



## Ataxia Myoclonus Syndrome in Mild Acute COVID-19 Infection

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Dear Editor,

The coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) triggered several new challenges around the world. Three COVID-19 infection phases have been described: (a) an acute phase (signs and symptoms lasting up to 4 weeks); (b) an ongoing symptomatic phase (signs and symptoms between 4 and 12 weeks); and (c) a post-COVID-19 phase (signs and symptoms that continue for more than 12 weeks) [1]. Neurological complications of SARS-CoV2 have been widely described [2], reported in over 35% of affected patients, especially when critically ill [3]. These neurological manifestations widely range from mild to severe complications, affecting both the central and peripheral nervous systems.

Despite the scarce prevalence of movement disorders in COVID-19 patients, new cases have been increasingly described during the last year, not only among hospitalized patients, but also in milder cases. Myoclonus and ataxia are the most frequently movement disorders observed in COVID-19 patients [4], and recent publications have highlighted the presence of an ataxia-myoclonus syndrome with or without opsoclonus as a common neurological complication resulting from a likely autoimmune etiology.

We aimed to present five patients with ataxia-myoclonus syndrome (AMS) as a post-infectious manifestation following a mild COVID-19 infection.

We report five male patients with an age ranging from 36 to 67 years. All of them presented mild COVID-19 symptoms and only one required hospitalization without the need for oxygen supplementation. All patients presented with AMS during the acute phase of COVID-19 once they were fully recovered from their initial respiratory symptoms, 8 to 15 days after the beginning of the disease. Axial and appendicular ataxia and myoclonus were seen in all patients and were the reason for their hospital admission. Myoclonus was mostly generalized and triggered by action, but in one patient, it was provoked by tactile stimulus. Two patients presented ocular flutter and one had opsoclonus. The rest of neurological examination was normal, except patient 3 who presented generalized areflexia (Table 1, Videos 1–5).

All patients underwent brain MRI that was normal. An extensive evaluation, including blood tests, CSF analysis, and onconeural antibodies, was performed in all patients. In two cases, a mild elevation in the CSF protein concentration was detected. PCR for EBV, CMV, and HZV as well as bacterial cultures were all negatives. Four patients received iv methylprednisolone (1 g/day for 3 days), combined with iv IgG (0.4 g/kg daily for 5 days) in one case. One patient resolved spontaneously without treatment and received only symptomatic management with levetiracetam 3 g/day and clonazepam 2 mg/day. Neurological symptoms dramatically improved and resolved completely in all patients over the course of days to weeks (Table 1).

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**Table 1** Demographic characteristics and clinical manifestations during COVID-19 infection and during AMS

Case	1	2	3	4	5
Age	60	67	36	44	33
Sex	Male	Male	Male	Male	Male
COVID-19 characteristics					
Infection severity	Mild	Mild	Mild	Mild	Mild
Diagnosis test	RT-PCR	RT-PCR	Antigen test	RT-PCR	RT-PCR
Hospitalization	No	No	No	Yes	No
Pulmonary involvement	No	No	No	Yes	No
Concomitant neurological involvement	No	No	No	No	Headache
AMS					
Latency between infection and first neurological signs (days)	10	11	15	13	8
Myoclonus	Yes (LL)	Yes (G)	Yes (G)	Yes (G)	Yes (G)
Type of myoclonus	Posture, action	Posture, action, stimulus-induced (tactile)	Posture, action	Posture, action	Posture, action
Ataxia	Yes	Yes	Yes	Yes	Yes
Ocular movements	Ocular flutter	Normal	Normal	Opsoclonus	Ocular flutter
Other neurological features	hyporeflexia	Dysarthria	Osteotendinous areflexia	Dysarthria	None
Brain MRI	Unremarkable	Unremarkable	Unremarkable	Unremarkable	Unremarkable
EMG	Demyelinating and axonal mixed polyneuropathy	Not done	Normal	Not done	Not done
Onconeuroal antibodies	Negative	Negative	Negative	Negative	Negative
CSF	Mild protein elevation	Not done	Normal	Mild protein elevation	Normal
Immunosuppressive treatment	IVIg/ Methylprednisolone	Methylprednisolone	Methylprednisolone	Methylprednisolone	None
Symptomatic treatment	Levetiracetam	None	Levetiracetam	None	Levetiracetam, clonazepam
Outcome	Full recovery in 18 days	Full recovery in 13 days	Full recovery in 4 weeks	Full recovery in 10 days	Full recovery in 6 weeks

AMS, ataxia-myoclonus-syndrome; CSF, cerebrospinal fluid; EMG, electromyography; G, generalized; IVIG, intravenous immunoglobulin; LL, lower limbs; MRI, magnetic resonance imaging; RT-PCR, real-time polymerase chain reaction

Herein, we presented five new cases characterized by the occurrence of AMS during the acute phase of a mild COVID-19 infection. To date, less than 50 cases of AMS secondary to COVID-19 have been described in the literature. A common hallmark of most reported patients was the delayed neurological presentation after COVID-19 infection, suggesting a post-infectious immunomodulated mechanism [5]. The pathogenesis of neurological complications in COVID-19 patients is still unknown. Different mechanisms are proposed: a direct damage from the virus, the effect of cytokines release, hypoxia, neuroinflammation, and endothelial dysfunction [6]. In the case of AMS, there is the hypothesis that a post- or para-infectious immune-mediated etiology could be the cause [7], whereby antibodies react against cerebellar Purkinje cells [8].

It was previously described that AMS could be seen not only in severe COVID-19 patients but also in mild cases [5, 7] and our study support this notion. All of our cases presented mild symptoms of COVID-19 infection and the main reason for hospitalization was the presence of AMS. In keeping with previously described cases, all of our patients had a benign course and an excellent response to immunosuppressive treatment, achieving a complete remission.

AMS is infrequent and the etiology includes paraneoplastic, para-infectious, toxic-metabolic, and idiopathic causes. AMS caused by COVID-19 either during the initial stages of COVID-19 infection (para-infectious syndrome) or with a delayed onset (post-infectious syndrome) should be suspected in acute cases with or without ocular movement impairment and recent history of COVID-19 infection, regardless of its severity.

In conclusion, our experience further supports the notions that SARS-CoV-2 should be seen as a potential cause for acute ataxia with or without myoclonus and/or opsoclonus [9]. The description of new cases will facilitate a better understanding of this neurological condition.

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## Declarations

**Ethics Approval** The authors 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. The authors confirm that the approval of an institutional review board was not required for this work.

**Consent for Publication** Patients signed informed consent regarding publishing their data.

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