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Case Report

Severe Carpal Tunnel Syndrome in a Pediatric Patient With a History of Congenital Adrenal Hyperplasia

Jeremy J. Eid, BS, * John W. Stelzer, MD, † Craig M. Rodner, MD †

* School of Medicine and Life Sciences, University of Toledo, Toledo, OH
† Department of Orthopedic Surgery, University of Connecticut, Farmington, CT

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The patient is a 17-year-old right-hand-dominant girl with a history of virilizing congenital adrenal hyperplasia (CAH) secondary to 21-hydroxylase enzyme deficiency. Her CAH had been managed with supplemental exogenous steroids, but unfortunately, she had been noncompliant for many years. She subsequently presented with severe progressive numbness and tingling in the bilateral upper extremities that were refractory to conservative management. Electromyography/nerve conduction studies confirmed bilateral carpal tunnel syndrome (CTS) with the right being more severe than the left, and she underwent uncomplicated carpal tunnel releases that relieved her symptoms immediately and completely. Carpal tunnel syndrome secondary to CAH may be associated with the effects of elevated sex hormones within the CTS, leading to inflammation and median nerve entrapment. Moreover, hyperandrogenism is associated with elevated acute phase reactants and inflammatory cytokines, contributing to progressive median neuropathy. To the author's knowledge, there have been no reported cases of severe pediatric CTS with associated hyperandrogenism from CAH.

Successful carpal tunnel release in a pediatric patient with severe bilateral carpal tunnel symptoms in the presence of uncontrolled congenital adrenal hyperplasia (CAH).

Case Report

The patient is a 17-year-old right-hand-dominant girl with a history of virilizing CAH secondary to 21-hydroxylase enzyme deficiency diagnosed at birth. Written informed consent was obtained from the patient for publication of this case report and accompanying images. The patient had a surgical history of genital reconstruction surgery for ambiguous genitalia. Her medical management of CAH consisted of dexamethasone, hydrocortisone, and fludrocortisone but has been noncompliant for many years. Annual androgen profiles demonstrated significantly elevated sex hormones and their precursors, confirming poorly controlled disease.

She presented with a 1-year history of severe progressive numbness and tingling in the volar thumb, index, and middle fingers bilaterally, the right worse than the left. She had no history of trauma or surgery to the bilateral upper extremities. In the prior 4–6 months, her symptoms were increasingly severe at night, would awake her from sleep, and would be slightly relieved with manual manipulation of her hands. Conservative management with wrist splints did not provide relief.

The patient's examination was significant for a Tinel's sign at the carpal tunnels and positive Phalen's and Durkan's compression tests bilaterally. Her strength was full bilaterally and displayed no evidence of thenar muscle atrophy. Electromyography/nerve conduction studies were obtained, given her age, the severity of her presentation, and the rapidly progressing nature of her condition. These studies revealed demyelinating and axonal sensory-motor median neuropathy across the right wrist and demyelinating median sensory neuropathy across the left wrist, suggestive of bilateral carpal tunnel syndrome (CTS) characterized as severe on the right and mild on the left (Figs. 1–3). The patient elected to proceed with a right endoscopic carpal tunnel release, and she received a stress dose of steroids prior to surgery, at the recommendation of her endocrinologist to prevent adrenal insufficiency.

An approximate 1 cm longitudinal incision was made in line with the radial border of the ring finger starting at the distal extent of Kaplan's cardinal line and extending proximal. Next,

Corresponding author: Jeremy J. Eid, BS, College of Medicine and Life Sciences, University of Toledo, 3000 Arlington Ave., Toledo, OH 43614.
E-mail address: Jeremy.eid@rockets.utoledo.edu (J.J. Eid).

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EMG

Side	Muscle	Nerve	Root	Ins Act	Fibs	Psw	Amp	Dur	Poly	Recrt
Left	Abd Poll Brev	Median	C8-T1	Nml	Nml	Nml	Nml	Nml	0	Nml
Left	1stDorInt	Ulnar	C8-T1	Nml	Nml	Nml	Nml	Nml	0	Nml
Left	Ext Digitorum	Radial (Post Int)	C7-8	Nml	Nml	Nml	Nml	Nml	0	Nml
Left	Biceps	Musculocut	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml
Left	FCR	Median	C6-7	Nml	Nml	Nml	Nml	Nml	0	Nml
Left	Deltoid	Axillary	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml
Right	Abd Poll Brev	Median	C8-T1	Incr	1+	1+	Incr	Incr	1+	Reduced
Right	1stDorInt	Ulnar	C8-T1	Nml	Nml	Nml	Nml	Nml	0	Nml
Right	Ext Digitorum	Radial (Post Int)	C7-8	Nml	Nml	Nml	Nml	Nml	0	Nml
Right	Biceps	Musculocut	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml
Right	FCR	Medain	C6-7	Nml	Nml	Nml	Nml	Nml	0	Nml
Right	Deltoid	Axillary	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml

Figure 1. Electromyography showing evidence of demyelinating and axonal sensory-motor median neuropathy across the right wrist as confirmed by fibrillations, increased amplitude and duration, and reduced recruitment.

Sensory Summary Table

Stim Site	NR	Peak (ms)	Norm Peak (ms)	P-T Amp (μV)	Norm P-T Amp	Site1	Site2	Delta-P (ms)	Dist (cm)	Vel (m/s)	Norm Vel (m/s)
Left Median D2 Sensory (2nd Digit)											
Wrist		4.5	<3.6	33.9	>10	Wrist	2nd Digit	4.5	14.0	31	>40
Right Median D2 Sensory (2nd Digit)											
Wrist		6.2	<3.6	6.8	>10	Wrist	2nd Digit	6.2	14.0	23	>40
Left Median D3 Sensory (3rd Digit)											
Wrist		4.7	<3.6	53.4	>10	Wrist	3rd Digit	4.7	14.0	30	>40
Right Median D3 Sensory (3rd Digit)											
Wrist		7.5	<3.6	2.6	>10	Wrist	3rd Digit	7.5	14.0	19	>40
Left Radial Sensory (Base 1st Digit)											
Forearm		1.8	<2.7	39.8	>5	Forearm	Base 1st Digit	1.8	10.0	56	
Right Radial Sensory (Base 1st Digit)											
Forearm		1.5	<2.7	74.0	>5	Forearm	Base 1st Digit	1.5	10.0	67	
Left Ulnar Sensory (5th Digit)											
Wrist		3.5	<3.7	34.7	>15	Wrist	5th Digit	3.5	14.0	40	>40
Right Ulnar Sensory (5th Digit)											
Wrist		3.0	<3.7	63.0	>15	Wrist	5th Digit	3.0	14.0	47	>40

Figure 2. Nerve conduction study—motor summary showing evidence of demyelinating and axonal sensory-motor median neuropathy across the right wrist as confirmed by increased onset of response, decreased compound muscle action potential amplitude, and decreased velocity.

dissection continued bluntly to the palmar fascia transverse carpal ligament (TCL), which was incised under direct visualization. The carpal tunnel was then entered in a retrograde fashion and released under endoscopic visualization. After surgery, her course was uncomplicated at 8 days and 4 weeks with immediate and complete resolution of symptoms, which continued until her final postoperative follow-up at 2 months. The patient was interested in a contralateral left carpal tunnel release as well because her previously mild symptoms progressed quickly to severe and constant in the months surrounding her right carpal tunnel release surgery and recovery.

Discussion

Carpal tunnel syndrome is the most common compressive mononeuropathy, which is caused by median nerve entrapment at the carpal tunnel.[1,2] The carpal tunnel is an inelastic fibro-osseous canal with carpal bones forming the floor and lateral walls and the roof formed by the TCL.[3] In contrast to adults, CTS is rare in the pediatric population, at times presenting with atypical symptoms, and is frequently secondary to an underlying condition.[1,4] Bilateral CTS is also generally associated with a systemic disorder.[1,2] Pediatric patients may present with atypical symptoms such as hand clumsiness or pain and muscle atrophy with a lack of sensory complaints leading to underdiagnosis.[1,4] Rüsch et al[1] noted that the most common etiologies of pediatric CTS were secondary to mucopolysaccharidoses, neoplasia's, and vascular malformations, followed by idiopathic CTS.[4] Endocrinopathies such as diabetes mellitus, hypothyroidism, and acromegaly have also been documented as potential causes of pediatric CTS.[1,4] To the author's knowledge, there have been no reported cases of severe pediatric carpal tunnel syndrome with associated hyperandrogenism from CAH.

Congenital adrenal hyperplasia is a group of autosomal recessive disorders caused by a deficiency in an adrenal enzyme involved in the steroidogenesis pathway, and the incidence of this disease ranges from 1:13,000 to 1:15,000.[5,6] The majority of cases are caused by mutations in *CYP21A2,* resulting in 21-hydroxylase enzyme deficiency, which accounts for 95% of cases.[5,6] A deficiency of this enzyme causes a decrease in the production of cortisol and/or aldosterone and the accumulation of sex hormones and their precursors. Hormone replacement therapy with a glucocorticoid and a mineralocorticoid is the mainstay of treatment.[5,6]

There is a known occurrence of CTS with pregnancy and menopause secondary to hormonal fluctuations and fluid accumulation within the carpal tunnel.[2] Similarly, patients with CAH have fluctuating hormone levels depending on the quantity of enzyme deficiency and medication compliance.[5,6] It has been postulated that inflammation of the TCL and tenosynovial tissue within the carpal tunnel can cause CTS.[7,8] Toesca et al[3] found high concentrations of estrogen and progesterone receptors in samples of the TCL and synovial tissue from CTS patients, suggesting the carpal tunnel to be a major target for hormonal action.[7] Patients with CAH who are obese and noncompliant will have elevated estrogen in addition to hyperandrogenism secondary to the aromatization of androgens by adipose tissue.[5] Subsequently, increased activity of these receptors within the carpal tunnel will contribute to inflammation of the TCL and synovial hyperplasia with a potential increased risk of median neuropathy.

Krishnan et al[9] performed a study using dihydrotestosterone, a potent androgen, for the induction of polycystic ovarian syndrome-like phenotype in prepubertal female rats. Their results demonstrated a significant increase in the level of proinflammatory cytokines, TNF-α and IL-6, resulting in a chronic inflammatory state. Elevated levels of estrogen are also associated with elevated levels of TNF-α, IL-6, and C-reactive protein, which is an acute phase reactant.[7] Maurizio et al[8,10] studied the synovial fluid of patients with rheumatoid arthritis and determined that increased estrogen concentrations enhance proinflammatory cytokine secretion and favor the development of immuno-mediated synovitis. Elevated levels of these cytokines can result in cellular proliferation, increased capillary permeability, and edematous changes followed by fibrosis, which can contribute to the development of CTS.[7] Patients with poorly controlled CAH are prone to an imbalance of sex hormones, specifically hyperandrogenism and elevated estrogen levels, which may contribute to a chronic inflammatory state and conditions such as CTS.

Nerve Conduction Studies
Motor Summary Table

Stim Site	NR	Onset (ms)	Norm Onset (ms)	O-P Amp (mV)	Norm O-P Amp	Site1	Site2	Delta-0 (ms)	Dist (cm)	Vel (m/s)	Norm Vel (m/s)
Left Median Motor (Abd Poll Brev)											
Wrist		4.1	<4.2	11.6	>5	Elbow	Wrist	4.0	21.5	54	>50
Elbow		8.1		10.9	>5						
Right Median Motor (Abd Poll Brev)											
Wrist		7.3	<4.2	3.2	>5	Elbow	Wrist	5.0	20.5	41	>50
Elbow		12.3		1.5	>5	Axilla	Elbow	4.0	0.0		>50
Axilla		8.3		3.0							
Left Ulnar Motor (Abd Dig Minimi)											
Wrist		2.3	<3.9	12.0	>3	B Elbow	Wrist	3.3	17.5	53	>50
B Elbow		5.6		12.1	>3	A Elbow	B Elbow	1.3	6.5	50	>50
A Elbow		6.9		12.4	>3						
Right Ulnar Motor (Abd Dig Minimi)											
Wrist		2.2	<3.9	14.8	>3	B Elbow	Wrist	3.7	20.0	54	>50
B Elbow		5.9		14.7	>3	A Elbow	B Elbow	0.8	4.5	56	>50
A Elbow		6.7		14.6	>3						

Figure 3. Nerve conduction study—sensory summary showing evidence of demyelinating and axonal sensory-motor median neuropathy across the right wrist as confirmed by increased peak latencies, decreased sensory nerve action potential amplitudes, and decreased velocity.

In summary, although causation of pediatric CTS cannot be mechanistically attributed to CAH from this case alone, the association of CTS and CAH, as presented in this case, is relevant to the pediatric hand evaluation. Providers should be aware of this potential etiology, which could expedite the diagnosis and treatment of pediatric patients, especially in those presenting with atypical presentations.

Conflicts of Interest

No benefits in any form have been received or will be received related directly to this article.

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