A challenging diagnosis of anti-NMDA receptor encephalitis in an adolescent male: a case series

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INTRODUCTION

Anti-NMDA receptor encephalitis is an autoimmune encephalopathy first described in 2005 in young women with ovarian teratomas. Despite increasing literature and data, psychiatric symptoms in the adolescent population have not been clearly elucidated. We present a case with diagnostic and treatment challenges in an adolescent male with anti-NMDA receptor encephalitis.

CASE

Our patient is a previously healthy 16-year-old male who presented with an episode of "blackout", confusion, anxiety, insomnia, auditory and visual hallucinations for past 6-8 weeks. These episodes manifested with purposeless bizarre behaviors such as laughing inappropriately, non-speech oral movements, pinching and gesturing in air. Progressively, these episodes became more frequent, bizarre, and violent in which he would often throw or kick around furniture. They started occurring one or two times in a week, with each lasting 24-36 hours.

Neuro-imaging, EEG, and CSF were done for infectious and autoimmune workup. Initial MRI brain was unremarkable. Lumbar puncture and initial CSF analysis revealed eight no signs of an infectious etiology. 24 hour continuous EEG monitoring captured behavioral episodes, changes in mental status, and abnormal motor movements without the presence of correlating epileptiform activity. His workup for autoimmune etiology and malignancies revealed no abnormalities.

Throughout his hospital stay, he had multiple episodes of agitation and aggression often requiring chemical and physical restraints. The majority of these episodes occurred during nighttime with accompanying insomnia. He also exhibited inappropriate behavior with hypersexuality.

The CSF immunofluorescence assay eventually came back with NMDA-R autoantibodies in serum and CSF. Patient was treated with 5 cycles of plasmapheresis and a course of rituximab as well as oxcarbazepine for seizure prophylaxis and quetiapine for psychosis. His condition improved substantially in the week following plasmapheresis.

In follow-up appointments, he has been symptom-free, and his mother reports that he is almost back to his normal self. He has been sleeping well and is back to his normal work schedule.

FIGURES AND MEDIA

Figure 1: Timeline and symptoms

Figure 2: EEG

Lab	Result	Normal range
CSF Glucose	66	60-82 mg/dL
CSF Protein	31	15-40 mg/dL
CSF Nucleated Cells	8	0-10
CSF RBC	0	0-5
CSF HSV 1+2 PCR	Not detected	Not detected
CSF Culture + Gram stain	Normal	Normal
TSH	0.42	0.35-4.95 uIU/mL
B12	484	211-911 pg/mL
ANA	Negative	Negative
HIV1/2 Ab + P24 Ag	Non reactive	Non reactive
Encephalitozoon Species PCR	Not detected	Not detected
CRP	0.4	<=0.50 mg/dL
ESR	6	0-15 mm/HR
Lead Blood	1	0-4 ug/dL
LDH Blood	186	140-260 U/L
AFP Blood Tumor Marker	1.2	0.0-8.3 ng/mL
HCG Beta Blood Tumor Marker	<1	<=1.0 mIU/mL
Cancer Antigen 125	5.1	0-35 U/mL

Table 1: Various Laboratory Tests during Admission

Lab	Result	Normal range
NMDA receptor Antibody, IgG	Positive Case1	Negative
Glutamic Acid Decarboxylase Antibody	0.01	<=0.02 nmol/L
Voltage-Gated Potassium Channel (VGKC) Antibody	0	<=0.02 nmol/L
GABA-B receptor Antibody	Negative	Negative
AMPA receptor Antibody	Negative	Negative
Leucine-rich Glioma-Inactivated (LGI) Protein 1 Antibody, IgG	Positive Case2	Negative
Contactin Associated Protein 2 Antibody, IgG	Positive Case3	Negative
Anti-Neuronal Nuclear Antibody Types 1-3	Negative	<1:240 titer
Amphiphysin Antibody	Negative	<1:240 titer
Purkinje Cell Cytoplasmic Antibody Types 1, 2, Tr	Negative	<1:240 titer

Table 2: Encephalopathy-Autoimmune Panel for Evaluation of CSF
Performing site: Mayo Clinic Laboratories – Rochester Main Campus

DISCUSSION

- The clinical phases of anti-NMDAR encephalitis can present with a broad range of neuro-psychiatric symptoms such as fear, agitation, aggression, insomnia, mood lability, bizarre behaviors, paranoia, grandiosity and hallucinations (Iizuka, 2008).
- In multiple studies, insomnia with irritability and agitation was an important identifying feature as the course of the disease progressed (DeSena, 2014).
- Presentation in our case is different from others in several ways: adolescent boy, sub-acute onset over 5-7 weeks, episodic nature of symptoms, poor response to antipsychotics, and no inciting event.
- Furthermore, despite the absence of a viral prodrome, the patient responded to immunotherapy. This brings into consideration a contributory role of the prodromal viral-like disorder, which by itself or in combination with a tumor sets off or enhances the autoimmune response.

CONCLUSION

- Due to the variety of symptoms anti-NMDA receptor encephalitis can present with in pediatric population and overlap with other neuropsychiatric diseases, it is difficult to discern anti-NMDA receptor encephalitis from others by the presenting symptoms.
- Recognizing the underlying organic cause of the neuropsychiatric symptoms in anti-NMDAR encephalitis is essential for prompt treatment and stabilization of the patient.
- The experience gained from the close clinical monitoring and long-term follow-up of this case has important implications for patients with atypical presentation and course.

References

- Iizuka T, Sakai F, Ide T *et al* Anti-NMDA receptor encephalitis in Japan: long-term outcome without tumor removal. *Neurology* 2008; 70: 504–511
- DeSena, Allen *et al*, "Light Switch" Mental Status Changes and Irritable Insomnia are Two Particularly Salient Features of Anti-NMDA Receptor Antibody Encephalitis *Pediatric Neurology*. 2014; 51: 151–153.