Generalised myoclonus associated with COVID-19 infection

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SUMMARY

Postinfectious generalised myoclonus has been reported after many viral and bacterial infections in the past. Recently, some case reports have described it in the context of COVID-19 infection. Most patients described in these case reports are either critically ill and intubated or have concurrent respiratory symptoms. Herein, we present a case of a 79-year-old man, who was recovering from a recent COVID-19 infection, presented with isolated generalised myoclonus. The patient was treated with levetiracetam, a short course (10 days) of dexamethasone, and required extensive rehabilitation. Outpatient follow-up at 2 months suggested complete resolution of symptoms and levetiracetam was subsequently discontinued. This case highlights that generalised myoclonus can occur as a delayed complication of COVID-19 infection.

BACKGROUND

COVID-19, caused by SARS-CoV-2, is primarily a viral pneumonia but can involve multiple-organ systems in the human body. Central nervous system (CNS) involvement is common and can occur either directly due to viral invasion to the CNS or indirectly in settings of widespread systemic inflammation, thrombosis and hypoxia.[1] CNS invasion of SARS-CoV-2 is not completely understood, but it is thought to possibly occur via two routes: retrograde spread through olfactory cells in the nasal mucosa and haematogenous spread.[1] The presence of SARS-CoV-2 in CNS has been confirmed by detection of viral particles via PCR in cerebrospinal fluids (CSF) and brain tissue of affected patients.[2 3]

Neurological manifestations of COVID-19 are broad and range from mild symptoms such as dizziness, headache, hyposmia/anosmia, hypogeusia/ageusia, to more severe clinical entities such as cerebrovascular accidents, viral encephalitis and acute disseminated encephalomyelitis.[4] Generalised myoclonus is an extremely rare complication of COVID-19 and only a few cases have been reported in the literature to date. Due to the lack of any standard guidelines, their diagnosis and management have been directed individually in different clinical settings.

CASE PRESENTATION

A 79-year-old man with no significant previous medical history presented to the emergency room for new-onset involuntary body movements for 1 day. These symptoms were preceded by worsening generalised fatigue for the past 2–3 days. The review of systems was negative otherwise. The patient was recovering from a recent COVID-19 lung infection that had manifested as cough and shortness of breath. He had been discharged 5 days prior from our facility in a stable condition after receiving 5 days of intravenous remdesivir, intravenous dexamethasone and supportive treatment for his COVID-19 lung infection.

On physical examination, the patient had intermittent, nonrhythmic, generalised myoclonic jerky movements, which were aggravated by various sensory stimuli such as auditory, tactile and painful stimuli and any voluntary movements. The examination was also significant for inability to track objects, marked startle and lack of coordination in voluntary movements. Besides, the haemodynamics were stable, and the systemic examination was unremarkable.

INVESTIGATIONS

Initial lab work including complete blood count, comprehensive metabolic panel, arterial blood gas analysis, urine drug screen (UDS), thyroid function test, vitamin B12, folate and ammonia levels were unrevealing. CT scan and MRI of the brain ruled out any obvious acute intracranial lesions. CT scan of the chest showed findings residual of recent COVID-19 lung infection. Lumbar puncture was obtained to further elucidate the cause of the patient's symptoms, and evaluation of CSF revealed normal proteins and glucose and no cells on cytology. Bacterial and fungal cultures of CSF did not show any growth. Extensive serum and CSF workup were negative for herpes simplex virus (HSV) type 1,2, HIV, West Nile virus, Lyme antibodies, Cryptococcus antigen, autoimmune panel and paraneoplastic panel. Electroencephalogram was considered however could not be performed due to limitations at the facility amidst patient with COVID-19 positive.

TREATMENT

Based on the review of a limited number of similar case reports and expert opinion from neurology, we started the patient on intravenous dexamethasone 6 mg/day and intravenous levetiracetam 1000 mg two times per day. The patient's symptoms started improving on day 3 and he displayed a very slow but progressive recovery. The patient was discharged on day 11 to a skilled nursing facility for rehabilitation, and oral levetiracetam was continued at discharge, and dexamethasone was discontinued.

OUTCOME AND FOLLOW-UP

Patient is discharged from rehabilitation facility and currently living at home and continues to

participate in home physical therapy. Outpatient follow-up at 2 months showed a complete resolution of symptoms and return to baseline functional status. Levetiracetam was tapered and subsequently discontinued after total 2 months.

DISCUSSION

Myoclonus is defined as sudden, brief, involuntary jerky movements characterised by sudden bursts of excessive muscular activity (positive symptoms) followed by brief muscular inactivity (negative symptoms).[5] It can be classified in many ways depending on its physiologic cause, anatomic origin, precipitating factors and electrodiagnostic findings. However, for ease, we will classify it based on the distribution of jerks into focal, segmental, multifocal and generalised myoclonus.[5 6] Myoclonus is not necessarily pathologic as it can be seen in physiologic conditions as well. Physiological myoclonus is seen during sleep and during the transition of sleep phases, called hypnic jerks.[5] Pathological myoclonus is seen in the context of epileptic disorders, neurodegenerative disorders, mitochondrial disorders, congenital disorders, cerebrovascular disorders, autoimmune disorders, metabolic disorders, acute and chronic posthypoxic states, para infectious and postinfectious states.[5]

Postinfectious generalised myoclonus is described in the literature in the context of various viral infections such as chickenpox, Nipah, influenza and HIV and some bacterial infections like group-A streptococcus, leptospira and mycoplasma pneumonia infections.[7–9] However, generalised myoclonus is rarely reported after the COVID-19 infection. Anand and colleague describe eight critically ill, intubated, COVID-19-infected patients with generalised myoclonus.[9] Another case series by Rábano and colleagues describes three cases of isolated generalised myoclonus after COVID-19 infection.[10]

Most patients described in the above case reports had some concurrent respiratory symptoms. In contrast, our patient presented with isolated generalised myoclonus few days after resolution of respiratory symptoms. Of note, our patient did not have any other neurological sequelae such as seizures, altered mentation or focal neurological deficits. This complication occurred in the absence of any evidence of encephalitis, anoxic brain injury, prolonged severe hypoxia, administration of sedative medications, metabolic abnormality or any neurological comorbidity; all of which are potential causes or triggers for generalised myoclonus.

It is unclear why this patient developed generalised myoclonus in the absence of significant clinical and investigative evidence of any CNS infection as MRI brain and CSF studies were nonrevealing. Historically, postinfectious generalised myoclonus has been thought to occur due to immune-mediated phenomenon, however, the exact immunopathological mechanism leading to myoclonus remains unknown.[11] Considering a delayed onset of symptoms, slow resolution of symptoms after giving steroid (dexamethasone) and supportive treatment, we also believe that it may have some immune-mediated origin. Nevertheless, further studies are needed to determine the exact pathophysiology of the complication.

There are no specific diagnostic modalities for generalised myoclonus associated with COVID-19 infection, and it is imperative to exclude alternative aetiologies such as seizures, encephalitis, anoxic brain injury, metabolic derangements and other neurologic abnormalities. There are no standard guidelines for treatment either, and treatment has been individualised based on clinical presentation and comorbidities. Antiseizure medications like valproic acid, levetiracetam and lorazepam with or without immune therapy such as steroids have been tried with variable outcomes.[8–11] Our patient received dexamethasone and levetiracetam and showed complete resolution of symptoms at 2 months follow-up. These patients may require long-term rehabilitation, as in our case, hence, expectations should be discussed with patients and families to prevent anxiety about the prolonged duration of symptoms.

Learning points

- Generalised myoclonus can occur as a delayed complication of COVID-19 infection.
- The diagnosis is clinical, and there are no specific diagnostic modalities for this condition. It is imperative to rule out an alternative diagnosis.
- Treatment is supportive and individualised in different clinical settings; antiepileptic medications such as levetiracetam, valproic acid, benzodiazepines with or without corticosteroids have been used in the treatment with variable outcomes.
- The recovery may take weeks to months and requires prolonged rehabilitation; hence, expectations should be discussed with patients and families at the time of diagnosis.

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