Anti-NMDA Receptor Encephalitis in an Adolescent

TK SHRUTHI, S SHUBA, PS RAJAKUMAR AND *S CHITRAMBALAM
*From Departments of Pediatrics and *Neurology, Sri Ramachandra Medical College, Chennai, Tamil Nadu, India*

Correspondence to:
Dr TK Shruthi,
Assistant Professor, Department of Pediatrics, SRMC and RI, Porur, Chennai 600 116, India.
shruthitarikere@gmail.com
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Background: Anti N-methyl-D-aspartate (NMDA) receptor encephalitis is an immune mediated disorder. **Case characteristics**: A previously healthy 14-year-old girl presenting with generalized tonic clonic seizures and altered behavior. **Observation:** In view of refractory seizures, hallucinations, psychobehavioral and catalepsy like symptoms, and CSF showing lymphocytic pleocytosis, possibility of autoimmune encephalitis was considered. Serum was positive for anti-NMDA receptor antibodies. **Outcome**: She recovered completely in six months without any sequelae. **Conclusion**: Anti-NMDA receptor encephalitis - a potentially treatable disease - should be considered in differential diagnosis of encephalitis when acute behavioral changes, seizures or dyskinesias are present.

Keywords: *Encephalitis, Catalepsy, Psychosis, Refractory seizures.*

Anti–N-methyl-D-aspartate (NMDA) receptor encephalitis is a disorder of the limbic system that largely affects children. It is often dismissed initially as a psychiatric syndrome or viral encephalitis. As this is a potentially treatable disorder, and occasionally the first indication of an underlying malignancy, prompt recognition and treatment is critical.

CASE REPORT

A previously healthy 14-yr-old girl presented to us with generalized tonic clonic seizures and altered behavior. Two weeks prior to the admission, she displayed personality changes, memory loss, psychosis and hallucinations. She was treated with antipsychotics.

On examination, she was drowsy (Glasgow coma scale 11/15), normotensive and euthermic. She was aphasic and not oriented to person, place or time but was able to localize painful stimulus. She had involuntary movements in the form of orofacial dyskinesia, pin-rolling movements, conjugate gaze and oral twitching; lead pipe rigidity and dystonia were present. Cranial nerves and fundus examination were normal. A probable diagnosis of viral encephalitis was considered and she was given empirical ceftriaxone, acyclovir, anticonvulsants and other supportive treatment.

Routine blood investigations and magnetic resonance imaging (MRI) of brain were normal. Electroencephalography (ECG) showed bilateral diffuse dysfunction. CSF examination revealed 1250 cells/hpf (polymorphs 25%, lympocytes 75%) with protein of 12 mg/dL and sugar 76 mg/dL. Polymerase chain reaction for herpes simplex virus was negative and bacterial cultures were negative. Subsequently, she developed refractory status epilepticus needing multiple antiepileptic drugs and ventilation.

In view of refractory seizures, hallucinations, psycho-behavioral and catalepsy like symptoms (mute, akinetic, unresponsive to verbal commands while keeping her eye open), and CSF showing lymphocytic pleocytosis, possibility of autoimmune encephalitis was considered. Child was treated with intravenous pulse methylprednisolone for 5 days, later changed to oral methylprednisolone. Child's serum was positive for anti-NMDA receptor antibodies but negative for anti-glutamate-receptor antibodies, GABA-B-receptor antibodies, LGi-1 antibodies and CASPR2 antibodies. Abdominal and pelvic ultrasonography done to screen for ovarian teratoma was unremarkable. Intravenous immunoglobulin (400 mg/kg/d) was administered for 5 days following which there was gradual clinical improvement. She was weaned off ventilator and antiepileptic drugs were tapered. She recovered gradually and discharged home after three months on oral steroids. At discharge parents were counseled regarding need for yearly tumor-screening. She is on regular follow-up and has recovered completely.

DISCUSSION

Anti-NMDA receptor encephalitis is a disorder mediated by antibodies to the NR1 subunit of the receptor [1]. Clinical manifestations include (*a*) prodromal phase with nonspecific symptoms like fever, headache and nausea (*b*) psychotic phase with emotional disturbances, amnesia, cognitive decline and strange behavior (*c*) unresponsive phase with catalepsy like symptoms and athetoid dystonic posturing (*d*) hyperkinetic phase with orofacial limb dyskinesia and orolingual dyskinesia and (*e*) recovery phase with gradual or complete recovery.

Diagnosis is made by characterstic clinical features, antibody to NMDA receptors in serum and/or CSF, CSF-pleocytosis, and EEG showing diffuse delta activity with paroxysmal discharge (extreme delta brush pattern) [2]. MRI brain FLAIR-sequence at presentation may be normal or it may demonstrate bilateral medial temporal lobe hyperintense signals, predominantly involving the hippocampus. First line therapy includes pulse methyl prednisolone and intravenous immunoglobulins or plasmapheresis [3]. Second line therapy includes rituximab, cyclophosphamide or both [1,3,4]. This child was treated with pulse methylprednisolone and intevenous immunoglobulins.

Anti-NMDA receptor encephalitis was originally described as a paraneoplastic syndrome, associated with ovarian teratomas containing neural tissue with antibodies cross reacting to the NMDA receptor [5]. Approximately 50% of adults and 70% of pediatric patients who presents with anti-NMDA receptor encephalitis have no identifiable tumour [1,4]. Ultrasound abdomen was normal in this child.

Armangue, *et al*. [2] in a case series of 20 pediatric patients from Spain observed more neurological and less psychiatric symptoms (67% *vs* 55%, respectively) at the onset in children less than 12 yrs, while older children had predominantly psychiatric symptoms. The child presented here had psychobehavioral symptoms followed by neurological symptoms.

Anti-NMDA receptor encephalitis is a potentially treatable disease but does not have uniformly good outcome. Recovery is usually protracted over months to years. 75% of patients may have complete or near complete recovery [1,4]. It should be considered in differential diagnosis of encephalitis when acute behavioral changes, seizures or dyskinesia are present.

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