“She Needs to Die”: Seronegative Autoimmune Encephalitis after COVID-19 Infection Presenting as Homicidal Ideation

Todd M. Stollenwerk, PhD, and Ana Navarro-Montoya, MD
Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

Introduction

- Autoimmune encephalitis is an immune-mediated disorder characterized by neuroinflammation and neuropsychiatric symptoms secondary to antibodies against neuronal cell surface proteins, ion channels, or receptors[1].
- Growing evidence suggests that COVID-19 infection can cause autoimmune encephalitis[2].
- We describe a previously unreported case of seronegative autoimmune encephalitis following COVID-19 infection manifesting as homicidal ideation in the context of delusions.

Case Presentation

A 25-year-old male presents to the ED for new-onset homicidal ideation directed towards his mother. He endorses delusions that his mother has been replaced by an imposter and needs to be crucified. He has had ongoing bizarre and grandiose delusions as well as auditory and visual hallucinations with impaired functioning for the past 11 months, beginning after COVID-19 infection.

2 years — **COVID-19** infection → psychosis for 3-5 days

11 months — Suspected **COVID-19** infection → paranoia, self-isolation, headache, hypersomnolence (18-20 hours/day), disorientation, visual hallucinations

9 months — Eloped from moving car, **violent** towards mother, became **unresponsive** to external stimuli with eyes open, arm **posturing**

7 months — **Lumbar puncture** for CSF studies → incidental improvement in symptoms for several days

6 months — **Indomethacin** for gout flare → incidental improvement

Lumbar puncture (opening pressure 20.2) → more conversational, emotionally appropriate, resolution of headache

5 months — Seen by optometrist – mild **papilledema**

2 months — **Ventriculoperitoneal shunt** placement (opening pressure 32) → improvement in symptoms for several days

Presentation — Brought to ED for **homicidal ideation** towards mother

Past Medical and Psychiatric History

12 y/o	13 y/o	14 y/o	15 y/o	16 y/o	17 y/o	18 y/o
TBI (bike) Emotions/smell 6 months	ADHD diagnosis	Narcolepsy with cataplexy, vivid dreams, and hypnopompic hallucinations	3 Psych Admissions (psychosis, SI, OD)	Auditory hallucinations and paranoia Aripiprazole (effective)		Prader-Willi syndrome Clinically diagnosed

Medications at Presentation

Acetazolamide 500 mg BID
Atomoxetine 100 mg QAM
Buspirone 10 mg TID
Risperidone 1.5 mg QHS
Sodium oxybate 5 g twice nightly
Solriamfetol 75 mg QD
Venlafaxine 37.5 mg QAM + 150 mg QHS

Imaging and Laboratory Studies

CSF Studies (7 months prior to presentation):
- Autoimmune encephalitis panel: negative
- Protein 29 (15-45 mg/dL)
- IgG 1.7 (≤8.1 mg/dL)
- Oligoclonal bands: negative

Serum autoimmune encephalitis panel (7 months prior): negative

ALT: **70 U/L**
AST: **45 U/L**
ESR: 10 mm/hr
CRP: **0.94 mg/dL**

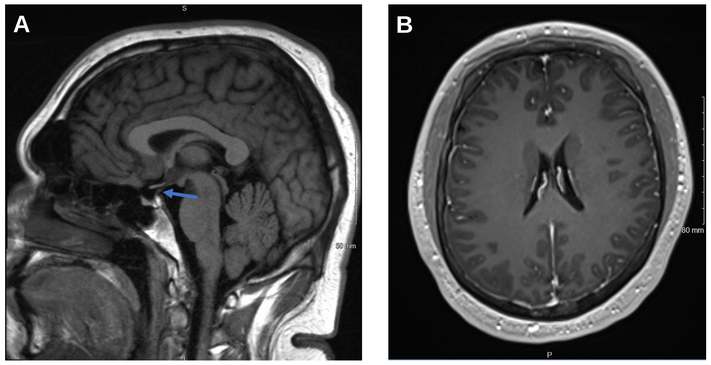

Figure 1. Brain MRI from 7 months prior. (A) Sagittal T1 FLAIR showing partially empty sella. (B) Axial enhanced 3D T1 FLAIR

Mental Status Exam

Orientation: fluctuating from fully oriented to oriented only to person

Thought process: illogical and tangential with flight of ideas

Thought content: paranoid and grandiose delusions based on video game and movie references regarding needing to find artifacts and crucify his mother. Endorses history of auditory and visual hallucinations; endorsed visual hallucinations on one occasion. Denied SI. Endorsing HI in the context of delusional need to crucify mother

Attention/Concentration: fluctuating between intact and impaired

Executive function: concrete, impaired abstraction

Studies and Interventions

- VP shunt interrogated and found to be patent
- CT head unremarkable with normal ventricles
- Continuous video EEG showed generalized slowing of the background with no epileptiform discharges nor seizures
- Olanzapine 10 mg → no response
- Indomethacin 50 mg TID for 4 days → mild improvement
- IV methylprednisolone 500 mg BID → stopped after 4 doses for behavioral concerns
- Intravenous immunoglobulin (IVIG) for 5 days → significant improvement in symptoms
- Patient discharged
- Psychotic symptoms recurred after 3.5 weeks but resolved with additional treatment of IVIG.
- Patient continues to receive IVIG infusions every 3 weeks with significant improvement.

Discussion

- The resolution of psychotic symptoms following IVIG treatment suggests a diagnosis of seronegative autoimmune encephalitis.
- Aspects of this case that implicate autoimmune encephalitis even in the absence of diagnostic laboratory findings include the temporal correlation between infection and symptom onset, elevated intracranial pressures, response to indomethacin, and abnormal findings on EEG.
- Previously undescribed autoimmune antibodies may be responsible for some cases of autoimmune encephalitis following COVID-19 infection.

References

[1]Dalmau J, Geis C, Graus F. Autoantibodies to Synaptic Receptors and Neuronal Cell Surface Proteins in Autoimmune Diseases of the Central Nervous System. *Physiol Rev*. 2017;97(2):839-887. doi:10.1152/physrev.00010.2016.

[2]Nabizadeh F, Balabandian M, Sodeifian F, Rezaei N, Rostami MR, Naser Moghadasi A. Autoimmune encephalitis associated with COVID-19: A systematic review. *Mult Scler Relat Disord*. 2022;62:103795. doi:10.1016/j.msard.2022.103795