



Isolated generalized myoclonus immune-mediated by SARS-CoV-2: an illustrative videotaped case

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Abstract

Myoclonus in the context of COVID-19 is an increasingly recognized condition. The occurrence in an ICU context in hypoxic patients, with metabolic disorders, taking several types of medication, makes difficult to establish a precise cause. Also, the implication of SARS-CoV-2 by direct invasion of the CNS or by immune-mediated phenomena is not yet clear. Currently, a dozen of cases of myoclonus as a predominant clinical manifestation, immune-mediated by SARS-Cov-2 are published. In all these cases, myoclonus was preceded by respiratory or other suggestive symptoms (e.g., anosmia) for this infection making straightforward the causal link. We describe a case of an isolated generalized myoclonus without other clinical complaints nor chest CT scan abnormalities nor SARS-CoV-2 RNA detection on nasopharyngeal swabs and on the CSF, as a para-infectious phenomenon of COVID-19 infection with excellent response to steroids perfusion. This challenging diagnosis was made upon confirmation of seroconversion (serology was negative at admission, then positive for IgM at day 6, then for both IgM and IgG at day 10) underlying that repeating serology is a diagnostic key to capture a similar findings.

Keywords Myoclonus · COVID-19 · SARS-CoV-2 · Immune-mediated · Movement disorders

Introduction

Movement disorders specialists are increasingly interested by Neuro-COVID-19 since the description of cases of ataxia, tremor, Parkinsonism, and myoclonus [1–3]. Very recently, some cases of myoclonus are reported [3–6] with variable phenomenology and diverse potential causes. Indeed, their occurrence in an ICU context in hypoxic patients, with metabolic disorders, taking several types of medication, makes difficult to establish a precise cause. Also, the implication of

SARS-CoV-2 by direct invasion of the CNS or by immune-mediated phenomena is not yet clear.

The case described here of an isolated generalized myoclonus without respiratory symptoms nor medication intake provides strong arguments in favor of a para-infectious condition, immune-mediated by SARS-CoV-2.

Case presentation

A 59-year-old man was hospitalized on October 15, 2020, because of a rapid-onset frequent falls. Two days before admission, he had noticed shock-like involuntary movements of both legs, without a fever or other clinical complaints particularly loss of smell, cough, or shortness of breath. His previous medical history was unremarkable except for a recent well-controlled diabetes. On examination (video 1), the patient was bedridden with normal consciousness and had a generalized typically myoclonic jerky movements including the torso, the four limbs, face, tongue, and larynx (responsible for a frank dysarthria). Myoclonus was clearly exacerbated by movements and acoustic stimuli (startle phenomenon). No oculomotor abnormality was noticed, particularly nystagmus. Otherwise, temperature, blood pressure, and oxygen

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saturation were normal. Except for a moderate elevation of C-reactive protein (48 mg/l), serum creatine kinase (650 ui/l), and a mild lymphopenia ($1100/\text{mm}^3$), an extensive laboratory workup (hemogram, glucose, thyroid, renal, hepatic functions, electrolytes, serum osmolality), cerebrospinal fluid (CSF) analysis, and cranial MRI revealed no abnormalities. EEG showed normal background rhythm and no epileptiform discharges. Nerve conduction study was normal, and no C reflex was found. Other laboratory workup including chest CT scan (day 4), real-time PCR of SARS-CoV-2 in nasopharyngeal swab (days 4 and 6) and in CSF (day 4), and serological IgM and IgG testing for SARS CoV-2 (day 4) were inconclusive. Symptomatic treatment with levetiracetam was initiated without improvement. At day 6, serology test for SARS-CoV-2 returned positive for IgM and negative for IgG. We assumed the myoclonus to be an immune-mediated manifestation of COVID-19, and we started immunotherapy by veinoglobulins, but the myoclonus seemed to improve only slightly. At day 10, serology test for SARS-CoV-2 returned positive for both IgM and IgG. Methylprednisolone 1000 mg/24 h for 5 days allowed a rapid and sustained improvement, and patient was discharged at home at day 15 (video 2). A full recovery was obtained at day 21 (video 3). Figure 1 summarized the timeline of all these events.

Discussion

This case gives a good evidence that generalized myoclonus can be the only manifestation of an immune-mediated reaction to SARS-CoV-2. Indeed, COVID-19 infection is diagnosed upon confirmation of seroconversion (serology was negative at admission, then positive for IgM (day 6), then for both IgM

and IgG (day 10)), but the virus was not detected on two nasopharyngeal swabs and on the CSF.

In the last few months, some cases in which myoclonus was the only or the predominant clinical manifestation in the context of COVID-19 infection were published [3–6]. In all these cases, myoclonus were preceded by respiratory or other suggestive symptoms (e.g., anosmia) for this infection, but in the case described here, the COVID-19 diagnosis was challenging because neither suggestive clinical complaints nor chest CT scan abnormalities were present.

SARS-CoV-2 can cause myoclonus via three mechanisms: (1) as a consequence of the associated hypoxic and systemic, particularly metabolic disturbances; (2) by direct viral CNS invasion; or (3) by immune-mediated para or post-infectious process. This case supports a dysimmune pathogenesis by the lack of other potential causes identified (neither hypoxic nor systemic disease) and the rapid improvement after corticosteroids. The brain MRI was normal, and the CSF analysis revealed no pleocytosis and no SARS-CoV-2 RNA, arguing against a direct viral CNS invasion.

The phenomenology of myoclonus as an immune-mediated condition by SARS-CoV-2 seems to be quite homogenous. Indeed, like our, patients presented with generalized myoclonus, predominantly action induced, involving trunk and the limbs [3–6] and accompanied in some cases, by cerebellar signs [1, 7] or opsoclonus [8, 9]). In the case described here, a brainstem reticular generator seems to be more likely according to the involvement of the axial muscles, the presence of a startle phenomenon, the normality of the EEG, the absence of a C reflex, and the lack of response to symptomatic treatment by levetiracetam. In the case described by Muccioli et al. [5], the electrophysiological testing performed argues also in favor of hyperactivation brainstem nuclei as an origin of the myoclonic jerks.

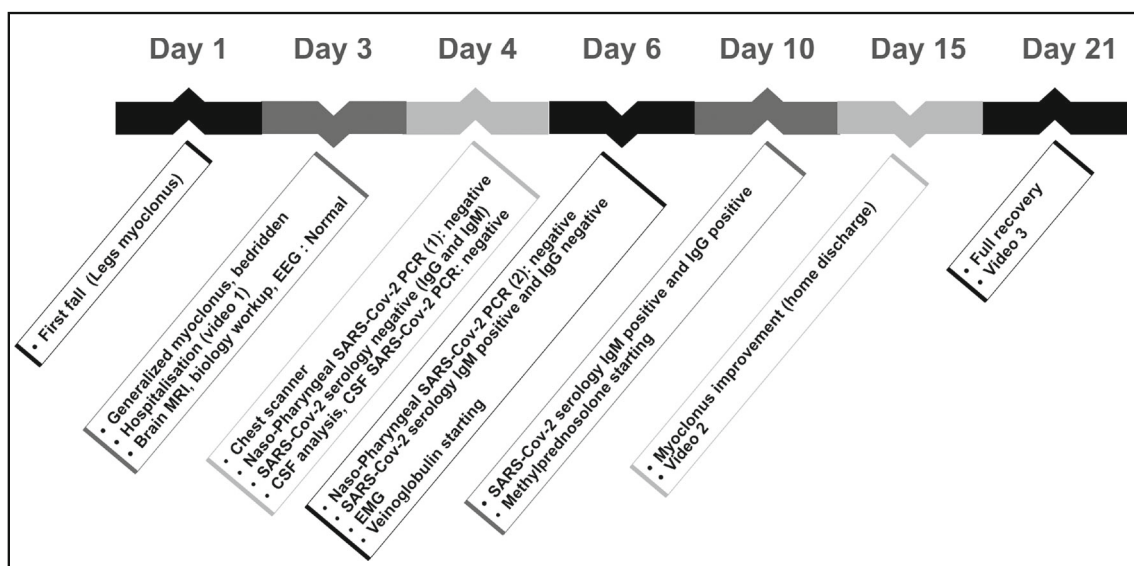


Fig. 1 This timeline summarizes clinical, laboratory assessment, treatment, and outcome of the patient

Conclusion

Our case is interesting because it demonstrates that generalized myoclonic movements can be the only manifestation of COVID-19 infection, without respiratory symptoms, chest CT scan abnormality nor SARS-CoV-2 RNA detection. Repeating serology is a diagnostic key. The outcome is very good after corticosteroids perfusion.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10072-021-05164-8>.

Declarations

Ethical approval None

Informed consent An informed consent to be filmed was obtained from the patient and his daughter.

Conflict of interest The authors declare no competing interests.

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