Acute Cerebellitis Following COVID-19 Vaccination: A Case Report

SeyedehNarges Tabatabaee[1], Fahimeh Akhoundi[1], Seyed Mohammad Tabatabaei[2], and Bahram Haghi[1]

[1]Iran University of Medical Sciences
[2]University of Tehran School of Electrical & Computer Engineering

December 15, 2022

Abstract

Various neurological symptoms have been reported as the side effect of COVID-19 vaccines. Vaccine-associated acute Cerebellitis is very uncommon. Here, we report a 45-year-old female with acute onset cerebellitis, beginning 10 days after administration of Sinopharm vaccine. Her CSF COVID-19 PCR was found to be positive, with no pulmonary symptoms.

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 the studies reporting their side-effects. To date, the most common post-vaccination 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. To the best of our knowledge, there is no similar case reported before**.**

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 10days prior to arrival. She had her first dose of Sinopharm COVID-19 vaccine two 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 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, she underwent different investigations. Brain MRI was taken with and without contrast from the head and neck. The MRI image showed a bilateral hyper intense 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 negative oligoclonal band (OCB). Accordingly, the most probable diagnosis was viral cerebellitis secondary to COVID-19 infection. Chest CT-scan and oropharyngeal COVID-19 PCR were negative. Infectious disease prescribed Remdicivir therapy along with 5grams of methylprednisolone. The LP was repeated after the completion of treatment and CSF COVID PCR was negative this time with no cells and a protein level of 38mg/dl. Since symptoms didn't 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 patient was provided with a walker for her ataxia at discharge and was scheduled to receive physiotherapy at home.

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. To the best of our knowledge, COVID-19 vaccination has not yet been reported as a cause of acute cerebellitis with positive CSF COVID PCR along with no associated respiratory symptoms and negative oropharyngeal swab test for COVID-19.

There have been various reports on extrapulmonary involvements of COVID-19 vaccines, like stroke, GBS, Bell's palsy and TM(3-5). The underlying etiology is still unknown. 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(10). In this mechanism, multiorgan spread of the virus occurs as a result of the wide distribution of the human angiotensin-converting enzyme-2 (hACE2) receptors (11). Another possible explanation could be a stimulation of the immune response following 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(12, 13), 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(14).

To diagnose cerebellitis, brain MRI and lumbar puncture are used which rule 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(15). 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. Laboratory evidence of vasculitis and connective tissue disease was also absent. As most of the possible causes were eliminated, the abovementioned feature was attributed to post vaccination cerebellitis following SARS-CoV-2 vaccination. The case shows close temporal association to a positive CSF COVID-19 PCR as a result of COVID-19 vaccination. The patient did not have any signs of previous COVID-19 infection, neither were COVID-19 antibodies detected in the serum. The acute attack of cerebellitis appeared within 2 weeks of COVID-19 vaccination. To our knowledge, no similar case has been reported yet. Specifically, we only found three reports of postvaccination cerebellitis which were secondary to influenza vaccine. The first case was a 16-year-old girl 12days after receiving H1N1 vaccine with cortical foci of hyperintensity on FLAIR in the cerebellar hemispheres with significant mass effect on the 4^{th} ventri-

cle(16). The second one was a 66-year-old woman presented with limb and gait ataxia and a history of H1N1 vaccination 3weaks prior to her symptoms. Her brain MRI had no abnormality but Technetium-99m hexamethyl propylene amine oxime-single photon emission computed tomography (HMPAO-SPECT) showed markedly cerebellar asymmetry, suggesting hypoperfusion in the right cerebellum(17). The third one was a 5 year-old girl with acute cerebellar ataxia after Influenza vaccination with marked Cerebellar Atrophy(7).

These reports may not be able to identify causality as no distinction can be made between infectious and other etiology. Our study lacks laboratory data analysis on autoimmune and paraneoplastic causes of acute cerebellitis. However, 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 seem 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 for finding of the actual relevance and potential risk. In this regard, we reported a case of post-vaccination acute cerebellitis with positive CSF COVID-19 PCR and no pulmonary symptoms for the first time.

Declaration of interest statement:

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

Author's contribution:

Seyedehnarges Tabatabaee: Resources, Writing – review & editing.

Fahimeh H Akhoundi: Data curation, Validation.

Seyed Mohammad Tabatabaei: Data curation, Writing – review & editing.

Bahram Haghi Ashtiani: Conceptualization, Supervision.

References:

1. Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie Z, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. Jama. 2020;324(10):951-60.

2. Control CfD, Prevention. Possible side effects after getting a COVID-19 vaccine. 2021.

3. Khan E, Shrestha AK, Colantonio MA, Liberio RN, Sriwastava S. Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature. Journal of Neurology. 2021:1-12.

4. McKean N, Chircop C. Guillain-Barré syndrome after COVID-19 vaccination. BMJ Case Reports CP. 2021;14(7):e244125.

5. Colella G, Orlandi M, Cirillo N. Bell's palsy following COVID-19 vaccination. Journal of Neurology. 2021:1-3.

6. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA neurology. 2020;77(6):683-90.

7. SAITO H, YANAGISAWA T. Acute cerebellar ataxia after influenza vaccination with recurrence and marked cerebellar atrophy. The Tohoku journal of experimental medicine. 1989;158(1):95-103.

8. Sawaishi Y, Takada G. Acute cerebellitis. The Cerebellum. 2002;1(3):223-8.

9. Van Samkar A, Poulsen M, Bienfait H, Van Leeuwen R. Acute cerebellitis in adults: a case report and review of the literature. BMC research notes. 2017;10(1):1-6.

10. Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain, behavior, and immunity. 2020;87:18-22.

11. Xia S, Zhu Y, Liu M, Lan Q, Xu W, Wu Y, et al. Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein. Cellular & molecular immunology. 2020;17(7):765-7.

12. Tishler M, Shoenfeld Y. Vaccination may be associated with autoimmune diseases. IMAJ-RAMAT GAN-. 2004;6(7):430-2.

13. I Hackett I, O'Sullivan R, Zaid A, Rea D, Walsh S. Acute cerebellitis associated with dual influenza A (H1N1) and B infection. 2013.

14. Blank M, Barzilai O, Shoenfeld Y. Molecular mimicry and auto-immunity. Clinical reviews in allergy & immunology. 2007;32(1):111-8.

15. De Bruecker Y, Claus F, Demaerel P, Ballaux F, Sciot R, Lagae L, et al. MRI findings in acute cerebellitis. European radiology. 2004;14(8):1478-83.

16. Lessa R, Castillo M, Azevedo R, Azevedo F, Azevedo H. Neurological complications after H1N1 influenza vaccination: magnetic resonance imaging findings. Arquivos de neuro-psiquiatria. 2014;72:496-9.

17. Park KM, Kim SE, Kim SE. An elderly case of acute cerebellitis after alleged vaccination. Journal of movement disorders. 2012;5(1):21.

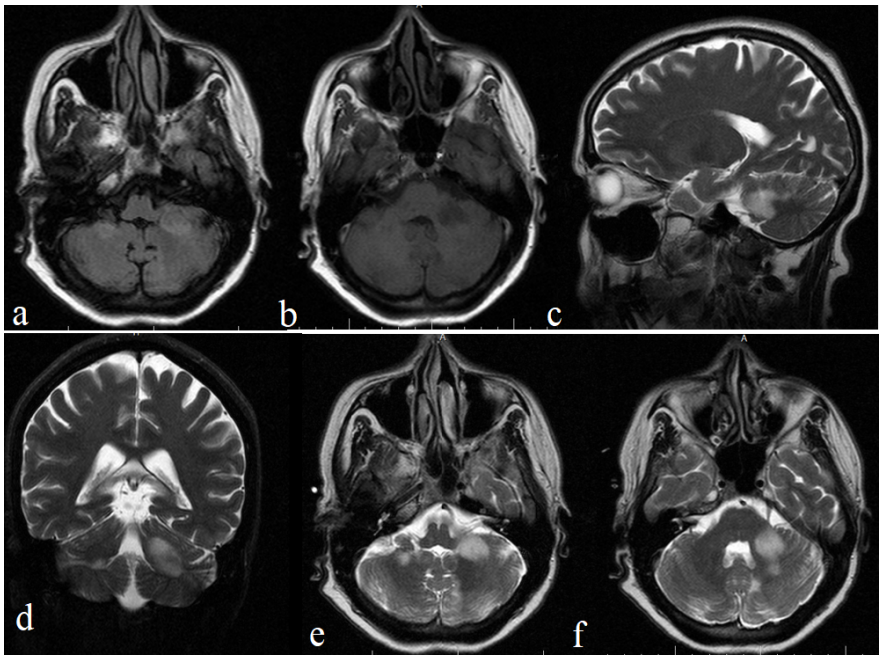

Fig.1 Brain MRI axial FLAIR image showing hyperintense bilateral MCP lesion(a), hypointense MCP lesion in axial T1 weighted(b), sagittal, coronal and axial T2 weighted showing hyperintense MCP lesions(c,d,e,f).