

Case Report

Autoimmune Encephalitis with Bipolar Disorder, Seizures, and Peripartum Symptom Fluctuation Associated with Serum-Positive, Cerebrospinal Fluid-Negative Contactin-Associated Protein-Like 2 Antibodies

Daren Liu; Luna Liu, BS; Yi Ding, PhD; Hongbiao Liu, MD, PhD*

Luna Medical Care, Amherst, NY

A case of a 47-year-old woman with a history of autoimmune encephalitis, bipolar disorder, and seizures, whose symptoms improved during pregnancy and worsened in the postpartum period. She was found to have serum-positive, cerebrospinal fluid (CSF)-negative contactin-associated protein-like 2 (CASPR2) antibodies. This case is unique due to the presence of serum-positive immune markers and negative CSF findings, despite clinical symptoms that were exclusively referable to central nervous system (CNS) involvement, with less evidence of peripheral nervous system pathology. The patient's neuropsychiatric symptoms and seizures responded to intravenous immunoglobulin (IVIG) and corticosteroid therapy. This report highlights the importance of considering autoimmune encephalitis in patients with neuropsychiatric comorbidities and CNS symptoms, even when immune markers are detected only in serum. Additionally, it underscores the modulatory and neuroprotective roles of sex hormones in autoimmune encephalitis, as evidenced by symptom improvement during pregnancy and exacerbation postpartum. [NAJ Med Sci. 2026;19(1):001-003. DOI: 10.7156/najms.2026.1901001]

Key Words: *Autoimmune Encephalitis, Contactin-Associated Protein-like 2 Antibodies, Central Nervous System, Sex Hormones, Neuropsychiatric Symptoms*

INTRODUCTION

Autoimmune encephalitis associated with contactin-associated protein-like 2 (CASPR2) antibodies is a rare, increasingly recognized disorder that causes neuropsychiatric symptoms, seizures, and cognitive dysfunction. The clinical spectrum ranges from limbic encephalitis to peripheral nerve hyperexcitability syndromes, including Morvan syndrome. Diagnosis relies on detecting contactin-associated protein-like 2 (CASPR2) antibodies in serum or cerebrospinal fluid (CSF), often with immunoglobulin G4 (IgG4) predominance, and is supported by magnetic resonance imaging (MRI) and electroencephalogram (EEG) findings. Sex hormones, especially during pregnancy and the postpartum period, modulate disease activity: pregnancy's high estrogen and progesterone levels promote immune tolerance and reduce inflammation, while postpartum hormonal withdrawal increases pro-inflammatory cytokines and relapse risk. Immunotherapy including corticosteroids, intravenous

immunoglobulin (IVIG), plasma exchange, and rituximab is effective, and early treatment improves outcomes.

CASE PRESENTATION

A 47-year-old woman with a complex medical history including obesity, chronic pain syndrome, anxiety, depression, post-traumatic stress disorder, bipolar disorder, and autoimmune encephalitis presented after two witnessed generalized seizure episodes at home. She had a longstanding history of absence seizures dating back to early adulthood and was amnesic to the recent events. The seizures occurred following a physical assault, which she identified as the inciting factor and after which she reported a subjective flare of her encephalitis symptoms. Her autoimmune encephalitis was previously characterized by CASPR2 antibody positivity in serum with negative cerebrospinal fluid testing.

Her neurological and psychiatric history was notable for chronic absence seizures with recent escalation to generalized tonic-clonic events, longstanding bipolar disorder, depression, anxiety, PTSD, and chronic pain. She also had chronic slurred

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*Corresponding Author: Luna Medical Care, Amherst, NY 14228.
(Email: hl75@buffalo.edu)

speech at baseline. A distinctive feature of her history was marked improvement in both neurological and psychiatric symptoms during each of her six pregnancies, followed by significant worsening in the postpartum period.

At the time of admission, her home medications included lamotrigine, baclofen, gabapentin, oxycodone, hydromorphone (Dilaudid), duloxetine, alprazolam, propranolol, and a proton pump inhibitor. In the emergency department, she received acute management with lorazepam, hydromorphone, morphine, baclofen, gabapentin, propranolol, and lamotrigine.

During her hospital course, she completed a five-day course of intravenous immunoglobulin and a five-day course of intravenous methylprednisolone, followed by a prednisone taper, for management of autoimmune encephalitis. Her lamotrigine dose was increased for seizure control. Electroencephalography demonstrated mild encephalopathy without epileptiform discharges. Brain MRI revealed stable, nonspecific T2 FLAIR hyperintensity, while MRI of the lumbar spine showed moderate central canal stenosis with degenerative changes. Her hospitalization was complicated by the development of urinary retention, which required Foley catheter placement. Laboratory evaluation was notable only for persistent CASPR2 antibody positivity in serum, with otherwise unremarkable results.

She was ultimately discharged to a subacute rehabilitation facility with plans for outpatient neurology follow-up and weight management care.

DISCUSSION

Autoimmune encephalitis associated with CASPR2 antibodies presents a complex clinical spectrum, often involving both central and peripheral nervous system manifestations. While CNS involvement is typically supported by the presence of antibodies in the CSF, serum-only positivity does not exclude CNS disease, especially when clinical features such as seizures, encephalopathy, and neuropsychiatric symptoms are prominent.^{1,2} This case highlights the importance of integrating clinical, serological, and neuroimaging data for accurate diagnosis.

Neuropsychiatric comorbidities, including mood disorders and psychosis, are well documented in autoimmune encephalitis and may overlap with primary psychiatric disorders such as bipolar disorder.³ Seizures are a hallmark of autoimmune encephalitis and are often refractory to standard antiepileptic therapy until immunotherapy is initiated.

A key feature in this case is the fluctuation of symptoms during the peripartum period, with marked improvement during pregnancy and significant worsening postpartum. This pattern is consistent with the immunomodulatory and neuroprotective **effects of sex hormones, particularly estrogens and progesterone.**^{4,5} During pregnancy, high levels of these hormones shift the immune system toward tolerance, reducing autoimmune activity and improving neurological symptoms.

Postpartum, the rapid withdrawal of these hormones increases pro inflammatory cytokines, potentially triggering autoimmune flares and worsening neurological symptoms.^{4,6}

Sex hormones exert neuroprotective effects through several mechanisms. Estrogens reduce neuroinflammation by suppressing microglial activation and pro inflammatory cytokines (eg, TNF α , IL 1 β , IL 6), enhance antioxidant defenses, and promote neuronal survival and synaptic plasticity via estrogen receptors in the CNS.^{6,7} Progesterone reduces neuroinflammation and oxidative stress, promotes myelination and neuronal survival, and modulates GABAergic neurotransmission, providing anticonvulsant effects.^{5,6} Androgens support neuronal growth and modulate immune responses, reducing pro inflammatory cytokine production.^{4,6}

The differential effects of estrogen receptor (ER) α and ER β ligand treatment have been shown to provide distinct neuroprotective and anti-inflammatory benefits, further supporting the therapeutic potential of targeting specific hormone pathways in neuroimmune disorders.⁷ These findings are corroborated by studies from Voskuhl and colleagues, which highlight the role of sex hormones in modulating neuroinflammation and immune responses in neurodegenerative and autoimmune diseases.^{7,8}

Immunotherapy with IVIG and corticosteroids remains the mainstay of treatment for CASPR2 antibody-associated encephalitis, with most patients responding to early intervention.^{1,2} The patient's improvement with IVIG and steroids supports the diagnosis of autoimmune CNS disease, despite the absence of CSF antibody positivity.

CONCLUSION

This case underscores the importance of integrating clinical, serological, and neuroimaging data in the diagnosis and management of autoimmune encephalitis. Serum-positive, CSF-negative CASPR2 antibodies do not exclude CNS involvement, particularly in patients with neuropsychiatric symptoms and seizures. The modulatory effects of sex hormones during pregnancy and postpartum should be considered in the disease course. Sex hormones provide neuroprotection and immune modulation through multiple mechanisms, including reducing neuroinflammation, oxidative stress, and autoantibody production. Hormonal fluctuations during pregnancy and postpartum significantly influence autoimmune encephalitis activity, explaining symptom improvement during pregnancy and worsening postpartum. Targeting sex hormone pathways may offer novel therapeutic strategies for neuroimmune disorders.

CONFLICTS OF INTEREST

None.

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