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Case Report

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COVID-19 Vaccine Related Cervical Radiculitis and Parsonage-Turner Syndrome: Case Report and Review of the Literature

Zachary C. TAYLOR, Ravi S. NUNNA, Angela TRAN, Matías COSTA, Maxwell GRUBER, Periklis GODOLIAS, Zachary LITVACK

Swedish Neuroscience Institute, Department of Neurosurgery, Seattle, WA, USA

Corresponding author: Ravi NUNNA ✉ ravisnunna@gmail.com

ABSTRACT

Parsonage-Turner Syndrome, or neuralgic amyotrophy, is an acute-onset upper limb and shoulder girdle palsy that can occur in a post-viral, post-surgical or idiopathic setting. There have also been some reported cases of the syndrome occurring following vaccinations. The pathophysiology of neuralgic amyotrophy is not completely understood and many of the commonly used diagnostic imaging modalities we use to try and diagnose this syndrome are inaccurate and misleading.

We present the case of a 40-year-old gentleman who presented with acute onset burning pain and fasciculations in his right upper extremity following vaccination with the second dose of the Pfizer-BioNTech COVID-19 vaccine. His symptoms progressed to weakness in isolated muscle groups with electromyographic evidence of decreased nerve conduction. MRI of the cervical spine demonstrated multilevel central and foraminal stenosis, suggesting a diagnosis of cervical radiculopathy. The patient underwent a C4-5/C5-6 and C6-7 laminoforaminotomy and tolerated the procedure well. Post-operatively, the patient has experienced gradual symptom improvement with residual right triceps and pectoralis muscle weakness as well as paresthesias of the right elbow and forearm.

Parsonage-Turner Syndrome is a brachial plexus palsy that can affect one or multiple branches of the brachial plexus. It causes acute-onset pain and weakness, and the diagnosis can be difficult to make with the commonly used diagnostic imaging methods. We reviewed other case reports about neuralgic amyotrophy following vaccinations as well as the current literature on more accurate diagnostic imaging modalities that may help our diagnosis and understanding of the pathophysiology of this condition.

KEYWORDS: Coronavirus vaccine, COVID-19 Vaccine, Parsonage-Turner Syndrome, Neuralgic Amyotrophy, Cervical Radiculitis

INTRODUCTION

Neuralgic amyotrophy and its many designations, including acute brachial neuropathy, acute brachial plexitis, localized neuritis of the shoulder girdle, and most commonly Parsonage-Turner syndrome (PTS), typically presents as acute onset of severe arm or shoulder pain, weakness, and sensory loss (29). Symptoms may also include patchy upper extremity paresis and associated scapular winging (32). The clinical presentation and symptom distribution vary, and often cannot be localized to any single nerve root distribution (29). The exact etiology of PTS is yet to be determined, although symptom onset has been implicated with any combination of autoimmune, hereditary, infectious, environmental, and biomechanical processes (32). Particularly for the idiopathic presentation of PTS, antecedent events such as immunizations and viral infections may trigger symptoms (32). Significant neurological complications have not yet been

Zachary C. TAYLOR : 0000-0002-9935-7936
Ravi S. NUNNA : 0000-0003-2516-5445
Angela TRAN : 0000-0003-2494-4842
Matías COSTA : 0000-0003-1833-4589
Maxwell GRUBER : 0000-0001-8778-0430
Periklis GODOLIAS : 0000-0001-6788-5200
Zachary LITVACK : 0009-0003-6784-5243

widely reported by initial trials on safety and efficacy of the mRNA-derived severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019 COVID-19) BNT162b2 (Pfizer, New York City, NY) vaccination (22). We describe a case report of PTS in which the patient developed less severe symptoms following an influenza vaccine in 2008, and more severe onset following both doses of the COVID-19 mRNA vaccine in 2021. We have used the CARE guidelines of standardized reporting of case reports to describe this interesting and educational case.

CASE REPORT

A 40-year-old male presented to our outpatient clinic with burning pain and nocturnal right upper extremity fasciculations two weeks after receiving the second dose of the COVID-19 vaccine. He experienced symptom aggravation with lifting of his right arm or tucking of his chin. He reported similar complaints following previous injections, including the first dose of the COVID-19 vaccine one month prior, in addition to a flu vaccine in 2008. Prior episodes had been self-limited and not as severe. On physical examination, there was mild (4+/5) weakness with right elbow flexion and slight (5-/5) weakness with shoulder abduction. Range motion was full but painful with activation of serratus anterior, biceps and rhomboids. A subsequent physical exam separated by about 4 weeks demonstrated mild (4+/5) elbow and wrist extension with an otherwise normal exam.

T2-weighted magnetic resonance imaging (MRI) of the cervical spine demonstrated C5-C6 and C6-C7 disc herniations with bilateral foraminal stenosis at those levels (Figure 1), in addition to C7-T1 facet hypertrophy and bilateral foraminal stenosis. Following the first dose of the COVID-19 vaccine and onset of symptoms similar to those described above, the patient had undergone electromyography (EMG) and nerve conduction velocity testing. These results demonstrated positive sharp waves in the biceps, rhomboids, serratus anterior and cervical paraspinal muscles suggesting acute right C5 and C6 radiculopathy with probable concomitant brachial neuritis (Table I). The patient was administered 40 mg oral prednisone, which was tapered down over 12 days, along with an epidural steroid injection that collectively offered significant, though temporary, symptom improvement.

A second EMG done four weeks after the second dose of the COVID-19 vaccine and subsequent worsening of symptoms revealed positive sharp waves in the triceps, pronator teres and C7 paraspinal muscles suggesting an acute right C7 neuropathy with subtle denervation over the ipsilateral C7 myotome (Table I). There were not any electrodiagnostic findings of brachial plexopathy of the upper trunk at this time.

Based on the correlation of symptoms, imaging and electrodiagnostic findings, consideration was given to a diagnosis of cervical radiculopathy - inflammatory worsening of underlying multi-level foraminal stenosis. With this working diagnosis, surgical intervention was determined to provide more definitive treatment. Our patient was taken to the operating room where right C4-5/C5-6 and C6-7 laminoforaminotomies were performed without complication. The patient's post-operative hospital stay was uneventful and at the time of discharge, he was neurologically intact and reported near resolution of symptoms. However, he complained of itching and burning pain at the incision site. Two weeks following surgery, he presented with serosanguinous drainage from the inferior aspect of his surgical incision site with accompanying neck pain. Ultrasound and MR imaging demonstrated a fluid pocket in the subcutaneous space (Figure 2). This fluid collection necessitated needle aspiration and evaluation for Beta-2 transferrin which was negative. Two days following aspiration, the patient developed worsening symptoms with reaccumulation of the fluid collection. Surgical exploration was carried out with further foraminotomy expansion to rule out CSF leak which was negative. All absorbable suture (polyglactin 910) was removed, following which the patient experienced symptom improvement, and subsequently was discharged home on POD 2. Upon follow-up, symptoms have been improving daily and the patient now only complains of decreased strength of his right triceps and pectoralis muscles and mild paresthesias over the lateral right elbow and forearm.

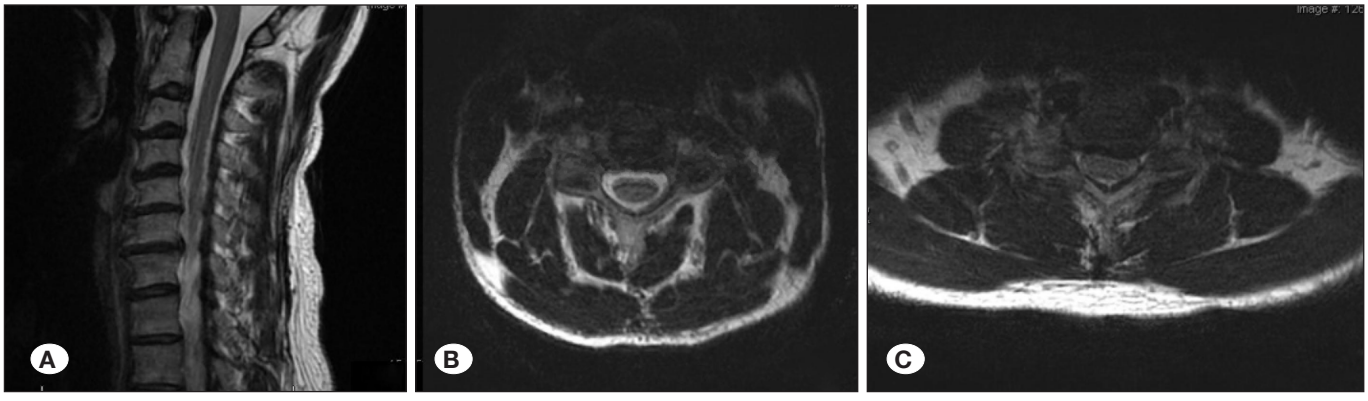

Figure 1: T2-weighted cervical spine MRI prior to surgery. **A)** Sagittal cervical spine image showing multilevel cord compression from vertebral disc herniations. **B)** Coronal cervical spine image at C3-4 disc space demonstrating normal CSF enhancement around spinal cord. **C)** Coronal cervical spine image at C6-7 disc space demonstrating cord compression and limited CSF enhancement around spinal cord.

Table I: EMG/NCV Study Results Upon First Presentation and Following Oral and Epidural Steroids

Side	Muscle	Nerve	Root	Insertional Activity	Fibrillation	Positive sharp waves	Amplitude	Duration	Polyphasics	Recruitment
EMG prior to steroids and surgery										
Right	Supraspinatus	Suprascapular	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Infraspinatus	Suprascapular	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Pectoralis major	Med./lat. pectoral	C5-6, C8	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Deltoid	Axillary	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Biceps	Musculocutaneous	C5-6	Increased	3+	3+	Nml.	Nml.	0	Mildly diminished
Right	Triceps	Radial	C6-7-8	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Pronator Teres	Median	C6-7	Nml.	Nml.	Nml.	Nml.	Nml.	0	Mildly diminished
Right	Opponens pollicis	Median	C8-T1	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Trapezius	Spinal accessory	CN XI, C3-4	Increased	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Rhomboid major	Dorsal scapular	C5	Increased	1+	1+	Nml.	Nml.	0	Nml.
Right	Serratus anterior	Long thoracic	C5-7	Increased	1+	1+	Nml.	Nml.	0	Nml.
Right	Cervical paraspinals	Rami	C4-6	Increased	2+	2+	Nml.	Nml.	0	Nml.
EMG following steroids and prior to surgery										
Right	Deltoid	Axillary	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Biceps	Musculocutaneous	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Triceps	Radial	C6-7-8	Increased	Nml.	1+	Nml.	Nml.	0	Nml.
Right	Pronator Teres	Median	C6-7	Increased	Nml.	1+	Nml.	Nml.	0	Nml.
Right	1st dorsal interosseous	Ulnar	C8-T1	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Levator scapulae	Dorsal scapular	C3-5	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Serratus Ant.	Long thoracic	C5-7	Nml.	Nml.	Nml.	Nml.	Nml.	2+	Nml.
Right	Ext. digitorum	Radial (post-int)	C7-8	Increased	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	Brachioradialis	Radial	C5-6	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.
Right	C7 paraspinal	Rami	C7	Increased	Nml.	2+	Nml.	Nml.	0	Nml.
Right	Latissimus dorsi	Thoracodorsal	C6-8	Nml.	Nml.	Nml.	Nml.	Nml.	0	Nml.

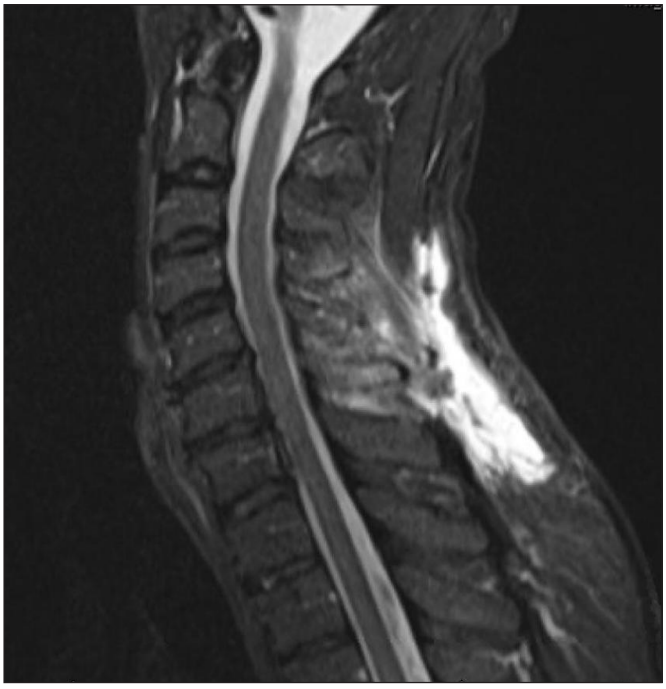

Figure 2: T2-weighted MRI cervical spine image following surgical decompression with multilevel laminoforaminotomy demonstrating fluid collection in the subcutaneous space.

DISCUSSION

Parsonage-Turner Syndrome (PTS), sometimes referred to as paralytic brachial neuritis (PBN) or neuralgic amyotrophy (NA), is a rare neurological disorder first formally described in the literature by Dr. Parsonage and Dr. Turner in 1948 (20). The two doctors observed military personnel during the second World War develop an acute onset of pain isolated to the shoulder girdle that lasted for several hours to several weeks (20). Once the pain had resolved, a flaccid paralysis developed in the shoulder with identifiable atrophy of the muscles (20). While the Parsonage and Turner paper identified the long thoracic nerve and serratus anterior muscle as the most commonly affected nerve-muscle pairing in their cohort of 136 patients, a newer and larger cohort study analyzing general characteristics of patients with PTS has identified the suprascapular nerve and the two muscles it innervates to be most commonly affected (20,35). There is a reported 2:1 male-to-female ratio and a median age of onset of 40 years in the idiopathic subgroup (35). While long thought to be a very rare entity with an estimated 1-3 cases per 100,000 per year, the incidence in the general population may be greater than previously suspected due to a combination of a lack of knowledge of the syndrome resulting in misdiagnosis, or misinterpretation of diagnostic studies early in the disease course.

Most of the published cases of PTS occur after a surgical procedure, in the peripartum period, after extreme exercise or as a result of a viral illness, including infection by COVID-19. The CDC Adverse Event Database (VAERS) lists a total of 27 reports of brachial radiculitis after any COVID-19 vaccination, more than half (10) of which are associated with the Pfizer-BioNTech COVID-19 vaccine (2). Only a handful of cases of PTS or neuralgic amyotrophy have been truly attributed to a vaccination and a list of those articles, published in English, are highlighted below in Table II. Interestingly, the two previously reported cases of PTS following administration of the COVID-19 vaccine, as well as the patient presented here, received the Pfizer-BioNTech vaccine (4,15). No major neurologic side effects were reported in the safety and efficacy trial for the vaccine (22). As has been suggested before in case studies, there does not seem to be a side concordance between the side the patient receives a vaccine on and the side that develops pain, paresthesias, and paralysis and that is affirmed here in our review of the literature. Another interesting observation is that there has been an increase in the number of reported cases of PTS following vaccination with 11 of the 18 papers reviewed below being published since 2008. Whether this is because the global population is increasing and more people are getting vaccinated, vaccines are being developed to initiate a stronger immunogenic response, or our diagnostic methods are improving, this diagnosis should be on our differential now more than ever. All the above causes of PTS fall under the domain of idiopathic neuralgic amyotrophy (INA).

While we do not currently understand what causes neuralgic amyotrophy, several hypotheses have been published. One of these is centered around the idea of repetitive microtrauma causing disruption of the blood-nerve barrier (37). This disruption then allows immune cells into the endoneurium causing a localized autoimmune reaction. This is reinforced by the observation of T-cell infiltrates and $CD20^+$ B-cell germinal centers surrounding nerves in biopsied or surgically excised regions of focal compression. Concomitant with these findings was the presence of active, multifocal axonal degeneration with replacement by fibrous tissue, in the absence of any vasculitic changes (19,33). Additionally, Sierra et al. discovered a decrease in the number of $CD8^+$ T-lymphocytes, which is a phenomenon seen in other autoimmune conditions affecting the peripheral nervous system including Guillain-Barré syndrome, idiopathic polyneuritis, and recurrent Bell's palsy (9,16,27,41). Another theorized etiology for NA focuses on the high mobility of the shoulder joint and proposes that already inflamed nerves become kinked and then twisted and constricted due to the rotation of the shoulder, causing the classic hourglass-like compressions that are often seen on imaging and intra-operatively in patients with PTS (14,18). Taken as a whole, all of these postulated explanations point to a complex interplay of autoimmune, biomechanical and genetic factors that contribute to the pathophysiology of this rare syndrome.

As alluded to above, the diagnostic tools we have long used to evaluate a patient with potential NA symptoms are not very accurate in the acute setting. Specifically, the common practice of ordering nerve conduction studies or an EMG immediately following initial onset of brachial plexus neuritis often has inaccurate results, and a normal conduction study in the acute setting should not rule out the diagnosis of PTS (34). One report about nerve conduction study (NCS) and EMG use in clinically affected nerves of patients with PTS documented a positive NCS or EMG in only 15% of cases

Table II: Articles (in English) about post-vaccination Parsonage-Turner Syndrome

Vaccine	Patient gender	Patient age	Site of vaccination	Side of PTS	Symptoms	Diagnosis method	Year published	Reference
Smallpox	M/F	Various	Deltoid	Bilateral	Arm pain, swelling, paresthesia, weakness	EMG	1949	Winkelman Jr. (40)
DTP	M	<1	Thigh	Right	Arm disuse, flaccid paralysis, hyporeflexia, decreased sensory withdrawal to pinprick	Clinical	1973	Martin and Weintraub (17)
Influenza	M	57	Left deltoid	Bilateral	Wrist pain and swelling followed by UE weakness progressing to paralysis	EMG	1977	Weintraub and Chia (39)
Tetanus (booster)	F	20	Gluteus	Right	Weakness with flexion at elbow, absent biceps reflex, no sensory deficits	EMG	1979	Baust et al. (1)
Tetanus (booster)	M	20	--	Left	Initial shoulder pain radiating into biceps followed by total paresis of left deltoid	EMG	1984	Kiwit (12)
HBV	F	24	Right deltoid	Right	Right shoulder pain and numbness of right thumb followed by winging of right scapula	EMG	1990	Reutens et al. (23)
DTP	F/M	< 1	Thigh	Left/ bilateral	Disuse of the arm, hyporeflexia, fever, and pain with passive ROM of arms	Clinical	1997	Hamati-Haddad and Fenichel (8)
HPV (Gardasil)	F	19	Left deltoid	Left	Severe shoulder/peri-scapular pain with weakness of infraspinatus/supraspinatus	EMG	2008	Debeer et al. (3)
HPV (Gardasil)	F	25	Left deltoid	Left	Burning LUE pain followed by decreased grip-strength and thumb flexion	EMG	2011	Taras et al. (30)
Influenza	M	52	--	Right	Rapid pain/weakness in separate distribution from prior radiation fibrosis radiculopathy	EMG	2011	Telhan et al. (31)
Influenza	F	46	Left deltoid	Left	Profound UE weakness and pain with ROM in all directions	EMG	2012	Shaikh et al. (26)
Influenza	M	47	--	Left	Left shoulder pain, numbness of posterior left arm, and weakness of left arm and hand	MRI	2012	Kasi and Couri (11) posterior aspect of upper left arm, medial aspect of left forearm

Table II: Cont.

Vaccine	Patient gender	Patient age	Site of vaccination	Side of PTS	Symptoms	Diagnosis method	Year published	Reference
HBV	M	25	Right deltoid	Right	Neck/shoulder pain, scapular winging and weakness/atrophy of suprascapular nerve	Clinical	2014	Fransz et al. (5) followed by weakness and atrophy of the upper extremity musculature, and a slow recovery requiring months to years. To our best knowledge, this is the first case describing symptoms and signs of PTS following the administration of a post-exposure prophylaxis (PEP)
DTP/MMR	F	6	--	Left/right	Arm pain, hyporeflexia, weakness	EMG	2017	Serin et al. (25)
TBE	F	62	--	Bilateral	Bilateral paresthesias in median nerve distribution without pain/weakness	EMG	2019	Pessa et al. (21)
Shingles	F	54	--	Bilateral	Bilateral UE pain and proximal weakness in C5-T1 distribution	EMG	2019	Lindgren et al. (13)
SARS-CoV2	M	50	Left deltoid	Left	Peri-scapular pain and weakness with hand-grip and wrist extension	EMG	2021	Mahajan et al. (15)
SARS-CoV2	F	35	Right deltoid	Left	Painless arm weakness, numbness, paresthesias and hyporeflexia	EMG	2021	Diaz-Segarra et al. (4)

(34). Some diagnoses are also made clinically based on a strong adherence of the patient's presenting symptoms and clinical time course to that of PTS. More recently though, research has been published validating the use of magnetic resonance imaging (MRI), magnetic resonance neurography (MRN) and high-resolution ultrasound of the brachial plexus and its branches to aid in the diagnosis. Commonly, increased MRI T2 signal intensity surrounding nerves, especially the suprascapular nerve, is seen about two weeks following the onset of shoulder pain, which is thought to reflect denervation injury (6,24). T2 hyperintensity and/or muscular atrophy have also been reported in those muscles directly innervated by the denervated nerves, most commonly the supraspinatus and infraspinatus, within 48 hours of the onset of pain. This hyperintensity on MRI of either the muscles or nerves certainly needs to be correlated clinically as the finding alone is nonspecific and could be related to trauma, myopathy or extrinsic compression. This is perhaps an advantage of MRI in the evaluation of acute onset shoulder pain as it can rule out other structural etiologies including rotator cuff pathology, nerve compression at the suprascapular notch, or quadrilateral space syndrome. Other studies evaluating the brachial plexus with use of MRN in patients with PTS and other forms of peripheral neuritis have identified increased T2 intensity of the affected nerve roots, trunks and cords as well as a phenomenon called hourglass-like compressions (HGCs). These compressions, which have been identified during surgical exploration for brachial plexopathies for almost 25 years, have only recently been identified on MRN and are thought to represent a non-extrinsic form of compression with adjacent inflammation and infiltration of immune cells. In fact, in a small cohort of six patients with symptoms consistent with neuralgic amyotrophy, MRN was able to identify a so-called bullseye sign indicative of these HGCs in 21 of 23 compression sites (28). The bullseye sign manifests immediately proximal to a nerve compression and is characterized by "peripheral signal hyperintensity and central hypointensity on intermediate-weighted FSE and/or fat-suppressed imaging, orthogonal to the longitudinal axis of the nerve" (28).

High-resolution ultrasound (HRUS) of the brachial plexus has been used to a lesser extent in the workup of neuralgic amyotrophy. One of the most recent studies of its effectiveness documents a statistically significant difference in cross-sectional area of the suprascapular nerve at the midclavicular line in 14 patients with confirmed NA compared to the nerves of 15 healthy volunteers (7). They noted focal enlargement of the nerve compared to the healthy volunteers and even compared to the contralateral side of the same patient regardless of the time from symptom onset, and proposed a diagnostic cutoff of 4.2 mm^2 for the cross-sectional area of the affected suprascapular nerve at the midclavicular line (7). Enlargement of other branches of the brachial plexus, including the long thoracic, median and radial nerves, has also been identified on HRUS in patients with NA, making for perhaps more accessible sites to evaluate when ultrasound is used as an adjunct to the clinical diagnosis.

While PTS is largely self-limited, with functional recovery ranging from 6-18 months, almost two-thirds of patients experience persistent pain or weakness after three years, as reported in one of the largest population-based studies of patients with PTS in the Netherlands (35). Adding to this poor long-term prognosis, there is a high recurrence rate of 25% in the idiopathic NA subgroup and almost 75% in the hereditary NA subgroup (35,37). In an attempt to expedite recovery, and based on the hypothesized etiology of neuralgic amyotrophy as an autoimmune process, high-dose steroids have been used quite extensively and while they do not seem to improve overall time to resolution or affect the rate of recurrence, several studies seem to validate steroid use in order to shorten the duration of pain in the acute setting (35,36,38). Use of intravenous immunoglobulin (IVIg) in addition to high-dose steroids has also been reported in several case reports with variable results. Unfortunately, these studies about combination therapy lack the power to draw any definitive conclusions about the utility of IVIg and this represents an area for further investigation. Finally, surgery has been reported as an option to repair the hourglass-like compressions with either excision of the HGCs and end-to-end anastomosis of the nerve or repair with a bridging nerve graft.

CONCLUSION

As occurred at our facility, the diagnosis of Parsonage-Turner syndrome is frequently overlooked as patients tend to have concomitant abnormal cervical spine MRI findings and radiculopathy in what seems like a single nerve root distribution. Upon closer evaluation, the pain and numbness are very frequently in different nerve distributions. EMG or nerve conduction studies, which are commonly used as a screening measure, are notoriously inaccurate in the acute setting of PTS as they can have normal results for close to four weeks after the onset of shoulder pain. With normal peripheral EMGs, the cervical spine is assumed to be the etiology of the radiculopathy and patients can undergo unnecessary surgical decompression. As such, knowledge and accurate diagnosis of this condition is critical to avoid unnecessary hospitalizations and surgeries.

AUTHORSHIP CONTRIBUTION

Study conception and design: RSN
Data collection: ZCT, RSN, MG, PG
Analysis and interpretation of results: AT, MC, ZL
Draft manuscript preparation: ZCT, RSN, MG, PG
Critical revision of the article: AT, MC, ZL
All authors (ZCT, RSN, AT, MC, MG, PG, ZL) reviewed the results and approved the final version of the manuscript.

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