Pediatric Neurology 50 (2014) 115–116

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Visual Diagnosis

NMDA Receptor Encephalitis: Late Treatment Also Effective

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Anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis is a severe form of encephalitis associated with antibodies against NR1-NR2 heteromers of the NMDA receptor.[1] Although more common in woman with ovarian teratomas, cases have been reported in males and females without detectable neoplasm.[1] Early treatment offers the best outcomes and often includes tumor resection and immunosuppression.[2] We describe a tumor-negative, symptomatic girl who went undiagnosed for more than 2 years before immunotherapy was begun. Her symptoms improved despite this late treatment.

A 9-year-old otherwise healthy African-American girl presented with headaches and new-onset seizures. She subsequently developed facial and extremity dyskinesias, encephalopathy with visual hallucinations, agitated behavior, and incomprehensible speech (Fig A). The patient continued to decline, ultimately developing autonomic instability with tachycardia and elevated blood pressure leading to respiratory failure and cardiac arrest requiring mechanical ventilation. Serial head magnetic resonance imaging, including fluid-attenuated inversion recovery and spectroscopy, were negative. Cerebrospinal fluid was inflammatory (leukocytes 41 per mm^3, predominantly lymphocytes; glucose 69 mg/dL; protein 21 mg/dL) but without viral antigens. Electroencephalography showed bihemispheric slowing, maximal over the right temporal region.

Extensive infectious, metabolic, and autoimmune evaluations were negative except for detection of glutamate decarboxylase 65 autoantibody in serum (0.07 nmol/L; normal range 0.00-0.02 nmol/L) but not in cerebrospinal fluid. Serum antiphospholipid antibodies were negative. Total body magnetic resonance imaging and meta-iodobenzylguanidine scintigraphy for occult malignancy were negative. Suspicion of autoimmune encephalitis prompted a 5-day course of intravenous immunoglobulin therapy (0.4 g/kg/day) and methylprednisolone (40 mg/kg/

FIGURE.
(A) Pre-treatment; 9-year-old girl presents with facial and extremity dyskinesias, acquired mutism, insomnia, and an inability to walk. (B) Post-treatment; 13-year-old girl now 2 years post-treatment is ambulatory with minimal dyskinesias. Cognitive deficits remain. (Videos accompanying these images may be viewed in the online version of the article at http://dx.doi.org/10.1016/j.pediatrneurol.2013.08.012.)

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0887-8994/$ - see front matter
http://dx.doi.org/10.1016/j.pediatrneurol.2013.08.012

day), then weekly steroids for three weeks. She did not improve and required tracheostomy.

Eighteen months later, she had not regained speech or ambulation. Spastic quadriparesis remained significant and was not responsive to botulinum toxin injections. Intermittent seizures persisted. Cerebrospinal fluid reevaluation showed oligoclonal bands and positive immunoglobulin G, immunoglobulin A antiphosphatidylserine, and immunoglobulin G anticardiolipin antibodies. Immunoglobulin G antiphosphatidlyethanolamine was found in serum. NMDA receptor antibody was not found in serum or cerebrospinal fluid. Empiric intravenous immunoglobulin (0.4 g/kg/day) and dexamethasone (15 mg daily) were started 4 days per month. She improved within 6 months, first showing more expressive speech and later normalized motor tone. She was able to speak, answer questions in short sentences, walk, run, ride a bike, read, and do simple math problems (Fig B).

A strong clinical suspicion for anti-NMDA receptor antibody prompted reanalysis of the cerebrospinal fluid obtained at the second admission, this time yielding positive results. Neuropsychological testing performed 6 months after beginning treatment revealed neuropsychological sequelae with receptive speech and verbal and performance intelligent quotients less than 70 (below 0.5%tile). At age 12, she is back in school with remediation.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.pediatrneurol.2013.08.012.

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Nine times out of ten, in the arts as well as in life, there is no truth to be discovered; there is only error to be exposed.

H. L. Mencken