



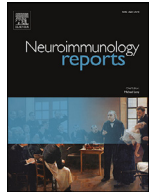
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Transverse myelitis as a first event of multiple sclerosis precipitated by Pfizer-BioNTech COVID-19 vaccination

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A B S T R A C T

Background: Neurological complications from COVID-19 vaccines are rare

Case Report: Herein, we present the case of a previously healthy woman who developed incomplete transverse myelitis (TM) immediately after receiving her first injection of the Pfizer-BioNTech COVID-19 vaccine.

Conclusion: This case is an example of TM as a first clinical event in the diagnosis of multiple sclerosis triggered by COVID-19 vaccination. A review of the FDA's Vaccine Adverse Event Reporting System (VAERS) reveals similar instances of TM. Clinicians should be aware of this potential complication from COVID-19 vaccination.

As COVID-19 infection spreads globally at alarming rates with new, more infectious variants, the effort to vaccinate populations has taken on great urgency. Three vaccines are approved for use in the United States under the FDA's Emergency Use Authorization (EUA). The Pfizer-BioNTech and Moderna vaccines, which use modified mRNAs that produce COVID-19 spike protein in vaccine recipients. The third is the Johnson & Johnson/Janssen vaccine (J&J/J), which uses DNA coding for COVID-19 spike protein transported via a non-replicating adenovirus (Wang et al., 2020; Silveira et al., 2021). Use of the latter vaccine was briefly suspended because of concerns over clotting in a small number of vaccine recipients (MISS, 2022)

Myelitis is a known, rare complication of several vaccines, including hepatitis B, measles-mumps-rubella, diphtheria-tetanus-pertussis, rabies, influenza, herpes zoster, yellow fever and COVID-19 (Klemen et al., 2020; Huynh et al., 2008; Baxter et al., 2016; Bartol et al., 2019; Huh et al., 2021). Other causes of transverse myelitis (TM) include post-infection reactions, autoimmune attack, metabolic disturbances and toxins. TM can also be caused by COVID-19 infection (Bhat et al., 2010; Ahmad and Rathore, 2020; Román Gustavo et al., 2021).

Here we wish to report an instance of TM associated with the Pfizer-BioNTech vaccine, and review other publically-reported cases associated with COVID-19 vaccines.

Case report

A 32 year old Caucasian woman was referred for evaluation of multiple sclerosis. She was in good health until January 16, 2021 when within

two hours of receiving the Pfizer-BioNTech COVID-19 vaccine she experienced a numbing sensation on the left lip. Three days later, she noted initially numbness of her right foot, which travelled proximally to her waistline, then the left foot and peroneal area. In addition, she felt a "tired" sensation in her legs and slight urinary incontinence. An MRI scan of the brain performed on February 28th, 2021 showed multiple, small periventricular and subcortical white matter lesions with subtle involvement of the corpus callosum, as well as a small contrast-enhancing lesion within the right temporal lobe. When she was evaluated on March 16th, she had reduced sharp touch sensation in her lower extremities and trunk with a T6 sensory level. Her past medical history was significant for chronic lower back pain since her teens with intermittent paresthesias of the right foot and gastric sleeve surgery for obesity in September of 2019 with subsequent weight loss of 80 lbs. Spinal cord imaging performed on March 21st showed a number of hyperintense signal abnormalities, including the left dorsolateral cord at C-4, a well-defined area of increased signal at T7-T8 with mild expansion of the cord and an ill-defined plaque on the right dorsolateral cord at T-10. The lesions did not enhance with contrast. She was diagnosed with incomplete transverse myelitis secondary to multiple sclerosis. Five days of high dose, intravenous methylprednisolone resulted mild improvement. She was referred for anti-CD20 treatment for long term therapy for MS.

Previous instances of TM associated with COVID-19 vaccination were obtained from the FDA's Vaccine Adverse Event Reporting System (VAERS) (United States Department of Health and Human Services (DHHS), 2021) (see Table 1). Listed are 25 cases of transverse myelitis. Sixteen are associated with the Pfizer-BioNTech vaccine, eight

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Table 1

Instances of Transverse Myelitis reported to the VAERS. Pf-BN = Pfizer-BioNTech, Mod = Moderna, J&J/J = Johnson & Johnson/Janssen.

No	Age	Sex		Vaccine	1st dose	2nd dose	Sx Onset	Adverse Event Summary	Diagnostic test(s)	Diagnosis
1	39	F	1	Pf-BN	12/23/2020	n/a	1/6/2021	Numbness tingling in feet, toes progressed to waist.		idiopathic
2	37	F	2	Pf-BN	12/21/2020	n/a	12/27/2021	Numbness and needle-like pain in both feet, ascending to waistline. Difficulty walking due to heavy sensation in legs. Burning erythematous rash present		idiopathic
3	39	F	3	Pf-BN	1/21/2021		1/22/2021	Numbness and tingling from chest distally. Girdle-like banding around trunk. Hand dysfunction. Impaired gait. Treated with IV steroids.	Results from blood work, lumbar puncture, MRI and CT scans unavailable.	idiopathic
4	69	F	4	Pf-BN	1/20/2021		1/22/2021	Upper and lower extremity weakness. Improvement with IV steroids.	MRI cervical and thoracic spine c/w transverse myelitis. Brain MRI showed T2/FLAIR white matter hyperintensities and global atrophy.	idiopathic
5	60	M	5	Pf-BN	12/17/2020		12/24/2020	Tingling in both hands following 1st dose. After 2nd dose, paresthesias in feet. weakness in left arm and both legs. Difficulty climbing ladder and fell in his home. Underwent L3-4 fusion, but paresthesia and weakness worsened. Uncontrolled twitching in both thighs and loss of function of left hand. Improved on corticosteroid therapy.	MRI spine c/w transverse myelitis. MRI brain and CSF results not available.	idiopathic
6	70	F	6	Mod.	1/28/2021		2/10/2021	Ascending numbness from feet to waist, hand tremors, gait ataxia, and upper spine pain. Treated with high dose dexamethasone.	MRI spine showed signal abnormalities at C3-7 and T1.	idiopathic
7	86	F	7	Mod.	2/5/2021		3/1/2021	Leg weakness, bladder/bowel dysfunction. Recovering.		idiopathic
8	34	F	8	Pf-BN	1/6/2021		1/25/2021	New onset seizures starting 1/25/21. Dx transverse myelitis on 2/5/21 and, later, multiple sclerosis with an atypical presentation.	Multiple MRIs, lumbar puncture x 2, extensive blood work	2 ^o to MS
9	NR	M	9	Pf-BN	1/1/2021		unknown	Left side numb, gait unsteady, left hand dysfunction over weeks. Treated with corticosteroids with recovery		idiopathic
10	54	F	10	Mod.	2/9/2021		2/25/2021	One day of severe upper extremity weakness and numbness. First Shingrix vaccine dose also administered 1/21/21		idiopathic
11	60	M	11	Pf-BN	1/7/2021	n/a	1/10/2021	Left side numb three days after vaccination in the left arm; right side weak three days after 2nd vaccine injected in the right arm.	MRI cervical spine showed T2 signal abnormalities.	idiopathic
12	73	M	12	Mod	2/3/2021	n/a	2/14/2021	Upper extremity proximal and distal weakness. Impaired light and sharp touch, temperature, vibration and proprioception on the right. Romberg positive.	MRI spine showed contrast enhancing lesion at C3-C5.	idiopathic
13	71	F	13	Pf-BN	2/12/2021	3/5/2021	3/5/2021	Headache, cramping after 2nd injection; chills, fatigue, leg pain and difficulty walking by the second day.	MRI Thoracic spine normal.	idiopathic
14	75	F	14	Pf-BN	1/23/2021	n/a	1/24/2021	Inability to walk. Bowel and urinary dysfunction. Left side numb from toes to breast and right side numb from toes to groin. Left leg weakness. Some recovery of sensation but ongoing bowel and urinary issues. Treated five days high dose steroids. Recovering.		idiopathic
15	50	M	15	Mod.	12/30/2020		1/7/2021	Electrical sensations, numbness and weakness lower extremities, unstable gait and sexual dysfunction.	MRI thoracic spine showed anterior lesions, and brain and cervical spine inconclusive. CSF nondiagnostic.	idiopathic

(continued on next page)

Table 1 (continued)

No	Age	Sex		Vaccine	1st dose	2nd dose	Sx Onset	Adverse Event Summary	Diagnostic test(s)	Diagnosis
16	70	F	16	Mod.	1/28/2021	n/a	2/9/2021	Bilateral shoulder and neck pain, lower extremity paresthesias. Bilateral ataxic tremors of the 5th digits. Bilateral pruritis from wrists to elbows. Improvement in weakness but residual numbness on left left trunk, ataxia and impaired word retrieval.		idiopathic
17	76	M	17	Pf-BN	1/12/2021	2/2/2021	2/2/2021	Dizziness and nausea 20 minutes after first vaccination, progressing to severe left upper and lower extremity weakness with inability to walk after two days. Sensation intact. Urinary retention, hyperreflexia and left Babinski sign. Treated with intravenous methylprednisolone	MRI brain showed global atrophy with nonspecific white matter T2/FLAIR hyperintensities c/w chronic microvascular ischemic disease. No intramedullary or cauda equina abnormalities on spinal MRI. CSF showed 6-8 oligoclonal bands. IgG index pending.	probable MS
18	80	F	18	Pf-BN	1/27/2021	n/a	1/28/2021	Generalized tonic-clonic seizure evening of 1st injection. Initially, awake and responsive, then disorientation. Bilateral multifocal pneumonia. Dx. meningoencephalitis. Intubated. Quadraplegic but able to follow commands with her eyes and mouth. Over previous six months, wt loss, night sweats and one week of paresthesias in her lower extremities. Felt that some neurological decline started prior to vaccination.	CSF studies: 220 WBCs (14% PMNs, 76% lymphs, 10% monos), 14 RBCs, Glu 59, Prot 145; GS 2+ WBCs, no orgs; india ink stain negative; Cx pending. Spine MRI showed longitudinally extensive transverse myelitis. Infectious and autoimmune panel pending.	meningo-encephalitis
19	73	F	19	Pf-BN	1/1/2021	n/a	2/26/2021	Ascending paralysis c/w transverse myelitis. CSF exam showed elevated cell count, elevated protein and low glucose.	CSF showed elevated cell count and protein; low glucose. Gram stain and culture neg.	idiopathic TM
20	75	F	20	Pf-BN	1/23/2021	n/a	1/24/2021	Acute left leg weakness and sensory loss and T10 sensory level, progressing to numbness and paresthesias in the right leg. Exam findings included mild hyperreflexia in the left leg and a T5-6 sensory level. Treated with IV methylprednisolone x5 days and transferred to rehab. Significantly improved with residual numbness in the left leg.	MRI brain and spinal cord initially normal. Repeat MRI showed contrast enhancing lesion at T5. CSF: 2 nucleated cells, protein 50 mg/dl, nml IgG index and negative oligoclonal bands.	idiopathic TM
21	49	M	21	Mod.	unknown	2/11/2021	2/12/2021	Incomplete transverse myelitis. Treated three days high-dose IV methylprednisolone followed by course of five plasma exchanges.		idiopathic TM
22	71	F	22	Mod.	1/25/2021		2/12/2021	Paresthesias and slight weakness in the right leg, worsening after two days. Onset left leg weakness and bowel and urinary retention with hydronephrosis. Treated with IV dexamethasone.	Brain and cervical spine MRI nml. Thoracic MRI scan showed ill-defined T2 hyperintensity at T5-T6. CSF nml. EMG/NCV nml.	idiopathic TM
23	71	F	23	Pf-BN		3/5/2021	3/5/2021	Headache fatigue and cramping evening of the second vaccination. Following evening: chills, fatigue, pain and heaviness in lower extremities legs, progressing to inability to walk. Treatment symptomatic.	MRI thoracic spine normal.	idiopathic TM
24	54	F	24	J&J	3/15/2021		3/29/2021	Transverse myelitis thoracic region, reported as first presentation multiple sclerosis.	MRI cervical and thoracic spine and CSF examination performed. Results not available	idiopathic TM
25	69	F	25	Pf-BN		2/19/2021	2/22/2021	Patient with Multiple Sclerosis. Developed pain in the right arm after 2nd COVID-19 vaccination, which steadily intensified and spread quickly to upper torso. Severe back pain. Ascending numbness and paresthesias in her legs to lower abdomen. Unable to stand. Received 1 gram IV solumedrol and high dose oral prednisone taper. Some improvement in right leg function improved but still unable to stand.		TM., MS

with the Moderna vaccine and one with the J&J/J vaccine. In three instances, the TM was associated with previously diagnosed or newly diagnosed MS. In addition to these cases, there are reports of two cases of transverse myelitis related to the AZ vaccine: one subject diagnosed with idiopathic TM 14 days after the booster injection and another within 10 days of the first injection. The latter was judged to have pre-existing multiple sclerosis after the event (C. et al., 2021, Voysey et al., 2021). The first case report, of which we are aware, of multiple sclerosis being diagnosed after an episode of transverse myelitis with the Pfizer-BioNTech vaccine, was recently reported (Havla et al., 2021).

Discussion

This is an example of incomplete TM secondary to multiple sclerosis, most likely triggered by the Pfizer-BioNTech vaccine. Our patient meets the MacDonald Criteria for multiple sclerosis based on her one clinical episode, multiple lesions in the brain and spine meeting the requirement for dissemination in space and an enhancing lesion in the brain meeting the requirement for dissemination in time (Thompson et al., 2018). Given the probable presence of lesions in the brain and possibly the spinal cord pre-vaccination, our patient likely would have been diagnosed with radiographically isolated syndrome, a precursor to multiple sclerosis (Hosseiny et al., 2020). Given the temporal relationship between COVID-19 vaccination and the onset of neurological symptoms, we believe that the vaccine triggered our patient's relapse.

To date, more than 130 million persons in the US have received at least one dose of the COVID-19 vaccine. Clearly, complications such as myelitis are rare. However, it is important that community physicians who will first encounter such patients be alert to the signs and symptoms of post vaccination myelitis so that such patients can receive expedient diagnosis and treatment.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nerep.2022.100074.

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