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CASE REPORT Open Access

Acute disseminated encephalomyelitis with optic neuritis and mononeuritis multiplex following COVID-19 vaccination: case report

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Abstract

Background Acute disseminated encephalomyelitis (ADEM) is an extremely rare complication of COVID-19 vaccination with very few reports worldwide. Concomitant peripheral nervous tissue involvement in ADEM is very uncommon.

Case presentation We report the case of a 52 year aged lady who developed headache and focal neurological deficits after 10 days of COVID-19 vaccination. Her evaluation suggested ADEM with optic neuritis and mononeuritis multiplex. She responded to pulse methylprednisolone therapy.

Conclusions COVID-19 vaccine may be associated with ADEM, optic neuritis and concurrent peripheral nervous system inflammation in rare instances.

Keywords Acute disseminated encephalomyelitis, Optic neuritis, COVID-19 vaccine, Mononeuritis multiplex

Background

Global mass vaccination campaigns have been the key strategy for effective containment of COVID-19 pandemic. The COVID-19 pandemic has been associated with numerous reports of parainfectious and postinfectious neurological complications, such as encephalitis, ADEM, Guillain Barre syndrome, transverse myelitis, peripheral neuritis etc., while COVID-19 vaccination-related adverse effects are less commonly described [1–3]. Acute disseminated encephalomyelitis (ADEM) is an extremely rare complication of COVID-19 vaccination with few reports world wide. The link between ADEM and COVID-19 is well-established but only eight cases of suspected ADEM have been reported in association with COVID-19 vaccination [4–11].

The first case of ADEM was reported in China who developed neurological symptoms 2 weeks after the first dose of Sinovac and responded to intravenous immunoglobulin therapy [4]. Vogrig et al. reported a case of a 56-year-old female who developed progressive neurological deficits 2 weeks after vaccination with the "Pfizer" COVID-19 vaccine and was diagnosed as probable ADEM [5]. Shimizu et al. reported an 88-year-old lady who developed ADEM after Pfizer COVID vaccine [6]. Bastide et al. reported atypical ADEM with a protracted course of illness following the ChAdOx1 nCoV-19 vaccine [8]. Al-Quliti et al. described ADEM in a 56 year aged female after her first COVID-19 vaccination (AstraZeneca) [9]. Gustavsen et al. reported a 31-year-old female with progressive right-sided weakness and numbness 4 weeks after she received the single dose COVID-19 vaccine Ad26.COV2.S from Johnson and Johnson [10]. Kenangil et al. described a patient with acute disseminated encephalomyelitis-like presentation after an inactivated coronavirus vaccine [11]. Permezel

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et al. described the clinical context and autopsy findings in the first reported fatal case of ADEM in the setting of recent Astra Zeneca COVID-19 vaccination [12]. Nagaratnam et al. described the case of a 36-year-old female presenting with bilateral optic neuritis following her first dose of the ChAdOx1 vaccine with radiological evidence of ADEM [13].

Concomitant central and peripheral nervous system involvement in our patient in the form of ADEM, optic neuritis and mononeuritis multiplex, as a post COVID-19 vaccine neurological complication is an exceedingly rare event and probably not yet reported.

Case presentation

We report the case of a 52 year aged lady, who was a known case of rheumatoid arthritis on treatment with leflunomide, presenting with severe holocranial throbbing headache and vomiting for 3 days associated with blurred vision, diplopia and unsteadiness of gait. There was no fever. Ten days back she had taken the first dose of COVID-19 vaccine (ChAdOx1 nCoV-19 vaccine (AZD1222) which was accompanied by myalgia and flu-like symptoms for 1 day. She had survived COVID-19 infection 3 months back without any neurological symptoms. Physical examination showed a conscious, drowsy and confused patient with preserved vital signs. There was left eye ptosis with esotropia and mild restriction of abduction bilaterally. The optic disc was edematous on both sides with pupils bilaterally equal in size and reacting sluggishly to light with no relative afferent pupillary defect. Visual acuity was 6/24 in right eye and 6/30 in left eye. The power was 4/5 by medical research council (MRC) grading on the right upper and lower limbs and 5/5 on the left, with extensor plantar response on

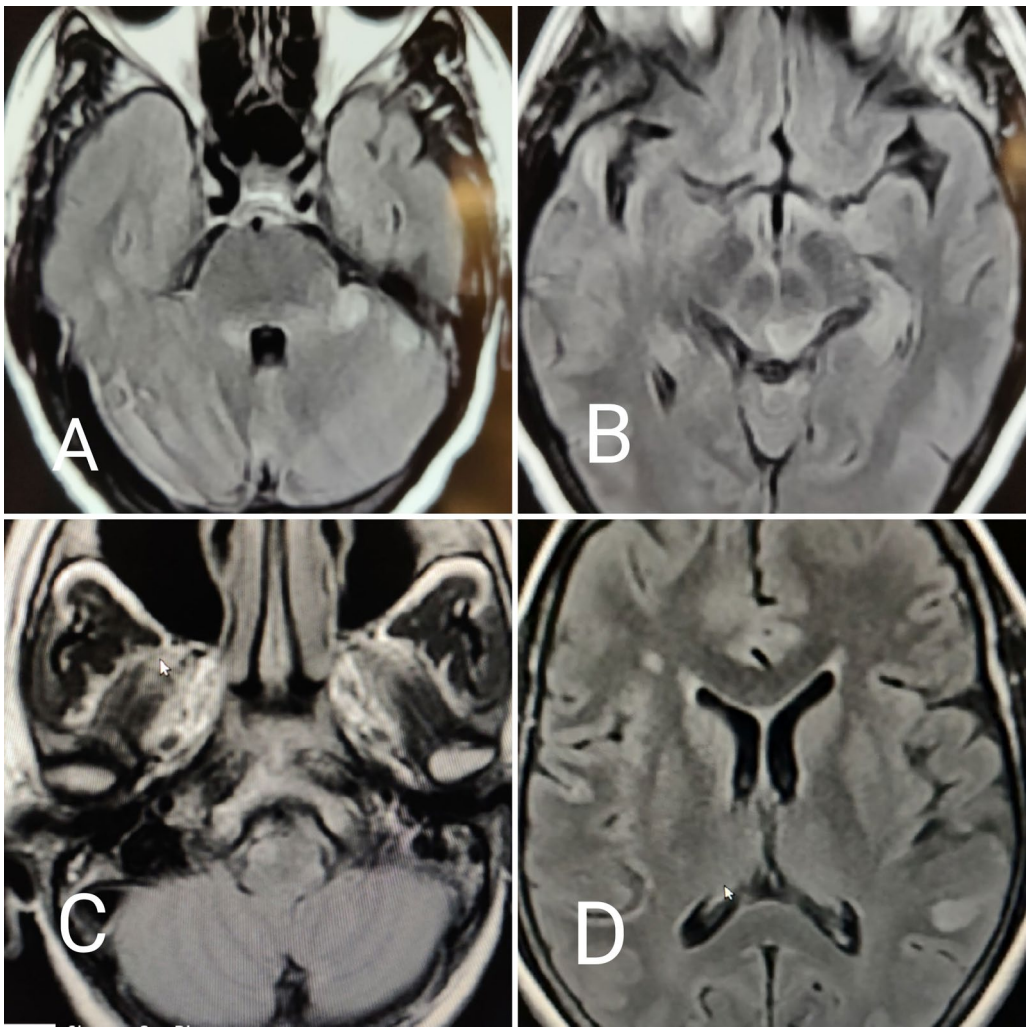

Fig. 1 MRI Brain axial FLAIR images showing hyperintensities involving **A** bilateral middle cerebellar peduncles (left>right) **B** left midbrain **C** right medulla and **D** left temporal juxtacortical white matter

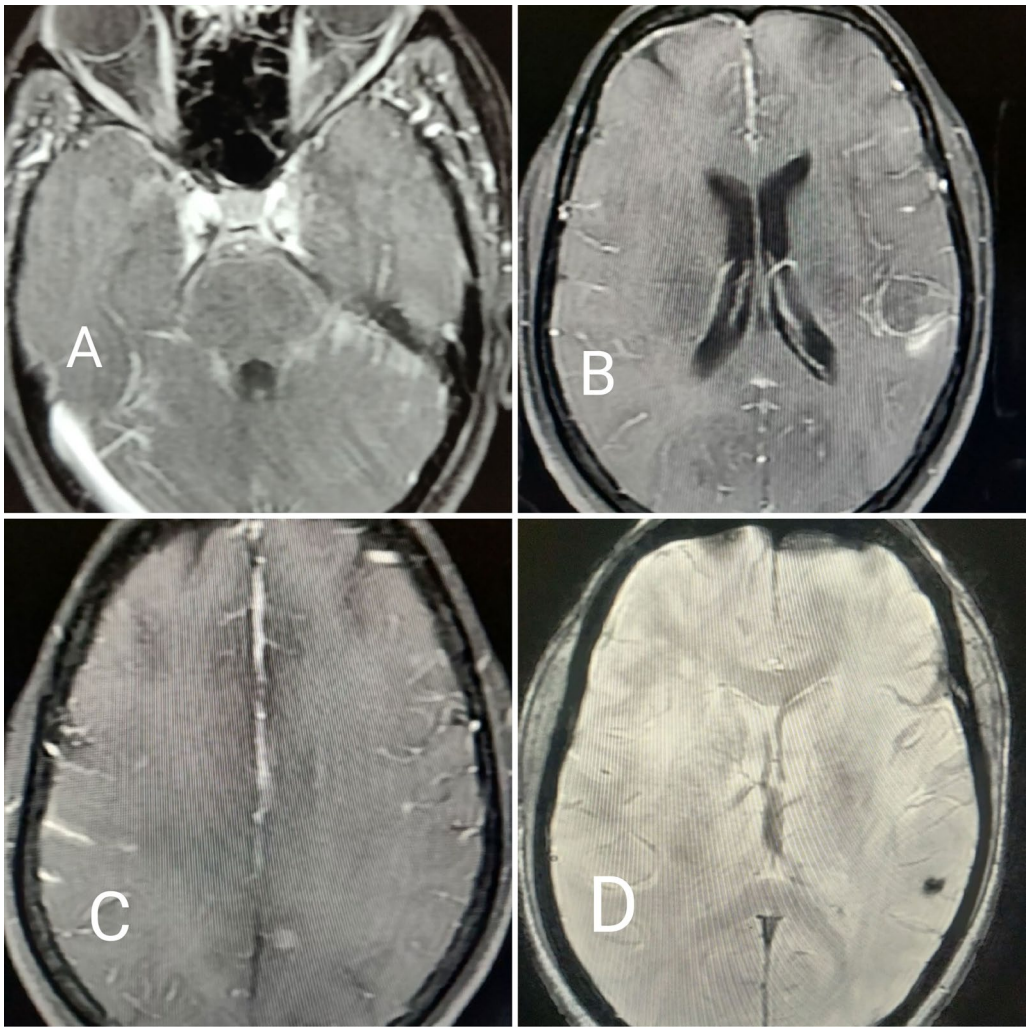

Fig. 2 MRI brain shows contrast enhancing lesions in **A** left middle cerebellar peduncle, **B** left temporal juxtacortical white matter and **C** shows leptomeningeal enhancement. **D** Susceptibility weighted imaging done after 12 wks shows microhemorrhage in the left temporal juxtacortical white matter

the right. Tandem walking revealed mild ataxia. There was no neck stiffness. The clinical localisation was left midbrain and thalamic lesion with corticospinal tract involvement causing right hemiparesis, somnolence, left ptosis and bilateral pseudoabducens palsy. Severe headache, disc edema, encephalopathy and focal neurological deficits with a recent history of vaccination suggested acute disseminated encephalomyelitis with optic neuritis and cerebral venous sinus thrombosis as the major differential diagnoses. An infective meningoencephalitic illness was less likely considering the absence of fever and neck stiffness.

Gadolinium enhanced MRI brain was performed which showed multifocal T2/FLAIR hyperintense lesions involving subcortical white matter, left thalamus, midbrain, right medulla and cerebellum with a few lesions showing contrast enhancement and a mild patchy leptomeningeal enhancement (Figs. 1, 2). MR angiogram and venogram were normal. The hematological and biochemical parameters were within normal limits. Serum RT PCR for COVID-19 was negative. A nontraumatic lumbar puncture showed cerebrospinal fluid (CSF) under high pressure with 110 leukocytes and lymphocytic pleocytosis (90%), few RBCs, elevated protein 68 mg/dL and

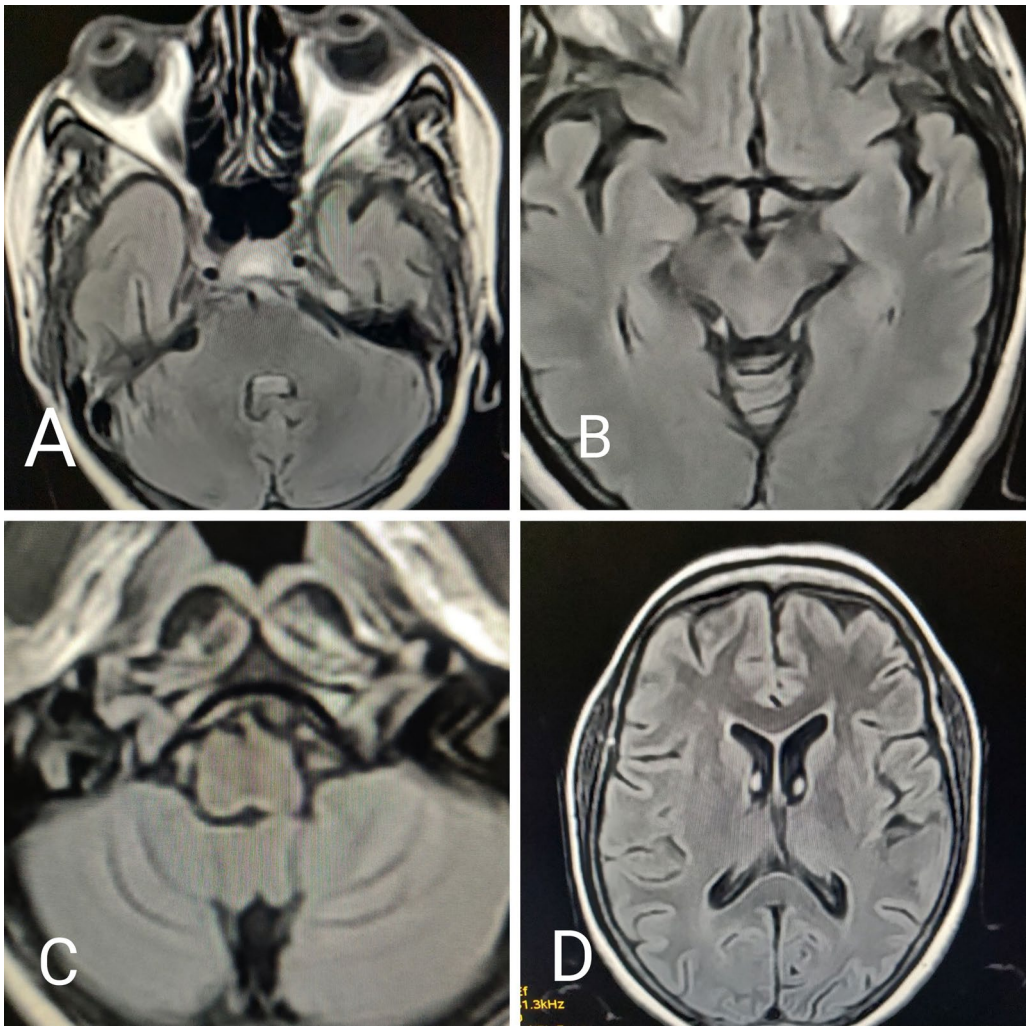

Fig. 3 MRI brain axial FLAIR images repeated after 12 weeks showing significant resolution of corresponding lesions shown in Fig. 1.

normal glucose (60 mg/dL). Gram stain, acid fast bacilli (AFB) stain and bacterial cultures were negative. CSF polymerase chain reaction (PCR) assays for Herpes simplex virus type 1, Varicella zoster virus, Cytomegalovirus, Streptococcus pneumoniae, Hemophilus influenzae, Neisseria meningitidis and Mycobacterium tuberculosis were negative. CSF oligoclonal bands were absent. The patient developed left foot drop after 3 days of admission and nerve conduction study (NCS) showed asymmetric sensorimotor axonal polyneuropathy of lower limbs suggesting mononeuritis multiplex. There was no prior history of numbness or weakness of hands and feet and the patient had not undergone NCS in the past.

The patient was started on injection methylprednisolone 1 g daily for 5 days followed by oral steroids in tapering doses over 6 weeks. She was also given Ceftriaxone and aciclovir empirically to cover the possible infectious etiologies. The patient's sensorium showed prompt improvement, while the motor deficits showed a gradual resolution over 12 weeks. Visual acuity normalised in 3 weeks. Repeat MRI brain and spine after 12 weeks showed significant resolution of lesions (Fig. 3).

Imaging was typical for ADEM showing multifocal contrast enhancing lesions except for leptomeningeal enhancement which is less commonly described. The lesions showed no hemorrhagic changes on initial imaging but the left temporal juxtacortical lesion showed mild hemorrhagic changes on repeat imaging which can occur due to microhemorrhages in ADEM. CSF showed atypical features for ADEM like moderate degree of cellularity with few RBCs and increased protein levels which raised the suspicion of a meningoencephalitic illness but the clinical features and microbiological studies precluded this possibility. Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein-associated disease (MOGAD) can present with bilateral optic neuritis

and cerebral parenchymal lesions but the antibody assays were negative. Apart from the central nervous system, our patient had peripheral nervous system involvement as well in the form of mononeuritis multiplex which is rarely described in association with ADEM and has been reported sparingly in the past particularly after rabies vaccination [14, 15]. This indicates that the target antigenic epitopes of myelin autoantigens are shared between central and peripheral nervous tissues. Rheumatoid vasculitis can cause mononeuritis multiplex but central nervous system involvement in rheumatoid arthritis is extremely rare and is unlikely considering the temporal association with vaccination [16]. Although the patient would have developed antigen specific autoreactive T cells during the COVID-19 infection 3 months prior to vaccination, it is noteworthy that she developed ADEM only following vaccination suggesting a probable reactivation of autoimmunity [15].

Conclusions

Antigenic cross reactivity and molecular mimicry following exposure to COVID-19 antigen either due to infection or vaccination causes autoimmune illness targeting both the central and peripheral nervous tissues in extremely rare instances as illustrated in this report. Vaccines remain the cornerstone of the humanity's defense against COVID-19 pandemic. However, they may be associated with a negligible but unavoidable risk of adverse effects which warrant close monitoring and a high clinical suspicion for early recognition and effective management.

Abbreviations

ADEM	Acute disseminated encephalomyelitis
CSF	Cerebrospinal fluid
NMOSD	Neuromyelitis optica spectrum disorder
MOGAD	Myelin oligodendrocyte glycoprotein-associated disease
NCS	Nerve conduction study

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Author contributions

JM analyzed and interpreted the patient data regarding the neurological illness. SV analysed the radiological investigations and interpreted the data. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in the published article.

Declarations

Ethics approval and consent to participate

The study was undertaken in accordance with the Helsinki Declaration after approval by the Institutional Ethical Committee. Informed consent was obtained for participation in the study and publication.

Consent for publication

Informed consent was obtained from relative of the patient for publication.

Competing interests

The authors disclose no conflicts of interest in the study.

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