Epileptiform activity and seizures in patients with COVID-19

INTRODUCTION

Acute symptomatic seizures have been reported in sporadic cases in patients with COVID-19.[1 2] However, a recent large retrospective cohort study suggested that there was no increased risk of acute symptomatic seizures in these patients.[3] As such, the association of seizures with COVID-19 has not been established. Admittedly, EEG studies have been significantly underused due to exposure concerns, and epileptiform activity has seldom been identified in this patient population. The aims of this study were to determine the prevalence of epileptiform activity and to assess the risk of seizures in patients with COVID-19.

METHODS

We retrospectively reviewed consecutive patients with COVID-19 from 1 March to 27 May 2020 in a single institution. Patients were included if they were (1) ≥18 years of age, (2) positive for nasal swab SARS-CoV-2 RNA qualitative PCR test and (3) underwent EEG monitoring. Patients with a prior active diagnosis of epilepsy were excluded. Patient data regarding demographics, medical history, neuroimaging, laboratory tests, complications, mortality, metabolic profiles and treatment were extracted from electronic medical records. COVID-19 disease severity was categorised according to WHO guideline into (1) non-severe: absence of viral pneumonia or hypoxia, or clinical signs of pneumonia but SpO_2 of >90% on room air; (2) severe: clinical pneumonia, respiratory rate of >30 and SpO_2 of <90% on room air; (3) critical: sepsis with organ dysfunction or requiring mechanical ventilation.

EEG studies were performed using standard international 10–20 system plus supplementary subtemporal electrodes (F9, T9, M1, F10, T10 and M2); in three cases, early in the pandemic, a limited montage consisting of eight channels was used. Two experienced epileptologists (FSdL and JT) visually interpreted the archived EEG recordings with differences resolved by consensus. EEG patterns, including ictal–interictal continuum patterns and interictal and ictal discharges, were determined.

RESULTS

Between 1 March and 27 May 2020 in the University of Chicago Hospital, routine or continuous video–EEG monitoring was performed in 38 patients with COVID-19. After excluding six patients who carried a prior diagnosis of epilepsy, data from 32 patients with COVID-19 were included in this study. The mean age was 61.9±17.8 years (mean±SD, range 18–91 years). Fourteen patients were female. With regard to the COVID-19 disease severity, 10 patients were non-severe; six were severe; and 16 were critical. Seven of 32 patients were intubated and sedated. Acute symptomatic seizures were observed clinically in 4 of 32 (12.5%) patients. Nine patients were treated with antiseizure medications. Six patients died during the admission, whereas 26 patients recovered. Older patients who were intubated with severe encephalopathy were more likely to die.

Indications for EEG studies included evaluation of unexplained encephalopathy and suspicion of seizures. Normal EEG background frequencies (8–10 Hz) were observed in six (18.8%) patients. Diffuse background slowing was observed in 26 (81.3%) patients, including mild (7–8 Hz) in 5 patients, moderate (6–7 Hz) in 4 patients and severe (≤6 Hz) in 17 patients. Focal slowing was observed in four patients. Ictal–interictal continuum patterns were observed in 8 (25%) patients, including generalised periodic discharges with or without triphasic morphology in six patients and lateralised periodic discharges in two patients. Focal interictal epileptiform discharges were observed in six (18.8%) patients, and electrographic seizures were recorded in three (9.4%) patients. Eight EEG studies were routine (1 hour) and 24 were continuous (4–144 hours).

Of the four patients with acute symptomatic seizures, patient 1 was a 36-year-old women with Dandy-Walker malformation. She was admitted for convulsive seizures and status epilepticus. A head CT did not reveal acute changes. Video–EEG monitoring showed sharp waves and frequent runs of epileptiform discharges lasting 3–7 s in the right frontocentral regions. She was treated with levetiracetam and valproic acid and recovered. Patient 2 was an elderly patient with Alzheimer's disease and diabetes mellitus, admitted for frequent body myoclonic jerks. Video–EEG monitoring showed frequent sharp waves and seven seizures in the right frontoparietocentral regions lasting 1–3 min. Brain MRI showed diffuse atrophy without acute changes. The patient was treated with levetiracetam and subsequently died during the admission. Patient 3 was a 43-year-old woman with sickle cell disease, admitted after a convulsive seizure. Video–EEG monitoring showed sharp waves and seizures in the right posterior temporo-occipital regions (figure 1). She progressed to status epilepticus with a total of 54 seizures. SARS-CoV-2 PCR tests on cerebrospinal fluid (CSF) were negative. Brain MRI showed extensive areas of T2 hyperintensity in bilateral hemispheres. She was treated with levetiracetam and lacosamide and recovered without focal neurological deficits. Patient 4 was a 52-year-old man with atrial fibrillation, hypertension, anaemia and liver cirrhosis. He was admitted after falling at home with body shaking. A head CT showed an acute subdural haematoma in the right hemisphere that was subsequently evacuated. An extended EEG monitoring showed marked diffuse encephalopathy without interictal or ictal epileptiform abnormalities. He recovered and was discharged on levetiracetam. All four patients were intubated and sedated with propofol during their hospitalisation.

DISCUSSION

That 18.8% of patients studied with EEG in the study period had interictal and ictal EEG patterns highlights the risk of seizures in patients with COVID-19, and is in line with the findings of Galanopoulou and colleagues.[4] The potential aetiologies of acute symptomatic seizures in patients with COVID-19 are likely heterogeneous, including hypoxaemia, metabolic derangements, stroke, infection and autoimmune responses.[1 3] One patient had extensive areas of T2 hyperintensity with minimal diffusion restriction, suggestive of encephalitis. Similar findings have been reported in a patient with COVID-19 with T2 hyperintensity in the temporal lobe.[1] Since SARS-CoV-2 RNA has rarely been identified in the CSF,[5] encephalitis-like patterns on MRI and associated seizures may be secondary to an inflammatory response rather than direct viral infection. In conclusion, there is a substantial risk of acute symptomatic seizures in patients with COVID-19. In patients with suspicious signs of

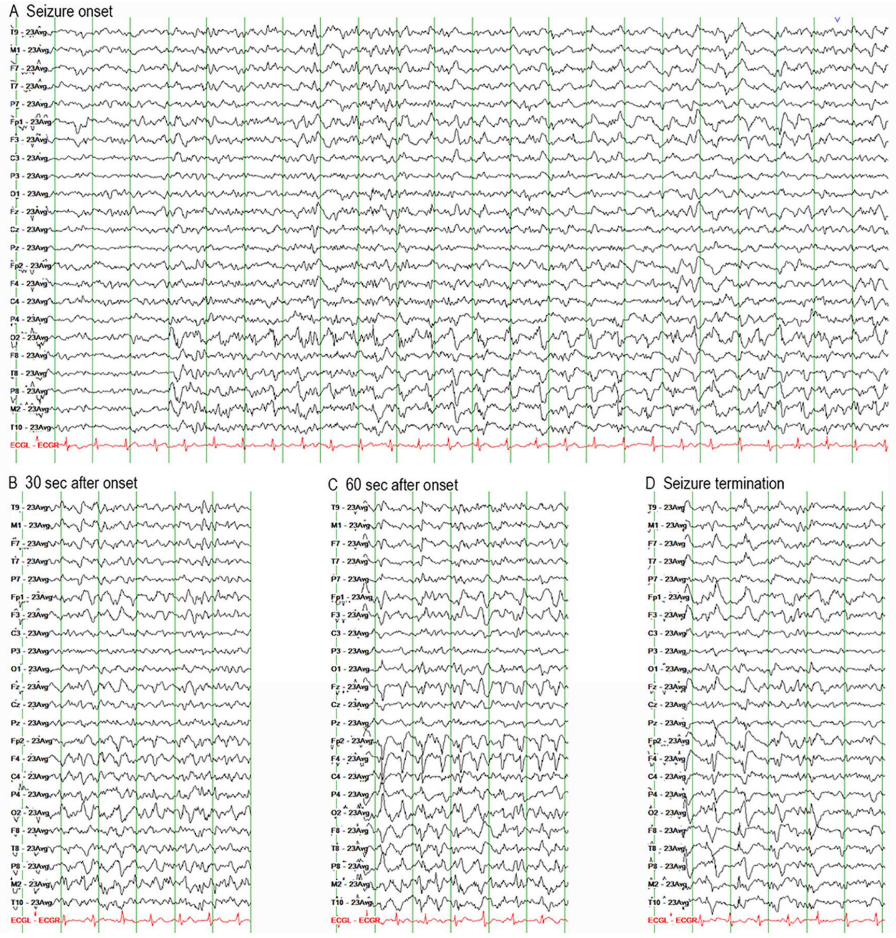

Figure 1 A right posterior temporo-occipital seizure with rhythmic ictal discharges on electrodes M2, P8 and O2 at the onset with spatiotemporal evolution over the right temporal and frontal regions correlating clinically with staring, eye blinking and left hand. High-pass filter, 1 Hz; low-pass filter, 50 Hz; sensitivity: 10 µV/mm.

seizures and unexplained encephalopathy, continuous EEG monitoring might be beneficial for the early diagnosis and treatment of non-convulsive seizures and status epilepticus, and may potentially improve the clinical outcomes.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval The study was approved by the University of Chicago Institutional Review Board (IRB20-1004).

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Santos de Lima F, Issa N, Seibert K, *et al*. *J Neurol Neurosurg Psychiatry* 2021;**92**:565–566.

Received 2 July 2020
Revised 23 September 2020
Accepted 14 October 2020
Published Online First 6 November 2020

J Neurol Neurosurg Psychiatry 2021;**92**:565–566.
doi:10.1136/jnnp-2020-324337

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