DOI: 10.7860/JCDR/2022/58310.16916

Case Report

Internal Medicine Section

SARS-CoV-2 Vaccination Associated Transverse Myelitis: A Case Report

BHARGAVI KUMAR[1], SARAVANAN THANGAVELU[2], SAKTHIVEL SELVAM[3], VIKRANTH RAJA[4], ADITYA CHANDRAN[5]

ABSTRACT

While policy makers around the globe have meticulously organised mass immunisation against Coronavirus Disease 2019 (COVID-19), its safety concerns and adverse events that need prompt evaluation are also emerging. Acute Transverse Myelitis (TM) is a rare neurological phenomenon where motor, sensory or autonomic disturbance occurs as a result of spinal cord injury. The aetiology of transverse myelitis is thought to be immune-mediated as a result of infection, parainfectious disorder, autoimmune disease or malignancy. Though a rare disease, acute TM warrants prompt recognition and aggressive therapy for favourable neurological patient outcomes. Hereby, authors presented this case of a 61-year-old male patient who developed symptoms of acute TM, 20 days after receiving an adenovirus vectored ChAdOx1 nCoV-19 vaccine against SARS-CoV-2. The patient was treated with intravenous steroids, supportive care with Foley's catheterisation and his weakness and bladder control improved over 1 week.

Keywords: Adverse reactions, Coronavirus, Immunisation, Severe acute respiratory syndrome coronavirus 2

CASE REPORT

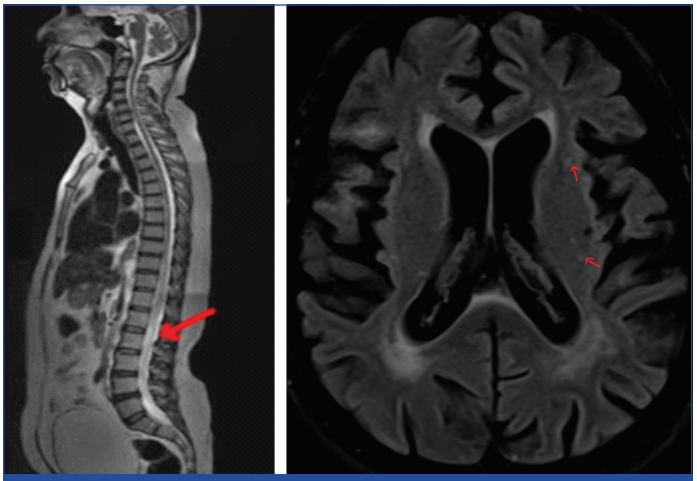
A 61-year-old male presented to the Medicine Department with complaints of constipation and urinary retention for three to four days accompanied by bilateral lower limb weakness. He had a past medical history of seizures 20 years ago and haemorrhagic cerebrovascular accident but was not on any regular medications. The patient had received the first dose of Coronavirus Disease 2019 (COVID-19) vaccine (ChAdOx1 nCoV-19) 20 days prior. His family history was unremarkable for muscular disorders, multiple sclerosis, stroke or any rheumatological disorders.

On physical examination, his heart rate was 72 beats per minute, respiratory rate of 15 breaths per minute, blood pressure was 130/80 mmHg, temperature of 98.4° Fahrenheit, and oxygen saturation of 99% on room air. He was conscious, oriented to time, place, person and did not have neck stiffness or signs of meningeal irritation.

On neurological examination, higher mental functions and cranial nerve examination was normal. He had asymmetrical paresis in lower limbs- power of 0 in the toes, 2 across the ankle joint, power 4 in the left knee, 3 in the right knee and power 3 in the hip joint. Deep tendon reflexes were absent in both the lower limbs and bilateral plantar response was mute. Sensory examination (fine touch, temperature, position sense, joint sense and vibration) was normal. Neurological examination of the upper limbs was within normal limits. Other systemic examination was unremarkable.

Initial laboratory analysis showed a normal complete metabolic profile, complete blood count, and a negative Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) nucleic acid amplification test. Echocardiography, ultrasonography abdomen was normal and Electroencephalography (EEG) showed no epileptiform discharges. Visual Evoked Potentials (VEP) for both eyes revealed bilateral optic neuritis. Antinuclear Antibody (ANA) profile was negative. The patient underwent Magnetic Resonance Imaging (MRI) of brain and spinal cord which was suggestive of acute demyelination [Table/Fig-1,2]. Lumbar puncture was performed and Cerebrospinal Fluid (CSF) analysis was done [Table/Fig-3].

Based on the investigations and clinical findings, a diagnosis of postvaccination- longitudinally extensive transverse myelitis was made. The patient was started on injection methylprednisolone at a dose of 1 g/day for 5 days. He was catheterised and given antiepileptics, laxatives, antipyretics and supportive care along with regular physiotherapy. The patient's symptoms of constipation, urinary retention, and weakness resolved over the next 1 week. The urinary catheter was removed and he was discharged home after 12 days of admission. Two weeks later, patient was followed-



[Table/Fig-1]: Magnetic Resonance Imaging (MRI) spine: Long segment T2 hyper-intense signal changes in the spinal cord and conus medullaris from the level of D9 - L1 predominantly involving the central cord with minimal cord expansion and Disc desiccation with mild disc bulge at L4-L5 level abutting the bilateral exiting nerve roots (red arrow). **[Table/Fig-2]:** MRI brain showed cerebral atrophy with chronic small vessel ischaemic changes (red arrow). (Images from left to right).

Parameters	Results
Colour	Straw yellow, clear
Volume	0.5 mL
Total count	260 cells/cumm
Differential count	Neutrophils- 24% Lymphocytes- 35% Monocytes- 41%
Background	Shows red blood cells
Adenosine Deaminase (ADA)	3.7 IU/L
Protein	433.36 mg/dL (15-60)
Glucose	64.4 mg/dL (50-80)
Mycobacterium tuberculosis complex (DNA)	Negative
Oligoclonal band	Normal pattern
Gram stain and culture	Normal and sterile

[Table/Fig-3]: Lumber puncture- Cerebrospinal Fluid (CSF) analysis.

up in the Outpatient Department (OPD) and he was able to walk without support.

DISCUSSION

The world is still combatting SARS-CoV-2. Many vaccines were given emergency approval after phase 3 trials. Intensive and mass Immunisation programs are being organised for vaccination and notable reduction in disease severity is noted. Nevertheless, adverse reactions post vaccinations were reported raising safety concerns adding to the vaccine hesitancy. According to the vaccine adverse event reporting system (VAERS), 51,755,447 doses of various COVID-19 vaccines have been administered in the United States until March 2, 2021 of which 9,442 adverse reactions were reported [1]. According to the Ministry of Health and Family Welfare, India has reported at least 70,102 cases of Adverse Events Following Immunisation (AEFI), and 1,013 deaths following the COVID-19 vaccines. Of this, Covishield contributed to 90.3% of the total adverse events and to 91% of the vaccine related mortality as of 30th January 2022 [2].

Neurological complications are already recognised rare adverse effects seen in certain vaccines namely diphtheria pertussis tetanus, measles mumps rubella, influenza and hepatitis B vaccines [3]. The vaccines against SARS-CoV-2 are either adenovirus vector based (ChAdOx1nCoV-19),m-RNA based (BNT162b2), protein based or inactivated virus based vaccines. All of these act by inciting an immune reaction against COVID-19 and include an antigen, a delivery system and an adjuvant. Vaccine associated adverse events may be attributable to any of these components. COVID-19 vaccine associated neurological complications that were reported worldwide include demyelinating disorders, cortical venous thrombosis, encephalopathy, stroke, seizures, myasthenic syndromes, Guillain-Barré syndrome and Bell's palsy [4].

Transverse Myelitis (TM) is a rare, acquired focal inflammatory disorder of one or more spinal cord sections [5]. The common etiologies are demyelinating illness such as multiple sclerosis, neuromyelitis optica, infections, autoimmune diseases ,malignancies, paraneoplastic and rarely vaccines. The commonly associated infections are cytomegalovirus, varicella-zoster virus, Epstein barr virus, and coxsackieviruses [6]. The incidence of COVID-19-related transverse myelitis has been reported as 0.5 case/per million people, roughly 1.2% of all COVID-19 related neurological complications [7]. The incidence of acute TM is estimated to be up to 3-5 cases per million people a year and vaccine-associated events are rarer [8]. Transverse myelitis could result due to acute or subacute dysfunction of the spinal cord and could be complete or partial as well. In the index patient, MRI showed long segment T2 hyperintense signal changes in the spinal cord from D9-L1 level. The incidence of acute TM varies between 1-8 million per year and peaks between 2nd-4th decades [9]. The index patient on the contrary is in the 7th decade of his life.

In a literature review of 39 articles discussing Central Nervous System (CNS) adverse effects of COVID-19 vaccines, five patients had developed transverse myelitis post vaccination [4]. However, all occurred within 4 days after vaccination contrary to the present case where the day of onset of symptoms was 20 days postvaccination.

According to the Vaccine Adverse Event Reporting System (VAERS), nine cases of acute transverse myelitis (incidence is approximately 1.739/per million people) were reported among the total 9442 adverse events following COVID-19 vaccines in the United States as of March 2021 [10]. Indeed a total of 119 postvaccination Acute Transverse Myelitis (ATM) cases were reported during the period from 1985 to 2017 [1]. Other than nine cases, neurological complications contributed to 2.69% of the total Adverse Events Following Immunization (AEFI) following Pfizer-BioNTech, Moderna, and Johnson & Johnson's [10]. So also, two serious events of transverse myelitis were noted following recombinant ChAdOx1 nCoV-19 vaccine [11,12].

Initially acute transverse myelitis was reported following viral vector vaccines and it was assumed that the viruses used for vaccination can induce autoimmunity, exhibit molecular mimicry, or have epitopes similar to the virus itself [1]. Nevertheless, in the mRNA vaccines, autoimmune interactions are probably though to occur between the Angiotensin Converting Enzyme-2 (ACE-2) receptors in the body and the virus spike protein antibody per se. Also, it was proposed that thrombogenic state induced by vaccination can cause spinal cord infarction leading to transverse myelitis [13]. Agmon-Levin N et al., proposed that post vaccination transverse myelitis may be the resultant of autoimmune reaction attributed to molecular similarity, accentuation of pre-existing autoimmune process or B lymphocytes' poly clonal activation leading to a cytokine storm [5].

A large population-based study of more than 32 million people done in the United Kingdom investigated the neurological adverse events associated with the ChAdOx1 nCoV-19 and BNT162b2 vaccines as well as SARS-CoV-2 infection [14]. It was found that increased risk of hospital admission was present for Guillain-Barré syndrome, Bell's palsy and myasthenic disorders in those who received the ChAdOx1 nCoV-19 vaccine. Increased risk of hospital admission for hemorrhagic stroke was observed in those who received the BNT162b2 vaccine. More importantly the risk of neurological outcomes following a positive SARS-CoV-2 test, such as acute CNS demyelinating events, encephalitis meningitis and myelitis, Guillain-Barré syndrome, Bell's palsy, myasthenic disorders, haemorrhagic stroke and subarachnoid haemorrhagic was documented. A crucial finding in this study was that the risk of neurological infections was far higher by the infection itself in comparison with the few events associated with the vaccine. This strongly advocates the need for vaccination rather than a vaccine reluctance.

Currently, there are no standard guidelines to treat post vaccination transverse myelitis. Conventionally transverse myelitis is managed with intravenous steroids as the first line therapy. Plasma exchange is done in steroid refractory cases [15]. Other immunomodulatory therapies include cyclophosphamide and rituximab. The index patient was treated with intravenous steroids for 5 days and showed significant improvement in his neurological symptoms.

CONCLUSION(S)

Any new disease comes with lot of challenges and new vaccines are to be closely monitored. Adverse events reporting system is not to sideline the vaccine importance or size down mass vaccination campaigns, rather only to add new data and share knowledge to raise global awareness. A causal link has not been conclusively established with the vaccine and side-effects except for the temporal association. The shared pathophysiological mechanism between the virus and vaccines may be central to the development of the adverse events. First contact physicians should be aware of acute TM after COVID-19 vaccination and maintain a high index of suspicion in patients presenting with neurological deficits after receiving the vaccine.

REFERENCES

[1] Shah S, Patel J, Alchaki AR, Eddin MF, Souayah N. Development of transverse myelitis after vaccination, A CDC/FDA vaccine adverse event reporting system (VAERS) study, 1985-2017. Neurology. 2018;90(Suppl. 15):5.099.
[2] The National AEFI Committee. Ministry of Health and Family welfare. Press release:4 February 2022. 70,102 adverse events after vaccination reported in India: Govt data - BusinessToday . https://main.mohfw.gov.in/Organisation/Departments-of-Health-and-Family-Welfare/immunization/aefi-reports.
[3] DeStefano F, Verstraeten T, Jackson LA, Okoro CA, Benson P, Black SB, et al. Vaccinations and risk of central nervous system demyelinating diseases in adults. Arch Neurol. 2003;60(4):504-09. Doi:10.1001/archneur.60.4.504.
[4] Srivastava S, Sharma K, Khalid SH, Bhansali S, Shrestha AK, Elkhooly M, et al. COVID-19 vaccination and neurological manifestations: A review of case reports and case series. Brain Sci. 2022;12(3):407. Doi.org/10.3390/brainsci12030407.

[5] Agmon-Levin N, Kivity S, Szyper-Kravitz M, Shoenfeld Y. Transverse myelitis and vaccines: A multi-analysis. Lupus. 2009;18(13):1198-204. Doi: 10.1177/0961203309345730.
[6] Khan E, Shrestha AK, Colantonio MA, Liberio RN, Sriwastava S. Acute transverse myelitis following SARS-CoV-2 vaccination: A case report and review of literature. J Neurol. 2022;269(3):1121-32. Doi: 10.1007/s00415-021-10785-2.
[7] Roman GC, Gracia F, Torres A, Palacios A, Gracia K, Harris D. Acute Transverse Myelitis (ATM): Clinical review of 43 patients with COVID-19-associated ATM and 3 post-vaccination ATM serious adverse events with the ChAdOx1 nCoV-19 vaccine (AZD1222) front. Immunol. 2021;12:653786. Doi: 10.3389/fimmu.2021.653786.
[8] Hsiao YT, Tsai MJ, Chen YH, Hsu CF. Acute transverse myelitis after COVID-19 vaccination. Medicina (Kaunas). 2021;57(10):1010. Doi: 10.3390/medicina57101010.
[9] Tahir N, Koorapati G, Prasad S, Jeelani HM, Sherchan R, Shrestha J, et al. SARS-CoV-2 vaccination-induced transverse myelitis. Cureus. 2021;13(7):e16624. Doi: 10.7759/cureus.16624. PMID: 34458035.
[10] Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates: neurological complications of COVID-19 vaccines. Ann Neurol. 2021;89(5):856-57. Doi: 10.1002/ana.26065.
[11] Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269):99-111.
[12] Knoll MD, Wonodi C. Oxford-AstraZeneca COVID-19 vaccine efficacy. Lancet. 2021;397(10269):72-74. Doi: 10.1016/S0140-6736(20)32623-4.
[13] Vojdani A, Kharrazian D. Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. Clin Immunol. 2020;217:108480.
[14] Patone M, Handunnetthi L, Saatci D, Pan J, Katikireddi SV, Razvi S, et al. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. Nat Med. 2021;27(12):2144-53. Doi: 10.1038/s41591-021-01556-7.
[15] Greenberg BM, Thomas KP, Krishnan C, Kaplin AI, Calabresi PA, Kerr DA. Idiopathic transverse myelitis: Corticosteroids, plasma exchange, or cyclophosphamide. Neurology. 2007;68(19):1614-17. Doi: 10.1212/01.wnl.0000260970.63493.c8. PMID: 17485649.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.
2. Professor and Head, Department of Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.
3. Student CRRI, Department of Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.
4. Student CRRI, Department of Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.
5. Student CRRI, Department of Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Bhargavi Kumar,
G 802,Purva Amaiti, Trichy Road, Singanallur, Cimbatore-641005,
Tamil Nadu, India.
E-mail: kmcbhargavi@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 16, 2022
- Manual Googling: Jul 16, 2022
- iThenticate Software: Aug 23, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jun 07, 2022**
Date of Peer Review: **Jul 07, 2022**
Date of Acceptance: **Jul 23, 2022**
Date of Publishing: **Sep 01, 2022**