Journal of the Neurological Sciences 407 (2019) 116502

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Letter to the Editor

Nerve transfer as a novel treatment for West Nile virus-associated acute flaccid paralysis

ARTICLE INFO

Keywords:
West Nile virus
Acute flaccid paralysis
Nerve transfer
West Nile neuroinvasive disease

Dear Editor,

West Nile virus-associated acute flaccid paralysis (WNV-AFP) is a well-known complication of West Nile neuroinvasive disease (WNND) [1,2]. Most cases of WNV-AFP occur as a result of anterior horn cell damage, resulting in a syndrome reminiscent of poliomyelitis. Brachial plexus involvement has been reported less commonly [3–5]. At present, supportive care is the mainstay of treatment for all forms of WNND [2]. The prognosis of WNV-AFP is generally poor, and recovery, if any, usually occurs within six months of onset [6].

Nerve transfer, or neurotization, is an established surgical treatment option for traumatic peripheral nerve injury and is optimally performed within 6 months of injury [7]. Alternative applications of nerve transfer are not novel. For instance, nerve transfer has been used to treat spastic limb paralysis [8] and even infectious motor neuron disease, particularly in the pediatric population. A case of poliomyelitis-like paralysis caused by enterovirus 71 [9] as well as several cases of acute flaccid myelitis caused by enterovirus D68A [10] in children have been reported to have been successfully treated with nerve transfer. The aforementioned six month time window is a reasonable period of observation for spontaneous recovery in these cases. Herein, we describe the first case of successful nerve transfer, to our knowledge, in the treatment of WNV-AFP.

A 63-year-old man presented with encephalopathy in the setting of a febrile illness. His diagnostic work-up showed a neutrophilic pleocytosis (92 nucleated cells/μL) on CSF analysis and a WNV IgM index value (IV) of 5.62 (positive is 1.11 IV or greater), a constellation of findings consistent with WNND. A brain MRI was normal. Approximately 2 weeks after symptom onset, the patient developed painless weakness of his bilateral shoulder-girdle muscles with minimal sensory symptoms. His shoulder-girdle weakness persisted for 3 months at which time he was referred for neuromuscular consultation.

His exam at the time of referral was notable for severely impaired bilateral arm abduction and external rotation, left worse than right, and mild weakness of left forearm flexion (Table 1). He had full strength of his bilateral trapezii, distal upper limbs, and lower limbs. Biceps reflexes were 1+ on the left, 2+ on the right, and he had 3+ bilateral lower extremity reflexes. He had no cranial nerve involvement, a normal sensory exam, and a normal gait. A cervical spine MRI was normal, including normal signal intensity in the ventral grey matter of the spinal cord. Nerve conduction studies (NCS) showed normal upper extremity compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitudes, including lateral antebrachial cutaneous SNAPs. Electromyography (EMG) of the left deltoid and bilateral infraspinati muscles showed active denervation with no voluntarily recruited motor unit action potentials (MUAPs), and the left biceps showed active denervation with moderately reduced recruitment of large, broad MUAPs. The left C5 paraspinal, left rhomboid, and right deltoid muscles were normal by EMG (Table 1).

At 6 months from symptom onset, he had full recovery of left forearm flexion strength and improved strength of his right shoulder girdle muscles. His EMG demonstrated volitional MUAPs in the left deltoid consistent with successful interval reinnervation. However, there were still no recruitable motor units present in the distribution of the left suprascapular nerve (supraspinatus/infraspinatus) on EMG (Table 1). At six months from symptom onset, he was deemed a surgical candidate for a left-sided end-to-end coaptation of the distal spinal accessory nerve to the suprascapular nerve. A dorsal approach was pursued, which takes advantage of the close proximity of the distal spinal accessory nerve to the suprascapular nerve near the suprascapular notch, an area where direct transfer is feasible. Intraoperatively, the supraspinatus was pale, consistent with denervation atrophy, and intraoperative nerve stimulation of the suprascapular nerve yielded no response. The spinal accessory nerve was visualized medial to the trapezius muscle, and following its course, a distal branch was selected and confirmed to have a normal response via intraoperative nerve stimulation. This distal branch of the spinal accessory nerve and the proximal suprascapular nerve were divided, and a coaptation of the nerves, with the assistance of an operative microscope, was performed.

The patient reported improved active range of motion of his left shoulder 4 months after surgery. There was also evidence of recovery by

Abbreviations: CMAP, compound muscle action potential; EMG, electromyography; EV-71, enterovirus-71; NCS, nerve conduction study; SNAP, sensory nerve action potential; WNND, West Nile neuroinvasive disease; WNV, West Nile virus; WNV-AFP, West Nile virus-associated acute flaccid paralysis

https://doi.org/10.1016/j.jns.2019.116502
Received 8 July 2019; Received in revised form 24 August 2019; Accepted 18 September 2019
Available online 15 October 2019

Table 1
Serial strength and electromyography data.

	3 months from onset		6 months from onset (4 days pre-neurotization)		24 months from onset (18 months post-neurotization)	
	Strength*	EMG	Strength	EMG	Strength	EMG
Left deltoid	0	*2+ fibs/PSWs no MUAPs*	0	*2+ fibs/PSWs Nascent MUAPs ↓↓ recruitment*	11	*Nl insertional activity ↑ D&A MUAPs ↓ recruitment*
Left biceps brachii	32	*2+ fibs/PSWs ↑↑ D&A MUAPs ↓↓ recruitment*	50+	*1+ fibs/PSWs ↑↑↑D & ↑A MUAPs ↓↓ recruitment*	50+	*Nl insertional activity ↑D & ↑↑ A MUAPs ↓ recruitment*
Left infraspinatus	0	*2+ fibs/PSWs no MUAPs*	0	*3+ fibs/PSWs no MUAPs*	11	*No fibs/1+ PSWs ↑↑D & ↑A MUAPs ↓↓ recruitment*
Left supraspinatus	0	*N/A*	0	*2+ fibs/3+ PSWs no MUAPs*	11	*2+ fibs/PSWs, ↑↑ D&A MUAPs ↓↓ recruitment*
Right infraspinatus	0	*3+ fibs, 3+ PSWs no MUAPs*	2/5	*N/A*†	12	*1+ fibs/PSWs ↑D & ↑↑ A MUAPs ↓↓ recruitment*

A – amplitude; D – duration; EMG – electromyography; fibs – fibrillations; MUAPs – motor unit action potentials; N/A – data not available; Nl – normal; PSWs – positive sharp waves; ↑↑↑ - greatly increased; ↑↑ - moderately increased; ↑ - mildly increased; ↓↓ - moderately reduced; ↓ - mildly reduced.
Three months from onset, all of the following muscles were normal by clinical exam and by electromyography: left triceps, extensor digitorum communis, first dorsal interosseous, rhomboid, and C5 paraspinal; right deltoid, biceps brachii, upper trapezius, and serratus anterior.

* Measured by MRC scale or handheld dynamometry (pounds of force). Note that dynamometry measurements of 11 and 12 pounds in the deltoid and spinati muscles and 32 pounds in the biceps brachii correspond to a 4/[] on the MRC scale.

† The right infraspinatus was not tested via EMG at 6 months as there was clinical evidence of improved strength.

neurologic exams and EMG studies performed at 12 and 18 months post-neurotization (Table 1). Two years after onset of symptoms (18 months post-neurotization), he graded his recovery as 90% of his premorbid baseline. External rotation of the left arm had improved to generating 11 pounds of force by dynamometry (MRC = 4/5, Table 1).

Herein, we present the first successful nerve transfer used for WNV-AFP. Residual disability is common in WNV-AFP, particularly in the absence of recovery within 6 months of onset [6]. Data from traumatic peripheral nerve injury suggest a similar timeframe for prognostication [7]. Improved strength and electrophysiologic evidence of successful interval reinnervation of the left infraspinatus and supraspinatus support therapeutic success in our patient.

The absence of sensory signs and the preserved left lateral antebrachial cutaneous SNAP in the setting of clear musculocutaneous nerve involvement (denervation in the biceps brachii) is consistent with anterior horn cell damage (C5/C6 myotomes) described in typical WNV-AFP. However, the lack of C5 paraspinal and rhomboid muscle involvement by EMG warrants consideration of a motor predominant lesion of the upper trunk of the brachial plexus, a pattern commonly reported in neuralgic amyotrophy. Nonetheless, from a clinical practice perspective, regardless of the ultimate localization, the presence of a viable donor nerve in proximity to the affected myotome or peripheral nerve is a more essential consideration when considering candidacy for nerve transfer in WNV-AFP. There is no reason to suggest nerve transfer would not be an option for a focal poliomyelitis-like syndrome or brachial plexopathy, which have both been described as neurological manifestations of WNV infection [1-5].

A reasonable concern could be raised that reinnervation in the distribution of the left suprascapular nerve was spontaneous, similar to that observed in the left axillary and right suprascapular nerves. However, given that an end-to-end transfer was performed, an intervention that eliminates the possibility of spontaneous recovery, we can state with confidence that the recovery observed in this case was directly attributable to the procedure. We were doubtful, in this case, of the possibility of spontaneous recovery of the left suprascapular nerve beyond 6 months, by which time other affected nerves had demonstrated signs of some recovery.

In conclusion, nerve transfer may be a treatment option for WNV-AFP when clinical and electrophysiologic evidence of spontaneous recovery within 6 months are lacking. Heightened awareness and further study of WNV-AFP and its best treatment, with a comparison of nerve transfer to supportive care, are warranted.

Study funding

None.

Author contributions

Dr. Wilks: Designed the study and wrote the paper.

Dr. Ray: Designed the study, performed the data collection/analysis and wrote the paper.

Dr. Al-Lozi: Performed the data collection/analysis and wrote the paper.

Dr. Bucelli: Designed the study, performed the data collection/analysis and wrote the paper.

Disclosure of conflicts of interest

Dr. Wilks has no relevant disclosures.

Dr. Ray has acted in a consultant capacity for Depuy/Synthes and Globus Medial, has an ownership stake in Acera Surgical, and has received grant support from the Department of Defense and NIH/NINDS.

Dr. Al-Lozi has no relevant disclosures.

Dr. Bucelli has served on an advisory board for MT Pharma, has Equity in Neuroquestions.LLC, and receives a recurring annual gift from a patient's family for research on neuralgic amyotrophy.

References

[1] J.J. Sejvar, A.V. Bode, A.A. Marfin, G.L. Campbell, D. Ewing, M. Mazowiecki, et al., West Nile virus-associated flaccid paralysis, Emerg. Infect. Dis. 11 (7) (2005) 1021–1027.

[2] J. Gea-Banacloche, R.T. Johnson, A. Bagic, J.A. Butman, P.R. Murray, A.G. Agrawal, West Nile virus: pathogenesis and therapeutic options, Ann. Intern. Med. 140 (7) (2004) 545–553.

[3] K. Almhanna, N. Palanichamy, M. Sharma, R. Hobbs, A. Sil, Unilateral brachial

plexopathy associated with West Nile virus meningoencephalitis, Clin. Infect. Dis. 36 (12) (2003) 1629–1630.
[4] S. Scholz, B. Kaas, A. Simpkins, J. Lyons, A. Venkatesan, J. Probasco, Brachial plexitis preceding encephalomyelitis in a patient with West Nile virus infection, BMJ Case Rep. (2013).
[5] M. Chahil, T.P. Nguyen, West Nile virus-associated brachial plexopathy, BMJ Case Rep. (2016).
[6] J.J. Sejvar, A.V. Bode, A.A. Marfin, G.L. Campbell, J. Pape, B.J. Biggerstaff, et al., West Nile virus-associated flaccid paralysis outcome, Emerg. Infect. Dis. 12 (3) (2006) 514–516.
[7] A. Forli, M. Bouyer, M. Aribert, C. Curvale, M. Delord, D. Corcella, et al., Upper limb nerve transfers: a review, Hand Surg Rehabil. 36 (3) (2017) 151–172.
[8] M.X. Zheng, X.Y. Hua, J.T. Feng, T. Li, Y.C. Lu, Y.D. Shen, et al., Trial of contralateral seventh cervical nerve transfer for spastic arm paralysis, N. Engl. J. Med. 378 (1) (2018) 22–34.
[9] E.B. Saltzman, S.K. Rancy, D.B. Sneag, J.H. Feinberg Md, D.J. Lange, S.W. Wolfe, Nerve transfers for Enterovirus D68-associated acute flaccid myelitis: a case series, Pediatr. Neurol. 88 (2018) 25–30.
[10] S. Funahashi, A. Nagano, M. Sano, H. Ogihara, T. Omura, Restoration of shoulder function and elbow flexion by nerve transfer for poliomyelitis-like paralysis caused by enterovirus 71 infection, J. Bone Joint Surg. (Br.) 89 (2) (2007) 246–248.

Anson W. Wilks[a], Wilson Z. Ray[b], Muhammad T. Al-Lozi[a], Robert C. Bucelli[a,*]
[a] *Department of Neurology, Washington University School of Medicine, United States of America*
[b] *Department of Neurosurgery, Washington University School of Medicine, United States of America*
E-mail addresses: awwilks@wustl.edu (A.W. Wilks), rayz@wustl.edu (W.Z. Ray), allozim@wustl.edu (M.T. Al-Lozi), bucellir@wustl.edu (R.C. Bucelli).

* Corresponding author at: Department of Neurology, Washington University School of Medicine, 660 S. Euclid Avenue, Campus Box 8111, Saint Louis, MO 63110, United States of America.