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**Case Report**

# COVID-19 associated meningoencephalitis or a neuropsychiatric manifestation of systemic lupus erythematosus-a diagnostic dilemma

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## ABSTRACT

The infection with SARS-CoV-2 is associated with fever and respiratory symptoms but is not limited to respiratory system only. Since its appearance, several neurological symptoms have been reported, most commonly headache and anosmia, as well as less frequent complications such as COVID-19-associated encephalitis and meningitis. In this case report, we report a 40-year-old female recently infected with SARS-CoV-2, who presented with history of high-grade fever, cough, breathlessness 12 days back followed by altered sensorium and restlessness. The patient was also found to have underlying systemic lupus erythematosus which surfaced post-COVID-19 infection. Cerebrospinal fluid (CSF) analysis was done and the patient received IVIG therapy and showed dramatic improvement. SARS-CoV-2 has been implicated in development of autoimmune diseases.

**Keywords:** Systemic lupus erythematosus, Post COVID-19, Meningoencephalitis, IVIG

## INTRODUCTION

Coronavirus disease 19 (COVID-19) is a respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The spectrum of clinical manifestations is broad, ranging from asymptomatic subclinical infection to acute respiratory distress syndrome and respiratory failure.[1]

COVID-19 also effects other systems, including the nervous system. The neurological manifestations of SARS-CoV-2 vary from central and peripheral nervous system manifestations, like headache, myalgias, and impaired consciousness, and also encephalopathy, skeletal muscle injury, acute polyradiculoneuropathy, acute cerebrovascular events, meningitis, encephalitis, and encephalomyelitis. The rate of neurological involvement is higher in severe cases of SARS-CoV-2 infections.[2,3]

The mechanism of neurological involvement in COVID-19 is not well described, although some authors reported detection of SARS-CoV-2 RNA in CSF and brain tissue.[4,5] Post COVID meningoencephalitis is a rare entity with very few cases report published yet.

## CASE REPORT

A 40 years old lady, with a known case of hypertension for the last 4 years and type 2 diabetes mellitus for 2 years, was alright 12 days before admission when she developed high-grade fever, cough, and shortness of breath for which she took symptomatic treatment and steroids at home for 10 days. This was followed by the development of altered sensorium, restlessness, disorientation to time, place, and person, and high-grade fever 3 days before admission. On the development of altered sensorium, she was admitted to a hospital outside. There, an NCCT brain scan was done which was normal**.** Since she was not improving later, an MRI brain was done which was suggestive of meningitis with no obvious focal intra-cerebral lesion. EEG was also done which showed diffuse cerebral dysfunction. A lumbar puncture was performed which showed clear CSF, raised protein, and sugars 256.2 mg/dl and 76.9 mg/dl respectively with

normal cell counts and negative culture. COVID-RTPCR was negative. ESR was also raised to 84 mm/hr. CSF for AFB and MTB X-pert was negative. CSF meningitis and encephalitis panel were negative. The patient received injection ceftriaxone, clarithromycin, and acyclovir empirically. As patient was not improving on this initial treatment, she was referred to us for further evaluation and management.

On presentation, the patient was conscious but disoriented to time, place, and person and was restless. On general examination, she had tachycardia (108/min) and tachypnoea (36/min), her BP was 126/80 mmHg and her temperature was normal, oxygen saturation was 93 percent on room air and pallor was present. On CNS examination patient had a GCS of 9/15 (E2V2M5). Neck stiffness was present. Kernig and Brudzinski were negative. Plantar B/L flexor, power, sensory, and coordination could not be assessed. Respiratory examination showed bilateral basal crepitations. Other systems were well within normal limits. She underwent a repeat CSF examination, which showed CSF cell counts 69 (lymphocytic 100%), and CSF protein was raised to 275 mg/dl. Her CSF HSV (herpes simplex virus) PCR, VZV (varicella zoster virus) PCR, MTB gene expert, crypto-la antigen was all negative. Her other infective diseases and fever work up including all routine cultures, COVID RT PCR and zoonotic diseases was negative.

She was started on I/V antibiotics (ceftriaxone) was continued, injection dexamethasone 4 mg twice daily, and other supportive treatment. Her investigation showed (Table 1).

**Table 1: CSF and initial investigation.**

| Variables | Results |
|---|---|
| **CSF Fluid** | Clear |
| **CSF protein** | 275 mg/dl |
| **CSF glucose** | 76.9 mg/dl |
| **CSF counts** | 69 (100% lymphocytes) |
| **CSF culture** | Negative |
| **CSF MTB gene X-pert, AFB, ADA** | Negative |
| **Hb/TLC/ platelet** | 10 gm/dl/ 11,000/µl/ 131000/µl |
| **ESR/CRP** | 85 mm/hr/ 12 mg/dl |
| **LFT/KFT** | Normal |
| **Ferritin** | 736 ng/ml |
| **D-DIMER** | 2.12 µ/ml |
| **CSF PCR panel encephalitis** | Negative |
| **CSF autoimmune encephalitis panel** | Negative |
| **CSF COVID antibodies** | Positive |

An HRCT chest was done which (Figure 1) revealed ground glass opacities in bilateral lower lobes suggesting a recent COVID-19 infection.

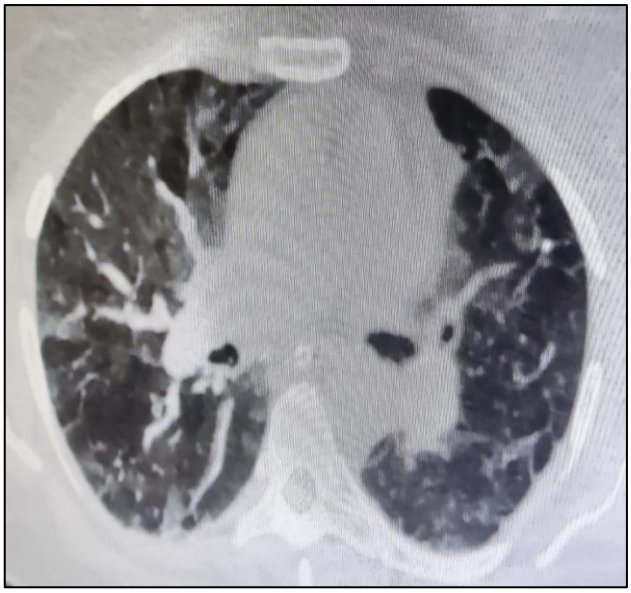

**Figure 1: HRCT chest showing bilateral ground glass opacities in lung fields.**

Since attendants also gave a history of photosensitive rash on and off, joint pains, and excessive hair fall, hence autoimmune panel was done which came out to be positive (Table 2). And the possibility of SLE was considered which got unmasked likely post-COVID-19. However, the cause of meningoencephalitis remained a dilemma as COVID-19-associated meningoencephalitis and SLE both could have been a likely aetiology. Hence autoimmune encephalitis panel was sent which came out to be negative.

**Table 2: Autoimmune panel.**

| Variables | Results |
|---|---|
| **ANA-IF** | positive (2+) |
| **ANA profile 3** | Ribosomal-P-protein+++, AMA-M2+, Sm+ |
| **C3, C4 levels** | Low (C3 – 147mg/L, C4-40 mg/L) |
| **Anti ds-DNA** | Positive |
| **DAT** | 2+ |
| **Urine routine** | Normal |

She was started on IVIG at 2 gm/kg (total of 120 mg in 3 days) and the dexamethasone dose increased to 4mg thrice daily. Ceftriaxone was continued and acyclovir was stopped.

Within 2 days, her altered sensorium progressively improved; she was oriented to time, place, and person, able to communicate, and was following commands. She was shifted out of ICU in a couple of days. Seven days later her repeat CSF analysis was done which came out normal (cell count of 3 (100% lymphocyte), protein 44 mg/dl, albumin 23 mg/dl, glucose 75 mg/dl, and ADA was 2.35 IU/L), AFB and gene X-pert for MTB negative. However, COVID total antibodies were still positive. A

repeat MRI brain was also normal. NCV study was done suggestive of sensory and motor demyelinating with axonal polyneuropathy involving bilateral lower limbs more than upper limbs. Her repeat EEG was suggestive of mild to moderate encephalopathy. The patient was started on physiotherapy. Her lower limb weakness improved within days and was soon discharged. This patient on follow-up is doing fine, with the SLE in remission.

## DISCUSSION

Neurotropism is one common feature of coronaviruses. The involvement of the nervous system can be due to a direct action of these viruses on the nervous tissue and/or to an indirect action through the activation of immune-mediated mechanisms. COVID-19 can have a pure neurological presentation and, on some occasions, precede the typical respiratory manifestations.[6] Besides, a myriad of neurological consequences following typical clinical presentation of COVID-19 has also been documented across the globe. There have been cases seen where active COVID-19 infection has shown meningoencephalitis and other neurological problems but this is the first case where meningoencephalitis is probably associated with post covid infection. Recognition of neurological disease associated with SARS-CoV-2 in patients whose respiratory infection is mild or asymptomatic proves challenging, especially if the primary COVID-19 illness has occurred weeks earlier.

Various neurological symptoms were reported in meningoencephalitis associated with SARS-CoV-2 infection. Confusion or disorientation to time and place or altered mental status was the most frequently reported symptom accounting for 22.22% of the cases.[7] This observation was also seen with our patient. It may therefore be assumed that in places reporting a high incidence of COVID-19, confusion or disorientation may prompt investigation for detection of SARS-CoV-2. While the classic Kernig's and Brudzinski's signs were not frequently documented, nuchal rigidity has been more commonly (9.25%) observed in COVID-associated meningoencephalitis, also a similar finding to our case.[7]

CSF parameters in COVID-19-associated meningoencephalitis had increased protein and lymphocyte count as the most notable observation.[7] Also, a finding was seen in post-COVID meningoencephalitis. A positive antibody test can help support a post-COVID diagnosis when patients present with complications of COVID-19 illness, such as multisystem inflammatory syndrome (with raised inflammatory markers) and other post-acute sequelae of COVID-19.

Our case report also has an underlying autoimmune SLE. Meningoencephalitis can be associated with SLE probably due to recent COVID status, immunological criteria, history, the results of CSF examination, and the response to steroid and IVIG, supporting the diagnosis. Infectious diseases have long been considered one of the triggers for autoimmune diseases, mainly via molecular mimicry. Probably SLE got unmasked by a recent COVID-19 infection in this patient. However, meningitis is a very rare CNS manifestation, observed in only 1.4-2.0% of patients with SLE.[8] While guidelines remain unclear, IVIg has potential benefits in the treatment of COVID-19-associated meningoencephalitis and neuropsychiatric manifestations of SLE.[9]

Though covid associated meningoencephalitis has a very much similar presentation as post covid meningoencephalitis. But note has to be taken on the delayed onset of symptoms and no active COVID infection in the former to differentiate the two. However, IVIG and steroid management showed favorable outcomes.

## CONCLUSION

Meningoencephalitis can be suspected even in post-COVID-19 infective patients not necessarily in active COVID patients and workup for autoimmune diseases should be done. COVID-19 can trigger unmasked autoimmune disorders and suspicion of autoimmune disorders should be kept in mind in such patients.

The importance of considering lupus and COVID-19's impact on the central nervous system (CNS) and IVIG may be of potential benefit.

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