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NEW ONSET SEIZURES EVOLVING INTO REFRACTORY STATUS EPILEPTICUS IN THE SETTING OF COVID-19: A CASE REPORT

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ABSTRACT

The novel Coronavirus disease (COVID-19) has been shown to involve the nervous system (both central and peripheral), with or without respiratory involvement in multiple ways. Although not much is known about this disease yet, seizures and status epilepticus which may evolve into refractory status epilepticus have been associated with it along with other manifestations like encephalopathy, neuropathies etc. The mechanism for development of seizures with COVID-19 related disease is not entirely known however it can be the consequence of "cytokine release syndrome" or "cytokine storm" which has been associated with this virus. Patients with COVID-19 infection who develop resistant status epilepticus may have increased morbidity hence early recognition and starting appropriate therapy are key to avoid possible poor outcomes. Here, we present a case of a patient with new onset seizures that rapidly progressed to refractory status epilepticus in the context of COVID-19 infection. Our case report highlights the need of testing for systemic viral infections like SARS-CoV-2 in refractory status epilepticus and using therapies like corticosteroids and IVIG that have shown a role in COVID-19 induced seizures and encephalitis.

Keywords

Covid-19, NORSE, SARS-CoV-2 infection, Encephalitis

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has presented an array of clinical challenges, including an evolving understanding of its impact on the nervous system.[1] Neurological manifestations associated with COVID-19 have garnered increasing attention, with reports of various central nervous system complications emerging.[2] These include (but are not limited to) encephalopathy, cerebrovascular diseases and seizures.[3] Seizures have emerged as a noteworthy neurological manifestation, warranting detailed investigation. New onset refractory status epilepticus (NORSE) is diagnosed when a patient who is not a known epileptic, has no structural neurologic disorder or any toxic or metabolic abnormality, develops refractory status epilepticus.[4] This case report aims to shed light on a distinctive presentation of COVID-19-related neurological involvement—specifically, the rapid evolution of new onset seizures into refractory status epilepticus. We present a comprehensive analysis of a patient who exhibited this unusual progression, emphasizing the diagnostic challenges, clinical management strategies, and potential mechanisms underlying such neurological complications in the context of COVID-19.[2,3]

CASE PRESENTATION

A young male with no known co-morbid conditions was admitted in Hospital with complains of fever, nausea and vomiting for one week, drowsiness for two days and two episodes of generalized tonic clonic seizures half an hour apart about five hours prior to presentation. There was no history of febrile seizure, previous history of seizure or no family history of seizures. On examination, he was drowsy but arousable and agitated, not following commands. No signs of meningeal irritation were noted and remaining examination was non-focal. Initial blood work-up including CBC, serum electrolytes, renal and liver function tests along with coagulation profile were all within normal limits. Inflammatory markers were also normal. Work-up for infection including Blood cultures, urine detailed report, urine culture, malaria and dengue serology and chest Xray were negative for any source of infection. However, his SARS-CoV-2 Antigen came out to be positive.

MRI brain with GAD with MRA and MRV showed gyral thickening in the bilateral frontal lobes without abnormal post contrast enhancement (Figure 1). Workup for viral, bacterial and autoimmune encephalitis work-up in CSF was negative. During hospital stay, initial treatment with anti-epileptics were given, the patient continued to have seizures intermittently so he was subsequently intubated and shifted to ICU, continuous EEG monitoring was done for eight days and anti-epileptics were escalated during that time.

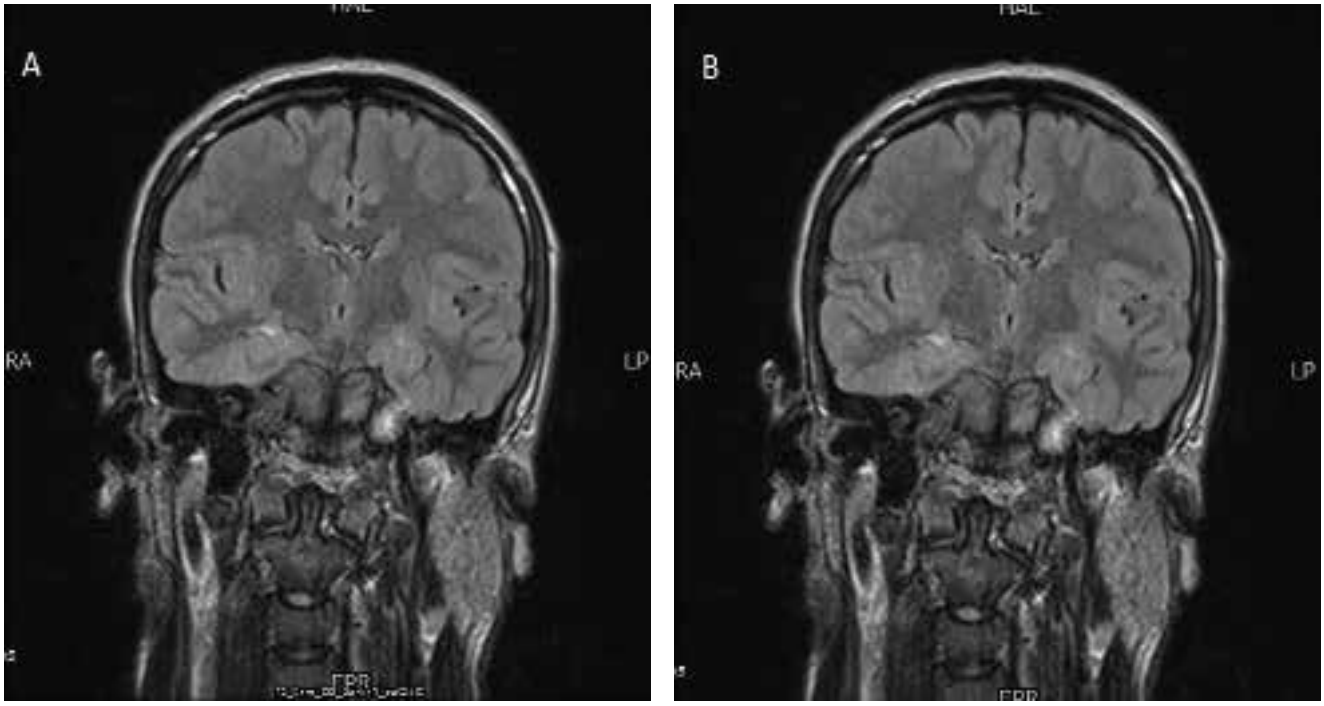

Figure 1
Coronal FLAIR (FIG. A) and post-contrast (FIG. B) showed gyral thickening in the bilateral frontal lobes without abnormal post contrast enhancement.

Despite being on multiple anti-epileptics including levetiracetam, valproate, lacosamide, topiramate, phenytoin and lorazapam, the patient continued to seize electrographically so he was given a trial of high-dose IV Methylprednisolone (1000mg) for five days followed by five doses of Intravenous Immunoglobulins (total 2g/kg bodyweight). His Interleukin-6 levels were elevated (36.9 pg/ml; normal: <7pg/ml). MRI Brain (Figure 2) and CSF studies were repeated and were within normal limits. Once burst suppression was achieved on EEG, sedation and anti-epileptics were gradually tapered. Ventilatory support was weaned off after 33 days with a tracheostomy in place.

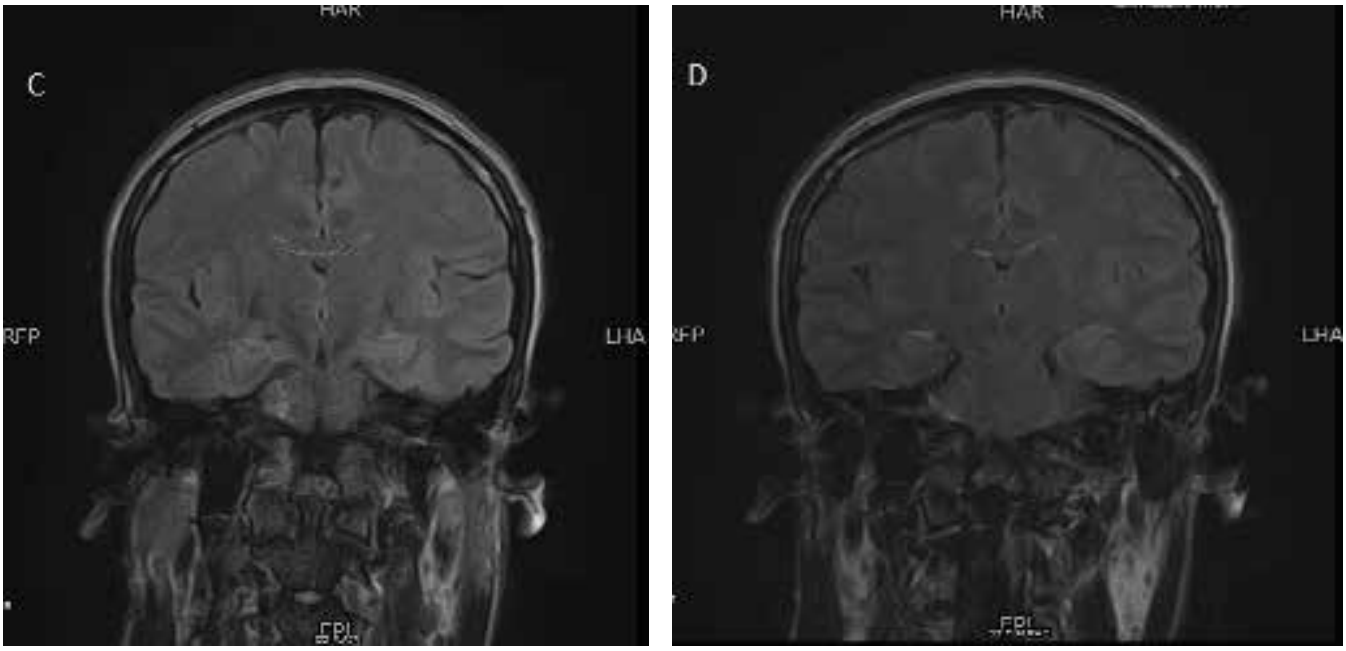

Figure 2: Coronal FLAIR (fig. C) and post-contrast (fig. D) showed interval resolution of previously identified gyral thickening involving the bilateral frontal lobes.

DISCUSSION

Since its advent, COVID-19 virus has been linked to multiple systemic complications apart from the respiratory symptoms. Neurological complications of this virus, both central and peripheral exist in various forms and can be debilitating.[1] The mechanisms underlying these neurological complications remain unclear and continue to be a subject of intense research. It is hypothesized that viral entry into the CNS, either via trans-synaptic spread or breach of the blood-brain barrier, could explain the neurological symptoms. Additionally, factors like hypoxia, vascular damage, and immune-mediated injury are believed to play significant roles in the pathogenesis of COVID-19-related neurological sequelae.[5]

Seizures and status epilepticus are recognized complications of COVID-19 infection.[3] According to Narula et al., there are three primary mechanisms that might explain the occurrence of seizures in COVID-19 patients: (1) direct viral invasion of the CNS, (2) an indirect mechanism where the cytokine storm leads to organ damage, hypoxia, and hypoperfusion, and (3) exacerbation of pre-existing epilepsy.[6,7] Such mechanisms are consistent with the case we present, where refractory status epilepticus (NORSE) occurred without obvious lung involvement, suggesting the possibility of direct or indirect immune-mediated effects of the virus.

A common cause for NORSE is autoimmune encephalitis. Of these, N-methyl-D-aspartate receptor (NMDA) encephalitis that may be a post-viral sequel with viral infections like Herpes Simplex Virus are amongst the most frequent. Refractory status epilepticus secondary to NMDA encephalitis have been recently reported in COVID-19 patients without lung involvement (similar to our patient). In our case, the patient's CSF studies were negative for any detectable autoimmune antibodies (including NMDA) however the response seen after initiation of IVIG hints to some aspect of immune mediated response.[8]

The COVID-19-related cytokine storm, particularly elevated levels of interleukin-6 (IL-6), has been postulated as a major contributor to the development of NORSE in our case. Treatment for NORSE should be initiated promptly given its high mortality rate (10-20%). Early intervention with immunosuppressive therapies such as steroids, IVIG, and plasma exchange is critical. In our patient, the response to IVIG, and possibly steroids, further emphasizes the immune-mediated nature of the disorder. Additional second-line therapies, such as Anakinra, Rituximab, or Cyclophosphamide, may also be considered, as well as alternative therapies like ketogenic diets or therapeutic hypothermia.[5]

CONCLUSION

NORSE is a rare but potentially devastating complication of COVID-19 infection that can result in permanent neuronal injury if not treated promptly and appropriately. This case highlights the importance of clinicians being vigilant in recognizing the signs of NORSE in the setting of COVID-19, even in the absence of significant pulmonary symptoms and the need for multidisciplinary care. Managing NORSE often requires a coordinated effort involving neurologists, intensivists, and other specialists to optimize care and improve prognosis. Early intervention with immunosuppressive therapies can significantly improve outcomes and should be considered as part of the treatment protocol for COVID-19-related NORSE.

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Mahira Mushtaq; concept, case management, manuscript writing
Zuha Amin; case management, manuscript writing
Shafaq Saleem: case management, manuscript writing
Fowzia Siddiqui; case management, manuscript revision

All the authors have approved the final version of the article and agree to be accountable for all aspects of the work.