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A Case of Transverse Myelitis After Moderna Severe Acute Respiratory Syndrome Coronavirus Vaccination

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Abstract

Transverse myelitis (TM) is an inflammatory syndrome of the spinal cord that presents with acute-to-subacute neurological deficits. The differential for TM is broad and includes demyelinating, infectious, neoplastic and paraneoplastic, autoimmune, and metabolic/toxic etiologies. With the novel severe acute respiratory syndrome coronavirus pandemic, more commonly referred to as the coronavirus infectious disease of 2019 (COVID-19), there have been increasing reports of neurological complications. In this case report, we describe a novel case of longitudinally-extensive TM associated with the Moderna vaccination.

Keywords

autoimmune diseases of the nervous system, neuroimmunology, myelitis, transverse, spinal cord diseases, COVID-19, imaging

Case

A 60-year-old, right-handed man with right hemispheric stroke in 2017 with residual left hemiparesis, non-alcoholic steatohepatitis, rheumatoid arthritis, hypertension, and type II diabetes mellitus was admitted for 4 days of bilateral lower extremity numbness and weakness. The patient received his 2nd dose of the Moderna COVID-19 vaccination 10 days prior to admission with no immediate adverse events. Prior to symptom development, he was self-ambulatory without assistance despite his residual left hemiparesis. Six days post-vaccination, he developed a tingling sensation in his feet. On day 7, the bilateral lower extremity tingling sensation travelled up to his knees. On day 8, the tingling progressed to his waist, transitioning to numbness later that day. He also started noticing weakness in his bilateral lower extremities and developed both urinary and bowel incontinence both with and without awareness that he was micturating or defecating. On day 10, his family brought him to our hospital.

His neurological exam was significant for reduced tone in his bilateral lower extremities. His bilateral iliopsoas, quadriceps, hamstrings, abductor, and adductor muscles were 2/5 on the MRC grading scale. His bilateral anterior tibialis, gastrocnemius, and foot invertors and evertors were 4+/5. From his residual post-stroke deficits, he demonstrated 4/5 strength in his left deltoid and bicep, 4−/5 in his left tricep and wrist extensors, and 3/5 in his left finger abductors. His right upper extremity was 5/5. His sensory exam was notable for a T9 sensory level to pinprick and perineal numbness with mildly reduced rectal tone. He had reduced lower extremity vibration in a length-dependent pattern. Reflexes were 2+ in his upper extremities and 1+ in the lower extremities. He had normal cranial nerve and coordination examinations.

Lumbar puncture revealed 5 white blood cells/mm^3 (22% neutrophils, 49% lymphocytes), 1271 red blood cells/mm^3, 124 mg/dL glucose, and 55 mg/dL protein. MRI of the brain, cervical, and lumbar spine were unremarkable. Thoracic spine MRI revealed a longitudinally-extensive hyperintense T2 signal from T8 to T12 without contrast enhancement. It also showed an incidental T5-T8 syrinx and mild-to-moderate diffuse degenerative disc disease (Figure 1). The findings suggested transverse myelitis which left a broad differential, including autoimmune, demyelinating, and paraneoplastic etiologies vs. possibly an acute cord infarction. Suspicion for an infectious etiology was low, and cultures were negative, so he was treated with methylprednisolone 1000 mg for 5 days.

Laboratory studies were overwhelmingly negative, including serum copper (138 µg/dL), zinc (63 µg/dL), heavy

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metals, RPR, and HIV 1/2; CSF HTLV 1/2, VDRL, and HSV; and several rheumatological studies including soluble IL-2 receptor (320 U/mL), anti-Jo, anti-Mi-2, anti-Ro/La, anti-Smith, anti-Scleroderma, anti-dsDNA, anti-ribosomal P, and anti-RNP antibodies. Serum neuromyelitis optica (NMO) and anti-myelin oligodendrocyte glycoprotein (MOG) antibodies from Mayo Clinic were also negative. He had an unremarkable chest X-ray. He had elevated ESR (37 mm/hr), CRP (37.4 mg/L), ANA (360 titer), and a positive VZV IgG and West Nile IgG (IgM negative for both).

With methylprednisolone, the patient's clinical course improved suggesting an autoimmune etiology. His lower extremity strength exam improved markedly (4+/5 on the right, 5−/5 on the left), and his pinprick sensation returned. He was discharged to inpatient rehabilitation and left with a walker after 2 weeks with no fall events. His bladder and bowel function normalized. He completed an oral prednisone taper (starting with 60 mg daily with 10 mg taper per week) over 6 weeks without worsening of myelopathic symptoms. On outpatient follow-up, his strength exam remained improved. Given negative aquaporin-4 (AQP-4) Ab and MOG Ab, suspicion of NMO spectrum disorder and MOG antibody associated disease was low. Sarcoidosis was low in suspicion due to no systemic symptoms, paucity of inflammatory markers in CSF, and normal chest X-ray. While CSF oligoclonal bands and IgG index were not checked, longitudinally-extensive transverse myelitis (LETM) is not typical of multiple sclerosis, so his transverse myelitis is suspected to be a post-vaccination autoimmune response.[1] He was advised to continue therapy, stretch daily, partake in water-walking to reduce leg stiffness, avoid further COVID-19 vaccinations, and monitor for any relapse or new symptoms in the neurology clinic.

Discussion

Myelitis is defined as an inflammatory disease state that affects the spinal cord. Transverse myelitis (TM) is an inflammatory syndrome that presents with acute-to-subacute neurological deficits stemming from the spinal cord.[2] Depending on the lesion location, impairments can include weakness of the upper or lower extremities (paraparesis), paresis of all extremities (quadriparesis), change in muscular tone (flaccidity, spasticity), increase or decrease in reflex responses (extremity reflexes, abdominal reflexes, genitourinary reflexes, etc.), sensory alteration or loss circumferentially at and below a dermatomal level (commonly referred to as a "sensory level"), and autonomic dysfunctions below the level of impairment (urinary, gastrointestinal, reproductive, cardiovascular, and thermoregulatory).[1,2] The lesion may cause a partial TM presenting as an asymmetric distribution of clinical findings, or it can manifest as a complete TM causing equal clinical findings bilaterally. The lesion can also be "longitudinally-extensive," spanning 3 or more vertebral segments on MRI. Longitudinally-extensive lesions are commonly seen in demyelinating conditions such as neuromyelitis optica (NMO) and MOG Ab associated disease (MOGAD).[1-3] The differential for TM is extensive with etiologies that include demyelinating, infectious, post-infectious, neoplastic, paraneoplastic, autoimmune, and metabolic/toxic etiologies. However, in the remaining 15-30% of patients, the diagnosis remains idiopathic without any identifiable cause.[2]

Given the broad differential, the physician must obtain a detailed clinical history from the patient. Evidence of antecedent infection (toxic symptoms, recent travel or exposures, etc.), systemic- and neoplastic-related symptoms (night sweats, weight loss, decreased appetite, fatigue, arthralgias, myalgias, rashes, etc.), onset and progression of symptoms, and prior diagnostic workup help eliminate less likely sources and narrow the clinician's differential. Other epidemiological factors, such as the patient's age, sex, and even geographical location, can help further tailor a physician's diagnosis.[2] Such practices can help eliminate features not diagnostic of TM, such as a preceding injury (which would suggest traumatic myelopathy), vascular risk factors, or recent abdominal-aortic surgical manipulation (suggesting a spinal cord infarction). Identifying the source is also important because the management differs drastically between etiologies. Equally if not more important, certain management strategies can worsen disease severity, such as mistakenly treating an infectious cause with steroids or discontinuing steroids too early in a case of anti-MOG disease.[2,3]

When more common and well-known culprits are exhausted from diagnostic workup, an astute clinician can turn to rare and uncommon explanations provided the history accounts for it. In this case, our patient presented a little over 1 year after the onset of the novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) pandemic, more commonly referred to as the coronavirus infectious disease of 2019 (COVID-19). COVID-19 was declared a pandemic on March 11, 2020, initially thought to be a respiratory pathogen as per its namesake.[4] Time, and numerous case reports, have shown that COVID-19 has system-wide effects on the human body. Among its systemic effects, neurological complications have become more frequently reported, including strokes, seizures, demyelinating disorders, Guillain-Barré Syndrome, myositis, and now spinal cord involvement.[4] Recent meta-analyses and systematic reviews vary in inclusion and exclusion criteria but show anywhere from 21 to 43 relevant cases of COVID-19-related spinal cord involvement, including but not limited to acute flaccid myelitis, transverse myelitis, acute disseminated encephalomyelitis, and undifferentiated demyelinating disease. The neurologic symptom onsets varied broadly from 15 hours to 6 weeks from infection onset. In all these cases, there was usually elevated protein and lymphocyte predominance in CSF studies.[4,5] While our patient did not have CSF pleocytosis, he did have elevated protein which can be a sign of CSF inflammation or myelitis.

Transverse myelitis post-vaccination is not a novel phenomenon. A meta-analysis between 1970 to 2009

demonstrated 37 reported cases related to vaccination against hepatitis B virus, measles-mumps-rubella (MMR) viruses, diphtheria-tetanus-pertussis (DTaP), and others.[6] The first reported case of TM following post-influenza vaccination occurred in 1995, in which the patient improved after an intravenous steroid regimen and physical therapy.[7] Other reports have appeared in the literature, including a case of LETM after the H1N1 vaccine in 2010, which also improved after intravenous steroids with outpatient taper and plasmapheresis.[8] While several spinal cord-related COVID-19 infection cases have been cited between 2020 and 2021, a review of acute TM by Román et al quotes only 3 post-vaccination cases, all from the phase III clinical trial of the Oxford-AstraZeneca COVID-19 vaccine ChAdOx1 nCoV-19 (AZD1222).[5,9,10] More recently, a report from the University of Iowa has demonstrated a suspected case of TM post-Moderna vaccination.[11] It is presumed that molecular mimicry, where a foreign antibody shares similarities with the host's molecular structures, is responsible for the autoimmune phenomena of COVID-19, triggering the production of an antibody that simultaneously attacks both the pathogen and the host.[12]

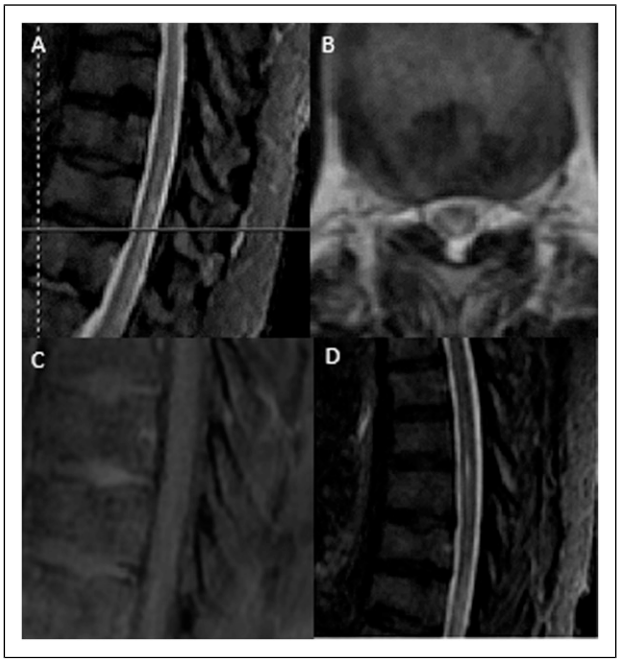

Figure 1. Thoracic spine MRI with 5-mm thickness slices. A. Sagittal STIR with longitudinally-extensive, T2-weighted hyperintense signal from T8 to T12 level. B. Axial plane at the level of T9/T10 demonstrating the same T2-weighted hyperintense signal. C. T1 sagittal post-contrast demonstrating no contrast enhancement in the region where the T2-weighted hyperintense signal was previously appreciated. D. Sagittal STIR revealing incidental syrinx located at T5-T8 level.

Given the timing of our patient's TM post-vaccine administration and thorough exclusion of other causes, we postulate that his TM is a potentially novel case of post-vaccine TM associated with the Moderna vaccination. This being said, the development of TM after vaccination is an incredibly rare event relative to the number of vaccinated individuals throughout recent history. Using the FDA VAERS data via the CDC WONDER search tool for all US licensed vaccinations, a review of any suspected post-vaccination spinal cord injury shows approximately 36 reports of "cervical or thoracic spinal cord injury or paralysis" and 452 reports of "abnormal MRI spinal imaging" without further elaboration or context. On the other hand, complications of the COVID-19 infection are more frequent, numerous, chronic, and multi-systemic in nature, including but not limited to pulmonary, cardiac, renal, vascular, and central and peripheral nervous system events.[13] Though post-vaccination myelopathy is a potentially debilitating condition if not treated, it is rare; thus the benefits of vaccination appear to outweigh the risks Figure 1.

Declaration of Conflicting Interests

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Supplemental Material

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