Received: 22 November 2022 | Revised: 21 December 2022 | Accepted: 5 January 2023

DOI: 10.1111/cen3.12742

Clinical & Experimental Neuroimmunology WILEY

CLINICAL LETTER

Transverse myelitis following bivalent COVID-19 booster vaccine and quadrivalent seasonal influenza vaccine

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KEYWORDS: adverse event, COVID-19, transverse myelitis, vaccine

1 | CASE PRESENTATION

A 78-year-old woman with a past medical history of osteoporosis, mitral regurgitation, and hyperlipidemia presented in September 2022 with left lower extremity weakness and numbness. Twenty-four h prior to presentation, the patient was at her neurologic baseline and ambulating when she acutely developed lightheadedness and left thigh paresthesia followed by generalized left leg weakness.

She presented to the emergency department unable to walk independently. She noted a painful, band-like sensation around her left upper abdomen but denied saddle anesthesia or fecal incontinence. On physical exam of the left lower extremity, strength was 4/5 for flexion and extension of the hip and knee, sensation to light touch was diffusely decreased across multiple dermatomes, and Babinski sign was positive. Examination of the right lower extremity was unremarkable. Laboratory workup including SARS-CoV-2 polymerase chain reaction, C-reactive protein, creatine kinase, thyroid-stimulating hormone, vitamin B12, angiotensin converting enzyme, antinuclear antibody, anti-HMG CoA reductase antibody, anti-SSA and-SSB antibodies, and antidouble strand DNA antibody were within normal limits or negative. Brain magnetic resonance imaging (MRI) without contrast was unremarkable. Initial thoracic MRI with contrast showed a nonspecific, nonenhancing lesion with T2 hyperintensity at T5-6 (see Figure 1A,B). Repeat thoracic imaging on hospital d 4 was again nonspecific, and the differential diagnosis remained broad.

Initially, the patient exhibited modest daily improvements in strength and functioning, but from hospital d 7 to 9 her functional improvements stalled and she developed urine retention and constipation. Urine retention gradually improved during the hospital stay, with successively lower post-void residual (PVR) volumes documented between hospital d 7 and 13. Lumbar puncture was performed on hospital d 8. Cerebrospinal fluid studies were within normal limits or negative, including cell count (zero nucleated cells in the fourth collected tube), Gram stain and culture, multipathogen meningitis panel (including varicella zoster virus and herpes simplex virus 1 and 2), and oligoclonal bands. On hospital d 9, a serum sample was sent to an outside laboratory to be tested for anti-MOG and anti-NMO/AQP4 antibodies with fluorescence-activated cell sorting (FACS) assay. Both tests results were negative.

Due to progression of symptoms and lack of an alternative diagnosis, thoracic MRI with contrast was repeated on hospital d 10. This demonstrated more conspicuous T2 hyperintensity, now extending from T3 to T7 along with pathologic contrast enhancement at T5–T6, consistent with transverse myelitis (TM; see Figure 1D–F). Of note, retrospective review of imaging from hospital d 3 revealed a faint, ill-defined enhancement on axial imaging (see Figure 1C). She denied any recent infectious event, sick contacts, or common infectious symptoms such as cough or rhinorrhea. She had no known family history of autoimmune disease. However, she had received the bivalent Pfizer-BioNTech COVID-19 booster vaccine and Fluzone quadrivalent influenza vaccine 6 d prior to symptom onset. The patient was diagnosed with transverse myelitis and completed 5 d of high-dose intravenous methylprednisolone, after which she was discharged to complete outpatient physical therapy. At 2 mo postdischarge, she was

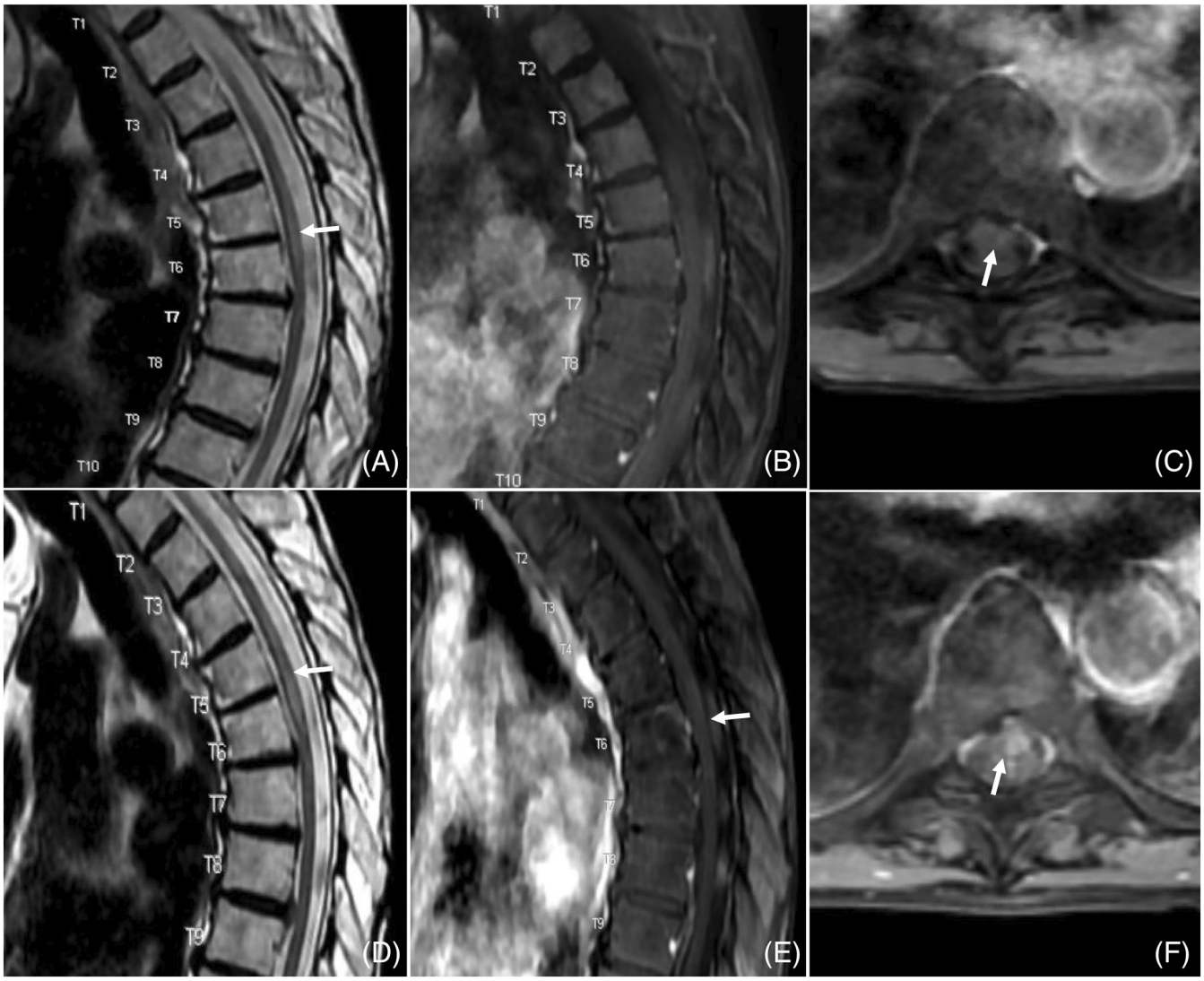

FIGURE 1 MRI of the thoracic spine was obtained pre- and postcontrast administration soon after presentation (upper row, A–C) and 1 wk later (lower row, D–F). T2-weighted image (A) demonstrates left paramedian hyperintensity centered at the T5–T6 level. There was no discernible enhancement on sagittal T1 postcontrast images (B). However, retrospectively a stippled ill-defined enhancement was noted at the T5–T6 level (C, white arrow). Follow-up images showed a more conspicuous T2 hyperintensity extending from T3 to T7 levels (D) along with more discernible enhancement in the left paramedian cord most confluent at the T5–T6 level (E). Additionally, more discrete enhancement was noted on the axial T1 postcontrast images at the T5–T6 level (F, white arrow).

able to ambulate independently with a cane but had not returned to her prior functional baseline. She was also found to have recurrence of urine retention with elevated PVR volume and was taught intermittent self-catheterization.

2 | DISCUSSION

TM is a rare inflammatory demyelinating disease associated with systemic autoimmune disorders, infection, and, less commonly, vaccination.[1] TM has been documented following different COVID-19 and influenza vaccines and can present days to weeks after the first vaccination or subsequent doses.[2] The pathogenesis is unclear. It is proposed that central nervous system (CNS) demyelinating syndromes following vaccination may involve mechanisms such as molecular mimicry or epitope spreading.[3] Parainfectious and postvaccination myelitis often has nonspecific findings on MRI, typically long-segment T2 hyperintensity with enhancement.[4] However, as seen in this case, enhancement is more common in subacute stages than at initial presentation.[4]

We present a case of acute partial TM following COVID-19 and influenza vaccination. The patient had previously received two Moderna and two Pfizer-BioNTech COVID-19 vaccines without issue. She developed symptoms 6 d after receiving the bivalent Pfizer-BioNTech booster vaccine and Fluzone quadrivalent influenza vaccine in early September 2022. Of note, initial MR imaging of her spinal cord lesion was considered nonspecific, delaying diagnosis of TM. However, given progression of symptoms and lack of an

alternative diagnosis despite extensive workup, repeat imaging was obtained and showed a T2 hyperintense lesion with contrast enhancement, consistent with TM. We could find no PubMed-indexed case reports of transverse myelitis following the bivalent Pfizer-BioNTech vaccine booster, which was authorized for use in the United States in August 2022 by the US Food and Drug Administration.[5] This booster covers the original SARS-CoV-2 strain along with the BA.4 and BA.5 lineages of the omicron variant. Due to coadministration of COVID-19 and influenza vaccines, we are unable to attribute this patient's TM to a single culprit.

Several studies have evaluated the safety of coadministration of COVID-19 and influenza vaccines. A United States-based multicenter clinical trial monitored adverse events following concomitant administration of a third booster dose of a COVID-19 vaccine (mRNA-1273, Moderna) and a seasonal influenza vaccine (Fluzone high-dose quadrivalent, Sanofi Pasteur), compared to administration of either vaccine alone.[6] This study found similar rates of adverse events between the covaccination group and COVID-19 vaccination-only group at 22 d follow-up, with slightly lower adverse event rates reported in the influenza vaccination-only arm. No serious adverse events were reported. A United Kingdom-based multicenter clinical trial evaluated concomitant administration of three different seasonal influenza vaccines with the second primary series dose of two different COVID-19 vaccines (ChAdOx1, Oxford–AstraZeneca and BNT162b2, Pfizer–BioNTech).[7] At 7-d follow up, two of the six treatment combinations failed to meet the noninferiority threshold, defined as a <25% increase in systemic adverse events compared to COVID-19 vaccination alone: ChADOx1 COVID-19 vaccine combined with MF59C adjuvanted trivalent influenza vaccine, and BNT162b2 COVID-19 vaccine combined with recombinant quadrivalent influenza vaccine. The rate of systemic adverse events in both of these covaccination groups narrowly exceeded the noninferiority threshold at the upper limit of their 95% confidence intervals. These adverse event findings were not felt to be clinically meaningful by the study's authors. The only serious adverse event reported was migraine requiring hospitalization in a patient receiving the ChADOx1 COVID-19 and cellular quadrivalent influenza vaccines. A United States-based retrospective cohort study evaluated rates of systemic adverse reactions following coadministration of either Pfizer-BioNTech or Moderna COVID-19 mRNA booster vaccine with seasonal influenza vaccine. At 7-d follow-up, self-reported systemic reactions were slightly more common in both covaccination groups compared to COVID-19 booster vaccine alone.[8]

3 | CONCLUSION

Acute TM is a rare but devastating condition that may be observed following vaccination. Patients presenting with characteristic findings should be evaluated for systemic disorders and asked about potential triggers such as recent infection and vaccination, including COVID-19 and influenza vaccines, which are increasingly coadministered. Postvaccination TM may present with nonspecific MRI findings, and clinicians with a high index of suspicion should consider the value of repeat imaging to guide diagnosis and treatment.

AUTHOR CONTRIBUTIONS

All authors have participated in preparation and review of this article. Ms. Xiao performed most of the literature review and wrote the majority of the article. Dr. Zaharia helped with writing and editing of the article. Dr. Al-Smadi provided MRI images and imaging commentary. Dr. Murphy helped with writing and literature review and oversaw preparation of the article.

ACKNOWLEDGMENTS

None.

FUNDING INFORMATION

This article was not supported by outside funding.

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

DISCLOSURE OF ETHICAL STATEMENTS

Approval of the research protocol: N/A.

Informed Consent: All informed consent was obtained from the subject(s) and/or guardian(s).

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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REFERENCES

1. Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates: neurological complications of COVID-19 vaccines. Ann Neurol. 2021;89(5):856–7. https://doi.org/10.1002/ana.26065
2. Eom H, Kim SW, Kim M, Kim YE, Kim JH, Shin HY, et al. Case reports of acute transverse myelitis associated with mRNA vaccine for COVID-19. J Korean Med Sci. 2022;37(7):e52. https://doi.org/10.3346/jkms.2022.37.e52
3. Morena J, Gyang T. COVID-19 mRNA vaccines associated with MOG-Ab disease and transverse myelitis: two case reports (P11-4.009). Neurology. 2022;98(18 Supplement):1185. [accessed 2022 Oct 24]. Available from: https://n.neurology.org/content/98/18_Supplement/1185
4. Goh C, Desmond PM, Phal PM. MRI in transverse myelitis. J Magn Reson Imaging. 2014;40(6):1267–79. https://doi.org/10.1002/jmri.24563
5. Coronavirus (COVID-19) Update: FDA Authorizes Moderna, Pfizer-BioNTech Bivalent COVID-19 Vaccines for Use as a Booster Dose. [accessed 2022 Nov 19]. Available from:. https://www.fda.gov/

news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-pfizer-biontech-bivalent-covid-19-vaccines-use.
6. Lazarus R, Baos S, Cappel-Porter H, Carson-Stevens A, Clout M, Culliford L, et al. Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): a multicentre, randomised, controlled, phase 4 trial. Lancet. 2021;398(10318):2277–87.
7. Izikson R, Brune D, Bolduc J-S, Bourron P, Fournier M, Moore TM, et al. Safety and immunogenicity of a high-dose quadrivalent influenza vaccine administered concomitantly with a third dose of the mRNA-1273 SARS-CoV-2 vaccine in adults aged ≥65 years: a phase 2, randomised, open-label study. Lancet Respir Med. 2022;10:392–402. https://doi.org/10.1016/S2213-2600(21)00557-9
8. Hause AM, Zhang B, Yue X, Marquez P, Myers TR, Parker C, et al. Reactogenicity of simultaneous COVID-19 mRNA booster and influenza vaccination in the US. JAMA Netw Open. 2022;5(7):e2222241–1. https://doi.org/10.1001/JAMANETWORKOPEN.2022.22241

How to cite this article: Xiao TL, Zaharia A, Al-Smadi AS, Murphy CJ. Transverse myelitis following bivalent COVID-19 booster vaccine and quadrivalent seasonal influenza vaccine. Clin Exp Neuroimmunol. 2023. https://doi.org/10.1111/cen3.12742