Immune Responsive NORSE in a Patient with COVID 19 Infection

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Abstract:
We report a case of new onset refractory status epilepticus (NORSE) in an adult patient with acute COVID infection who was ventilated for long with continuous fits and finally responded dramatically to Immunoglobulin therapy.

Keywords: NORSE, COVID 19, Immunoglobulin therapy

Introduction
There is a broad range of neurologic manifestation which are reported with Covid 19 infection. The central nervous system complication can range from non specific manifestations to encephalitis, myelitis, necrotising encephalopathy, endothelitis and stroke. One of the mechanism for the neurovirulence of Corona virus is related to the virus' ability to induce proinflamatory cytokines and resultant hyperimmune response.

Case report
A young lady with no premorbid illness, was diagnosed as Covid-19 by PCR of nasal swab when she presented with cough and mild fever. She was home quarantined. 2 days later she developed sudden onset tonic posturing of both upper and lower limbs with uprolling of eyes. She was brought to emergency deparment where she had multiple episodes of fits. She was given diazepam and loading dose phenytoin. She was started empirically on ceftriaxone and acyclovir in meningitic dose along with dexamethasone. Since she was continuing to have seizures she was intubated. Simultaneously she was being given parenteral sodium valproate and Levetiracetam. After the patient was mechanically ventilated she was started on midazolam infusion. Lumbar puncture was done on same day. CSF (cerebrospinal fluid) was normal, less than 5 cells/mm$^3$, protein of 15 mg/dl, CSF gram stain was negative, no growth in CSF culture and CSF viral panel was negative. CT brain was normal. She was continuing to have subtle seizures. On second day she had recurrent seizures with twitching of face and mild clonic movements of hands. She was started on phenobarbital infusion on third day and continued on oral phenobarbitone. Still she continued to have subtle seizures. She was subsequently given propafol and thiopentone without much benefit. Her CT brain and CT
venogram of brain was normal. Her MRI brain could not be done at the time since she had to be shifted out to nearby facility which was not possible considering the critical situation and continuous seizure. She continued to have seizures with multiple medications. She was started on ketamine also on day 10. Her CSF study was repeated after 4 days of admission which was also normal. Initially she was given ceftriaxone and acyclovir for 5 days. It was discontinued when repeat CSF also came as normal. She was given dexamethasone 6 mg once daily for the initial 10 days. She was deteriorating and could not be weaned from ventilator. So she was tracheostomised.

Since the patient attendant was not willing for auto immune work up, it was not done. As there was no clinical improvement regarding patient sensorium and seizure, we planned to give trial of immunoglobulin. She was given intravenous immunoglobulin at 0.4 g/kg for 5 days from day 10 of admission. After 2 days of starting of immunoglobulin no more seizures were noted. Her anaesthetic medications were tapered and stopped. She gradually regained consciousness and on fifth day of immunoglobulin she was opening eyes and moving all limbs to painful stimuli. She became fully conscious and began to obey commands after 5 more days. There was no further seizures. Her tracheostomy wound was closed later. 15 days after immunoglobulin infusion she was discharged from hospital. She was conscious, conversing normally and there was no focal neurologic deficit. Her antiseizure drugs were tapered. At the time of discharge she was on carbamazepine 600 mg, Levetiracetam 3000 mg and Clonazepam 2 mg. Also she was on prednisolone 20 mg daily. She had few episodes of focal seizures when she missed her medication. Her EEG done after she recovered showed only occasional theta slowing of background. No epileptiform activity was present. MRI brain showed flair hyperintensities in cortical areas - right parasagittal and right anterior temporal cortex.

Discussion

Central Nervous System (CNS) manifestations of SARS CoV 2 are diverse. Other than stroke, the COVID can present as acute necrotising encephalopathy, encephalitis, Acute Demyelinating Encephalomyelopathy (ADEM), endothelitis like involvement, Toxic/Wernicke like encephalopathy. Mechanisms of CNS damage can be direct viral injury, inflammatory mediated injury, thrombotic injury, hypoxia mediated injury and encephalopathy of critically ill [1,3].

NORSE is a condition defined as the occurrence of refractory status epilepticus in patients without active epilepsy and without a clear acute or active structural, toxic or metabolic cause. The most frequently identified cause of NORSE is autoimmune encephalitis [2]. Antibodies against NMDA receptor or voltage gated potassium channels are the most common antibodies identified in an adult [4]. Early treatment is recommended for NORSE due to autoimmune encephalitis as delay can lead to irreversible neurological sequelae.

In our patient although though we cannot rule out a direct infectious mechanism of SARS CoV 2, since the CSF parameters are normal, this is unlikely. There has been a few case reports of NORSE associated with COVID. Our patient was deteriorating daily but once initiated with IVIG she showed dramatic improvement. This case report highlights the importance of early initiation of IV immunoglobulin in suspected immune mediated NORSE related to Covid to prevent irreversible neuronal damage. If infectious, structural and metabolic causes of NORSE are excluded by appropriate investigations, patient should be initiated on immunoglobulin.

Conclusion

The main implication is that physicians should be aware of the Covid -19 infection presenting
as encephalitis or as refractory epilepsy due to activation of inflammatory pathways and early initiation of treatment is critical to avoid neurologic sequelae.

References


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