Transverse Myelitis Unmasking Multiple Sclerosis After mRNA COVID-19 Vaccine: A Case Report

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Abstract

Introduction: Demyelinating central nervous system (CNS) disorders such as transverse myelitis (TM) and multiple sclerosis (MS) have been reported with mRNA Covid-19 vaccine. Some cases were relapses of a pre-existing condition but *de novo* and initial presentation of MS after BNT162b2 COVID-19 mRNA vaccine has very rarely been documented.

Case Description: We report a 72-year-old female, right-handed, Filipina, with a one-month history of bilateral lower extremity weakness which occurred 7 days after she received her first booster dose of BNT162b2 mRNA vaccine. This was later accompanied by fecal and urinary incontinence. On examination, she had motor deficit below L1 myotome manifesting with loss of hip flexion, knee extension, dorsiflexion, and plantar flexion. There was also sensory deficit below T10 level with relative 80% sensation of vibration, proprioception, light touch and complete loss of pain and temperature sensation. The initial impression was Transverse Myelitis which may be related to a post-vaccination state. Spinal magnetic resonance imaging (MRI) revealed long segment enhancing T2W hyperintense lesion at T2 to T7. Cranial MRI revealed ovoid areas of heterogeneous, predominantly T2/FLAIR hyperintense signals exhibiting restricted diffusion in the periventricular white matter of the fronto-parietal lobes. Cerebrospinal fluid (CSF) analysis was negative for infectious causes such as tuberculosis but with high levels of CSF immunoglobulin G. She was then diagnosed to have Multiple Sclerosis (MS) and was treated with high dose oral prednisone. However, there was no improvement in neurological deficits on follow-up.

Conclusion: This case adds to the reported rare cases of initial presentation of MS occurring after vaccination for COVID-19 and the first reported case in the Philippines. Early recognition and prompt treatment is important to improve outcomes.

Keywords: *Demylenating CNS disease, Transverse Myelitis, Multiple Sclerosis, COVID-19 vaccination*

Introduction

Transverse myelitis (TM) and multiple sclerosis (MS) are both inflammatory diseases of the central nervous system (CNS). TM may present as weakness, sensory deficits and bowel or bladder symptoms.[1] It may occur independently or as a continuum of another neuro-inflammatory disease such as MS. The diagnosis of MS is met in individuals with evidence of damage occurring in multiple parts of the CNS over the course of time.[1] This condition has been rarely associated with vaccination, and to date, there are very few cases of MS with initial manifestations occurring post COVID-19 vaccination.

Case Presentation

A 72-year-old female, right-handed, Filipina, previously ambulatory and able to perform activities of daily living unassisted, presented at the emergency room due to ascending bilateral lower extremity weakness. One month prior, she received her booster dose of BNT162b2 mRNA vaccine. Her primary series was Ad26.COV2-2 vaccine which she had six months prior to her booster dose without any adverse reactions. Seven days post-vaccination, the patient experienced weakness and pain on her distal lower extremities after prolonged ambulation. There was no gait abnormalities nor sense of imbalance. She then noted progression of weakness which initially started at the distal lower extremities now at the level of L2. Furthermore, weakness progressed to paraplegia with associated numbness. Two weeks thereafter, she started to have fecal and urinary incontinence, however no intervention was done. Loose stools of around 5 to 8 episodes per day associated with

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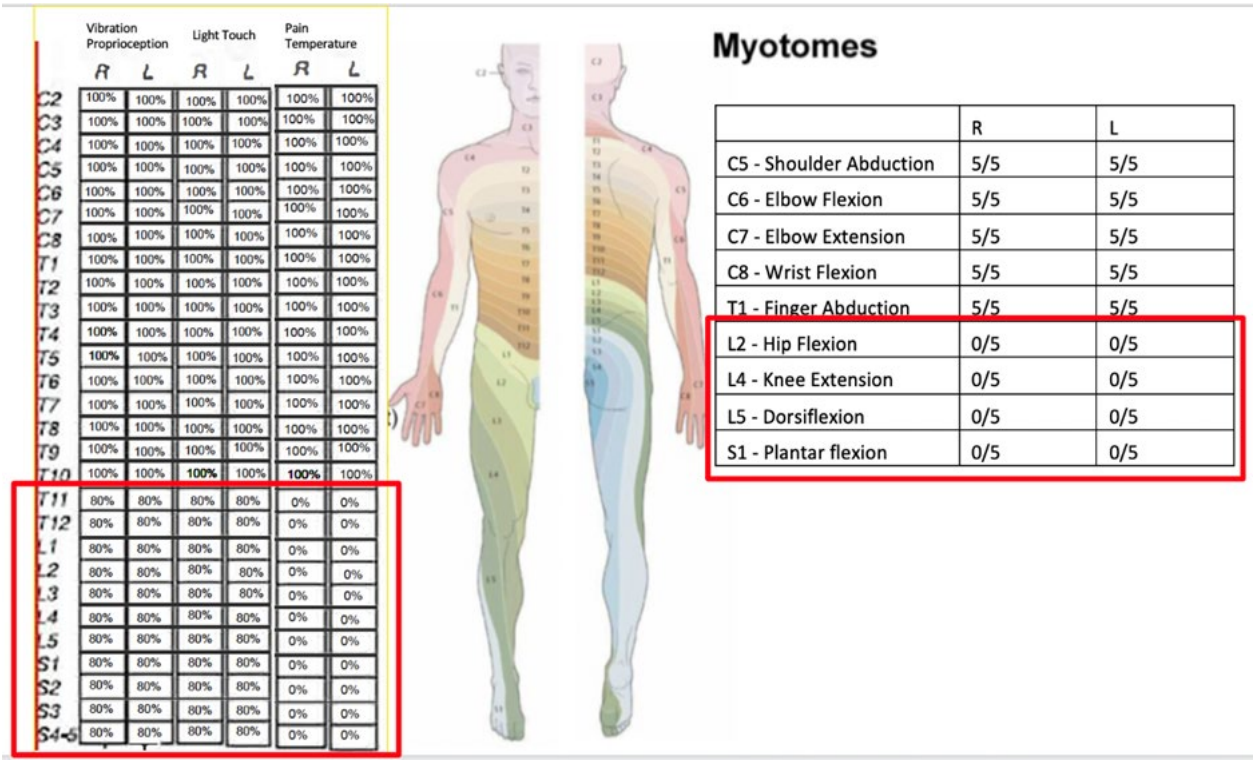

	Vibration Proprioception		Light Touch		Pain Temperature	
	R	L	R	L	R	L
C2	100%	100%	100%	100%	100%	100%
C3	100%	100%	100%	100%	100%	100%
C4	100%	100%	100%	100%	100%	100%
C5	100%	100%	100%	100%	100%	100%
C6	100%	100%	100%	100%	100%	100%
C7	100%	100%	100%	100%	100%	100%
C8	100%	100%	100%	100%	100%	100%
T1	100%	100%	100%	100%	100%	100%
T2	100%	100%	100%	100%	100%	100%
T3	100%	100%	100%	100%	100%	100%
T4	100%	100%	100%	100%	100%	100%
T5	100%	100%	100%	100%	100%	100%
T6	100%	100%	100%	100%	100%	100%
T7	100%	100%	100%	100%	100%	100%
T8	100%	100%	100%	100%	100%	100%
T9	100%	100%	100%	100%	100%	100%
T10	100%	100%	100%	100%	100%	100%
T11	80%	80%	80%	80%	0%	0%
T12	80%	80%	80%	80%	0%	0%
L1	80%	80%	80%	80%	0%	0%
L2	80%	80%	80%	80%	0%	0%
L3	80%	80%	80%	80%	0%	0%
L4	80%	80%	80%	80%	0%	0%
L5	80%	80%	80%	80%	0%	0%
S1	80%	80%	80%	80%	0%	0%
S2	80%	80%	80%	80%	0%	0%
S3	80%	80%	80%	80%	0%	0%
S4-5	80%	80%	80%	80%	0%	0%

Myotomes

	R	L
C5 - Shoulder Abduction	5/5	5/5
C6 - Elbow Flexion	5/5	5/5
C7 - Elbow Extension	5/5	5/5
C8 - Wrist Flexion	5/5	5/5
T1 - Finger Abduction	5/5	5/5
L2 - Hip Flexion	0/5	0/5
L4 - Knee Extension	0/5	0/5
L5 - Dorsiflexion	0/5	0/5
S1 - Plantar flexion	0/5	0/5

Figure 1. Dermatome and Myotome Cuts Elicited in the patient

anorexia, fatigue and generalized weakness prompted her to finally seek consult and subsequent admission.

On review of systems, she denied fever, back pain, night sweats, weight loss, cough, hemoptysis, and seizure episodes. She was previously diagnosed with hypertension maintained on losartan. She had no known autoimmune disorders and any recent history of viral infection. The patient was a never-smoker and denied alcohol use. On physical examination, vital signs were normal and physical examination was unremarkable. Digital rectal examination was unremarkable.

Neurologic examination showed intact judgement, fund of knowledge, calculation, and concentration with a mini mental status exam (MMSE) score of 21 denoting mild cognitive impairment. Cranial nerves were intact. There was no anisocoria or pupillary defects. On fundoscopy, the media was clear, with yellow-orange disc and distinct borders, cup disc ratio was 0.3, retinal arterio-venous ratio was 2:3 and no exudates. The pertinent neurological examination is shown in *Figure 1* with manual muscle test grade of 0/5 in the lower extremity from L2 downwards. Vibration, proprioception, and light touch descending from T10 dermatome were all noted to be decreased at 80% whereas pain and temperature sensation were completely absent from the same dermatomal levels. Deep tendon reflexes elicited gave a brisk normal response.

The lesion was localized in the spinal cord due to presence of weakness, demarcated sensory loss, and autonomic dysfunction in a patient presenting with intact cortical and cranial nerve functions. The patient had presence of sensory level along the umbilicus at the dermatomal level of T10, hence the lesion was further localized at the level of T7-T8. Given the temporal profile of illness, with early presentation of upper motor neuron signs, ascending sensory involvement, and delayed sphincter involvement, it was classified as an extramedullary spinal cord lesion.

Patient was then admitted and managed as a case of spinal cord compression T7-T8, probably extramedullary, probably secondary to 1) Pott's Disease 2) neoplasm; to consider multiple electrolyte imbalances secondary to gastrointestinal losses. Initial and subsequent workup are summarized in *Table I*. The hemogram was essentially normal. The serum creatinine was initially elevated but normalized after hydration. There were abnormalities in the serum electrolytes which were attributed to dehydration and acute kidney injury.

Imaging studies were also done. The thoracolumbar MRI revealed a long segment enhancing T2W hyperintense lesion at T2 to T7 levels suggestive of TM (*Figure 2*). Hence, a post-vaccination TM was considered at this time. She was started on prednisone at 0.5 mg/kg/day. On further work-up, cranial MRI revealed ovoid areas of heterogenous, predominantly T2/FLAIR hyperintense

Table I. Blood Chemistry Done During the Course of Admission

Laboratory Tests	On admission	Normal range
Complete Blood Count		
Hemoglobin	12.2 g/dL	14.0-18.0
Hematocrit	0.37%	0.40-0.54
White Blood Cells	10.4	4.0-11.0
Platelet	167	150-450
Segmenters	68%	50-70
Lymphocytes	27%	20-40
Monocytes	5%	2-5
Blood Chemistry		
Blood Urea Nitrogen	36.35	3.2-7.4 mmol/L
Creatinine	269.33	64-100 umol/L
Sodium	134	136-145 mmol/L
Potassium	5.3	3.5-5.1 mmol/L
Chloride	106	98 – 107 mmol/L
Magnesium	1.11	0.66-0.99 mmol/L
Phosphorus	2.13	0.81-1.45 mmol/L
Ionized Calcium	1.15	1.12-1.32 mmol/L

Table II. Cerebrospinal fluid tests and results

Cerebrospinal fluid analysis parameters	Result, units
Color	Straw colored/Clear
White blood cells	5.9
Red blood cells	19.9
Total cell count	25.8
Cell cytology	No malignant cells with noted hypocellular smears
Glucose	80 mg/dL
Protein	100 mg/dL
Immunoglobulin G	15.50 mg/dL
Mycobacterium Tuberculosis Polymerase Chain Reaction	Negative

signals exhibiting restricted diffusion in the periventricular white matter of the fronto-parietal lobes with no associated effacement of the involved sulci (*Figure 3*). Since there were multiple lesions and areas of inflammation in the CNS, our patient was diagnosed to have MS. To support a diagnosis of MS, a lumbar tap was done. CSF analysis revealed elevated levels of immunoglobulin G at 15.50 mg/dL which is consistent with MS (*Table II*). Oligoclonal Band testing was requested but not done due to diagnostic challenges.

On the 15th day of admission, there was no noted progression of sensorimotor deficits and the patient was discharged, on high dose oral corticosteroids. On follow-up two weeks after discharge, there was no improvement in motor strength in both lower extremities and no recovery in sensation and autonomic function. She was bedridden and sacral decubitus ulcer was seen. She returned a generally unremarkable complete blood count with no leukocytosis, and blood chemistry with creatinine levels and electrolytes within normal range.

Good compliance on her previously prescribed home medications was elicited on history from both the patient and her relative who is also her caregiver. There were no new subjective complaints as per the patient with no

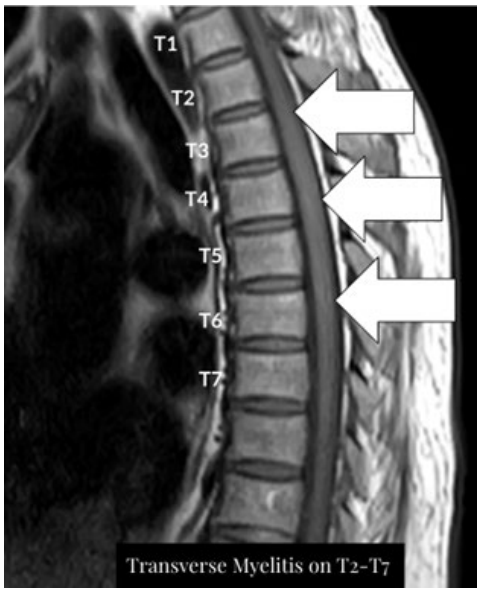

Figure 2. Thoracolumbar magnetic resonance imaging (sagittal view) showing long segment enhancing T2W hyperintense lesion spanning from T2 to T7 findings suggestive of transverse myelitis

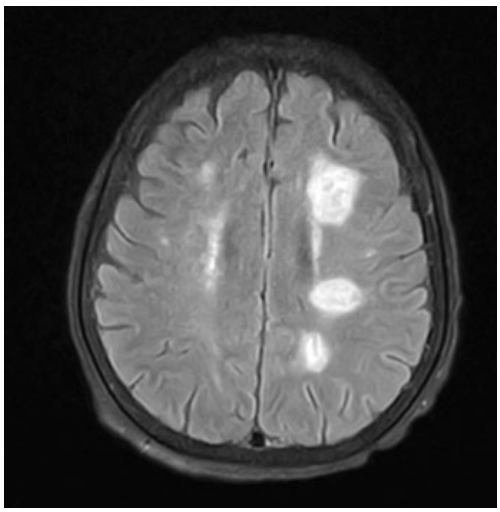

Figure 3. Cranial MRI (axial view) with IV contrast showing ovoid areas of heterogeneous T2/FLAIR hyperintense signals exhibiting restricted diffusion in the periventricular white matter of the fronto-parietal lobes

adverse reactions noted from treatment regimen. She was advised to continue oral corticosteroids for a total of at least three months, with regular follow-up and no changes to therapeutic intervention.

Discussion

Vaccination has been established to be the most effective tool, for protection from "infection, severe disease and death."[2] Since the initiation of vaccine administration for COVID-19, the most common side effects reported are

pain on injection site, fatigue, headache, muscle pain and fever.[3] Rare complications involving the CNS such as MS, neuromyelitis optica spectrum disorders and longitudinal extensive TM have been reported after administration of mRNA COVID-19 vaccine (BNT162b2).[4-9]

TM is a spinal cord disorder which may present with motor, sensory and autonomic dysfunction.[1] There were three cases of TM in clinical trials for ChAdOx1 nCoV-19 vaccine.[10] Nevertheless, the two were found to be unrelated to the vaccine and only one was considered to be possibly related to the vaccination. After the introduction of mRNA vaccine in the market, the first reported case of TM that was temporally associated with the vaccine was that from McLean and Trefts.[11]

The incidence of vaccine related acute TM is approximately 1.739 per million people.[12] Although not clearly understood, TM from COVID-19 vaccinations may be due to different mechanisms, depending on the type of vaccine. Molecular mimicry and autoimmune reactions are the possible mechanisms for the live or recombinant virus whereas for the mRNA vaccine, it is inferred that there is an interaction in spike proteins and angiotensin converting enzyme-2 (ACE-2) receptors.[13] In our patient, given the temporal relationship between the vaccination, and the onset within seven days, TM secondary to the mRNA Covid-19 vaccine was considered. In a meta-analysis by Agmon-Levin, TM may be associated with vaccine if symptoms occur a few days to three months post-vaccination.[14] In general, TM is commonly due to an autoimmune disorder but may also be due to infections or part of MS or neuromyleitis optica spectrum disorder.[15] Hence, in our case, we requested for cranial MRI to rule out affectation of the other parts of the CNS. The imaging studies showed multiple sites of CNS involvement; thus, a final diagnosis of MS was reached.

MS is the most common neurological auto-inflammatory disease, usually with a chronic setting. Manifestations of MS are generalized including numbness, weakness, loss of autonomic function, and visual disturbance. There have been quite a few reports of MS after administration of mRNA COVID-19 vaccine.[16,17] It is also highly important to note, based on these previous studies that MRI showing admixed old and new lesions points to a possibility of previous dormant disease process further exposed by CNS-demyelination post-vaccination. These instances however are generally not of new-onset MS, rather focus on recurrence of previous illness.

Only a few cases, to our knowledge, has been reported of initial presentation of MS occurring post COVID-19 vaccination. In a case report by Taglafierri et al., a 32-year-old female had progressive right-sided weakness one week post-vaccination and on further workup was diagnosed to have MS. She was managed with intravenous steroids and eventually sent home on oral prednisone.[5] Guarnaccia et al also reported a case of a 69-year-old female, known case of MS who presented with ascending numbness and paresthesia in her legs to her abdomen. She was treated with IV solumedrol and tapered with high dose oral prednisone which eventually led to some improvement in function of the right leg but the patient was still unable to stand.[18] In the case series by Toljan et al., there were a few cases of patients who were diagnosed with MS after vaccination.[19] A 29-year old female who presented with limb weakness in the week after mRNA COVID-19 vaccination was initially treated with methylprednisolone and was eventually started on ocrelizumab with improvement of neurologic symptoms. In the same series, a 43-year-old female had right arm weakness and numbness five weeks after mRNA COVID-19 vaccination. This patient was initially given prednisolone for three days which afforded some improvement and was also eventually started with rituximab-pvrr.

Generally, the cause and factors leading to MS are not definite but it is agreed upon that it is due to an array of factors including genetic predisposition, environment and medications. One of the common environmental affectations leading to the eventual development of MS are viruses. This is theorized to come from various mechanisms, that may involve "molecular mimicry, epitope spreading, and bystander activation."[20,21]

There are a few postulated mechanisms by which MS is developed post-vaccination after mRNA vaccination. Generally, molecular mimicry is one of the most common theories on the activation of autoimmune response which is brought about by cross-reactivity. This is due to similar protein structure from host and newly-introduced molecule which stimulate auto-reactive T-Cells and autoimmune B-Cell response.[22] Another mechanism involves the patient's self-reactive T-Cells attacking the CNS as discussed by Savarin and Bergmann.[23] In those receiving mRNA vaccination, there is immune-stimulation brought about by exogenous mRNA which in turn activates the dendritic cell maturation, hence leading to greater T-cell and B-cell responses which lead to demyelination.[24]

The presence of ovoid lesions in the periventricular area, as seen in our case, is a hallmark of MS.[25] Using the McDonald criteria, our patient's case falls under having one attack and two lesions. One attack pertains to the single episode of neurologic symptoms as reported by the patient as weakness and numbness in bilateral lower extremities and had two lesions occurring in different areas of the CNS. Lesions in the periventricular areas of the brain are usually asymptomatic. Hence, in our case, it is difficult to establish the chronicity of the disorder. Other differentials that would present similar clinically, such as myelopathy, acute flaccid myelitis and Guillan-Barre syndrome was ruled out given these highly suggestive radiographic findings.[26] The Lumbar tap revealing elevated levels of immunoglobulin G and negative *Mycobacterium tuberculosis* Polymerase Chain Reaction (MTB PCR), further supported this diagnosis.[27]

Signs and symptoms of demyelinating spinal cord disorders, even in the first reported case of TM after Covid-19 vaccination, is potentially reversible with early diagnosis and treatment. Unfortunately, in our case, there

was a delay in the patient's consultation and failure to recognize and report initial symptoms as manifestation of a possible major adverse reaction from the vaccine. This might have affected the outcome of our patient.

Lastly, the issue regarding second booster should be addressed in our patient. In Taiwan, heterologous vaccine regimen is being advised for those who develop major adverse effects such that the second dose should be a vaccine with different mechanism.[28] In patients with pre-existing MS, vaccination against COVID-19 did not significantly increase the risk of relapse.[29] Thus, after an informed consent, patient may still receive second vaccine booster dose of a different mechanism of action.

Conclusion

Careful follow-up is recommended to identify adverse events after the administration of mRNA vaccines for COVID-19. Few cases, only three to our knowledge, have been reported of initial presentation of MS occurring post COVID-19 vaccination. This case is the first reported case of MS post-administration of an mRNA vaccine for COVID-19 in the Philippines that we know of.

Despite the occurrence of rare complications such as this, it is still imperative to note that vaccination is a vital preventative mechanism for infectious diseases and despite the temporal profile of findings on imaging in this case, there is no definite established association between MS and COVID-19 vaccination.

Conflict of Interest. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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