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Case Report

Chiari I malformation and syringomyelia in mucopolysaccharidosis type I (Hurler syndrome) treated with posterior fossa decompression: Case report and review of the literature

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Abstract

Background: Hurler Syndrome is the most severe phenotype of mucopolysaccharidosis type I. With bone marrow transplant and enzyme replacement therapy, the life expectancy of a child with Hurler syndrome has been extended, predisposing them to multiple musculoskeletal issues most commonly involving the spine.

Case Description: This is the case report of a 6-year-old male with Hurler syndrome who was diagnosed with Chiari I malformation and cervicothoracic syringomyelia on a preoperative magnetic resonance imaging (MRI) for his thoracolumbar kyphosis. This report details the successful management of a Chiari I malformation and syringomyelia with posterior fossa decompression in a child with Hurler syndrome.

Conclusion: Children born with MPS I can have complex spine issues that require surgical management. The most common orthopedic spinal condition for these patients, thoracolumbar kyphosis, requires evaluation with an MRI before performing surgery. This resulted in the diagnosis of a Chiari I malformation and syringomyelia in our patient with Hurler syndrome. This was successfully treated with decompression of the posterior fossa.

Key Words: Chiari I Malformation, Hurler syndrome, mucopolysaccharidosis type I, posterior fossa decompression, syrinx

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INTRODUCTION

Mucopolysaccharidosis type I (MPSI) is an autosomal recessive lysosomal storage disease caused by deficient or absent activity of the α-L-iduronidase enzyme (IDUA), which catalyzes the degradation of the glycosaminoglycans (i.e., dermatan and heparan sulfates), the most severe form of which is Hurler syndrome (HS).[25] Without treatment, patients with HS suffer from multisystem manifestations including mental retardation, skeletal deterioration, severe

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cardiopulmonary disease, hepatosplenomegaly, visual impairment, and deafness, usually leading to death within the first decade of life.[8] The advent of allogeneic hematopoietic stem cell transplantation from bone marrow, peripheral blood, or unrelated umbilical cord has resulted in the reversal of organomegaly, preservation of neurocognitive development, and improved hearing, vision, and cardiopulmonary function in most transplanted patients.[1,8,9,13,18,20,21] With improvement in treatment, not only is the life expectancy of a child with HS increased, so is the risk of development of other medical conditions. To our knowledge, there have been only two papers published in the English medical literature describing syringomyelia in patients with mucopolysaccharidosis type II (Hunter syndrome)[14] and type VI (Maroteaux–lamy syndrome).[10] There have been no reports on the diagnosis and management of a Chiari I malformation (CM-I) and syringomyelia in a patient with HS. In this manuscript, we present a case of a 6-year-old child with HS who was diagnosed with CM-I and a cervicothoracic syrinx during a preoperative magnetic resonance imaging (MRI) for the surgical management of his thoracolumbar kyphosis.

CASE REPORT

The patient is a 6-year-old male who was referred to a pediatric clinic for an incidentally found CM-I and cervicothoracic syrinx [Figure 1] identified during a preoperative workup prior to the surgical management of a progressive thoracolumbar kyphosis [Figure 2]. The child has been experiencing daily headaches, but denied dysphagia, neck pain, or numbness or weakness in the upper extremities. His family also noted difficulty with hand coordination and strength when compared to his peers. Born via caesarian section at 41 weeks with a birth weight of 8 pounds and 12 ounces, he was diagnosed with HS and underwent a bone marrow transplant at the age of 14 months.

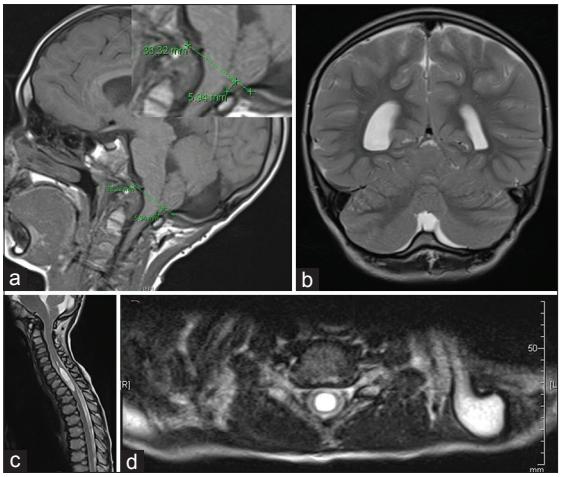

Figure 1: Preoperative MRI findings. (a) MRI brain, T1WI sagittal view. Demonstrates cerebellar ectopia, measuring approximately 5.9 mm with crowding within the foramen magnum. (b) MRI brain, T2WI coronal view. Demonstrates prominent retrocerebellar cystic space. The differential diagnosis includes major cisterna magna versus an arachnoid cyst. (c) MRI cervicothoracic spine, T2WI sagittal view. Demonstrates 8 mm syrinx from C_5 to T_{1-2}. (d) MRI cervicothoracic spine, T2WI axial view at the level of C_{6-7}

On physical examination, the patient was noted to be alert and oriented with clear speech and normal cranial nerve function. Muscle strength was 5/5 in bilateral biceps, triceps, and deltoids, 4+/5 in hand grip and finger abduction. Deep tendon reflexes were grade 2/4 in the upper and lower extremities with a negative Hoffman's sign bilaterally, no ankle clonus, and a downgoing Babinski test bilaterally. The patient was unable to perform single-leg stance.

On August 4, 2015 the patient was taken to the operating room where he underwent a successful suboccipital craniectomy measuring 3 × 3 cm, C_1 laminectomy, intradural exploration with coagulation of cerebellar tonsils, lysis of arachnoid adhesions, resection of thick posterior arachnoid membrane, and duraplasty measuring 3 × 3 cm utilizing Dura-Guard™ (Baxter Healthcare Corporation, Mountain Home, Arizona) and DuraSeal™ (Medtronic, Minneapolis, Minnesota). Intraoperatively, he was noted to have numerous arachnoid adhesions, an arachnoid cyst, and cerebellar tonsillar herniation to the level of C_1 was confirmed. Postoperative course was unremarkable, and he was ultimately discharged home on postoperative day 3.

At his first 2-week postoperative follow-up, his mother reported more stability with his gait and improved balance. The patient returned to school. The patient's physical examination was unchanged from his preoperative exam except that he was now able to perform a single-leg stance. At his 3-month

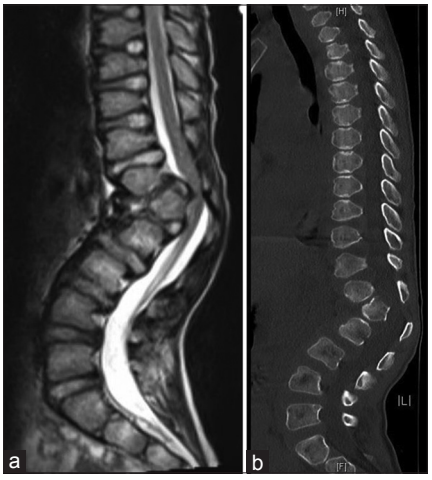

Figure 2: Spinal Imaging. (a) MRI thoracolumbar spine, sagittal view. (b) CT thoracolumbar spine, sagittal view. Both demonstrate severe gibbus deformity centered at L1 causing moderate to severe bony spinal canal stenosis

follow-up visit, his parents reported that he continued to improve. His daily headaches had resolved, and the MRI of the cervicothoracic spine revealed improvement in the size of the syrinx measuring 3.5 mm at its widest point [Figure 3].

Six months after suboccipital craniectomy, the patient underwent an uncomplicated anterior release and posterior spinal fusion with correction of his thoracolumbar kyphosis. During the most recent 3-month follow-up visit, the patient was found to have complete resolution of his gibbus deformity and no changes with his neurologic exam. The MRI of the cervical and thoracic spine revealed a stable syrinx. This case report was approved by the University of Missouri Health Sciences Institutional Review Board, and an informed consent was obtained from the patient's parents.

DISCUSSION

In 1891, Hans Chiari documented three cases of congenital defects of the rhombencephalon, classified as type I, II, and III.[6] The most common type is CM-1, which is present in 0.56–1% of the population.[16] The radiologic diagnosis of CM-I is best made on cranial midsagittal MRI studies, with cerebellar tonsil herniation of at least 3 mm below the basion-opisthion line suggesting the condition [Table 1].[3,11,15] The symptoms of CM-I include head, neck, and back pain, cape pain (shoulders), nonradicular limb pain, weakness, paresthesias, vestibular symptoms, diplopia, tinnitus, hearing loss, syncope, slurred speech, dysphagia, urinary incontinence, and sleep disturbance.[16] A syrinx is present in 30–70% of cases of CM-I.[15]

MPSI is an autosomal recessive lysosomal storage disease caused by mutation in the *IDUA* gene located on chromosome 4p16.3,[12] resulting in deficient or absent activity of the *IDUA*, which catalyzes the degradation of the glycosaminoglycans (i.e., dermatan and heparan sulfates).[25] These molecules can be found in free form in the extracellular matrix or as part of the structure of different types of proteoglycans, with important functions both in the structure of tissues and intercellular communication. Intralysosomal accumulation of these substrates results in pathological processes that produce a progressive dysfunction resulting in multiorgan deterioration that includes hepatosplenomegaly, dysostosis multiplex, short stature, coarse facial features, corneal clouding, joint contractures, umbilical hernias, failure to thrive, intellectual disability, and developmental delay.[5,12] The extensive storage of these glycosaminoglycans is also known to cause meningeal thickening.[4] Intraoperatively, our patient was noted to have thickened arachnoid membrane, which was biopsied and sent for pathological assessment. The sample did not reveal any intracellular storage of Luxol Fast Blue or Periodic Acid-Schiff positive contents, which neither supports nor refutes the clinical diagnosis of mucopolysaccharidosis.

Historically, MPSI has been divided into three clinical subtypes – Hurler (severe), Scheie (mild/attenuated), and Hurler–Scheie (intermediate).[1] This classification is based on clinical factors such as the age of onset, the rate of functional deterioration, and the range of affected organs (i.e., CNS involvement).[1] HS is the most severe phenotype in the spectrum of MPSI, with a prevalence of approximately 0.69 cases per 100,000 births.[2] Diagnosis of MPSI is based on *IDUA* enzyme analysis in leukocytes or dried blood spots followed by molecular confirmation of the *IDUA* gene mutations in individuals with low enzyme activity.[12]

HS progresses rapidly from 6 to 24 months resulting in significant multiorgan dysfunction.[5] Historically, the natural history of HS involved death before the age of 10 due to respiratory complications or cardiomyopathy.[17] Because new therapies such as allogeneic hematopoietic stem cell transplantation became a viable treatment option, reversal of organomegaly, preservation of neurocognitive development, and improved hearing, vision, and cardiopulmonary function in most transplanted patients have been observed.[1,8,9,13,18,20,21] To our knowledge, there have been only two papers published in the English language medical literature describing the diagnosis and treatment of syringomyelia

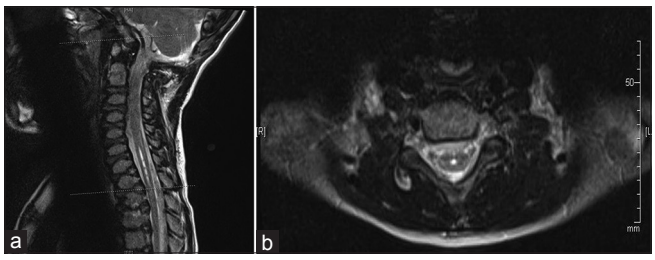

Figure 3: 3-month postoperative MRI. (a) MRI cervicothoracic spine, T2 WI sagittal view. Demonstrates improvement in syrinx from C_5 to T_{1-2}. (b) MRI cervicothoracic spine, T2 WI axial view at the level of C_{6-7}

Table 1: Diagnostic quick reference for Chiari I malformation and variants. This table is reproduced with the permission of the authors and the Neurologic Clinics

Definition	Measurement of Tonsillar Descent Below the Basion-Opistion Line on MR Sagittal Images
Cerebellar tonsillar ectopia (considered normal)	< 3 mm
Chiari 0	< 3 mm with syringomyelia or syringohydromyelia
Borderline Chiari I	3-5 mm
Chiari I (>15 y)	> 5 mm
Chiari I (<15 y)	> 6 mm

in mucopolysaccharidosis patients. No one has reported this diagnosis in a patient with HS.

Manara *et al*.,[14] reported a case of CM-I and holocord syringomyelia in a patient who was diagnosed with Hunter syndrome at the age of 18 months. Patient was ultimately treated with enzyme replacement therapy with idursulfase. A brain MRI revealed enlarged cisterna magna along with cerebellar tonsils ectopia consistent with CM-I. MRI of the cervical spine failed to reveal a syringomyelia, whereas a repeat MRI at the age of 5 years revealed a focal thin syrinx. The child only complained of upper limbs numbness and loss of sphincter control without any other neurological deficits. A follow-up MRI 1 year later showed a holocord syrinx extending from the cervicomedullary junction to the conus medullaris. The child underwent posterior fossa decompression (PFD) for CM-I. At 7-months follow-up preoperative symptoms had resolved, whereass the MRI demonstrated significant decreased in size of the syrinx.

Hite *et al*.,[10] reported the case of a 6-month-old boy who initially presented for evaluation of hepatosplenomegaly and increased head circumference. He was diagnosed with mucopolysaccharidosis type VI (Maroteaux–lamy syndrome) and treated with allogeneic bone marrow transplantation at the age of 14 months. Pretransplant spinal MRI was essentially normal, however, by 4 years of age a follow-up MRI revealed a holocord syringomyelia from C2 to L1. The syrinx remained stable on serial MRIs and the patient continued to have no focal motor or sensory abnormalities. Thus, no neurosurgical intervention was performed.

In 2003, Zafeiriou *et al*.,[26] summarized typical brain and spine MRI findings in patients with mucopolysaccharidosis. It was noted that the most prominent brain features identified in almost all types of mucopolysaccharidosis were white and gray matter changes, ventriculomegaly and hydrocephalus, cortical atrophy, and enlargement of the perivascular spaces. Spinal MRIs usually revealed canal stenosis and cord compression with spinal cord signal changes [Table 2].[26] Looking specifically at the posterior fossa, mega cisterna magna was the most common radiologic finding. Ultimately, the correlation between imaging findings and the disease severity remains unclear. Intraoperatively, in our patient, the posterior fossa thickened membrane versus arachnoid cyst appeared to be causing compression on the surrounding tissue, which may have played a role in the tonsillar ectopia.

Tandon *et al*.,[22] published a case series among 12 patients with HS with a mean of 4.5 years follow-up after undergoing bone marrow transplantation. High lumbar kyphosis was noted in 10 patients, which was associated with thoracic scoliosis in one, whereas isolated thoracic scoliosis was seen in another. One patient did not have any significant problems in the thoracic or lumbar spine but had odontoid hypoplasia, which was also seen in three other children. Four of the 8 patients in whom MRI of the cervical spine had been performed had abnormal soft tissue around the tip of the odontoid. Neurological problems were only seen in two patients. In one it was caused by cord compression in the lower dorsal spine 9.5 years after posterior spinal fusion for progressive kyphosis, and in the other by angular kyphosis with thecal indentation in the high thoracic spine associated with symptoms of spinal claudication.

Table 2: Overview of the most frequent brain and spinal MRI abnormalities identified in MPS according to disease type. This table is reproduced with the permission of the authors and the American Journal of Neuroradiology

	Signal Alternations	Enlarged PVS	Hydrocephalus/ Ventriculomegaly	Atrophy	Spinal Stenosis
MPS I					
Hurler	+++	+++	+++	++	++
Hurler/ Scheie	++	++	++	+	++
Scheie	++	++	++	+	++
MPS II	+++	+++	+++	+++	+
MPS III					
III A	++	++	++	+	+
III B	++	++	+	+++	-
III C	-	-	-	-	-
III D	+		±	+	-
MPS IV					
IV A	±	-	+	-	+++
IV B	±	-	-	-	+++
MPS VI	+	+ +	+	+	+++
MPS VII	+ +	-	-	-	+
MPS IX	-	-	-	-	-

Note: +++: indicates a constant finding, ++: a frequent finding, +: a less frequent finding, ±: rare, -: not described in the literature to our knowledge

PFD has long been performed to relieve compression and restore normal CSF pathways at the craniocervical junction.[24] A survey on surgical treatment of CM-I with syringomyelia conducted by the American Society of Pediatric Neurosurgeons showed that 85% of the respondents perform PFD as first-line treatment, whereas less than 3% offer syrinx drainage as first-line therapy.[7,19] In addition, routine practice consisted of bony decompression alone for 7%, decompression with duraplasty in 36%, and additional tonsil reduction for 27%.[7] Xie *et al*.[24] examined 87 patients aged 5–18 years who had undergone PFD. They noted 72.4% improvement of symptoms at final follow-up. In 90.8% of the cases, significant syrinx resolution was also noted.

Wu *et al*.[23] reported that typically the syrinx resolved within 6 months after PFD. In their retrospective review of patients with CM-I who had undergone PFD, Chotai *et al*.[7] noted that 87% of the patients indicated they would choose to undergo the surgery again.

CONCLUSION

MPSI is an autosomal recessive lysosomal storage disorder causing a chronic, progressive multiorgan disease by deficient or absent activity of the α-L-iduronidase enzyme, which catalyzes the degradation of glycosaminoglycans.[25] Bone marrow transplant and enzyme replacement therapy has led to an increased life expectancy for this once fatal disease. Patients with HS are now at an increased risk of developing other medical conditions associated with their disease, including progressive TL kyphosis, symptomatic carpal tunnel syndrome, angular deformity of the lower limbs, and hip dysplasia that may require surgical treatment. Diagnosing and properly managing a CM-I and syrinx in this patient population is necessary to avoid neurologic complications and spinal cord injury that could occur from anesthesia and surgical management of HS patients. Though these three reports represent a small case series, given the fact that all three patients developed a syrinx on serial imaging, and two of the three demonstrating neurologic abnormalities, we would suggest that patients with mucopolysaccharidosis require routine follow-up for clinical assessments with spinal imaging as indicated by history and physical examination.

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Conflicts of interest
There are no conflicts of interest.

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