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Combined peripheral and central nervous system demyelination post-COVID-19 vaccination: A case report.

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ABSTRACT

Background: During the era of the Coronavirus disease 2019 (COVID-19) pandemic, various neurological syndromes were reported during or after the infection. Fortunately, efforts were made to successfully develop various vaccines with high efficacy and safety. Despite the promising results of those vaccines, they are too novel to be fully understood. Here we are shedding light on a neurological case presentation that may be attributed to one of the COVID-19 vaccines.

Case presentation: A 23-year-old male patient with no prior comorbidities presented with quadriparesis and numbness that were clinically and electrophysiologically consistent with Guillain-Barré Syndrome (GBS). The condition started 10 days after the first dose of the AstraZeneca vaccine. Moreover, MRI of the brain and spinal cord has shown evidence of non-specific central demyelination. Despite the radiological finding, the patient is not fulfilling the diagnosis of a known demyelination disorder and the lesions regressed on follow-up. Since no better explanation or trigger could be found, a post-vaccination immune-mediated reaction was considered.

Conclusion: We still cannot assume the certainty of the causality association between the vaccine and the neurological presentation. Meanwhile, we suggest vigilance for cases of GBS or myelitis following vaccination for Covid-19 and that post-vaccination surveillance programs ensure a statistically significant tool to prove or disprove the causality.

1. Introduction

Demyelination in the peripheral or central nervous system is an immune-mediated phenomenon that has been observed after both infection and vaccination (Stohlman and Hinton, 2001). Guillain-Barre Syndrome (GBS) is the prototype and the most common form of post-infectious immune-mediated peripheral demyelinating neuropathy. In two-thirds of GBS patients, preceding infectious symptoms are present, while the remainder has no overt trigger for their illness. Recently, it has been also reported after coronavirus disease 2019 (COVID-19) infection (Abdullahi et al., 2021).

Here we report a case that developed both central and peripheral demyelination after Astra-Zeneca vaccination as proven through both nerve conduction studies, neuroimaging, and cerebrospinal fluid (CSF) examination.

2. Case report

A 23-year-old male patient with no prior comorbidities was admitted to Alexandria university neurology department on 28th May 2021 with a history of subacute onset of ascending motor weakness progressing over three weeks prior to his admission associated with numbness in hands, lower limbs, and the trunk. The onset of his symptoms was on 7th May 2021. The patient received the first dose of AstraZeneca vaccine on 28th April 2021 i.e. 10 days before the date of the onset.

On examination, the patient was fully conscious, readily responsive, and cooperative. His general observations and cranial nerves examination were unremarkable. His motor examination revealed hypotonia and areflexia all over, unelicited planter reflexes and weakness in lower limbs (2/5) more than the upper limbs (3\5) symmetrically distributed on both sides. Sensory examination yielded no specific superficial sen-

Abbreviations: CD, cluster of differentiation; ChAdOx1, a chimpanzee (Ch) adenovirus-vectored vaccine (Ad), which was developed by the University of Oxford (Ox); CRP, C-reactive protein; CSF, cerebrospinal fluid; CT, computerized tomography; CV, cervical vertebra; COVID-19, coronavirus disease 2019; FLAIR, Fluid-attenuated inversion recovery; GBS, Guillain-Barré Syndrome; IgG, immunoglobulin G; INF-γ, interferon-γ; PCR, polymerase chain reaction; NCS, nerve conduction study; MRI, magnetic resonance imaging; MS, multiple sclerosis; NMO, neuromyelitis optica; OCB, oligoclonal bands; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SWI, susceptibility-weighted imaging; T2, T2 weighted; TNF- α, tumour necrosis factor-α; WBC, white blood cell.

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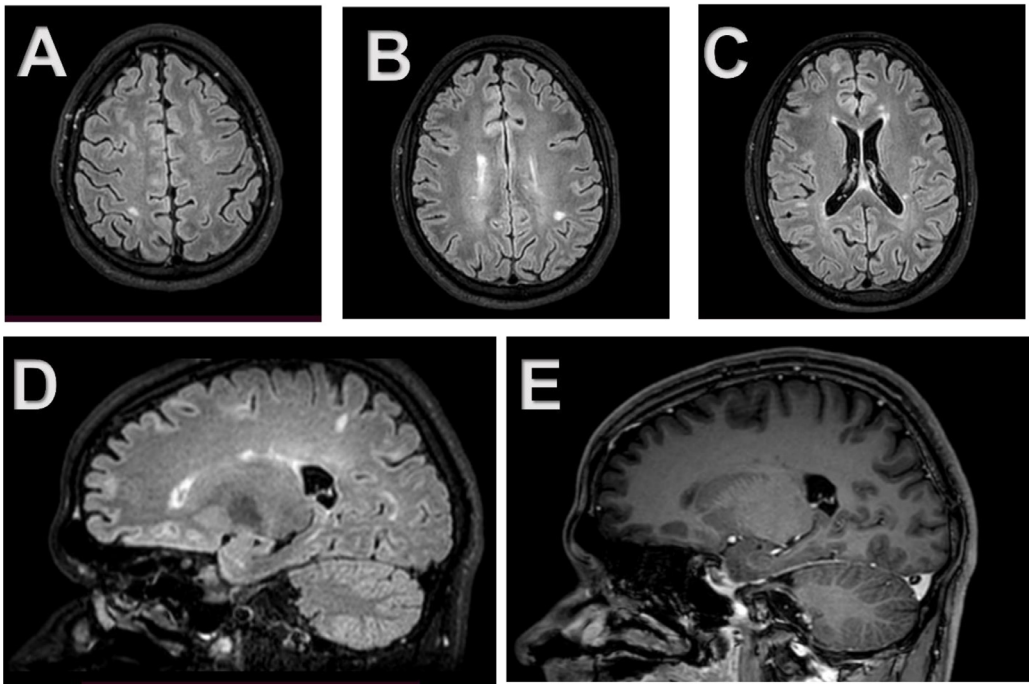

Fig. 1. A,B and C are axial FLAIR MRI brain cuts showing the location of different subcortical and periventricular hyper-intense patches. D is a sagittal FLAIR cut through some of the patches, and E is post-contrast sagittal cut showing no enhancement of the lesions.

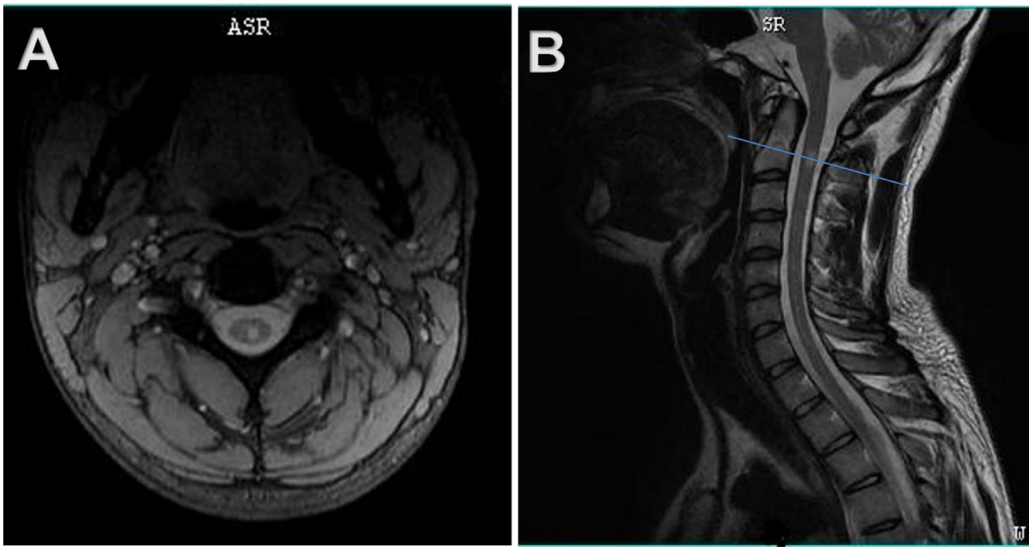

Fig. 2. Cervical spine MRI. A axial T2 cut and B sagittal T2 cut through a short hyperintense patch at CV2 level.

sory pattern, yet the deep sensation was impaired bilaterally to the clavicle.

NCS has shown sensorimotor mixed demyelinating neuropathy suggesting GBS, bilateral sural and superficial sensory nerves showed no response. Peroneal nerves showed delayed distal latency, temporal dispersion, decreased conduction velocity and delayed F wave. Tibial nerves showed delayed distal latencies, conduction block and prolonged F wave. Additionally, magnetic resonance imaging (MRI) brain showed multiple T2 and FLAIR hyperintense foci involving the subcortical white matter, none of them showing SWI blooming or diffusion restriction and no post-contrast enhancement could be noted.Fig. 1 This was associated with T2 and FLAIR hyperintense central short patch within the cervical cord opposite to CV2 level with no post-contrast enhancement. Fig. 2 CSF examination came up with clear protein-cell dissociation (WBC was 6 Cells/μL 4 lymphocytes and 2 polymorphnuclear cells, while protein was 395 mg/dL) and a negative infection screen. Isoelectric focusing immunoassay of the CSF revealed no oligoclonal immunoglobulin bands (OCB). Recent infection with COVID-19 was excluded through negative nasal and pharyngeal polymerase chain reaction (PCR) swab, clear CT Chest on admission, and negative CRP and D-dimer in serum.

Before admission he was on prednisolone 40 mg/day for one week during which he was still worsening clinically. We started plasma exchange sessions on alternate days on 30th May, he started to show improvement after the 3rd session. After the 9th session, he regained his full power in the upper limb and his power in the lower limbs improved to 4/5. He was discharged on physiotherapy for the residual weakness. On follow-up assessment after 3 months, his motor power was 5/5 allover, deep tendon reflexes were elicited on both upper limbs

and lower limbs. MRI brain and cervical cord showed complete regression of the previously noted demyelinating patches.

Discussion

To the best of our knowledge, this the first case to be reported having both peripheral and central nervous system demyelination that may be an immune-mediated reaction to the AstraZeneca vaccine. While the diagnosis of the reported case was somehow challenging, the neurological examination was consistent with lower motor pathology which was confirmed by the electrophysiologic studies and CSF albuminocytologic dissociation. There was an interval of 10 days between the date of vaccination and the onset of his symptoms, this would coincide with the time of the anticipated maximal immune response to the vaccine. The patient had also impaired deep sensation up to the clavicles which is not a usual finding in a pure peripheral neuropathy case and so central imaging was requested. Surprisingly, MRI brain and cervical cord were not normal or showing the classical finding of root enhancement as expected in a scenario of a GBS case (Gorson et al., 1996). MRI cervical cord showed a short demyelination patch and MRI brain showed multiple subcortical and periventricular patches. This signifies that the demyelination was not exclusive to the peripheral nerves. Differential diagnoses of a focal cord lesion entail a long list of diseases as multiple sclerosis (MS), neuromyelitis optica (NMO), vasculitis, infections, and sarcoidosis. The diagnostic constellation of peripheral demyelinating neuropathy, CSF findings of albuminocytologic dissociation, absence of OCB, negative infectious screen, and regressive monophasic course of the illness make the abovementioned diagnoses less likely albeit extended follow-up would be more confirmimg.

The association between neurological disorders and COVID-19 infection is well-described, ranging from cerebrovascular thrombosis, peripheral neuropathies as GBS, post-infectious encephalopathies, transverse myelitis, and acute disseminated encephalomyelitis (Varatharaj et al., 2020). In terms of post-infection or post-vaccination syndromes, we tend to discuss both temporal and causal correlations. For the former, GBS associated with COVID-19 typically has a median onset of eleven days following the initial manifestations of infection (Rahimi, 2020). Despite the reported temporal relation between different variants of GBS and COVID-19, causality is still debated. That is because there is no evidence that the overall incidence of GBS has increased during the COVID-19 pandemic despite the reported cases of GBS after COVID-19 infection (Rahimi, 2020).

ChAdOx1 vaccine (AstraZeneca) is composed of a single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector that codes for the S glycoprotein of SARS-CoV-2 (ChAdOx1-S recombinant). Replication-deficient adenoviruses are attractive for use in the development of new vaccines for their favourable safety profiles and high immunogenicity in both healthy and immunocompromised individuals (Coughlan et al., 2018; Gilbert and Warimwe, 2017; Ndiaye et al., 2015). These vectors are knowingly potent inducers of both antibodies as well as cytotoxic T cells targeted for infection control (Sridhar et al., 2013). In a study of the immunological profile of the ChAdOx1 vaccine in a phase 1/2 clinical trial, it was described that the vaccine induces both neutralizing antibodies and antigen-specific T cells against the SARS-CoV-2 spike protein (Ewer et al., 2021). Moreover, the study demonstrated that the pattern of immune response was Th1-biased, which is characterized by interferon-γ (INF-γ) and tumour necrosis factor-α (TNF- α) cytokine secretion by CD4+ T cells, and immunoglobulins production mainly of IgG1 and IgG3 subclasses. CD8+ T cells of monofunctional, polyfunctional and cytotoxic phenotypes were also induced (Ewer et al., 2021).

Similar neurological syndromes were reported before with the Covid-19 infection itself suggesting a similar immunologic response to both the virus and the vaccine. This can be attributed to the production of host antibodies that cross-react with myelin proteins. These antibodies may be generated in direct response to the Covid-19 spike protein (Gigli et al., 2020). Knowing that the ChAdOx1 is a viral vector based vaccine, a hypothesis that the immunologic reaction is directed toward the adenovirus vector, not to the viral material itself was postulated (Velikova and Georgiev, 2021). As with other immune-mediated pathologies, host vulnerability plays an important role specifically the human leucocyte antigen haplotype profile (HLA) (Gigli et al., 2020).

Conclusion

We still cannot assume the certainty of the causality association between the vaccine and the neurological presentation. Meanwhile, we suggest vigilance for cases of GBS or myelitis following vaccination for Covid-19 and that post-vaccination surveillance programs ensure a statistically significant tool to prove or disprove the causality.

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Declaration of Competing Interest

All authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Supplementary materials

Supplementary data associated with this article can be found, in the online version, at 10.1016/j.nerep.2022.100057.

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