Abnormal Saccadic Oscillations Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Encephalopathy and Ataxia

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Neurological manifestations can complicate patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and may be the predominant clinical feature in patients with minimal or no respiratory symptoms.1,2 In this report, we describe a patient with parainfectious saccadic oscillations and ataxia complicating SARS-CoV-2 infection and provide a video illustration of the eye movement abnormalities.

Case Report

A 79-year-old previously independent man was admitted to a regional hospital with an 8-day history of progressive decline in physical function, confusion, and diarrhea. His nasopharyngeal sample tested positive for SARS-CoV-2 on reverse-transcriptase polymerase chain reaction 8 days prior to admission. He had a stable chronic nonproductive cough without new respiratory symptoms and was tested for SARS-CoV-2 because of close contact with a confirmed case. His past history includes asbestosis, previous nondisabling stroke, mild cognitive impairment, type 2 diabetes mellitus, hypertension, and prostatic hypertrophy. His preadmission medications were clopidogrel, atorvastatin, cilazapril, tamsulosin, finasteride, and solifenacin. On admission he was confused but could maintain appropriate eye contact, had no focal neurological deficit, and was apyrexial. He was maintaining oxygenation on room air without respiratory distress.

Admission laboratory investigations showed elevated C-reactive protein (53 mg per L) and a mild lymphopenia at (900 per μL). Chest radiograph was normal. He had an isolated low-grade pyrexia (37.8°C) on day 2 of admission without an alternative infective focus identified. Cilazapril was ceased on day 5 and substituted for losartan in an attempt to manage his cough. He developed worsening confusion with agitation and gait ataxia (wide-based gait) during the first 7 days of admission. The agitation was mild, and he did not require medication treatment. Repeat neurological examination on day 7 of admission demonstrated ocular flutter (see Video S1) and opsoclonus (earliest section of Video S1) and truncal ataxia without limb ataxia or long-track signs. There were no other additional brainstem or cerebellar ocular eye movement abnormalities. Myoclonus was not observed. Noncontrast magnetic resonance imaging on day 9 of admission (day 17 since SARS-CoV-2 diagnosis) showed chronic white ischemic change on background of moderate cerebral atrophy without abnormalities in the cerebellum or brainstem. Cerebral spinal fluid examination was not obtained as he would have required anesthetic support, which was unavailable at the regional hospital. At this juncture, C-reactive protein and lymphopenia had normalized. Remote tele-neurological consultation was sought, and SARS-CoV-2 encephalopathy with parainfectious opsoclonus was diagnosed. The patient was managed expectantly with initial improvement of his cognitive function and resolution of the eye movement abnormality (second part of the Video S1). However, the encephalopathy subsequently declined, and he was discharged to high-level care 35 days after admission and passed away from general physical decline 43 days after SARS-CoV2 diagnosis. A postmortem examination was not performed. A timeline of the his clinical and laboratory features is presented in the Figure 1.

Discussion

Opsoclonus myoclonus syndrome (OMS) is a rare immune-mediated neurological manifestation comprising opsoclonus, myoclonus, and ataxia and is usually parainfectious or associated with an active malignancy.3 OMS and ocular flutter have been described in the setting of a range of infectious, predominantly viral, as part of a postinfectious or parainfectious autoimmune...
phenomenon.\textsuperscript{4,5} A summary of the reported cases in the past 30 years in the English literature is presented in Table S1. Myoclonus and/or opsoclonus may not be present in these\textsuperscript{5} cases, and so the absence of myoclonus and predominance of flutter over opsoclonus in the present case is not atypical.

Two cases of SARS-CoV-2 myoclonus and ocular flutter associated with brainstem encephalitis have been reported,\textsuperscript{7,8} and the present similar case with ocular flutter, opsoclonus, and ataxia, but absence of myoclonus, adds to the clinical spectrum. Management in non-malignancy-related OMS is symptomatic, with or without immunosuppressant therapy, with significant improvement or resolution of neurology symptoms in majority of patients.\textsuperscript{4}

Opsoclonus comprises omni-directional back-to-back saccades without an intersaccadic interval, whereas the related phenomenon, ocular flutter, comprises purely horizontal saccadic oscillations without an intersaccadic interval.\textsuperscript{9} The pathophysiological mechanism underlying ocular flutter and opsoclonus is not certain. Earlier suggestions that lesions encompassing the omnipause neurons in the pons have not been substantiated by neuroimaging or neuropathological examination. Current thinking is that these phenomena relate to either membrane instability of saccadic burst neurons in the brainstem or, perhaps more likely, disinhibition of the fastigial nuclei of the cerebellum.\textsuperscript{4}

The time course of manifestations suggests SARS-CoV-2 as the causative etiology in the patient’s neurological presentation. Neurological involvement is observed in approximately one third of SARS-CoV-2–infected patients and can be the presenting feature in patients without typical SARS-CoV-2 respiratory or systemic symptoms. Although encephalitis in the setting of SARS-CoV-2 infection may be via immune-mediated cytokine and chemokine release triggered by direct viral invasion of the central nervous system, other neurological complications of SARS-CoV-2, including acute disseminated encephalomyelitis, Miller Fisher syndrome, and Guillain-Barré syndrome, are likely to be parainfectious.\textsuperscript{9,10} That is, in these cases it is presumed that autoimmune cross-reactivity is the mechanism as in other viral infections with similar parainfectious manifestations.\textsuperscript{8,10} In the same vein, we suggest that the present case of saccadic oscillations and ataxia is related to immune-related dysfunction within the brainstem or cerebellum.

This case adds to the expanding spectrum of SARS-CoV-2–associated neurological manifestations.

**Author Roles**

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

D.W.: 1A, 1B, 1C, 2A, 2B
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P.H.-W.: 1C, 2A, 2B
T.A.: 2A, 2B
T.Y.W.: 1A, 1B, 1C, 2A, 2B

**Disclosures**

**Ethical Compliance Statement:** The authors confirm that written consent for publication was obtained. We confirm that we have read the journal’s position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. As per local regulations, case report with written consent does not require approval from institutional review board.

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Supporting Information

Supporting information may be found in the online version of this article.

**Video S1.** First part: patient video demonstrating opsoclonus with ocular flutter 15 days after diagnosis of severe acute respiratory syndrome coronavirus 2. Second part: resolution of the abnormal eye movements 17 days later.

**Table S1.** Reported cases in literature of parainfectious opsoclonus or flutter since 1990.