A Rare Case of Longitudinally Extensive Transverse Myelitis Following Pfizer-BioNTech COVID-19 Vaccination with a Favourable Outcome

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ABSTRACT
Introduction: mRNA COVID-19 vaccines are very safe, but rare adverse events such as transverse myelitis have been reported after COVID-19 vaccination.
Case Description: We report the case of 50-year-old man who presented with progressive lower extremity weakness, back pain and urinary retention after his second dose of the Pfizer COVID-19 vaccine. MRI of the spine revealed longitudinally extensive transverse myelitis (LETM). He recovered completely after treatment with intravenous methylprednisolone and physical therapy.
Discussion: This case highlights the rare association between LETM and COVID-19 vaccines and encourages clinicians to maintain a high index of suspicion for prompt diagnosis and treatment.

LEARNING POINTS
• Longitudinally extensive transverse myelitis (LETM) is rare adverse events after mRNA COVID-19 vaccination.
• Clinicians should maintain a high index of suspicion for prompt diagnosis of vaccine-induced transverse myelitis.
• Vaccine-induced LETM should show marked clinical improvement after appropriate treatment.

KEYWORDS
COVID-19, transverse myelitis, mRNA COVID-19 vaccines, autoimmune disease

INTRODUCTION
Longitudinally extensive transverse myelitis (LETM) is a rare subtype of transverse myelitis (TM) which extends over three or more vertebral segments and presents with spinal cord dysfunction, including rapid onset weakness, sensory loss, and bowel and bladder dysfunction [1]. Central nervous system (CNS) demyelination disorder, systemic inflammatory disorders, infectious and paraneoplastic syndromes and vaccination are known causes of TM [2, 3]. Headache, dizziness, muscle pain and spasm, myalgia and paraesthesia are common neurological symptoms; however, rare cases of stroke, Guillain-Barre syndrome, facial palsy, seizures, acute disseminated encephalomyelitis and TM have been reported after COVID-19 vaccination [4]. We report the case of a 50-year-old man admitted to hospital 20 days after his second dose of the Pfizer COVID-19 vaccine with progressive lower extremity weakness and numbness, back pain and urinary retention. Investigation and imaging results were consistent with LETM.
CASE DESCRIPTION
A 50-year-old man with no significant past medical history presented to the emergency department with progressive weakness and numbness of the bilateral lower extremities, back pain, and difficult urination for 2 days. He denied fever, chills, headache, dizziness, vision changes, chest pain, shortness of breath, abdominal pain, nausea and vomiting. He had no history of recent trauma, travel or contact with a sick person. He reported COVID-19 infection 10 months earlier with complete recovery without treatment. He had received his second dose of the Pfizer COVID-19 vaccine 20 days previously.

His initial vital signs were blood pressure of 136/72 mmHg, temperature of 36.7°C, heart rate of 76 beats/min, and respiratory rate of 16 breaths/min with 98% saturation on room air. The physical examination revealed decreased strength in the bilateral lower extremities (muscle power 4/5), decreased vibration sense and proprioception in the bilateral lower extremities with sensory level at T4, and brisk reflexes (3+) in all four extremities with a positive Babinski reflex and ataxic gait. The rest of the physical examination was unremarkable. The laboratory studies, including complete blood count and comprehensive metabolic panel, were unremarkable. A COVID-19 PCR test was negative. MRI of the brain was unremarkable. However, MRI of the spine (cervical/thoracic/lumbar) revealed multiple relatively long segments of increased cord signal diffusely throughout the cervical and thoracic cord with lesions mainly affecting C2–C5 (Fig. 1) and T2–T7 (Fig. 2).

Cerebrospinal fluid (CSF) studies revealed pleocytosis and elevated protein with normal glucose, as shown in Table 1.

| Variable            | Reference range | Reported values |
|---------------------|-----------------|-----------------|
| Nucleated cells     | 0–10/µl         | 129/µl          |
| Neutrophils         | 0–6%            | 17%             |
| Lymphocytes         | 40–80%          | 12%             |
| Monocytes           | 15–45%          | 71%             |
| Glucose             | 55–88 mg/dl     | 59 mg/dl        |
| Protein             | 15–45 mg/dl     | 68 mg/dl        |
| Oligoclonal bands   | 0–1 bands       | 0 bands         |

Table 1. Cerebrospinal fluid study results during hospitalization
Additional work-up including CSF oligoclonal band, angiotensin-converting enzyme, aquaporin 4 receptor antibody (NMO-IgG), antimyelin oligodendrocyte glycoprotein (MOG) antibody, Lyme antibodies, meningitis panel, West Nile virus IgG and IgM, HIV, syphilis rapid plasma reagin, serum vitamin B12, serum copper, antinuclear antibody, antibody to an extractable nuclear antigen, rheumatoid factor and a paraneoplastic CSF panel, was unremarkable. The diagnosis of LETM secondary to COVID-19 vaccination was made by a diagnosis of exclusion.

The patient was started on intravenous methylprednisone 1000 mg daily for 5 days. After five doses of methylprednisolone and physical therapy, his lower extremity weakness had improved (muscle power 5/5). He reported improved sensation in both feet, although numbness and tingling persisted. He was started on oral prednisone 1 mg/kg/day for 2 weeks, followed by a gradual taper, and discharged to the acute rehabilitation unit (ARU) to continue physical therapy. After 1 week of extensive physical therapy at ARU, he was discharged home. He continued outpatient physical therapy three times a week and completed recovery in about 1 month.

DISCUSSION

Acute TM is a rare, acquired neuro-immune spinal cord disorder with an incidence of 1.34–4.6 cases per million annually[5], and vaccine-associated myelitis is even more rare[6]. CNS demyelinating disorders (multiple sclerosis, neuromyelitis optica spectrum disorder (NMOSD), MOG antibody disorder, acute disseminated encephalomyelitis (ADEM)), systemic inflammatory disorders (systemic lupus erythematosus (SLE), sarcoidosis, Sjogren’s syndrome), infectious (enterovirus, HIV, syphilis) and paraneoplastic syndromes and vaccines (hepatitis B, measles, mumps, rubella, diphtheria, tetanus, pertussis) have been associated with TM[2, 3, 6]. TM has been reported as a complication of both COVID-19 infection and COVID-19 vaccination[7]. The pathogenesis of vaccine-associated myelitis is unclear. It is proposed that infectious agents and vaccine adjuvants may induce immune reactions by various proposed mechanisms such as molecular mimicry, epitope spreading, upregulation of cytokines, and polyclonal activation of B and T lymphocytes leading to TM[8]. However, mRNA COVID vaccines do not use adjuvants, and TM is less common with mRNA COVID vaccines than with viral vector COVID vaccines such as Johnson and Johnson and AstraZeneca[7]. mRNA COVID vaccines encode the pre-fusion SARS-CoV-2 spike protein; autoimmune reactions between SARS-CoV-2 spike protein antibody and tissue proteins or ACE2 receptors have been the proposed mechanism of mRNA COVID vaccine-induced TM[9].

COVID-19 vaccination has played a significant role in curbing the COVID-19 pandemic. mRNA COVID vaccines are very safe. However, with mass immunization against COVID-19, various adverse events have been reported, including severe neurological adverse effects such as TM[4]. A literature review revealed 12 cases of TM after mRNA COVID-19 vaccination, which are summarized in Table 2. However, TM is a rare adverse event and marked clinical improvement can occur with prompt diagnosis and appropriate treatment, as shown in our case. Intravenous methylprednisone followed by oral prednisone is the most common therapeutic approach in reported cases of vaccination-induced TM. However, a few cases have been treated with subsequent plasma exchange and IV immunoglobulins along with methylprednisone therapy (Table 2). Further studies will be needed to determine the exact pathogenesis, risk factors, and treatment for mRNA COVID-19 post-vaccination TM.

CONCLUSION

This case highlights the rare association between LETM and mRNA COVID-19 vaccination and encourages clinicians to maintain a high index of suspicion for vaccine-induced TM for prompt diagnosis and treatment.
| Author           | Country         | Age/Gender | Vaccine and doses | Clinical presentation                                      | Symptom onset | MRI Finding | Management                                                                 | Outcome                      |
|------------------|-----------------|------------|-------------------|------------------------------------------------------------|---------------|-------------|----------------------------------------------------------------------------|-------------------------------|
| Gao et al.[10]   | Taiwan          | 76/F       | Moderna mRNA-1273 1st dose | Unsteadiness and abnormal sensation in the lower limbs     | 6 Days        | Cervical cord C2-C5 on T2 images | Intravenous methylprednisone (IVMP) for 5 days followed by oral | Marked improvement |
| Alabak et al.[11]| Canada          | 26/F       | Pfizer 1st dose    | Progressive saddle numbness and allodynia                  | 3 Days        | T2 short segment and diffusely enhancing lesion at T5                     | IVMP for 5 days, pregabalin | Minimal improvement of symptoms |
| Hirose et al.[12]| Japan           | 70/M       | Moderna 1st dose   | Progressive sensorimotor dysfunction in bilateral lower limbs | 7 Days        | Intramedullary lesion T1-T2, T3-T6                                      | IVMP for 5 days followed by oral prednisone, gradual taper | Complete improvement |
| Fernandes et al.[13]| West Indies     | 26/F       | Pfizer 1st dose    | Progressive lower limb weakness and left upper limb weakness | 2 Days        | Medulla to T1 level                                                     | IVMP for 5 days followed by oral taper prednisolone, rituximab | Complete improvement |
| Miyae et al.[14] | Japan           | 75/M       | Pfizer 1st dose    | Sensory loss below the umbilicus and complete paraparesis in both legs | 3 Days        | Longitudinally hyperintense lesion from the lower thoracic to lumbar spine | Steroids and plasma exchange | Limited recovery |
| Khan et al.[15]  | USA             | 67/F       | Moderna 1st dose   | Tingling sensation in right lower extremity and difficulty walking | 5 Days        | MRI cervical spine, hyperintense lesion C1-C3                           | IVMP for 3 days, no improvement, followed by plasmapheresis for 5 days | Marked improvement |
| Fitzsimmons et al.[16] | USA          | 63/M       | Moderna 2nd dose   | Severe pain in lower back, legs, feet, unable to walk, urinary difficulty | 2 Days        | MRI spine, T2 cord signal distal spinal cord and conus                  | IV immunoglobulin for 2 days, followed by IVMP for 5 days, prednisone taper | Marked improvement |
| McLean et al.[17]| USA             | 69/F       | Pfizer 1st dose    | Bilateral upper and lower extremity weakness               | 2 Days        | MRI spine, noncompressive myelitis C3-C4, T2-T3                        | IVMP for 5 days               | Residual weakness with gradual improvement |
| Nakano et al.[18]| Japan           | 85/M       | Pfizer 2nd dose    | Progressive gait disturbance and urinary retention         | 15 Days       | MRI spine, longitudinally hyperintense lesion T3-T5                     | IVMP for 3 days followed by oral prednisone | No improvement, developed pneumonia and later died in hospital |
| Eom et al.[19]   | Korea           | 81/M       | Pfizer 2nd dose    | Bilateral hand weakness and numbness                        | 3 Days        | MRI spine, high signal intensity C1-C3                                 | IVMP for 5 days, oral prednisone taper for 2 weeks | Marked improvement |
| Albokhari et al.[20]| Saudi Arabia   | 16/F       | Pfizer 2nd dose    | Tingling sensation in both thighs and leg weakness         | 3 Weeks       | MRI spine, high signal intensity on conus medullaris                    | IVMP for 5 days, followed by oral prednisone taper for 2 months | Marked improvement |

Table 2. Cases of transverse myelitis after mRNA-based COVID-19 vaccination
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