Myelin-Oligodendrocyte Glycoprotein Antibody-Positive Longitudinally Extensive Transverse Myelitis following ChAdOx1-S/nCoV-19 Vaccine

Sir,

Longitudinally extensive transverse myelitis (LETM) is an uncommon subtype of transverse myelitis (TM) in which the pathology involves three or more contiguous or consecutive vertebral segments of the spinal cord.[1] LETM usually manifests as a part of underlying primary central nervous system demyelinating disorders, especially neuromyelitis optical and anti-MOG antibody disease.[2] The other causes are systemic autoimmune diseases such as systemic lupus erythematosus (SLE), Sarcoid, Behcet, infections, paraneoplastic, and vascular etiologies.[2] Recent reports also showed that autoantibodies against the myelin oligodendrocyte glycoprotein (MOG) can also precipitate LETM rarely.[3] LETM following vaccination is very rarely reported in the literature.[1,4] Here, we present a case of MOG-antibody-positive LETM following the first dose of ChAdOx1-S/nCoV-19 vaccination.

A 40-year-old male presented to the emergency department with history of new-onset pruritus involving the trunk and both lower limbs on the 10th day after receiving the first dose of ChAdOx1-S/nCoV-19 vaccine. He developed difficulty in passing urine and had to strain harder to void, lower abdominal fullness, and constipation after 2 days. He also developed aching pain over the upper back followed by ascending paresthesia involving both lower limbs, trunk, and upper limbs, up to the neck, within the next 1 week period. Sensory symptoms were also accompanied by weakness of both lower limbs. He had difficulty getting up from a sitting position and could not walk without support. Neurological examination showed gaze-evoked nystagmus without any other cranial nerve findings. Power in the upper limb was normal with proximal and distal weakness of both lower limbs (grade 4). All the deep tendon reflexes were brisk, and plantar was bilaterally extensor. Tone was normal. Joint position sense and vibration were impaired in both lower limbs and Romberg test was positive. Position sense and vibration were normal in both upper limbs. His magnetic resonance imaging (MRI) showed extensive demyelinating lesion spanning from brainstem to thoracic cord. Lesions extended more than three vertebral segments in both cervical and thoracic segments [Figure 1]. USG KUB (Ultrasound Kidney, Ureter, Urinary Bladder) showed significant residual urine suggestive of voiding dysfunction. His cerebrospinal fluid study showed mild lymphocytic pleocytosis with elevated protein and normal sugar. His antinuclear antibody, rheumatoid arthritis factor, Sjogren syndrome (SS)-A, SS-B, angiotensin-converting enzyme, and serum calcium were normal. Studies for HIV, Venereal disease research laboratory test (VDRL), and Viral PCR for Herpes simplex virus (HSV), human T-lymphotropic virus (HTLV), Epstein–Barr virus (EBV), Cytomegalovirus (CMV), human herpesvirus (HHV) 6, RT-PCR for COVID-19, were negative. Serum was also sent for anti-aquaporin 4 antibody and MOG IgG, which showed strong positivity for MOG antibody. He responded excellently to intravenous methylprednisolone 1 g once daily for 5 days. After 5 days of methylprednisolone treatment, he was able to walk without support, and bowel and bladder functions were normal. There was no recurrence of the symptoms while writing this report.

Here, to our knowledge, we present the first report of a patient with anti-MOG antibody-positive LETM after COVID-19 vaccination. The myelin-forming cells of the CNS (oligodendrocytes) produce several proteins including the

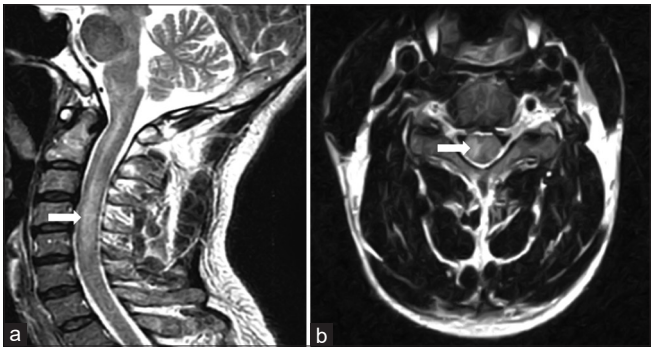

Figure 1: (a) Sagittal T2-weighted MR image of the cervical spine demonstrates cord hyperin-tensity extending from the C5-C6 level to the lower medulla associated with subtle cord ex-pansion (arrow). (b) Axial T2-weighted MR images of cervical cord show hyperintensity (arrows) affecting more than two-thirds of the cross-sectional area of the cord

myelin oligodendrocyte glycoprotein, which is an important component of the oligodendrocyte surface membranes with critical roles in the formation, maintenance, and disintegration of myelin sheaths.[5] The pathogenicity of MOG antibodies in human beings is still a matter of debate. Even though evidence indicates its role in antibody-mediated cell-induced tissue destruction, the exact mechanism is still unclear.[5] Recently, it was reported that autoantibodies against MOG are found in patients with a spectrum of inflammatory demyelinating diseases of the CNS.[3] However, the mechanisms of development and function of anti-MOG antibodies, especially in the setting of COVID-19 infection or vaccination, remain unclear. One theoretical speculation is that SARS-CoV-2 can disturb self-tolerance and trigger autoimmune responses through cross-reactivity with host cells.[6] Varied presentations of myelin oligodendrocyte glycoprotein (MOG)-associated degenerative disorders of the central nervous system had been reported in the literature, with isolated transverse myelitis as the most common initial presentation.[3] LETMS has also been reported rarely, especially in young people, where low parts of the spinal cord are inflamed, including medullary cone, with acute flaccid myelitis presentation.[3] However, to our knowledge, there is no published literature regarding MOG-associated LETMS following COVID-19 infection or COVID-19 vaccination till date.

COVID-19 infection triggers various autoimmune diseases, such as Guillain–Barré syndrome or SLE.[6] There are also reports of acute transverse myelitis (ATM) following COVID-19 infection. A recent study analyzed 43 patients with COVID-19-associated ATM from 21 countries and found that 28 cases (70%) had longitudinally extensive ATM (LEATM) involving ≥4 spinal cord segments (cervicothoracic in 18 cases and thoracolumbar-sacral in 10 patients).[7] However, not only COVID-19 infection, COVID-19 vaccination could be a possible cause of CNS demyelinating diseases. The safety and efficacy report of four randomized controlled trials conducted in Brazil, South Africa, and Great Britain for the AZD1222 COVID-19 vaccine informed the occurrence of three cases of ATM as serious adverse events.[7] A recent report by Pagenkopfa and Südmeyer also reported longitudinally extensive transverse myelitis (LETM) following COVID-19 vaccine (AZD1222, AstraZeneca) with MRI showing T2 hyperintense signal of the spinal cord with wide axial and longitudinal extent reaching from C3 to Th2 without gadolinium enhancement.[1]

The case of anti-MOG antibody-positive LETM presented here shows a close temporal association to vaccination, as symptoms occurred within 10 days after injection of the first dose of ChAdOx1-S/nCoV-19 vaccine. A very extensive diagnostic workup has been performed to rule out other differential diagnoses. One of the major limitations of our report is that we could not perform SARS-CoV-2-IgG serum antibody in our patient's blood to rule out prior asymptomatic COVID-19 infection. However, temporal association with vaccination and no past history of symptoms of COVID-19 infection indicates that a postvaccination immune-mediated inflammation is highly likely in our case.

In conclusion, to our knowledge, we have reported the first case of LETM following ChAdOx1-S/nCoV-19 vaccination in India. Moreover, there are no published reports of anti-MOG antibody-mediated demyelinating illness following ChAdOx1-S/nCoV-19 vaccine. Physicians should keep in mind this rare possibility while evaluating patients with neurological symptoms following COVID-19 vaccination. Moreover, well-structured epidemiological longitudinal studies are needed to understand the prevalence of acute TM following COVID-19 vaccination and differentiating features of classical myelin oligodendrocyte glycoprotein antibody-associated disease transverse myelitis and acute TM postvaccine.

Ethics approval and consent to participate

This case report has been described in accordance with the ethical standards laid down in the "Declaration of Helsinki 1964".

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Conflicts of interest

There are no conflicts of interest.

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