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CASE REPORT

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Acute cerebellitis following COVID-19 vaccination: A case report

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Key Clinical Message

A plethora of neurological symptoms have been reported as the side effects of COVID-19 vaccines. Vaccine-associated acute cerebellitis is quite rare. Here, we report a 45-year-old female with acute onset cerebellitis, beginning 10 days after administration of Sinopharm vaccine. The patient's CSF COVID-19 PCR was found to be positive, with no pulmonary symptoms.

KEYWORDS

acute cerebellitis, COVID-19, CSF, Sinopharm, vaccine

1 | INTRODUCTION

The outbreak of COVID-19 has severely affected the whole world. As vaccines are being distributed around the globe to fight this pandemic, we are also witnessing an increase in studies reporting their side effects. To date, the most common postvaccination side effects have been injection site reactions, flu-like complaint, headache, and asthenia that were fortunately mostly mild and self-limiting.[1] Furthermore, neurological symptoms including headache, pain, and rarely tremor, diplopia, tinnitus, seizures, and reactivation of herpes zoster have been reported.[2] Other neurological manifestations such as stroke, Guillain–Barre syndrome (GBS), Bell's palsy, and transverse myelitis (TM) have also been observed.[3–5]

Acute cerebellitis (AC) is a very uncommon condition, and rarer is the vaccine-associated AC. However, some studies have reported its occurrence following administration of the influenza vaccine. As the number of reports on the side effects of COVID-19 vaccines increases, we will be able to better prevent and cure such dreaded outcomes. Here, we report a case of acute cerebellitis after COVID-19 vaccine administration.

2 | CASE

A 45-year-old female with no past medical history presented to the emergency department with onset of progressive nausea, slurred speech, and difficulty walking due to imbalance for 10 days prior to arrival. She had her first dose of Sinopharm COVID-19 vaccine 2 weeks prior to her presentation. She reported some difficulty walking at initiation, but then had difficulty speaking and showed dysmetric movements in her left limbs which prompted her to come to the emergency department. She denied headache, unilateral weakness, vision changes, cough, fever, shortness of breath, chest pain, or neck pain. She

denied any COVID-19 contacts. Her initial vital signs were normal with oxygen saturation of 99% in room air. The physical exam was significant for dysarthria, incoordination, trouble reaching for items in left hand, and imbalance. On exam, she was significantly ataxic and her symptoms were more prominent on her left side. Her examination revealed mild horizontal nystagmus to left, dysdiadochokinesia, moderate appendicular ataxia, left dysmetria with finger-nose testing, and inability to stand unassisted. The patient was alert and oriented. Her motor force was 5/5 in upper and lower extremities with no pronator drift. No meningeal signs observed on exam. The initial laboratory work including CBC, TSH, ESR, CRP, urinalysis, and urine drug screen were obtained and all were essentially normal. As acute cerebellitis could be related to various etiologies, the patient underwent different investigations. Brain MRI was taken with and without contrast from the head and neck. The MRI image showed a bilateral hyperintense lesion in both cerebellums which was more prominent in the left middle cerebellar peduncle (MCP) along with a fade enhancement in the same region and no cervical lesion (Figure 1). A lumbar puncture (LP) revealed an elevated protein level of 90 mg/dL with 10 WBCs with a lymphocyte predominance of 80%. CSF analysis revealed a positive COVID PCR and was negative for neurotropic viruses including varicella zoster virus, herpes simplex virus 1, herpes simplex virus 2, cytomegalovirus, and enteroviruses. CSF culture showed no growth. Oligoclonal band (OCB) was negative as well. Accordingly, the most probable diagnosis was viral cerebellitis secondary to COVID-19 infection. Chest CT scan and oropharyngeal COVID-19 PCR were negative. Treatment was started with Remdesivir therapy along with 5 g of methylprednisolone. The LP was repeated after the completion of treatment and, this time, CSF COVID PCR was negative with no cells and a protein level of 38 mg/dL. As symptoms did not improve significantly, she remained hospitalized for 10 days more and treatment with 7.5 liter of plasmaphereses was performed with some improvement in neurological symptoms. The

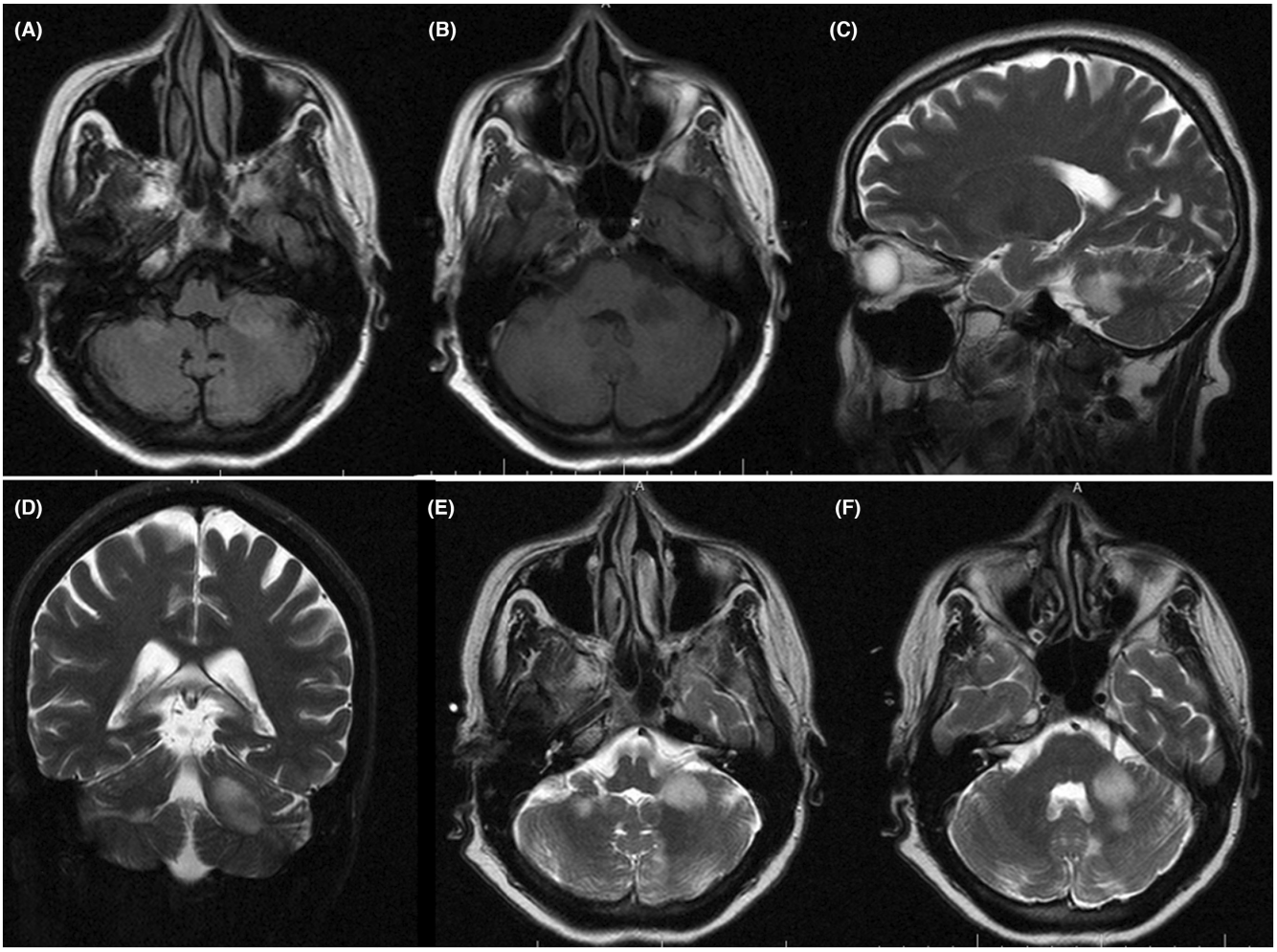

FIGURE 1 Brain MRI axial FLAIR image showing hyperintense bilateral MCP lesion (A), hypointense MCP lesion in axial T1 weighted (B), sagittal, coronal, and axial T2 weighted showing hyperintense MCP lesions (C–F).

patient was provided with a walker for her ataxia at discharge and was scheduled to receive physiotherapy at home. At the culmination of the 1-month follow-up of the patient, despite receiving physiotherapy, no improvement was observed and she was even worse. So, the patient was hospitalized again and diagnostic examination was repeated for her. Routine analysis of CSF once again showed mild lymphocytic pleocytosis with elevated protein. Full infectious, autoimmune, and paraneoplastic panel of serum and CSF have been checked and the result was negative. Serum vasculitis tests were negative. This time, HIV-Ab test was positive but other viral studies were still negative. Patient's CD4 count was under 100 at this time. Antiretroviral treatment started immediately but the patient did not respond to drug and went through a progressive course of deterioration. The patient died in a course of 1 month.

Retrospective detailed history revealed that patient's husband was an intravenous drug abuser and had multiple partners.

3 | DISCUSSION

The main clinical manifestation of COVID-19 is respiratory involvement. However, there also have been reports of neurological manifestations besides pulmonary involvement.[6] Acute cerebellitis is a rare disease, characterized by cerebellar dysfunction. Acute cerebellitis has been attributed to infectious, parainfectious, paraneoplastic, ischemic, and systemic autoimmune diseases.[7] Acute cerebellitis caused by viral agents such as varicella zoster, herpes simplex, Epstein–Barr, rotavirus, echovirus, coxsackie, mumps, measles, and rubella[8] happens most commonly in children[9] but it could be seen in adults as well.

There have been various reports on extrapulmonary involvements of COVID-19 vaccines, like stroke, GBS, Bell's palsy, and TM.[3–5] One case of acute cerebellitis after COVID-19 vaccination has been reported in a multiple sclerosis (MS) patient using ocrelizumab.[10] Moreover, there are few reports on acute cerebellitis after COVID-19 infection.[11–13] Virus can gain access to the central nervous system either through the hematogenous route or through olfactory bulbs. The possible etiopathogenic mechanisms responsible for the neurological involvement are direct neuronal injury, immune-mediated injury, and injury secondary to hypoxemia.[14]

As the Sinopharm vaccine contains inactivated virus, one possible neuroinvasive mechanism that can lead to neurologic manifestations could be a direct viral injury to the central nervous system (CNS) via blood circulation.[15] In this mechanism, multi-organ spread of the virus occurs as a result of the wide distribution of the human angiotensin-converting enzyme-2 (hACE2) receptors.[16] Another possible explanation could be a stimulation of the immune response following the administration of vaccine. When distinguishing between foreign antigens and host antigens becomes difficult for the immune system, it triggers autoimmunity which results in destruction of host cells,[17,18] an immune response similar to those observed for various infections mentioned above. One of the most common mechanisms attributed to this process is molecular mimicry between infectious antigens and self-antigens.[19] The patient showed positive PCR for COVID-19 in the CSF, making the neuroinvasive hypothesis more plausible. Nonetheless, she did not exhibit any symptoms of systemic COVID-19 involvement.

To diagnose cerebellitis, brain MRI and lumbar puncture are used which help ruling out other differential diagnoses.[9] Brain MRI in acute cerebellitis demonstrated bilateral or unilateral diffuse cerebellar hemispheric abnormalities in T2-weighted images and pial enhancement in contrast enhanced T1-weighted images.[20] The diagnosis of multiple sclerosis was unlikely due to the absence of multiple sclerosis-like lesion in brain and oligoclonal bands in CSF. The imaging studies were also negative for acute disseminated encephalomyelitis and vascular lesions. Extensive workup to exclude infectious, autoimmune and paraneoplastic causes was performed and no pathogen was identified. Vasculitis and connective tissue disease panels were also negative. However, on follow-up, patient's HIV-Ab got positive.

As most of the possible causes were eliminated, the abovementioned feature was attributed to acute cerebellitis following SARS-CoV-2 vaccination secondary to immune suppressive state. There has been just one reported case of acute cerebellitis after receiving COVID-19 vaccine, that similar to our case, was for a immunosuppress patient, using ocrelizumab for MS.[10] Her CSF examination revealed 22 leukocytes with 21 lymphocytes and protein level of 64 mg/L and normal glucose. CSF COVID-19 PCR was negative. Brain MRI showed diffuse cytotoxic edema of cerebellar cortex with restriction of diffusion sparing deep white matter and brainstem. Her CD-19/20 lymphocyte counts were zero, which could have caused some level of immune dysregulation.[10]

In analyzing our case, two factors should be considered. First, the case shows close temporal association with COVID-19 vaccination that can suggest possible causality. On the other hand, the possible association of HIV infection cannot be excluded.

There were also three reports of postvaccination cerebellitis which were secondary to influenza vaccine. The first case was a 16-year-old girl 12 days after receiving H1N1 vaccine with cortical foci of hyperintensity on

FLAIR in the cerebellar hemispheres with significant mass effect on the fourth ventricle.[21] The second one was a 66-year-old woman presented with limb and gait ataxia and a history of H1N1 vaccination 3 weeks prior to her symptoms. Her brain MRI had no abnormality but technetium-99 m hexamethyl propylene amine oxime-single photon emission computed tomography (HMPAO-SPECT) showed markedly cerebellar asymmetry, suggesting hypoperfusion in the right cerebellum.[22] The third one was a 5-year-old girl with acute cerebellar ataxia after Influenza vaccination with marked cerebellar atrophy.[7] None of these three cases had a history of immunodeficiency and none had a progressive course. However, our case like the case by Gregor Brecl Jakob et al. had a fulminant and deteriorative course which was treatment resistant.[10]

Primary cerebellar degeneration in HIV patients are mostly related to other opportunistic pathogens, such as the EBV in acute cerebellitis.[23]

These reports may not be able to identify causality as no distinction can be made between infectious and other etiology. Nonetheless, the close temporal association along with positive CSF COVID-19 PCR in our case, makes it very likely. More studies have to be done to determine the causal relationship and, as of now, vaccination seems to outweigh the risks.

As the number of vaccinated people worldwide are growing, vaccine-related disorders are coming to our notice. Certainly, accurate reporting is needed to have findings of actual relevance and capable of assessing potential risks. In this regard, we reported a case of postvaccination acute cerebellitis with positive CSF COVID-19 PCR and no pulmonary symptoms in a HIV-positive patient.

AUTHOR CONTRIBUTIONS

SeyedehNarges Tabatabaee: Resources; writing – review and editing. **Fahimeh. H. Akhoundi:** Data curation; validation. **Afsaneh Khobeydeh:** Data curation; writing – review and editing. **Seyed Mohammad Tabatabaei:** Data curation; writing – review and editing. **Bahram Haghi Ashtiani:** Conceptualization; supervision.

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COFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationship that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

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