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COVID-19

Post ChAdOx1 nCoV-19 vaccination frontal lobe syndrome

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Dear Editor,

The stepping up of an effective mass vaccination programme against the novel SARS-CoV-2 virus worldwide has led to the emergence of a host of adverse events involving various systems, a majority of which are self-limiting. Central nervous system inflammation is one of the rare adverse effects of post-COVID vaccination and has been described in a few case reports. We hereby report a reversible frontal lobe syndrome in a patient following ChAdOx1 nCoV-19 vaccination.

A 45-year-old male without any prior comorbidities developed behavioural abnormalities and weakness of both the lower limbs, 3 days after receiving the first dose of ChAdOx1 nCoV-19 vaccination (COVISHIELD). The patient was apparently asymptomatic prior to the vaccination. Three days after vaccination, he developed mild fever, became confused, had short-term memory impairment, and had decreased attention span. Over the next 2 days, he became dependent on family members for walking, and developed buckling of the knees, with slippage of slippers with knowledge. Almost at the same time, family members noticed he had developed aggressive behaviour and started to use abusive language to his family members. He began to defecate and urinate at inappropriate places and was not concerned for the same. There was no past history of any fever, focal neurological deficit, seizure, head injury, drug or toxin exposure, high-risk behaviour, or any other systemic illness.

For the abovementioned complaints, he consulted a local physician and was started on antipsychotics medication without any improvement in his symptoms.

After 2 weeks of illness, he presented to the neurology ward and was found to be afebrile, with stable vitals and a Glasgow Coma Score of 14 (E4M6V4). His attention span forward was 2 and backward was 1 and patient was disoriented to time, place, and person. His power in both the upper limbs was at least MRC grade 3/5 in both the lower limbs and normal in both the upper limbs, deep tendon reflexes were normal in both the upper limbs, and were brisk in both lower limbs. The plantar response was bilaterally extensor. All the frontal release signs were present. His routine haematological and biochemical parameters were normal. Thyroid profile, HIV, vasculitis workup, anti-TPO, autoimmune and paraneoplastic panel workup, and USG abdomen and X-ray chest were normal. (A CT chest abdomen and pelvis was planned but could not be done due to financial constraints.) Cerebrospinal fluid analysis was unremarkable including a panel for common regional aetiologies of viral encephalitis. An initial magnetic resonance imaging (MRI) of the brain had revealed diffusion restriction and patchy and flair hyperintensity in b/l frontal subcortical and deep white matter without any contrast uptake (Fig. 1).

The patient was managed with intravenous pulse methylprednisolone (1 gm) for 5 days, after which he had a dramatic improvement. His aggressive behaviour became normal, started to tell regarding urination and defecation, started to walk by taking support of one stick, and had significant improvement in his attention. He was discharged on oral steroids. Repeat MRI done 4 weeks later showed a significant decrease in lesion load (Fig. 2).

Thus, our patient presented with a frontal lobe syndrome, with features of acute central nervous system inflammation on MRI consistent with ADEM (acute disseminated encephalomyelitis), 3 days after vaccination. This may be explained possibly by either direct local effect of S protein or noxious effect of anti-S protein

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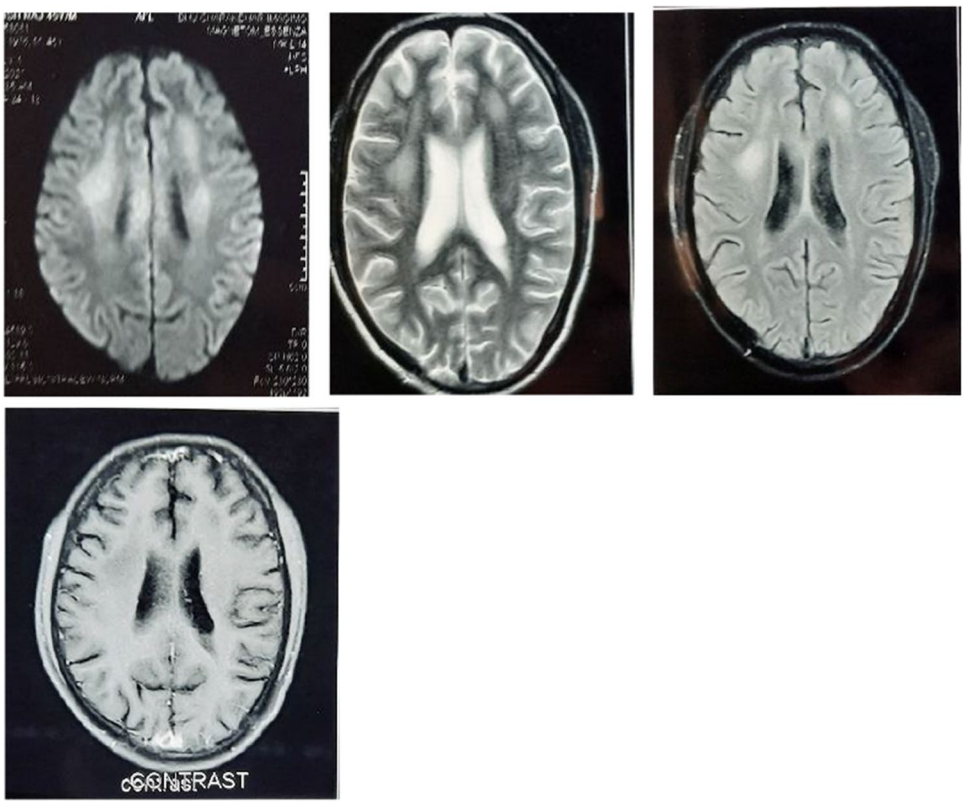

Fig. 1 MRI of the patient prior to treatment

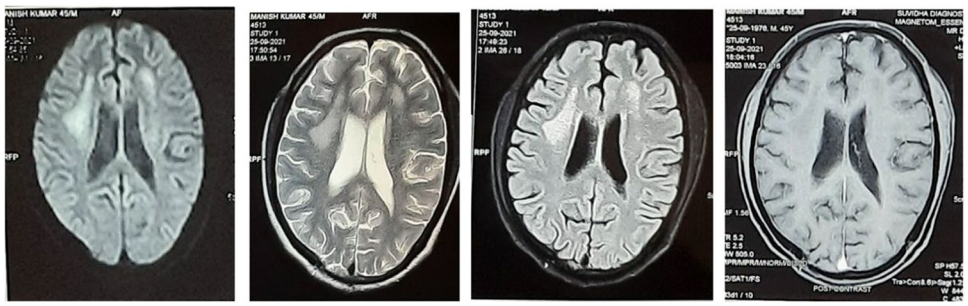

Fig. 2 MRI of the patient after treatment with steroids

antibodies. At the injection site, adenovirus vector or lipid nanoparticle (LNP) encapsulated mRNA which encodes the full-length S protein could assess different types of host cells, leading to the expression of the S protein which could be either transferred to the cell surface or secreted outside [1–3]. When this S protein is presented by the antigen-presenting cells (APCs) to immune cells at the draining lymph nodes, a strong adaptive immune response by different types of activated B and T lymphocytes is elicited. The second possibility is of host autoimmune response producing anti-S protein that cross-reacts with neural tissue antigen of the host in response to the unfamiliar antigen. A similar mechanism mediated by cross-reactive antibodies would have possibly caused the CNS inflammation in our case as has been reported in other post-COVID vaccination complications like immune thrombotic thrombocytopenia, Guillain-Barré syndrome, and stroke events, and exacerbations of demyelinating diseases [4–6].

A recent in vitro study recognizes multiple host antigens from various tissues including the brain that could cross-react to diverse extent with antibodies specific to SARS-CoV-2 proteins including the Spike [7]. ADEM-like manifestations can follow COVID-19 vaccination due to T cell–mediated autoimmune response, a humoral response, and nonspecific response to myelin basic protein among [8].

Further following COVID-19 vaccination, auto-antibodies against platelet factor 4 have been linked to cerebral venous thrombosis and thrombocytopenia [9].

There have been five published cases of ADEM, 2 or more weeks following COVID-19 vaccination, with favourable response to steroids [10–14]. However, to the best of

our knowledge, a presentation with a frontal lobe syndrome has not been described previously. Also, the onset of symptoms was only after 3 days in our patient, while it was 2 or more weeks in various cases described earlier. In another case series of 7 patients, vaccination triggered an acute CNS inflammation [15]. In that series, 4 patients had an exacerbation of multiple sclerosis, 2 developed new-onset MS, and 1 developed NMOSD. Possibly in a subset of patients, the vaccine induces an overactive immune response with the resultant CNS inflammation. However, larger prospective studies are needed to establish this relationship. Notwithstanding the rare risk of CNS inflammation following COVID-19 vaccination, the benefits of vaccination are clearly overwhelming. Nevertheless, the adverse effects must be identified at the earliest with prompt institution of treatment. Clinicians must be aware of these self-limiting effects.

Declarations

Ethics approval Individual case reports do not require approval as per local policies. No human experimentation performed. Written informed consent to publish was taken from the legal guardian of the patient.

Conflict of interest No conflict of interest declared.

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