# Atypical COVID-19-associated Non-convulsive Status Epilepticus Case

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Status epilepticus is a neurological emergency requiring immediate evaluation and management to prevent significant morbidity or mortality. Previously, status epilepticus was defined as a seizure with a duration equal to or greater than 30 minutes or a series of seizures in which the patient does not regain normal mental status between seizures. The Neurocritical Care Society guidelines from 2012 revised the definition to a seizure with 5 minutes or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures.

Status epilepticus may be convulsive, non-convulsive, focal motor, or myoclonic, and can become refractory. Convulsive status epilepticus consists of generalized tonic-clonic movements and mental status impairment. Non-convulsive status epilepticus is defined as seizure activity identified on an electroencephalogram with no accompanying tonic-clonic movements. Focal motor status epilepticus involves the refractory motor activity of a limb or a group of muscles on one side of the body with or without loss of consciousness. Refractory status epilepticus refers to continuing seizures (convulsive or non-convulsive) despite appropriate antiepileptic drugs [1].

## PATIENT DESCRIPTION

An 88-year-old male, whose co-morbidities included diabetes mellitus type 2, hypertension, and hypercholesterolemia, was admitted to the emergency department due to a confusional state that began one day prior to admission. A cervical vertebral fracture at the level of C2 occurred 4 days prior to presentation due to head trauma. He was treated conservatively with a neck brace. He had no prior history of seizures and had not been treated with antiaggregants or anticoagulants.

Relatives reported that he was not oriented to time and place and repeated the same questions. During his stay in the emergency department, the patient abruptly stopped communicating and a stroke code was declared.

During a neurological examination, the patient did not open his eyes in response to painful stimuli, did not vocalize at all, and did not obey commands. His only response to painful stimulus was grimacing. He had gaze deviation to the left and grasped a pole at the bed side firmly with his left arm. His left leg was firmly in dorsiflexion and his right leg had increased tone. There was a positive Babinski sign on the left, but on the right there was no plantar reaction.

Suspecting non-convulsive status epilepticus, the patient was administered 10 mg of diazepam (Assival®) IV, with resolution of the pole-grasping and the dorsiflexion in his left leg. The patient was then rushed to the computed tomography (CT) facility to complete a head and neck CT, perfusion, and angiography, which were unremarkable for any acute findings. No space occupying lesions or cortical encephalomalacia, which would precipitate epileptic activity, were found. Following the imaging, the patient's oxygen saturation in room air lowered to 80%, and he was put on oxygen supplementation with a reservoir mask. He was unresponsive to pain and still had gaze deviation to the left. He was then administered 2400 mg of valproic acid IV, after which automatisms were observed manifesting as repeated bilateral hand movements in the air resembling the action of pulling down his pants. The gaze deviation to the left was still maintained. Consequently, he was administered 1000 mg of levetiracetam IV.

On further examination, the automatisms ceased, the patient firmly closed his eyelids, vocalized incoherently, and withdrew his limbs in response to painful stimuli. The increased tone in the right leg was maintained, and the patient shifted repeatedly from side to side in the bed, resembling an encephalopathic state, which was maintained until the following day.

A positive coronavirus disease 2019 (COVID-19) test was detected. The blood work demonstrated decreased white blood cell count of 3.88 K with a decreased absolute lymphocyte count of 0.65 and an elevated C-reactive protein of 3.45 mg/dl. There were no significant electrolyte disturbances. Creatine phosphokinase was not measured. A lumbar puncture was performed to rule out a co-existing central nervous system infection; however, the tap was traumatic and no relevant information was

yielded besides negative HSV-1 HSV-2 and enterovirus polymerase chain reaction (PCR) tests.

The patient was admitted to the COVID-19 ward where a repeat lumbar puncture was performed, which yielded 0 white blood cell count and 3900 red blood cell count. Glucose was slightly elevated at 91 and cerebrospinal fluid (CSF) protein was elevated at 78 (15–45 normal range). Furthermore, parechovirus PCR was negative and west Nile virus immunoglobulin M was negative. Interleukin 6 was 38 (normal range 0–7).

## COMMENT

Status epilepticus manifestation may vary widely and may be hard to discern when presenting as non-convulsive status epilepticus (NCSE). The evidence for causality of status epilepticus by the COVID-19 virus is lacking, and to the best of our knowledge, no significant evidence has been published to ascertain increased incidence of status epilepticus during the COVID-19 pandemic [2,3]. However, it has been suggested that lack of electroencephalogram recordings of COVID-19 positive patients [4] due to isolation measures may cause under-diagnosis of NCSE and obfuscate the incidence of NCSE in COVID-19 positive patients. Furthermore, a meta-analysis conducted in 2022 demonstrated increased incidence of seizures as the presenting feature of epileptic patients with COVID-19 [5].

Several mechanisms have been suggested as a cause of seizures in COVID-19 positive patients, including direct invasion of the central nervous system (CNS), cytokine storm, microglial activation, mitochondrial dysfunction, and breakdown of the blood–brain barrier.

Our patient presented with his first seizure at the age of 88 years as NCSE during an acute COVID-19 infection; however, he experienced significant head trauma 4 days prior to his current admission to the emergency department. Traumatic brain injury could have contributed to his susceptibility to developing NCSE. Further differential diagnosis for his NCSE included a hyperacute minor ischemic cortical stroke, which would not have been visible in perfusion CT and post-concussive seizure. Other precipitants of seizures, which were ruled out in this patient, included space occupying lesion (e.g., meningioma) and a metabolic condition (e.g., hyponatremia, hypoglycemia).

## CONCLUSIONS

The CSF was unremarkable for signs of CNS infection. The elevated protein count was attributed to the patient's diabetes mellitus, spinal stenosis, and the number of red blood cells. During his stay in the COVID-19 ward, his consciousness improved. He opened his eyes to painful stimuli, vocalized incoherently, and obeyed simple commands.

This patient's NCSE cannot be positively attributed solely to COVID-19 infection due to his recent concussion; however, encephalopathic states secondary to this viral infection are well documented, suggesting a significant effect on the CNS, direct or indirect.

Once sufficient immunity is developed in the population, whether natural or due to more efficient vaccinations, isolation measures could be eased and additional information on the manifestations, complications, and sequelae of COVID-19 infection should emerge due to increased accessibility to non-critical diagnostics, which were avoided to curb the pandemic.

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Capsule

## Sparking T cell response

The mitochondrial electron transport chain (ETC) is required for T cell immune responses to antigens. **Mangalhara** and colleagues explored whether modulating the mitochondrial ETC could influence cancer growth and tumor. Increasing electron flow through mitochondrial complex I elevated succinate levels and led to transcriptional and epigenetic activation of major histocompatability complex class I (MHC-I) and antigen presentation and processing genes. Induction of MHC-I occurred independently of the cytokine interferongamma and resulted in potent T cell responses to melanoma, suggesting an approach for improving tumor immunogenicity.

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