SVOA Neurology

ISSN: 2753-9180

ScienceVolks Open Access

Case Series

A 22-Year-Old Woman with NMDA Receptor Antibody Encephalitis Possibly Triggered by SARS-CoV-2 Infection

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DOI: https://doi.org/10.58624/SVOANE.2024.05.0128

***Received:** January 11, 2024* ***Published:** January 30, 2024*

Abstract

A 22-year-old woman presented to the emergency department (ED) on two occasions with seizures, altered mental status, psychoses, and behavioral changes. Analysis of both serum and cerebrospinal fluid revealed positive anti-NMDA receptor (NMDAR) antibodies, confirming the diagnosis of NMDAR antibody encephalitis. Interestingly, 5-6 weeks before her ED visits, she had experienced a SARS-CoV-2 infection, potentially serving as a triggering factor for her autoimmune encephalitis. This case adds to the limited instances documented in the literature, highlighting the potential link between SARS-CoV-2 infection and the onset of autoimmune encephalitis.

***Keywords:** NMDA receptor antibody; Autoimmune encephalitis; SARS-CoV-2*

Introduction

In recent years, autoimmune encephalitis has gained increasing recognition and attention within the medical community. The reported incidence is approximately 0.8 per 100,000, with a prevalence of around 13.7 per 100,000 (1). Among recognized cases of autoimmune encephalitis, anti-NMDAR encephalitis is a rare disorder with the estimated incidence of 1.5 per million population per year (2).

Since the onset of Covid-19 pandemic, a handful of cases were reported suggesting a potential association between SARS-CoV-2 infection and autoimmune encephalitis (3). However, the reported cases are limited in number, highlighting the imperative for comprehensive, high-quality studies to deepen our understanding of this relationship. In this context, the author presents a case involving a 22-year-old woman diagnosed with anti-NMDAR encephalitis, possibly triggered by SARS-CoV-2 infection. Timely diagnosis and treatment are pivotal for a more favorable prognosis.

Case Presentation

This 22 –year-old right handed woman initially presented to emergency department (ED) because seizures. She was making strange noise on the phone with her sister. Family members noted that her arms raised and she was posturing. She had jaw-clenching, followed by shaking, foaming at the mouth which lasted about 2-3 minutes in duration. She then had post-ictal drowsiness, confusion and combative behavior. In the ED, she had second event. She was noted to have a tonic-clonic seizure lasting 90 seconds in duration, accompanied by tongue biting. Lorazepam 1 mg and Levetiracetam 1,500 mg were administered in ER. She had post-ictal sleepiness and confusion.

Her past medical history included syncope twice (2 years ago, related to dehydration and taking cough medication). Interestingly. 5-6 weeks prior to the ED visit, she had Covid-19 which was confirmed by RT-PCR for positive SARS-CoV-2, which recovered within a week. No past surgical history was present. Family history was negative for neurological diseases. She only took multivitamins.

She studied in a community college. She did not smoke; no alcohol or recreational drugs were used. She had no known allergies.

In ED, neurological examination showed no neurological focal deficit other than drowsiness. Drug screen was negative; complete blood counts, comprehensive metabolic panel and urine analysis were normal. Her head CT was normal. She was admitted to the hospital. Initial MRI brain showed 3 punctate foci of T2/FLAIR hyperintense signal in the bilateral frontal subcortical white matter which were entirely nonspecific. EEG was normal. She was discharged in hospital day 3 with maintenance dose of Levetiracetam 500mg twice daily.

She was back to normal for one day after discharge. On the second day she was brought to the ED again because she was confused, forgot people's name and saw people who were not there. She had mainly visual hallucinations. She speaks sentences that did not make much sense. Family said patient has had a lot of stresses lately. She was admitted to the hospital again. Her vital signs showed mild sinus tachycardia (Pulse:110). Neurological examination revealed that she was alert but only intermittently oriented to person, place, time and she was able to state president's name, but unable to determine situation without reorientation. Paranoid delusions were noted. Other neurological examinations were unremarkable.

Because of possible behavioral side effects, Levetiracetam was stopped, and switched to Lacosamide 100mg twice daily and subsequently Valproic Acid 500mg q8hr was added. Valproic Acid was stopped later due to side effects.

Head CT was again normal. Repeated MRI brain showed no acute changes, again noted were punctate foci of T2 prolongation noted throughout the subcortical white matter, nonspecific in etiology. No pathological enhancement was present. Right cerebellar developmental venous anomaly and mild cerebellar tonsillar ectopia were noted.

Continuous video EEG (3 days) revealed bilateral temporal slowing (right greater than left) without epileptiform discharges or electrographic ictal discharges. CT and MRI of abdomen revealed no teratoma.

Blood tests for CBC, CMP, PT, PTT, hepatitis panel, TSH, RPR, ESR, CRP, ANA panel, ammonia, Vitamin B1, B12, lactic acid, Quantiferon TB gold, West Nile, HIV, CMV were all normal. Urine analysis was normal,

CSF obtained and showed normal protein, cells and glucose. HSV-1, HSV-2, enterovirus PCR all negative.

A few days later, the blood and CSF autoimmune encephalitis panels came back and showed presence anti-NMDAR antibodies in both serum and CSF, both with titer of 1:100 (using cell based IFA).

Empirically intravenous Methylprednisolone was started; then intravenous immunoglobulin followed. The patient showed only subtle improvement. She still has intermittent confusion, agitation, delusional thoughts "people trying to kill her" and her thoughts were disorganized.

Plasma exchange started afterwards and she was able to finish the entire session. She showed gradual improvement over weeks.

Then oral Prednisone 60mg daily started with slowly tapering down.

In the meantime, intravenous Rituximab 1000 mg was given once, then 1000mg in 2 weeks, and then every 6 months. After first dose of Rituximab was given, she still showed fluctuating symptoms and she still was not well communicative and wondered around. But no aggressive behavior was noted. So she was discharged to a rehabilitation facility.

5 months later she had follow up visit in clinic. She stated that she started feeling much better; the confusion became less and felt back to baseline for 3 months after being discharged.

She had no more seizures, no more confusion. She is back to work in a retail store; She resumed studying in college. She has some residual memory issues. Her sister noticed that she might forget excess information and trivial things.

Rituximab was continued and Prednisone was reduced to 10 mg a day and Lacosamide 100mg twice daily was continued currently.

Discussion

Over the past decade, despite the growing recognition of autoimmune encephalitis within the medical community, it remains largely underappreciated. During the Covid-19 pandemic, the incidence of autoimmune encephalitis seems rise sharply (3, 4). Some case review series suggest that SARS-CoV-2 might act as a trigger, instigating an autoimmune mechanism that leads to autoimmune encephalitis (5).

The autoimmune encephalitis may be mediated by antibodies against neuronal cell-surface/synaptic proteins or by antibodies against intracellular neuronal proteins. Anti-NMDAR encephalitis falls into the former category, characterized by antibodies against neuronal cell-surface proteins. It is a rare disorder, with an estimated incidence of 1.5 cases per million population per year (2). Therefore, clinicians must maintain vigilance for such cases when confronted with unusual presentation of encephalitis. Early identification and prompt treatment with immunosuppressant yield a better prognosis.

The symptoms in this case started 5 weeks after prior Covid-19 infection. While comprehensive data are lacking to definitively link SARS-CoV to autoimmune encephalitis, clinicians and researchers should acknowledge the need for heightened attention in this realm. Large-scale prospective studies may be essential in the future to substantiate this potential relationship. Clinicians should contribute case reports to accumulate evidence supporting this link.

In clinical practice, autoimmune encephalitis should be among the primary considerations in the differential diagnosis for patients with unexplained encephalitis to prevent multiple admissions and delays in diagnosis and treatment.

Conclusion

Autoimmune encephalitis is frequently under-recognized, underdiagnosed, and underreported. Anti-NMDAR encephalitis, being even rarer, emphasizes the importance of early treatment for improved outcomes. While a few case reports suggest a plausible association between Covid-19 infection and autoimmune encephalitis, it is crucial to recognize that more high-quality studies are needed to substantiate this possibility.

Conflict of Interest

The author declare no conflict of interest.

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Citation: Wang CC. A 22-Year-Old Woman with NMDA Receptor Antibody Encephalitis Possibly Triggered by SARS-CoV-2 Infection. Literature Review. *SVOA Neurology* 2024, 5:1, 61-63.