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Tumefactive Demyelinating Brain Lesion Developing after Administration of Adenovector-Based COVID-19 Vaccine: A Case Report

Ravindra K Garg, Hardeep S Malhotra, Neeraj Kumar, Shweta Pandey, Manish R Patil, Ravi Uniyal, Imran Rizvi

Abstract:

Background: Postmarketing surveillance of COVID-19 vaccination reveals that the COVID-19 vaccine administration is associated with several rare but serious neurological complications.

Case Report: We report a case of new-onset tumefactive demyelinating brain lesion that developed after administration of an adenovector-based COVID-19 vaccine. A middle-aged female presented with recent right hemiparesis, which was noticed 2 days after she received the first dose of the vaccine. Magnetic resonance imaging (MRI) revealed a large subcortical T2/FLAIR hyperintensities involving corpus callosum as well. The patient responded to oral methylprednisolone. At 4 weeks, a follow-up MRI revealed a reduction in size of the lesion.

Conclusion: To conclude, adenovector-based COVID-19 vaccination may be associated with a tumefactive demyelinating lesion.

Key Words:

Acute disseminated encephalomyelitis, brain tumor, corticosteroids, multiple sclerosis

Key Messages:

We report a case of tumefactive demyelinating brain lesion after adenovector-based coronavirus vaccination. In postvaccinal hemiparesis, besides cerebral venous thrombosis, a possibility of demyelinating brain lesion should be considered.

The latest global data, as per World Health Organization, indicated that till 27 August 2021, there have been 214,468,601 confirmed COVID-19 cases along with 4,470,969 deaths.[1] Early this year many COVID-19 vaccines were given emergency use approval in different countries. As of 18 October, 2021, a total of 6,495,672,032 COVID-19 vaccine doses have been administered.[1]

There are four main types of COVID-19 vaccine that are currently being administered: Messenger RNA (mRNA) vaccine (the Moderna and Pfizer/BioNTech), viral Vector vaccines (Oxford/AstraZeneca), inactivated virus vaccines (Covaxin Bharat Biotech, Sinopharm and Sinovac), and the protein subunit (Novamax) vaccine.

Postmarketing surveillance of COVID-19 vaccines reveals that these vaccines are associated with several rare but serious neurological complications. For example, vaccine-induced thrombotic thrombocytopenia (VITT) is characterized by venous or arterial thrombosis and thrombocytopenia generally following adenovirus vector-based vaccine administration. Antibodies against platelet factor 4 are generated leading to a prothrombotic state. In addition, many cases of postvaccinal encephalitis, acute disseminated encephalomyelitis, acute transverse myelitis, Bell's palsy, and Guillain–Barré syndrome, following the administration of various types of COVID-19 vaccine, have been reported. All these neurological complications generally represent the postvaccinal autoimmune phenomenon.[2-4]

Department of Neurology, King George Medical University, Lucknow, Uttar Pradesh, India

Address for correspondence:
Dr. Ravindra K Garg, Department of Neurology, King George Medical University, Lucknow, Uttar Pradesh - 226 003, India. E-mail: garg50@yahoo.com

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We report a patient who developed a demyelinating brain lesion after administration of an adenovector-based COVID-19 vaccine.

Case Report

A 56-year-old housewife presented to Neurology patient-care services with weakness of the right upper and lower limbs 2 days after she received the first dose of adenovector-based ChAdOx1 nCoV-19 (COVISHIELD™) vaccine. Weakness progressed for the next 3 days and the patient needed support for her activities of daily living. She was hypertensive and did not have any history of COVID-19. Neurological examination revealed normal mental status and cranial nerves. The patient had right hemiparesis of grade 4/5 by Medical Research Council (MRC), both in right lower and upper limbs; the left side was normal. Deep tendon reflexes were brisk on the right side, while the right plantar response was extensor. The modified Rankin Scale was three. There was no sensory abnormality.

Hematological laboratory investigations revealed a hemoglobin level 12.4 g/dL, total leukocyte count 21,400 per mm^3 (polymorphs 86%; lymphocyte 12%; eosinophils and monocytes 1% each), platelet count 3,13,000/mm^3, blood urea 28 mg/dL, blood sugar (fasting 117 mg/dL, postprandial 178 mg/dL), glycosylated hemoglobin 5.4%, and vitamin B12 level 717 pg/ml. Thyroid profile was normal (T3 1.4 ng/ml, T4 12.0 ug/dl, and thyroid-stimulating hormone 1.7 ulU/ml). C-reactive protein level was 3.0 mg/L. Testing for connective tissue disorders and vasculitis did not reveal any abnormality. Prothrombin time was 14 s, the International Normalized Ratio (INR) was 1, and activated partial thromboplastin time was 27 s. Visual evoked responses and the brainstem auditory evoked responses were normal. Magnetic resonance imaging (MRI) revealed T2/fluid-attenuated inversion recovery (FLAIR) hyperintensities involving the white matter of the left parietal lobe and extending into the body of the corpus callosum. There was no suggestion of blooming on gradient recall echo sequence; lesional gadolinium-contrast enhancement or leptomeningeal uptake was not seen. Optic nerves were not involved [Figure 1].

The patient was treated with oral methyl-prednisone (32 mg/day) for 2 weeks, followed by a weekly tapering of dose by 8 mg/week. A follow-up MRI, done after one month, showed a reduction in the size of the demyelinating lesion [Figure 2]. At 12 weeks, the patient had improved remarkably and had become independent for all her activities of daily living (modified Rankin Scale = 1). There were no suggestions of any relapse and the patient continues to be in follow-up.

Discussion

We present the first report of tumefactive demyelination in a middle-aged lady following the administration of recombinant ChAdOx1 nCoV-19 vaccine. Establishing a causal association between vaccination and an adverse effect is always challenging. Many autoimmune neurological complications like Guillain–Barre syndrome, transverse myelitis, or acute disseminated encephalomyelitis, though rare, are thought to be causally associated with coronavirus vaccination.[2-4] In our case as well, a temporal association between vaccination

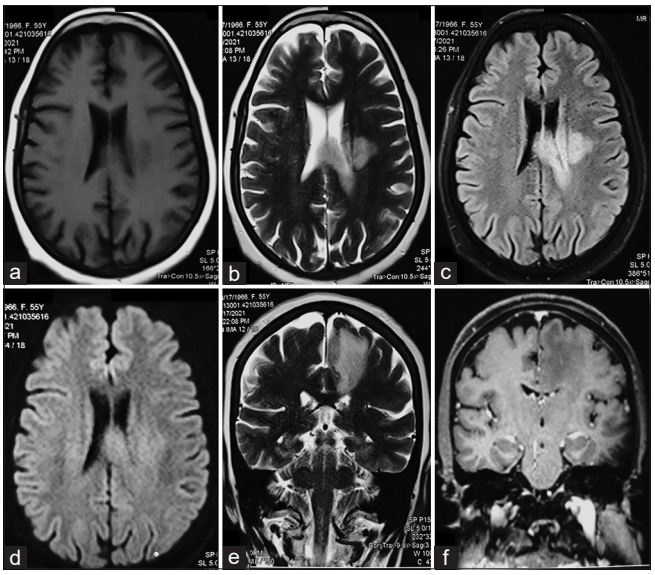

Figure 1: MRI of the brain (axial sections) depicts a periventricular hypo- to iso-intense lesion on T1W sequence (a); the white matter lesion is hyperintense on T2W (b) and FLAIR (c) sequences and shows minimal diffusion-restriction on diffusion-weighted imaging (DWI) (d) sequence. On T2W coronal section (e), the subcortical hyperintense lesion can be seen to involve the corpus callosum; no contrast enhancement is evident in T1W-gadolinium enhanced image (f)

and occurrence of tumefactive demyelinating lesion favors a probable causal link between two conditions.

Tumefactive demyelinating lesions are large lesions (greater than 2 cm) that dominantly affect subcortical areas of the brain.[5] Tumefactive demyelinating lesions are seen in many acute demyelinating disorders of the brain. Tumefactive brain lesions are generally reported in multiple sclerosis but in the Indian subcontinent, the incidence of multiple sclerosis is quite low; tumefactive lesions are seen as a manifestation of either neuromyelitis optica spectrum disorder or acute disseminated encephalomyelitis. In addition, large demyelinating lesions are reported in neuromyelitis optica spectrum disorder and acute hemorrhagic leukoencephalitis.

The exact pathophysiology of tumefactive demyelinating lesions is poorly understood. Acute disseminated encephalomyelitis is an autoimmune disorder that is often triggered by infection or vaccination. In our case, it is possible that antibodies, developed against SARS-CoV-2 spike proteins following ChAdOx1 nCoV-19 vaccination, cross-react with the structurally similar protein present in host cells by a phenomenon of molecular mimicry.

Our case illustrates another important issue of differential diagnosis. Tumefactive demyelination lesions can mimic a space-occupying lesion (brain abscess, a granuloma, or metastasis) and stroke. Our case presented with acute hemiparesis mimicking the presentation of VITT, a recently recognized complication of ChAdOx1 nCoV-19 vaccination. VITT is associated with an enhanced risk of thrombocytopenia as well as of arterial and venous thrombosis. It is notably seen in young females presenting with cerebral venous thrombosis within 2 weeks of administration of adenovirus vector-based ChAdOx1 nCoV-19 vaccine.[6] Patients may

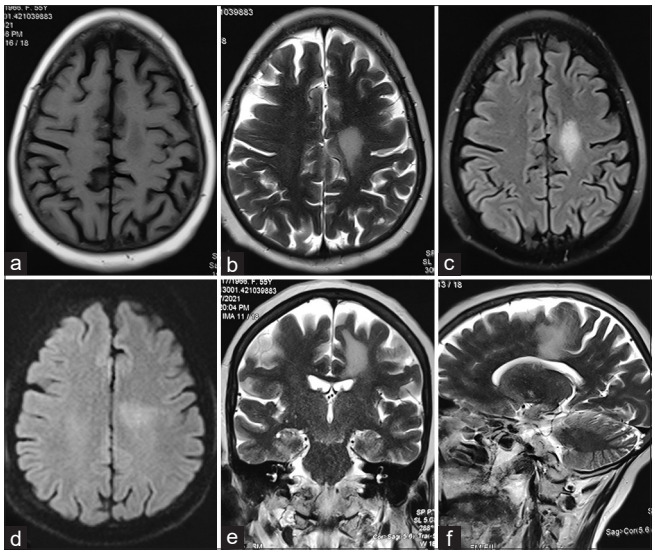

Figure 2: Follow-up MRI at 3 weeks depicts reduction in the size of periventricular hypo- to iso-intense lesion on T1W sequence (a); reduction in the size of the hyperintense lesion is also evident in T2W (b) and FLAIR (c) sequences and minimal diffusion-restriction is noted on DWI (d) sequence. On T2W coronal (e) and sagittal (f) sections, the hyperintense lesion has reduced in size

present with headaches, hemiparesis, and presence of large arterial infarcts.[7,8] Patients with VITT respond to intravenous immunoglobulin and/or corticosteroids.[6]

Sullivan and colleagues described a patient, who was diagnosed to have a tumefactive demyelination lesion because of acute disseminated encephalomyelitis following administration of a COVID-19 mRNA vaccine. The patient was treated with corticosteroids. However, the patient's clinical condition kept on deteriorating and later she was diagnosed with glioblastoma.[9] On neuroimaging, lack of mass effect and an open-ring form of contrast-enhancement are said to be suggestive tumefactive demyelination lesion.[10]

To conclude, not all patients presenting with hemiparesis represent relatively dangerous VITT; the possibility of a tumefactive demyelinating lesion, readily treatable with corticosteroids, should also be considered.

Declaration of patient consent

Written consent was obtained from the son of the patient.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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