=72-280) |
| Beta-galactosidase enzyme assay in leukocytes | 84 nanomoles /hour/mg prot (VN=72-280) |

Source: The Authors.



**Figure 2.** A 6-year-old patient already showing somatic traces of the disease. Source: The Authors.

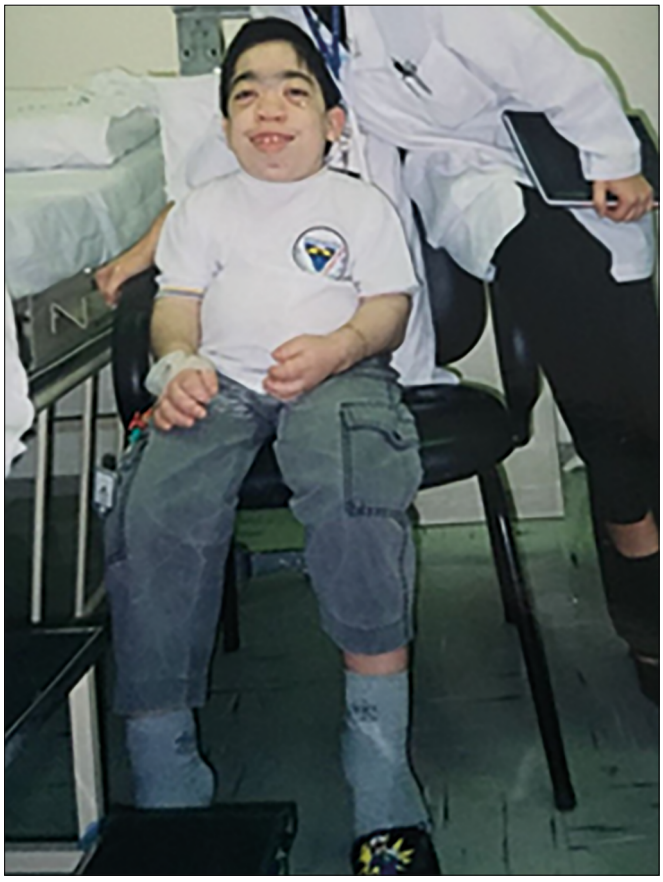


**Figure 3.** Patient, aged 14, when performing the first infusions with recombinant enzyme. Source: The Authors.

also due to increased intracranial pressure. About half of patients have optic disc alteration with mild to moderate edema[7,12]. This compression can lead to permanent visual loss, as happened in our patient.

Usually, the most advanced form of the disease presents from early childhood, progressive growth deceleration, skeletal deformities, facial dysmorphism, upper airway obstruction, and recurrent airway infections and otitis. As the disease progresses, patients become wheelchair-bound or bedridden due to joint skeletal deformities, cardiovascular deformities, blindness, and spinal cord compression. Without proper treatment, patients with rapidly progressing disease may have a life expectancy of less than 20 years. These patients usually die from cardiopulmonary disease, infection or surgical complications[13].

In terms of specific therapy for Maroteaux-Lamy syndrome, two strategies have been developed: hematopoietic stem cell transplantation (bone marrow transplantation) and, more recently, enzyme replacement therapy (ERT).

Bone marrow transplantation has been done in rare cases in recent years for the treatment of MPS VI in small case series. Although the leukocyte ASB enzyme is elevated, skeletal abnormalities remain difficult to correct and bone marrow transplantation is considered a limited treatment due to its high risk of mortality (30% mortality)[7]. Recently, clinical trials have demonstrated a positive impact on enzyme replacement therapy with rhASB (*galsulfase, Naglazyme ®*) which has become the first line of pharmacological treatment for the disease, especially when started early, delaying the involvement that affects cardiovascular function, facial dimorphism, hepatomegaly and physical development, although skeletal and ophthalmological abnormalities continue to progress[10].

The introduction of enzyme replacement with galsulfatase was a clinical milestone for the treatment of patients with MPS VI, who previously did not have many alternatives other than bone marrow transplantation and supportive care. Enzyme replacement showed better clinical results when using the 1.0 mg/kg dose of rhASB , many patients showed improvement in resistance tests (12-minute walk test and 3-minute stair test) and also a reduction in urinary levels of GAGs[10].

Currently, many case reports have demonstrated that the initiation of enzyme replacement therapy in younger patients has a clear benefit in preventing the progression of the pathophysiological aspects of the disease[14]. In a study by Horovitz[15], 4 unrelated children with MPS VI were followed up, who started ERT in the first year of life (1 mg/kg IV weekly of *Galsulfase / Naglazyme ®* for 6 years) and who have older siblings affected with the same disease. The study demonstrates that, even with early enzyme replacement therapy, many clinical aspects of the disease still persist, but when we compare some systemic changes in patients who used ERT for 6 years, such as manifestations

of the nervous, cardiac and orthopedic systems in relation to their brothers, it is observed that they are in a different degree of progression (slower)[15]. Thus, the study reports that the severity of the disease may be related to the age of initiation of treatment, as it was shown that the 4 patients who started ERT in the first year of life had a slower disease progression than that of their siblings[15].

Early initiation of enzyme replacement therapy (ERT) has demonstrated clinical benefits in patients with MPS VI. A study by Furujo[16] describes a 10-year follow-up of 2 Japanese brothers, both with MPS VI who were started on ERT with weekly infusions of 1mg/kg Galsulfase / Naglazyme ®. The older brother started treatment at 5.6 years old, reached puberty and although he had a growth spurt, his height was 3 deviations lower than expected on the growth curve[16]. He had the phenotypic characteristics of the disease and although his skeletal deformity remained, he exhibited a significant improvement in shoulder joint motion and practically no loss of cardiac function and hearing. In contrast, the younger sibling who started treatment at 6 weeks of age had virtually no symptoms typical of MPS VI such as facial dysmorphism, hepatosplenomegaly, and hearing impairment. Their joint mobility was preserved, but skeletal changes such as the claw hand were observed. Both brothers showed progressive corneal opacity. The follow-up of these 2 siblings demonstrates that the initiation of ERT in newborns can be well tolerated and contribute to the prevention or possible delay of the progression of the disease, some of the clinical symptoms may be milder or practically non-existent, but the skeletal and ophthalmologic tests remained present[16].

Even though our patient was one of the first patients to start enzyme replacement therapy in Brazil in 2003[13], the patient could not fully benefit from the treatment, due to his age at the time (13 years) and the progression of some manifestations of the disease. that are considered irreversible, such as weight and height deficit, joint contractures and bilateral optic atrophy, as well as corneal opacity. Even so, the patient's quality of life changed a lot after starting SBT, and one of the most significant clinical changes of the treatment was the recovery of much of his hearing. With proper treatment, the patient completed a higher education course and is currently back in college. Although he has some systemic manifestations of the disease present, he lives a relatively normal life with his family[13].

A study by Harmatz , Paul, et al with 10 patients aged between 6 and 22 years, 7 of whom had a rapidly evolving form of the disease, was carried out to assess endurance (resistance to physical activity), joint mobility and some biochemical parameters. After 24 weeks of treatment, patients had an average improvement of 155-m (98%) on the 12-minute walk test, they also had an improvement of 64-m (62%) at the sixth minute of the 12-minute walk and showed a 110% improvement in the 3-minute stair climb test. Additional improvements were seen after 48 weeks of treatment including mean values of 221 m (138%) in the 12-minute walk test and 75 m (80%) in the sixth minute of the 12-minute walk test and a 147% improvement in the 12-minute walk test. 3 minute stair climb test. On the joint pain and stiffness questionnaire, the score improved by at least 50% at week 24 and remained at week 48, however there were small improvements in shoulder joint range of motion (< 10 degrees) and in the time required to stand. , walk and turn *(expanded timed get up and go test)*[11].

Our patient also showed improvements in *endurance.* Before starting the treatment, he did not have the strength to stand, thus using a wheelchair, after ERT, the patient abandoned the wheelchair and now has the ability to walk independently. However, due to the late age at the beginning of treatment, the range of motion of the joints did not improve significantly.

Has brought many benefits and increased survival for patients, which implies a change in the morbidity and mortality profile. However, there are still many limitations, one of which is spinal cord compression myelopathy that occurs with or without therapy. With access to treatment, patients are having a longer life expectancy and many will need surgery to correct spinal cord compression. Before ERT, patients died of cardiorespiratory problems, but today with treatment they have more problems related to spinal cord compression[17].

Spinal cord compression is a serious complication of MPS VI and typically arises from spinal canal stenosis secondary to malformations of the spinal canal, skull base, and/or GAG accumulation in tissues surrounding the spinal cord. Compression is caused by diffuse thickening of the dura and extradural soft tissues in the cervical region. Atlantoaxial instability is another important cause of cervical cord compression especially in patients with MPS VI[18].

Compression usually occurs in the cervical region and may involve multiple levels and may also lead to compressive myelopathy or myelomalacia. Cervical cord compression is potentially debilitating and life-threatening[18]. MRI is considered the gold standard test for diagnosing cervical cord compression. Early signs of myelopathy can be detected by clinical neurological examination. Surgical interventions usually involve decompression, however airway management and anesthesia during surgery are challenges[18].

It is not possible to obtain accurate data on the age range of onset of cervical cord compression because most patients discover spinal cord compression at the first MRI scan. However, as shown in the study by Solanki , Guirish A., et al cervical cord compression can develop early, in a sample of 4 children under 2 years of age were reported to have compression already in the first MRI. Approximately 75% of subjects evaluated by MRI had documented cervical spinal cord compression indicating the frequency of

cervical compression [20]. Even among individuals without signs of compression on MRI, almost all (93.9%) had cervical spine abnormalities such as stenosis and dysmorphic vertebrae . Taken together, these findings suggest that all patients with MPS VI are at significant risk of developing cervical spine compression at a young age and underscore the importance of routine MRI at the time of diagnosis of Maroteaux - Lamy syndrome[17].

A detailed neurological assessment should be performed in patients treated with ERT, especially during the period of improvement in the osteoarticular condition. ERT has not been successful in preventing cervical myelopathy and surgical decompression is required in order to achieve a satisfactory outcome and it may be crucial to perform surgery at an early age[17].

The presence of neurologic abnormalities such as quadriparesis and/or spasticity, urinary retention secondary to neurogenic bladder, hyperreflexia with or without clonus , or a history of decreased exercise tolerance or difficulty standing up should alert the physician to the possible need for cervical surgery. decompression because it allows a significant neurological improvement. Therapeutic decisions and approaches vary and depend on the clinical picture, functional tests and radiological findings. Factors such as institutional resources and physician experience play a significant role in determining when to perform surgery. Mortality from surgery is related to anesthesia and may occur during or after the cervical decompression procedure. In one case involving a 12-year-old patient there were episodes of desaturation followed by cardiac arrest that occurred 36 hours after surgery. In another case intubation failure resulted in hypoxia and death in a 13-year-old patient. Both cases illustrate the high anesthetic risk of individuals with MPSVI. Obstructed airways, COPD, heart problems, cervical instability, and myelopathy all contribute to an increased risk of anesthesia-related complications. Careful preoperative care, anticipation of problems and the involvement of anesthesiologists with the physician accompanying the case can be fundamental to minimize the risk of perioperative mortality[18].

Therefore, ERT has positively modified the course of the disease, but it still does not represent a cure. Although it has significantly improved the quality of life of patients with MPS VI as exposed in the patient's case, avoiding fatal complications, there are still several open questions. Among them, the fact that myelopathy has become a reality for many patients due to their current longevity[11,12]. There is a need to train more neurosurgeons and spinal orthopedists to be able to perform adequate surgical interventions, as many patients are dying during or after spinal decompression surgeries, since many of the complications presented by these patients do not have their pathophysiology completely clarified, in addition to from the very challenge of complications associated with the anesthetic procedure[17,18].

## REFERENCES


1. Turtelli CM. Manifestações radiológicas da mucopolissacaridose tipo VI. Radiol Bras. 2002 Out;35(5):311-4.
2. Borges MF, Tavares FS, Silva PCL, Oliveira ZAR, Ballarin MAS, Gomes RA, et al. Mucopolissacaridose tipo VI (síndrome de Maroteaux-Lamy): avaliação endócrina de três casos. Arq Bras Endocrinol Metab. 2003 Fev;47(1):87-94.
3. Costa-Motta FM, Bender F, Acosta AX, Abe-Sandes K, Machado T, Bomfim T, et al. A community-based study of mucopolysaccharidosis type VI in Brazil: the influence of founder effect, endogamy and consanguinity. Hum Heredity. 2014 Jul;77(1-4):189-96.
4. Cardoso-Santos A, Azevedo ACMM, Fagondes S, Burin MG, Giugliani R, Schwartz IVD. Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome): assessment of joint mobility and grip and pinch strength. J Pediatr (Rio J). 2008 Abr;84(2):130-5.
5. Harmatz P, Shediac R. Mucopolysaccharidosis VI: pathophysiology, diagnosis and treatment. Front Biosci (Landmark Ed). 2017 Jan;22(3):385-406.
6. Neufeld EF, Muenzer J. The mucopolysaccharidoses. In: Scriver CR, Beaudet AL, Sly WS, Valle D (eds.). The metabolic and molecular bases of inherited disease. New York: McGraw-Hill; 2001. p. 3421-52.
7. Valayannopoulos V, Nicely H, Harmatz P, Turbeville S. Disease name with synonyms. Orphanet J Rare Dis. 2010 Abr;5:5.
8. Swiedler SJ, Beck M, Bajbouj M, Giugliani R, Schwartz I, Harmatz P, et al. Threshold effect of urinary glycosaminoglycans and the walk test as indicators of disease progression in a survey of subjects with mucopolysaccharidosis VI (Maroteaux-Lamy syndrome). Am J Med Genet A. 2005 Abr;134(2):144-50.
9. Walkley SU, Thrall MA, Haskins ME, Mitchell TW, Wenger DA, Brown DE, et al. Abnormal neuronal metabolism and storage in mucopolysaccharidosis type VI (Maroteaux-Lamy) disease. Neuropathol Appl Neurobiol. 2005 Out;31(5):536-44.
10. Lourenço CM, Giugliani R. Evaluation of galsulfase for the treatment of mucopolysaccharidosis VI (Maroteaux-Lamy syndrome). Expert Opin Orphan Drugs. 2014;2(4):407–17.
11. Mitchell, John, et al. "Unique medical issues in adult patients with mucopolysaccharidoses." European journal of internal medicine 34 (2016): 2-10.
12. Mizuno CA, Figueiredo JB, Tavares I, Teza V, Tai- LGN. Aspectos clínicos da mucopolissacaridose tipo VI * Clinical aspects of mucopolysaccharidosis type VI. Rev Bras Clin Med. 2010;8(4):356–61.
13. Harmatz, Paul, et al. "Direct comparison of measures of endurance, mobility, and joint function during enzyme-replacement therapy of mucopolysaccharidosis VI (Maroteaux-Lamy syndrome): results after 48 weeks in a phase 2 open-label clinical study of recombinant human N-acetylgalactosamine 4-sulfatase." Pediatrics 115.6 (2005): e681-e689.
14. J.J. McGill, A.C. Inwood, D.J. Coman, M.L. Lipke, D. de Lore, S.J. Swiedler, J.J. Hopwood, Enzyme replacement therapy for mucopolysaccharidosis VI from 8 weeks of age–a sibling control study, Clin. Genet. 77 (2010) 492–498, http://dx.doi.org/10.1111/j.1399-0004.2009.01324.x.
15. Horovitz DDG, Acosta AX, De Rosso Giuliani L, Ribeiro EM. Mucopolysaccharidosis type VI on enzyme replacement therapy since infancy: Six years follow-up of four children. Mol Genet Metab Reports [Internet]. 2015;5:19–25. Available from: http://dx.doi.org/10.1016/j.ymgmr.2015.09.002

14. Furujo, Mahoko, et al. “Enzyme replacement therapy attenuates disease progression in two Japanese siblings with mucopolysaccharidosis type VI.” Molecular genetics and metabolism 104.4 (2011): 597-602.

17. Jurecka, Agnieszka, et al. “Spinal cord compression in Maroteaux-Lamy syndrome: case report and review of the literature with effects of enzyme replacement therapy.”Pediatric neurosurgery 48.3 (2012): 191-198.

18. Solanki, Guirish A., et al. “Cervical cord compression in mucopolysaccharidosis VI (MPS VI): Findings from the MPS VI Clinical Surveillance Program (CSP).” Molecular genetics and metabolism 118.4 (2016): 310-318.