Received: 26 December 2021 | Revised: 29 March 2022 | Accepted: 30 March 2022

DOI: 10.1111/cen3.12700

CASE REPORT

Clinical & Experimental Neuroimmunology WILEY

Post-infectious cerebellar ataxia following COVID-19 in a patient with epilepsy

Sidhartha Chattopadhyay[1] | Judhajit Sengupta[1] | Sagar Basu[2]

[1]Department of Critical Care Medicine, R.N Tagore International Institute of Cardiac Sciences, Mukundapur, Kolkata, India

[2]Department of Neuro-medicine, KPC Medical College & Hospital, Jadavpur, Kolkata, India

Correspondence
Sidhartha Chattopadhyay, Department of Critical Care Medicine. R.N Tagore International Institute of Cardiac Sciences, Mukundapur, Kolkata, West Bengal, India.
Email: sidharthachatterjee111@gmail.com

Funding information
This research did not receive any grant from funding agencies in public, commercial or not-for-profit sectors.

Abstract

Background: Various neurological manifestations have been described in relation to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19). However, the development of cerebellar ataxia after recovery from COVID-19 is rare. We present a case of cerebellar ataxia 3 weeks after recovery from COVID-19.

Case Presentation: A 70-year-old male patient from an urban area of India presented with ataxia. He was hypertensive and had been receiving treatment for post-traumatic epilepsy for the previous 3 years. He had previously had laboratory-confirmed COVID-19 infection with mild symptoms that resolved within 2 weeks. However, 3 weeks after symptom improvement, he developed severe pan-cerebellar ataxia. Investigations were suggestive of post-infectious cerebellar ataxia. Other causes of ataxia were excluded. He responded well to pulse methylprednisolone therapy and was discharged with mild tremor and ataxia.

Conclusion: Post-infectious cerebellar ataxia is an unusual presentation after COVID-19. The clinician should be aware of such complications following COVID-19 infection as early diagnosis and proper management leads to better outcomes in many patients.

KEYWORDS
ataxia, cerebellitis, covid-19, epilepsy, miller fisher syndrome, tremor

1 | INTRODUCTION

Neurological manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; coronavirus disease 2019 [COVID-19]) have been increasingly documented in various literature since the start of the pandemic.[1,2] Cases of seizures, meningitis, headache, encephalopathy, Guillain-Barré syndrome, and others during COVID-19 infection have been recorded.[2] But ataxia as a post-COVID-19 manifestation has rarely been described (<1% of patients).[3] These include acute cerebellar ataxia, ataxia due to Miller Fisher syndrome, opsoclonus myoclonus ataxia syndrome, and ataxia associated with encephalopathy as described in the literature.[4] We describe a very unusual case of a 70-year-old man with known epilepsy who developed cerebellar ataxia 5 weeks after documented SARS-CoV-2 infection.

2 | CASE REPORT

A 70-year-old male patient with epilepsy and hypertension presented to our neurology clinic with sudden onset of severe imbalance leading to difficulty walking and maintaining a sitting posture with tremulousness of both hands for the previous 2 days. He had no history of alcoholism, gluten hypersensitivity, significant weight loss, substance abuse, nausea, vomiting, dizziness, tinnitus, visual disturbance, headache, altered sensorium, convulsion, paresis, or sphincteric involvement. The patient had tested positive for SARS-CoV-2 infection with real-time reverse transcriptase polymerase chain reaction (rRT-PCR) testing 5 weeks previously. His COVID-19 symptoms were mild and had resolved after 2 weeks, which correlated with a negative rRT-PCR result and high titers of serum immunoglobulin G antibody. He had

been receiving levetiracetam 500 mg twice daily for post-traumatic seizures for the previous 3 years. Hypertension was adequately controlled with cilnidipine 10 mg. On examination, he was afebrile, had normal cognitive function (Montreal Cognitive Assessment score = 95/100), and had no signs of meningeal irritation. Cranial nerves, motor power, and sensory functions were intact with hypotonia. Deep tendon reflexes were exacerbated in both upper and lower limbs. The plantar response was bilaterally flexor. Cerebellar examinations showed dysarthria, dysmetria, bilateral dysdiadochokinesia, no nystagmus, truncal ataxia, and severe intention tremor with abnormal finger nose, and the knee–heel and Romberg tests were negative with broad base ataxic gait and gross difficulty in tandem walking. Based on these cerebellar signs and symptoms, a clinical diagnosis of pan-cerebellar ataxia was made. His full blood count, metabolic parameters such as electrolytes, thyroid function test, serum vitamin B_{12} assay, calcium profile, x-ray chest, and non-contrast computed tomography brain plain were normal. Brain magnetic resonance imaging (MRI) with contrast showed multiple old lacunar infarcts without any other abnormal signal changes. Hepatitis B and C and HIV serology were negative. Ultrasonography abdomen and pelvis were unremarkable. Examination of the cerebrospinal fluid (CSF) showed a normal cell count and glucose, with mildly increased protein (60 mg [N = 20–40 mg]). CSF for Gram stain, Ziehl-Nielsen, India-ink, BIO FIRE FILMRRAY, and multiplex PCR panel were also negative. His serum autoimmune profile, including anti-nuclear antibody profile, anti-thyroid peroxidase antibody, and paraneoplastic antibody panel, were negative. Neuromyelitis optica spectrum disorders were ruled out with negative aquaporin 4 antibody and anti-myelin oligodendrocyte glycoprotein antibody in serum. Visual evoked potential showed normal p100 latencies. Nerve conduction velocity studies of all limbs were normal. The patient was diagnosed as having post-infectious pan-cerebellar ataxia as a sequelae of COVID-19 infection. He was treated with pulse therapy of intravenous methylprednisolone 1 gm/day for 5 days, along with rehabilitation with physical and occupational therapy. He was also given antiplatelets (clopidogrel 75 mg) and statins (atorvastatin 10 mg) in addition to his regular anticonvulsant and antihypertensive medications as the brain MRI with contrast revealed evidence of cerebral small vessel disease. His walking and speech improved significantly on the 7th day. At discharge on the 10th day, he was experiencing mild tremors and ataxia.

3 | DISCUSSION

The neurological manifestation of COVID-19 is probably due to the invasion of SARS-CoV-2 virus particles in the central nervous system (CNS) via a neuronal or hematogenous route.[1] It has also been hypothesized that SARS-CoV-2 virus can attach to the angiotensin-converting enzyme-2 receptor on neuron and glia and circulates in various parts of the CNS such as the hypothalamus, basal ganglia, midbrain, pons, medulla, and cerebellum.[5] The cerebellum is also believed to modulate seizure activity, but the concept of cerebellar epilepsy is controversial. Ataxia is a presenting manifestation of various epilepsies such as *SCN1A*, *SCN2A*, *KCTD7*, *KCNJ10*, and *CACNA1A* gene mutations and of various deficiency disorders and metabolically conditioned diseases (such as folic acid transport disorders, vitamin E deficiency, and glucose transporter 1 deficiency).[6] Ataxia may also be seen as a consequence of epilepsy, possibly due to cerebellar atrophy (but the pathogenesis not yet clear) or as an adverse effect of antiepileptic drugs such as phenytoin, carbamazepine, clobazam, clonazepam, and zonisamide, among others. Levetiracetam also caused ataxia in about 1.5% of patients in a randomized placebo-controlled study.[7] Our patient had epilepsy for 3 years, and it was well controlled with levetiracetam, so levetiracetam-induced ataxia was unlikely after so many years. Cerebellar ataxia is very uncommon and is not frequently seen after SARS-CoV-2 infection. Cases of ataxia associated with COVID-19 were well recognized in a systemic review of the literature by Chan et al., who described 33 cases of ataxia, of which 18 cases were para- and post-infectious ataxia, and only one was cerebellar ataxia with orthostatic tremor.[8] The timing of the development of ataxia subsequent to COVID-19 suggests a link between the two. Other possible causes of ataxia such as other viral infections, intoxication, or para-neoplastic diseases were excluded based on history, laboratory investigation, and course of illness. We found no other auto-immune complications of COVID-19 illness such as Miller Fisher syndrome,[9,10] opsoclonus myoclonus ataxia syndrome,[11] or acute cerebellar ataxia with myoclonus only.[12] This patient had no history of COVID-19-related encephalopathy. Sensory ataxia was excluded by the presence of normal deep tendon reflexes and normal posterior column sensations. Ataxia was unlikely to be due to direct invasion of the cerebellum by SARS-CoV-2, which was ratified by a negative PCR test and normal CSF cell count, although SARS-CoV-2 RNA analysis was not done in the CSF. The MRI did not show any abnormal signals, although various abnormal neuroimaging changes in SARS-CoV-2 have been described in the literature, possibly due to cytokine-induced immune-mediated tissue damage.[13] The cause of ataxia without any abnormal MRI signal in our patient is likely a post-infective phenomenon, causing a delayed humoral or cell-mediated immune response due to cross-reactive cerebellar antigens with viral antibodies and/or T cells. However, other possibilities remain.

This is a rare presentation of post-infective cerebellar ataxia due to COVID-19 infection, probably due to an immune-mediated mechanism. However, further research is needed for a better understanding of the pathophysiology. Clinicians should be aware of such complications of COVID-19 infection, which often respond to treatment.

ACKNOWLEDGMENT

Not applicable.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

ETHICS STATEMENT

Approval of the research protocol: Not Applicable; *Informed consent*: informed consent was obtained from the subject; *Registry and the Registration No. of the study/trial*: Not Applicable; *Animal Studies*: not Applicable.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Sidhartha Chattopadhyay https://orcid.org/0000-0001-9697-7761

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How to cite this article: Chattopadhyay S, Sengupta J, Basu S. Post-infectious cerebellar ataxia following COVID-19 in a patient with epilepsy. Clin Exp Neuroimmunol. 2022. https://doi.org/10.1111/cen3.12700