

# Carpal Tunnel Syndrome in the Setting of Mucopolysaccharidosis II (Hunter Syndrome)

Anne E. Argenta, MD\*  
Alexander Davit, MD†

**Background:** Carpal tunnel syndrome (CTS) is a rare finding in children, but heavily represented in pediatric patients with mucopolysaccharidoses. Diagnosis is a challenge due to lack of the stereotypical symptomatic complaints and relies on examination and objective nerve conduction studies.

**Methods:** We present a case of delayed presentation of CTS in a 12-year-old boy with Hunter syndrome, followed by a review of the literature.

**Results:** Patient Z.D. presented with minimal reported CTS symptoms but advanced median nerve damage on electromyography. He underwent bilateral carpal tunnel release with median nerve neurolysis and flexor tenosynovectomies. Intraoperative examination demonstrated the presence of a “waist sign” of the median nerve and moderate flexor tenosynovial hypertrophy bilaterally. Parents reported mild subjective improvement of dexterity and fine motor skills postoperatively.

**Conclusion:** To optimize functional outcome, routine screening for CTS and intervention at an early age are emphasized in the mucopolysaccharidoses population. (*Plast Reconstr Surg Glob Open* 2017;5:e1477; doi: 10.1097/GOX.0000000000001477; Published online 24 August 2017.)

**M**ucopolysaccharidosis II (Hunter syndrome) is a heterogeneous, X-linked, lysosomal storage disorder caused by deficiency of iduronate-2-sulfatase. Glycosaminoglycan accumulation throughout the body manifests as facial dysmorphism, enlarged liver and spleen, stiff contracted joints, cardiac valve dysfunction, obstructive sleep apnea, visual and auditory abnormalities, cognitive delay, and developmental regression.<sup>1–3</sup> Severe forms become clinically apparent between 1 and 4 years of age and are generally fatal by the mid-20’s; attenuated forms develop later and may not impair neurocognitive function.<sup>1,4</sup> The broad spectrum of presentation commonly results in late diagnosis.<sup>5</sup>

Because of the historically dismal prognosis, treatment of Hunter syndrome and related mucopolysaccharidoses has emphasized comfort and limited intervention. With the advent of hematopoietic stem cell transplantation and enzyme replacement therapy, patient survival has markedly improved. Consequentially, efforts to improve quality of life are warranted.

An estimated 85–95% of patients with Hunter syndrome develop carpal tunnel syndrome (CTS), confirmed by abnormal nerve conduction studies (NCS) as early as age 2.<sup>6</sup> Because communication barriers limit symptom reporting and subtle signs are often shadowed by more pressing medical problems, this population is at risk for advanced CTS at the time of diagnosis.

## CASE

Patient Z.D. is a 12-year-old male with Hunter syndrome. He was diagnosed at age 3, after demonstrating delay in developmental milestones. Genetic workup revealed the I007-1G<C mutation on the iduronate-2-sulfatase gene and undetectable levels of iduronate-2-sulfatase enzyme. He was started on enzyme replacement therapy with Elaprase at 4.5 years old. Despite comprehensive care including occupational and speech therapy, he began showing signs of developmental regression at age 7. These included incontinence, inability to follow commands, loss of speech, aggression, increased sensitivity to being touched, toe walking, repetition, difficulty with activities of daily living, wandering, twitching, and staring spells. He was subsequently referred to the Lysosomal Storage Disorders Program at our tertiary referral center. Brain magnetic resonance imaging, video electroencephalogram lumbar drain placement, and intracranial pressure monitoring revealed no explanation for his regression, which stabilized after 6 months. At age 10, he was enrolled in an ongoing multicenter phase I/II trial to receive

From the \*Department of Plastic Surgery, Medical College of Wisconsin, Milwaukee, Wis.; and †Department of Plastic Surgery, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, Pa.

Received for publication June 15, 2017; accepted July 11, 2017.

Presented, in part, at the Rangos Research Symposium at the Children’s Hospital of Pittsburgh of UPMC, June 2015, Pittsburgh, Pa.

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DOI: 10.1097/GOX.0000000000001477

**Disclosure:** The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.

Elaprase experimentally via monthly intrathecal injections under sedation.<sup>5</sup>

When he was 11 years old, Z.D.'s mother first reported concern that he would grab hot objects without pain and pick at his fingers. His neurology team subsequently recommended NCS. These were done under sedation in conjunction with his monthly injection. NCS demonstrated prolonged motor and sensory latency of the median nerve at the wrist bilaterally (motor latency 7.4ms on left and 5.7ms on right; sensory latency 4.3ms on left and 4.9ms on right). He was referred to our Pediatric Plastic Surgery Hand Clinic. At the time of his appointment, the patient's mother reported that Z.D. had started dropping objects more frequently and appeared irritable when she trimmed his nails. Examination demonstrated intact grip and moderate thenar atrophy bilaterally. Single-stage bilateral carpal tunnel release was recommended. He subsequently underwent bilateral carpal tunnel release, in conjunction with his intrathecal injection. An open, extended incision approach was used. Inspection of both median nerves revealed a "waist sign," median nerve narrowing within the carpal canal, and moderate flexor tenosynovial hypertrophy. Bilateral median nerve neurolysis and flexor tenosynovectomies were performed. Pathologic analysis of the excised tenosynovium revealed fibrosis. He was placed in resting volar splints for 2 weeks. His incisions healed without complications. At his 1-month follow-up appointment, his mother stated that Z.D. resumed using his hands for all activities, without any apparent discomfort or new impairments.

## DISCUSSION

CTS is a rare finding in children, but heavily represented in pediatric patients with mucopolysaccharidoses, including Hunter and Hurler syndromes. In contrast to adult patients, who present with classic clinical symptoms (numbness, tingling, weakness, and/or pain), symptomatic reporting is unusual in the mucopolysaccharidoses population. This is likely due to developmental delay, difficulty with communication, and inability to express symptoms, although in many reported cases patients deny pain.<sup>2,6,7</sup> Often, it is the caretaker who reports the first signs.<sup>3</sup> Thus, a higher level of vigilance among medical community is needed to educate caretakers for objective signs of CTS, including difficulty with activities of daily living, clumsiness with fine motor tasks, wrist swelling, and thenar atrophy. Unfortunately, many objective signs correlate with advanced disease and unrecoverable nerve injury. Therefore, multiple studies have recommended annual screening NCS as early as age 3.<sup>1,3,6</sup> NCS generally require sedation due to patient intolerance and should be performed in a setting competent with the pediatric difficult airway, as upper airway obstruction contributes significantly to morbidity in this population.<sup>1</sup> Other authors advocate prophylactic carpal tunnel releases, without presurgical NCS.<sup>8</sup>

Anatomically, there are several notable differences between mucopolysaccharidoses patients and adults with CTS. Haddad et al.<sup>2</sup> demonstrated radiographically that children with mucopolysaccharidoses have distorted bony architecture in the distal wrist, including distal radio-ulnar

dissociation, small irregular carpal bones, and short tubular metacarpals. Tenosynovial hypertrophy and thickened flexor retinaculum are also more common, contributing to triggering of digits and joint stiffness, which can mask the signs of CTS. These concurrent abnormalities contribute to hand dysfunction and complicate attempts to objectively measure pre- and postoperative hand function.

Interestingly, several studies have been unable to document postoperative improvement in nerve conduction velocity (NCV) or objective physical examination findings.<sup>2,6,7,9</sup> This may be due to growth altering nerve conduction velocity baselines, inability to follow commands for testing, difficulty with repeated examinations, or global developmental regression.<sup>2</sup> Regardless, these studies have shown subjective improvement in pain and manual dexterity with daily tasks and play.

At 12 years of age, Z.D. is a late presentation of CTS associated with Hunter syndrome. By his first meeting with a hand specialist, the patient showed moderate thenar atrophy, manual clumsiness, changes in play patterns, and withdrawal to touch. Findings of "waist sign" intraoperatively imply a long-standing compressive neuropathy. While parents may report subjective improvement in dexterity postoperatively, we recommend all patients with mucopolysaccharidoses be routinely and serially screened for CTS starting at age 3. Acknowledging that these patients often have several simultaneous medical issues and a higher risk for anesthetic complications, we advocate a concerted effort to coordinate invasive procedures requiring sedation.

## SUMMARY

CTS in the mucopolysaccharidoses population has received increased attention over the past 2 decades in large part because medical advances have greatly extended the anticipated lifespan for these patients. As these advances continue, improvements in the quality of life of affected patients should be emphasized. We therefore advocate multidisciplinary management, including vigilant monitoring of hand function, serial NCS, and early involvement of a hand specialist in the comprehensive treatment protocols for these patients.

Alexander Davit, MD

Department of Plastic Surgery  
Children's Hospital of Pittsburgh of UPMC  
One Children's Hospital Drive  
4401 Penn Ave  
Faculty Pavilion, #7105  
Pittsburgh, PA 15224  
E-mail: Alexander.Davit@chp.edu

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