ORIGINAL RESEARCH • CASE SERIES

Radiology

Parsonage-Turner Syndrome Following COVID-19 Vaccination: MR Neurography

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Vaccination is one of the several known triggers of Parsonage-Turner syndrome (PTS). This case series describes two individuals with clinical presentations of PTS whose symptoms began 13 hours and 18 days following receipt of the Pfizer-BioNTech BNT162b2 and Moderna mRNA-1273 COVID-19 vaccine, respectively. The diagnosis of PTS was confirmed by using both electrodiagnostic testing and 3.0-T MR neurography. Although research is needed to understand the association between PTS and COVID-19 vaccination, MR neurography may be used to help confirm suspected cases of PTS as COVID-19 vaccines continue to be distributed worldwide.

Parsonage-Turner syndrome (PTS; neuralgic amyotrophy) is a rare peripheral neuropathy typically characterized by sudden-onset severe upper arm pain followed by muscle weakness (1). Muscle weakness can be debilitating and up to two-thirds of patients experience long-term functional deficits (1). Vaccination precedes PTS onset in an estimated 4.3%–15.5% of cases (1–3). Other known triggers of PTS include infection, strenuous exercise, and surgical procedures, but approximately half of all affected individuals have no identifiable antecedent event (1,2). Peripheral neuropathies have been reported following COVID-19 vaccination, but only three studies describe PTS and none include associated imaging findings (4–9).

Materials and Methods

Two patients were referred for MR neurography between February and March 2021 due to clinically suspected PTS that developed 13 hours following the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine and 18 days following the Moderna (mRNA-1273) COVID-19 vaccine. With informed consent from each participant, medical records were retrospectively reviewed for pertinent clinical and electrodiagnostic testing data as part of an ongoing institutional review board–approved PTS registry compliant with the Health Insurance Portability and Accountability Act. A single musculoskeletal radiologist (D.B.S., with more than 7 years of MR neurography experience) reviewed 3.0-T MR neurography and cervical spine MRI examinations.

Results

Patient 1

A 49-year-old man was awoken by severe, electric, shooting pain in his left volar forearm, 13 hours after receiving the first dose of the BNT162b2 vaccine (Pfizer-BioNTech) in his contralateral right shoulder. Because of persistent severe pain, he went to the emergency department where he received intravenous nonsteroidal anti-inflammatory medications, but these provided only mild relief. Laboratory tests performed in the emergency department, including C-reactive protein test, erythrocyte sedimentation rate, complete blood count, and comprehensive metabolic panels were all normal. His past medical history was significant for Lyme disease manifesting with an erythema migrans lesion, fatigue, and myalgias 2 months prior and treated with doxycycline, although Lyme immunoglobulin M and immunoglobulin G antibodies also obtained in the emergency department were negative. The patient was discharged and treated with an oral 8-day prednisone taper, at the end of which his pain subsided.

Electrodiagnostic testing performed 9 days after onset was normal; specifically, no median nerve abnormality was identified on the nerve conduction or electromyography portions of the examination. The patient developed weakness in wrist flexion and forearm pronation the day after electromyography, along with numbness along a 1-inch strip in the middle volar forearm region. Cervical spine and brachial plexus MRI performed 9 days after onset of initial pain symptoms did not demonstrate any findings to account for the patient's symptoms.

Eight weeks after onset of initial pain, physical examination by a neurologist revealed mild atrophy in the left volar forearm and mild weakness in forearm pronation and wrist flexion (British Medical Research Council scale, muscle strength grade 4+/5). MR neurography demonstrated prominent denervation edema pattern of the pronator teres (PT) and flexor carpi radialis (FCR) muscles within the forearm (Fig 1A). Within the arm, four severe hourglass-like constrictions and T2-weighted signal hyperintensity of the anteromedially positioned fascicular bundle of the median nerve were detected; this bundle represents the PT/FCR bundle based on the known topographic fascicular

Abbreviations

FCR = flexor carpi radialis, PT = pronator teres, PTS = Parsonage-Turner syndrome

Summary

The authors report MR neurography findings in two individuals with Parsonage-Turner syndrome who developed symptoms within 13 hours and 18 days of receiving a COVID-19 mRNA vaccine.

arrangement of the median nerve (Fig 1B, 1C) (10). Repeat electromyography, consistent with imaging findings, demonstrated severe denervation and no motor unit recruitment within the PT or FCR muscles. Muscles in the anterior interosseous nerve distribution were normal at MRI and electromyography.

At 3-month follow-up after onset, the patient reported no residual pain but increased weakness. He had not yet received the second dose of his COVID-19 vaccine.

Patient 2

An otherwise healthy 44-year-old man developed sudden-onset, intense, cramping pain in the left lateral deltoid region, 18 days after receiving his second dose of mRNA-1273 in the same arm. Three weeks later, he noticed the inability to abduct the left shoulder beyond 20 degrees. He otherwise experienced only minor symptoms attributed to the vaccine, including erythema at the injection site as well as headache and mild fatigue that lasted 2 days.

Twenty-four days after onset, cervical spine MRI demonstrated no findings to explain his symptoms. Two days later, physical examination revealed severe weakness in left shoulder abduction (Medical Research Council grade 2 of 5) and external rotation (Medical Research Council grade 3 of 5). He also described hyperesthesias in the left lateral shoulder and had diminished sensation to pinprick in the radial nerve distribution. Nerve conduction studies demonstrated mild slowing of the left median and radial sensory responses. Electromyography showed denervation and poor motor unit recruitment in the infraspinatus muscle. The supraspinatus muscle was not tested.

Five weeks after symptom onset, left brachial plexus MR neurography demonstrated enlargement, T2-weighted signal hyperintensity and multiple focal hourglass-like constrictions of the suprascapular nerve (Fig 2A) with accompanying denervation edema pattern of the supraspinatus and infraspinatus muscles (Fig 2B).

The patient was treated 3 weeks after onset with 300 mg of gabapentin 3 times a day for pain and began physical therapy 7 weeks after symptom onset. Three months after onset, his range of motion and strength subjectively improved but did not return to baseline levels.

Discussion

Parsonage-Turner syndrome (PTS) after vaccination typically ensues within 28 days of immunization and has been reported as early as the same day as vaccination (2). PTS is most frequently associated with tetanus vaccination, but it has also been reported following human papilloma virus, influenza, shingles, and tick-borne encephalitis vaccines (1–3,11–13). To date, three published cases describe PTS after COVID-19 vaccination (4–6), but none include imaging to substantiate the diagnosis. One of these cases involves the ulnar nerve (4), which is rarely reported in PTS (1,14). Another describes painless onset of weakness localized to the upper trunk (5), rather than more classic individual nerve involvement (1,10,14).

Intrinsic hourglass-like constrictions of affected nerves or nerve fascicles have been recognized in the acute (≤4 weeks) phase of PTS (10) and to date, they have not been observed in other spontaneous neuropathies (10,14). Patients 1 and 2 developed symptoms 13 hours and 18 days, respectively, after receiving a COVID-19 vaccine, with MR neurography helping to confirm the diagnosis by 8 weeks and 5 weeks, respectively. Although approximately half of all individuals with PTS report no identifiable trigger (1), the close temporal association between events suggests that vaccination may have been linked to PTS in these patients.

The pathophysiology of PTS is poorly understood, but it is thought to have genetic, environmental, and immune-mediated components (1). Possible immune-mediated mechanisms include molecular mimicry and bystander activation, both of which may ensue following either infection (eg, hepatitis E and SARS-CoV-2 [15]) or vaccination. The mRNA vaccines elicit potent type I interferon responses, which induce inflammation and may be associated with increased risk of autoimmune reactions (1,16). It is unlikely that PTS is secondary to direct nerve insult from vaccination, because PTS after vaccination and other peripheral neuropathies are often reported contralateral to the injected side, as observed in patient 1 (2–5,11–13).

Patient 1 received a clinical diagnosis of Lyme disease 2 months prior to PTS symptom onset despite negative immunoglobin M and immunoglobin G serologic tests, which have low sensitivity during early infection (17). He was treated with doxycycline and recovered prior to receiving the COVID-19 vaccine. Although Lyme disease has been associated with neurologic sequelae including PTS (18), the patient's PTS symptoms developed just 13 hours following vaccination; as such, vaccination alone or a combination of vaccination and recent infection may have been a trigger.

In the United States, three COVID-19 vaccines have received Food and Drug Administration Emergency Use Authorization. These include mRNA vaccines developed by Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273), as well as a one-dose, replication-incompetent human adenovirus vector vaccine developed by Johnson & Johnson/Janssen (Ad26.COV2.S) (19–21). Peripheral neuropathies were rare during phase 3 clinical trials, which included 30 000–40 000 participants randomized to either vaccine or placebo. In trials for BNT162b2 and mRNA-1273, Bell palsy occurred in four and three vaccinated individuals, respectively, compared with zero and one individuals, respectively, in the placebo groups (19,20). A modest increase (29%) in peripheral neuropathies was also seen in the Ad26.COV2.S vaccine cohort compared with placebo (21). In all cases, evidence was insufficient to directly link the vaccines to these occurrences. Recently, however, regulatory agencies in the United States and Europe have revised the labels of Johnson & Johnson's Ad26.COV2.S and AstraZeneca's Vaxzevria vaccines,

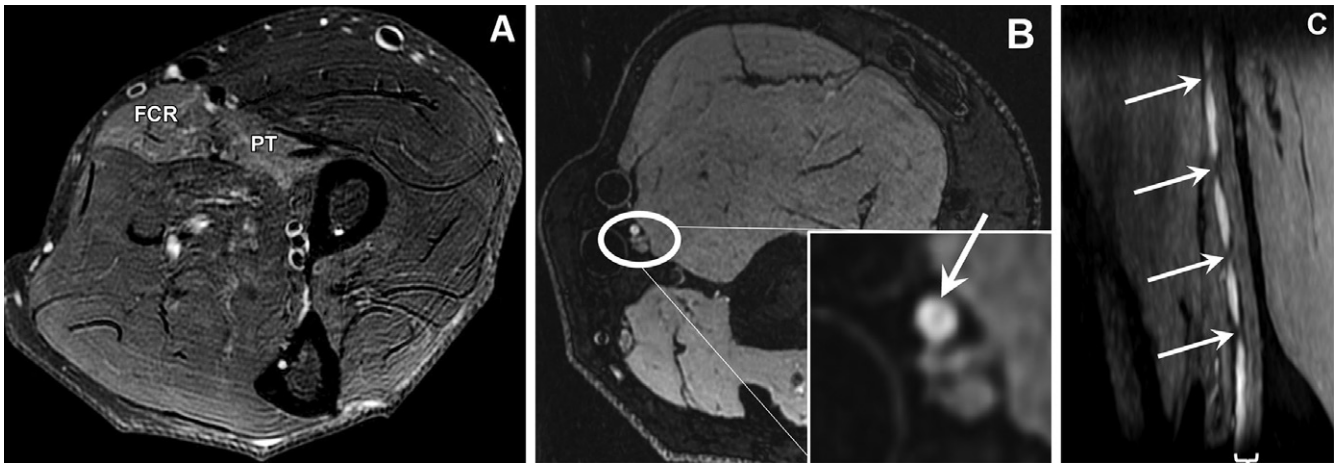

Figure 1: Patient 1: A 49-year-old man with Parsonage-Turner syndrome that developed 13 hours following the first dose of the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine. **(A)** Axial T2-weighted fast-spin echo fat-suppressed image 8 weeks after symptom onset demonstrates denervation edema pattern of the pronator teres (PT) and flexor carpi radialis (FCR) muscles. **(B)** Axial T2-weighted gradient-echo image demonstrates abnormal signal hyperintensity of the PT/FCR, anteromedially positioned, fascicular bundle (arrow, magnified inset) of the median nerve (oval) within the distal arm. **(C)** Oblique sagittal curved multiplanar reformatted T2-weighted gradient-echo image demonstrates multiple severe intrinsic constrictions (arrows) of the PT/FCR bundle of the median nerve (bracket).

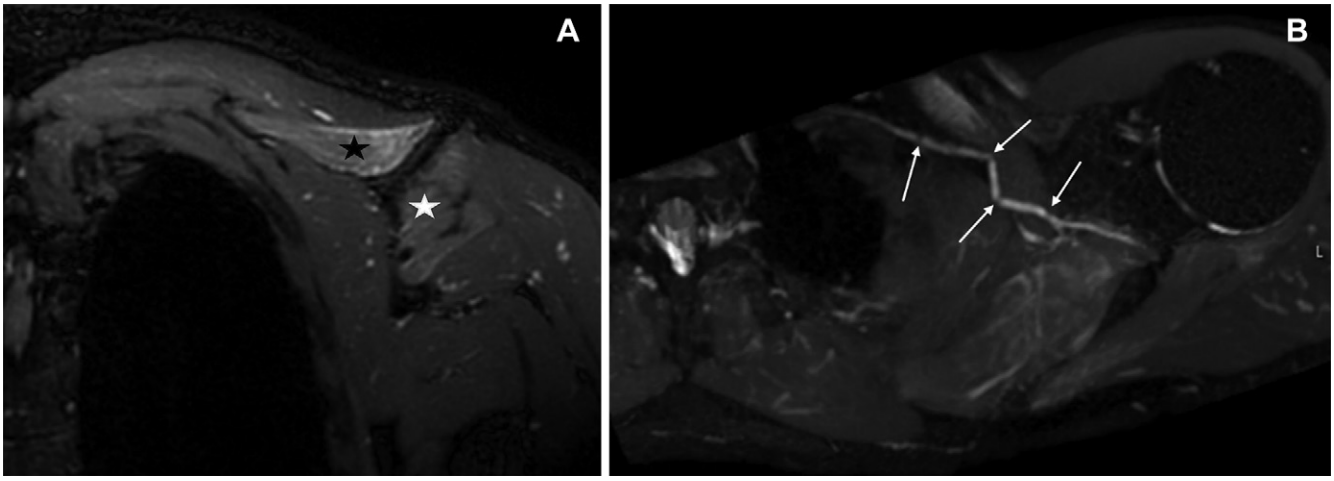

Figure 2: Patient 2: A 44-year-old man with Parsonage-Turner syndrome that developed 18 days following the second dose of the Moderna (mRNA-1273) COVID-19 vaccine. **(A)** Coronal T2-weighted fat-suppressed fast-spin echo (FSE) image 5 weeks after symptom onset demonstrates denervation edema pattern of the supraspinatus (black star) and infraspinatus (white star) muscles. **(B)** Oblique axial curved multiplanar reformatted T2-weighted fat suppressed FSE image demonstrates four severe intrinsic constrictions (arrows) of the suprascapular nerve.

which are both viral-vectored vaccines, to reflect an observed increased risk of Guillain-Barré syndrome following vaccination (22). Postauthorization surveillance is therefore needed to monitor for rare adverse events that may have not been observed or observed only sparsely during clinical trials.

As of July 15, 2021, nearly 2 billion people worldwide, including approximately 184 million in the United States, have received at least one COVID-19 vaccine dose (23). A search in the Vaccine Adverse Event Reporting System, or VAERS (24), for "Parsonage-Turner syndrome," "neuralgic amyotrophy," and "brachial neuritis" (other common terms for PTS) generated 56 reports of PTS occurring within 30 days of BNT162b2 (24 reports), mRNA-127 (23 reports), or Ad26.COV2.S (one report) COVID-19 vaccines. This search was manually sorted to only include nonduplicated reports and to exclude cases for which descriptions were inconsistent with PTS. An important limitation of VAERS is that it is subject to reporting bias, and is open to both health care workers and the lay population. Additionally, some individuals will develop PTS within the postvaccination window by chance alone.

MR neurography is a useful diagnostic tool for Parsonage-Turner syndrome (PTS) and may be particularly relevant as worldwide COVID-19 vaccinations increase. Although there are currently no approved treatments, early oral prednisone may reduce PTS symptom duration and severity (25). In recalcitrant cases, surgical neurolysis has also demonstrated efficacy (26). The timely and accurate diagnosis of PTS, which is often delayed, can help to lleviate any undue stress for the patient and direct appropriate management.

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References

1. van Alfen N, van Engelen BG. The clinical spectrum of neuralgic amyotrophy in 246 cases. Brain 2006;129(Pt 2):438–450.
2. Tsairis P, Dyck PJ, Mulder DW. Natural history of brachial plexus neuropathy. Report on 99 patients. Arch Neurol 1972;27(2):109–117.
3. Hamati-Haddad A, Fenichel GM. Brachial neuritis following routine childhood immunization for diphtheria, tetanus, and pertussis (DTP): report of two cases and review of the literature. Pediatrics 1997;99(4):602–603.
4. Mahajan S, Zhang F, Mahajan A, Zimnowodzki S. Parsonage Turner syndrome after COVID-19 vaccination. Muscle Nerve 2021;64(1):E3–E4.
5. Diaz-Segarra N, Edmond A, Gilbert C, Mckay O, Kloepping C, Yonclas P. Painless idiopathic neuralgic amyotrophy after COVID-19 vaccination: A case report. PM R 2021. 10.1002/pmrj.12619. Published online April 22, 2021.
6. Antonio Crespo Burillo J, Martínez CL, Arguedas CG, Pueyo FJM. Amyotrophic neuralgia secondary to Vaxzevria (AstraZeneca) COVID-19 vaccine [in Spanish]. Neurologia 2021. 10.1016/j.nrl.2021.05.007. Published online June 3, 2021.
7. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological Complications of COVID-19: Guillain-Barre Syndrome Following Pfizer COVID-19 Vaccine. Cureus 2021;13(2):e13426.
8. Waheed W, Carey ME, Tandan SR, Tandan R. Post COVID-19 vaccine small fiber neuropathy. Muscle Nerve 2021;64(1):E1–E2.
9. Patel SU, Khurram R, Lakhani A, Quirk B. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. BMJ Case Rep 2021;14(4):e242956.
10. Sneag DB, Arányi Z, Zusstone EM, et al. Fascicular constrictions above elbow typify anterior interosseous nerve syndrome. Muscle Nerve 2020;61(3):301–310.
11. Pessa ME, Verriello L, Valente M, Gigli GL. A rare case of pure sensitive Parsonage-Turner syndrome. Neurol Sci 2019;40(7):1499–1501.
12. Lindgren B, Rivers D, Clark J. Bilateral Parsonage-Turner Syndrome After Initial Unilateral Presentation: A Case Report. Cureus 2019;11(12):e6422.
13. Shaikh MF, Baqai TJ, Tahir H. Acute brachial neuritis following influenza vaccination. BMJ Case Rep 2012;2012:bcr2012007673.
14. Sneag DB, Saltzman EB, Meister DW, Feinberg JH, Lee SK, Wolfe SW. MRI bullseye sign: An indicator of peripheral nerve constriction in parsonage-turner syndrome. Muscle Nerve 2017;56(1):99–106.
15. Mitry MA, Collins LK, Kazam JJ, Kaicker S, Kovanlikaya A. Parsonage-turner syndrome associated with SARS-CoV2 (COVID-19) infection. Clin Imaging 2021;72:8–10.
16. De Beuckelaer A, Grooten J, De Koker S. Type I Interferons Modulate $CD8^+$ T Cell Immunity to mRNA Vaccines. Trends Mol Med 2017;23(3):216–226.
17. Moore A, Nelson C, Molins C, Mead P, Schriefer M. Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States. Emerg Infect Dis 2016;22(7):1169–1177.
18. Wendling D, Sevrin P, Bouchaud-Chabot A, et al. Parsonage-Turner syndrome revealing Lyme borreliosis. Joint Bone Spine 2009;76(2):202–204.
19. Vaccines and Related Biological Products Advisory Committee Meeting. FDA Briefing Document. Pfizer-BioNTech COVID-19 Vaccine. https://www.fda.gov/media/144245/download. Published December 10, 2020. Accessed July 2021.
20. Vaccines and Related Biological Products Advisory Committee Meeting. FDA Briefing Document. Moderna COVID-19 Vaccine. https://www.fda.gov/media/144434/download. Published December 17, 2020. Accessed July 2021.
21. Vaccines and Related Biological Products Advisory Committee Meeting. FDA Briefing Document. Janssen Ad26.COV2.S Vaccine for the Prevention of COVID-19. https://www.fda.gov/media/146217/download. Published February 26, 2021. Accessed July 2021.
22. FDA News Release. Coronavirus (COVID-19) Update: July 13, 2021. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-july-13-2021. Published July 13, 2021. Accessed DATE.
23. Our World in Data. Coronavirus (COVID-19) Vaccinations. https://ourworldindata.org/covid-vaccinations?country=OWID_WRL. Accessed May 28, 2021.
24. Centers for Disease Control and Prevention. The Vaccine Adverse Event Reporting System (VAERS). https://wonder.cdc.gov/controller/saved/D8/D165F867. Accessed July 16, 2021.
25. van Eijk JJ, van Alfen N, Berrevoets M, van der Wilt GJ, Pillen S, van Engelen BG. Evaluation of prednisolone treatment in the acute phase of neuralgic amyotrophy: an observational study. J Neurol Neurosurg Psychiatry 2009;80(10):1120–1124.
26. Krishnan KR, Sneag DB, Feinberg JH, et al. Outcomes of Microneurolysis of Hourglass Constrictions in Chronic Neuralgic Amyotrophy. J Hand Surg Am 2021;46(1):43–53.