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CASE STUDY

Acute cerebellar ataxia and myoclonus with or without opsoclonus: a para-infectious syndrome associated with COVID-19

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Abstract

Background and purpose: Patients with COVID-19 can have central or peripheral neurological manifestations.

Methods: The cases of two patients with acute cerebellar ataxia and myoclonus associated with COVID-19 are reported (with Video S1) and five previously reported patients are discussed.

Results: Acute cerebellar ataxia and myoclonus started between 10 days and 6 weeks after the first manifestations of COVID-19. Opsoclonus or ocular flutter was present in four patients. Patients were treated with intravenous immunoglobulins and/or steroids except for one patient, resulting in a striking improvement within a week.

Conclusion: Acute cerebellar ataxia and myoclonus with or without opsoclonus belongs to the wide spectrum of neurological manifestations associated with COVID-19. It is important to recognize this possible manifestation since early treatment allows for rapid recovery.

KEYWORDS
encephalopathy, immune-mediated disorder, movement disorders, para-infectious, SARS-COV-2

INTRODUCTION

Patients with COVID-19 infection can have neurological manifestations reflecting involvement of the central nervous system (mainly subacute encephalopathy and stroke), the peripheral nervous system (mostly Guillain–Barré syndrome and cranial nerve palsy) or a combination thereof[1]. Opsoclonus myoclonus ataxia syndrome (OMAS) is an immune-mediated movement disorder and is mostly para-infectious or paraneoplastic [2] It is characterized by the variable association of opsoclonus, myoclonus, cerebellar ataxia, and behavioural and sleep disturbances [2] Immune-mediated acute cerebellar ataxia and myoclonus (ACAM) in the absence of opsoclonus is rare. It is not clear whether ACAM belongs to the spectrum of OMAS or is a distinct entity close to OMAS [2]

Two cases of ACAM associated with COVID-19 are reported. Detailed characteristics of the patients are shown in Table 1. ACAM started 10 days and 6 weeks respectively after the onset of typical features of COVID-19 infection (Table 1). Patient 1 had confusion with myoclonic jerks of the four limbs, ataxic dysarthria and an opsoclonus (Video S1). Patient 2 presented a rapidly progressive cerebellar syndrome with stimulus-sensitive action myoclonus (Video S1). Cerebral magnetic resonance imaging and cerebrospinal fluid analysis were normal. There was no epileptic activity on electroencephalogram. Video-oculography confirmed the opsoclonus in patient 1. Auto-immune and paraneoplastic anti-neuronal antibodies were negative. COVID-19 diagnosis was established by the presence of COVID-19 specific antibodies in the patient's serum. Both patients were treated with intravenous immunoglobulins associated with steroids in patient 1, resulting in a striking improvement within a week.

Cendrine Foucard and Aurore San-Galli contributed equally to the work.

TABLE 1 Characteristics of patients with acute cerebellar ataxia and myoclonus associated with COVID-19

Patient	COVID-19 diagnosis[a]	ACAM onset	Neurological manifestations	Investigations	Treatment[b]	Follow-up[c]
Patient 1 83 years/male	Yes	10 days	• Opsoclonus • Myoclonus of the four limbs, trunk and face worsened with stimulation, posture and action • Ataxic dysarthria • Confusion	• Normal cerebral MRI • Normal CSF • Negative serum and CSF auto-immune and paraneoplastic anti-neuronal antibodies • Blood tests excluded other infectious, metabolic or auto-immune diseases • EEG: no epileptic anomaly • Thoracic CT scan: minimal form of COVID-19 pneumonitis, no occult neoplasm	IVIG (0.4 g/kg daily for 5 days) + steroids (1 g/day during 5 days) and diazepam	Few days
Patient 2 63 years/male	Yes	6 weeks	• No opsoclonus • Action myoclonus sensitive to stimulation involving the four limbs, trunk and face • Static and kinetic cerebellar syndrome involving the four limbs with ataxic dysarthria • No cognitive impairment	• Normal cerebral MRI • Normal CSF • Negative serum and CSF auto-immune and paraneoplastic anti-neuronal antibodies • Blood tests excluded other infectious, metabolic or auto-immune diseases • Whole-body PET FDG and TAP CT scan: no occult neoplasm	IVIG (0.4 g/kg daily for 5 days)	Few days/3 months
MA/male[3]	Yes	3 weeks	• Opsoclonus • Cortical myoclonus • Cerebellar syndrome involving the four limbs and trunk with ataxic dysarthria	• Normal cerebral MRI • Normal CSF • Negative serum and CSF auto-immune and paraneoplastic anti-neuronal antibodies • Blood tests excluded other infectious, metabolic functions or auto-immune diseases	Steroids (1 g/day during 7 days), sodium valproate (20 mg/kg/day), levetiracetam (2 g/day), clonazepam (2 mg/day)	Few days/1 week
44 years/male [4]	Yes	2 weeks	• Ocular flutter • Myoclonic jerks sensitive to tactile and auditory stimuli of the four limbs, trunk and face • Cerebellar syndrome involving the four limbs • Mild neurocognitive symptoms • Insomnia	• Normal cerebral and spinal cord MRI • Normal CSF • Negative serum and CSF auto-immune and paraneoplastic anti-neuronal antibodies • Blood tests excluded other infectious, metabolic functions or auto-immune diseases • Whole-body PET FDG: no occult neoplasm • Normal dermatological screening and testicular echography	Steroids (1 g/day during 5 days) then IVIG (0.4 g/kg daily for 3 days)	5 days/2 months
57 years/male [5]	Yes	10 days	• Opsoclonus • Action myoclonic jerks of the four limbs • Ataxic gait	• Normal cerebral MRI • CSF analysis not conducted • No blood test abnormality mentioned • Negative screening for an occult neoplasm with TAP CT scan	Clonazepam, IVIG (0.4 g/kg daily for 5 days) and steroids (40 mg twice a day for 5 days)	Few days/2 weeks

(Continues)

TABLE 1 (Continued)

Patient	COVID-19 diagnosis[a]	ACAM onset	Neurological manifestations	Investigations	Treatment[b]	Follow-up[c]
72 years/ male [6]	Yes	17 days	• No opsoclonus • Myoclonic jerks sensitive to stimulus of the four limbs • Cerebellar syndrome with ataxic dysarthria	• Normal cerebral MRI • CSF: mildly elevated protein without elevated cell counts • Autoantibodies directed against the nuclei of Purkinje cells, striatal neurons and hippocampal neurons in the CSF • Brain PET FDG showed putaminal and cerebellum hypermetabolism associated with diffuse cortical hypometabolism • Whole-body PET FDG: no occult neoplasm • Blood tests excluded other auto-immune diseases	IVIG (0.4 g/kg daily for 5 days) then steroids (1 g/day during 5 days)	Few weeks
48 years/ male [7]	Yes	13 days	• No opsoclonus • Myoclonic jerks of the four limbs, trunk and face (not stimulus sensitive) • Cerebellar syndrome involving the four limbs	• Normal cerebral MRI • Normal CSF • Negative serum and CSF auto-immune and paraneoplastic anti-neuronal antibodies • Blood tests excluded other infectious, metabolic functions or auto-immune diseases	Levetiracetam	Improved/not entirely after 49 days (since neurological symptoms onset)

Note: Patients with opsoclonus myoclonus ataxia syndrome post-COVID-19 characteristics.

Abbreviations: ACAM, acute cerebellar ataxia and myoclonus; CSF, cerebrospinal fluid; CT scan, computed tomography scan; EEG, electroencephalogram; IVIG, intravenous immunoglobulin; MA, middle-aged; MRI, magnetic resonance imaging; PET FDG, positron emission tomography fluorodeoxyglucose; TAP CT scan, thoraco-abdomino-pelvic CT scan.

[a]Positive real-time reverse polymerase chain reaction in nasopharyngeal swab and/or positive COVID-19 specific antibody in serum.

[b]Type and duration of treatment.

[c]Improvement time/full recovery time.

All procedures were done according to our institution's ethical standards in accordance with the Declaration of Helsinki. The patients consented to videotape and publication.

Including the two patients reported here, seven patients have been reported with ACAM associated with COVID-19 [3–7] (Table 1). They were male and aged from 44 to 83. ACAM started between 10 days and 6 weeks after the first manifestations of COVID-19. Opsoclonus was present in three patients, ocular flutter in one patient. One was treated with intravenous immunoglobulins, one with intravenous steroids, and four with the combination thereof. The remaining patient only received symptomatic treatment with levetiracetam. They all had a clear improvement within a week after treatment onset. As for various viral infections, such as human immunodeficiency virus, cytomegalovirus, herpes simplex virus, adenovirus and enterovirus [2] a variable combination of opsoclonus, myoclonus and ataxia could be observed in association with COVID-19. The mechanism is probably immune-mediated, as supported by the normality of the magnetic resonance imaging and cerebrospinal fluid [8] These observations are important for clinical practice since early treatment with immunoglobulin and/or steroids allows rapid recovery [8]

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CONFLICT OF INTEREST

The authors have no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

All the data are available in the Department of Neurology at the Pitié-Salpêtrière hospital.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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