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Post-infectious SARS-CoV-2 autoimmune encephalitis associated with N-type calcium channel antibodies

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ABSTRACT

Objective: To report the association between SARS-CoV-2 and Anti-N-Type Calcium Channel antibody positive, EEG and MRI-negative encephalitis with a treatment response to plasmapheresis.

Background: Postinfectious SARS-CoV-2 neuropsychiatric complications are common but the pathogenesis and response to treatment remains poorly understood.

Case: We report a case of autoimmune encephalitis with subacute onset after SARS-CoV-2 infection with positive cerebrospinal fluid serology for Anti-N-Type-Calcium Channel antibodies. CSF profile showed cytoalbuminologic dissociation (CSF WBC 4, Protein 88). MRI and EEG were normal. Plasmapheresis resulted in significant improvement and resolution of cognitive and neuropsychiatric manifestations.

Conclusion: Anti-N-Type-Calcium Channel antibody encephalitis should be considered in patients who develop new neuropsychiatric symptoms after SARS-CoV-2 infection even in absence of positive EEG and MRI findings.

Introduction

SARS-CoV-2 post-infectious autoimmune encephalitis is an evolving condition that has been associated with anti-NMDA receptor, anti-GD1b and anti-Caspr2 antibodies (Guilmot et al., 2021). Psychosis can be the presenting symptom for autoimmune encephalitis no abnormalities on EEG and MRI. Autoimmune encephalitis is treatable but underrecognized, particularly in the post-infectious state of SARS-CoV-2. We report plasmapheresis-responsive postinfectious autoimmune encephalitis after SARS-CoV-2 with anti-N-type calcium channel antibodies in the cerebrospinal fluid (CSF).

Case presentation

A 56-year-old Hispanic male with a history of end-stage renal disease, diabetes and hypertension presented for new-onset cognitive decline and hallucinations two months after severe SARS-CoV-2 infection. One week prior to admission, the patient’s family reported non-sensical speech, visual and auditory hallucinations and getting lost. History from the patient and family was negative for prior neurological, cognitive, or psychiatric disorders. On admission, vital signs and physical exam were normal. The patient was alert but disoriented to time, date, year, or place. He could not register or recall three words after five minutes and could not perform simple calculations. Speech was tangential. Cranial nerve exam was normal except for prior vision loss bilaterally. Spontaneous myoclonus was seen diffusely. Motor exam was normal; deep tendon reflexes and Babinski sign were normal. Complete blood counts, metabolic panel, thyroid stimulating hormone and urinalysis were normal. SARS-CoV-2 polymerase chain reaction, HIV, hepatitis panel, Rapid plasma regain, and urine toxology screen were normal. CT of the head was normal. Chest X-ray showed moderate right pleural effusion with atelectasis.

The patient was started on ceftriaxone and azithromycin for treatment of community acquired pneumonia. Electroencephalogram demonstrated diffuse background slowing with frequencies in the theta range, posterior dominant rhythm of 7.8 Hz, and no epileptiform discharges were observed. Brain magnetic resonance imaging with and without contrast demonstrated temporal atrophy without T2 hyperintensity, diffusion restriction, or enhancement. Lumbar puncture revealed cytoalbuminologic dissociation (CSF WBC 4, protein 88 mg/dL). The remainder of his laboratory evaluation was normal including meningoencephalitis PCR panel in CSF, B12, homocysteine, erythrocyte sedimentation rate, C-reactive protein and antinuclear antibody. The admitting and neurology consultation team were concerned about the possibility of a SARS-CoV-2 post-infectious autoimmune encephalitis. Serum and CSF autoimmune encephalitis panel was sent to the Mayo Clinic Laboratories (Encephalopathy, Autoimmune Evaluation, Serum and CSF 2). After three days without improvement on antibiotics, he was started on plasmapheresis daily for five days. After 5 days of plasmapheresis, the patient was fully oriented, and no longer reported auditory or visual hallucinations. Given his significant cognitive improvement and medical stability, the patient was discharged home with family.

At the one-month hospital follow-up appointment, autoimmune panel returned positive for N-type calcium channel antibodies.
(0.24 nmol/L, normal 0.03). At one-month follow-up, mental status exam remained normal. All hallucinations, behavioral abnormalities and myoclonus resolved. Outpatient screening for neoplasm including a prostate specific antigen, fecal occult blood test was unremarkable.

**Discussion**

N-type calcium channel antibody positive autoimmune encephalitis has not previously been described as a sequela of SARS-CoV-2. The presentation, time course, response to plasmapheresis, and absence of prior psychiatric history is consistent with autoimmune encephalitis (Graus et al., 2016). Anti-N-type calcium channel autoimmune encephalitis commonly present with psychotic symptoms (paranoia, hallucinations) and cognitive decline. Each reported case responded well to immunosuppressive therapy in the form of either high dose corticosteroids, plasmapheresis, or Intravenous immunoglobulin (Thakolwiboon et al., 2020; Kornitzer et al., 2019; Simutis et al., 2020).

Understanding of the full spectrum of neuropsychiatric complications of SARS-CoV-2 is still in progress. Symptoms may be secondary to SARS-CoV-2 activation of immune mediated processes and IL-6 mediated cytokine storm (Boldrini et al., 2021). Similar to other infections, patients can develop new neuropsychiatric complications after infection due to autoimmune encephalitis (Galeotti and Bayry, 2020). Patients at risk for autoimmune encephalitis after SARS-CoV-2 may benefit from empiric immunomodulatory therapy including plasmapheresis. At the earliest state of clinical suspicion, both serum and CSF should be sent for autoantibody testing. However, treatment initiation should not await antibody characterization confirmation labs (Graus et al., 2016).

Multiple case reports of suspected and confirmed autoimmune encephalitis associated with SARS-CoV-2 have been reported since the outbreak of the pandemic. Anti-NMDA receptor, anti-GD1b, and anti-Caspr2 autoantibody associated encephalitis has been documented (Guilmot et al., 2021). Similar to non-SARS-CoV-2-associated autoimmune encephalitis, a specific autoantibody is not identified in all cases, despite successful treatment with empiric immunosuppressive treatment or symptomatic management alone (Guilmot et al., 2021).

This case report expands on the emerging literature of postinfectious SARS-CoV-2 immune mediated neuropsychiatric complications. We identified previously undescribed N-type calcium channel antibody in the CSF of a postinfectious SARS-CoV-2 patient who responded fully to plasmapheresis. Clinicians should consider screening and immune-based treatment for autoimmune encephalopathies presenting after SARS-CoV-2 infection.

**Data availability statement**

We confirm that Drs. Torrico, DeGiorgio, and Kerr have full access to all the patient information and the right to publish any and all data separate from any sponsor. Anonymized data not published within this article will be made available by request from any qualified investigator.

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**Declaration of Competing Interest**

None.

**Authorship**

All authors contributed to writing the manuscript.

**Research ethics and informed consent**

Our local IRB and ethical standards committee does not review case reports as they are observational reports only. The patient consented to permission for publication and this is on file by request.

**Consent to disclose**

Written informed consent-to-disclose from the patient was obtained.

**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neurep.2021.100039.

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