

Autoimmune Encephalitis: A Case Presentation with Recurrent Febrile Seizures and Psychiatry Problems

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Abstract

Background: Autoimmune encephalitis is being diagnosed more and more often in the pediatric age group. It should be suspected in children with psychiatric symptoms, encephalopathy, abnormal movements or epileptic seizures. The most frequent autoimmune encephalitis in the pediatric is anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis.

Case report: We report a four-year-old boy with encephalitis signs and symptoms and focal tonic-clonic seizures followed by behavior disorders. CSF and MRI results were normal; but in view of EEG showing delta waves, possibility of autoimmune encephalitis was considered. Then child was treated with plasmapheresis and symptoms were disappeared.

Conclusion: Autoimmune encephalitis is a treatable disorder and there might be a negative result in patient's CSF antibody's panel of autoimmune encephalitis. Electroencephalogram validated the diagnosis in this case. Considering the fact that autoimmune encephalitis is curable disorder, we recommend that the process of treatment should be started if strong clinical suspicions exists.

Keywords: Anti-NMDAR Encephalitis, Behavior disorders, Plasmapheresis

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Background

Psychic alterations such as hallucinations, agitation, inattention, mutism, emotional lability (abnormal laughing or crying) may occur in children with neurologic origin including temporal lobe seizures, non-convulsive status epilepticus, status absence and autoimmune encephalopathies (1-3).

Autoimmune encephalitis also named immune mediated encephalitis, in which patients present with psychiatric symptoms associated with antibodies directed against ion channels, synaptic receptors, or related proteins of neuronal cells, are now well-recognized in adults and children (4). The most frequent disorders in the pediatric population are anti-N-methyl-D-aspartate (anti-NMDA)

receptor encephalitis, and limbic encephalitis, which refers to inflammation in the limbic system, including the medial temporal lobes, amygdala, and cingulate gyrus (5).

Most patients with anti-NMDAR encephalitis have a multistage illness that progresses from psychosis, memory deficits, epileptic seizures, and language disintegration into a state of coma often associated with movement disorders, dysautonomia and breathing instability. Although first described as a paraneoplastic syndrome associated with ovarian teratoma in young women, NMDAR-antibody encephalitis is increasingly recognized in children, often unassociated with tumors, less frequent than in adults, and responds to treatment but

it is reversible (5-7).

Antibodies to voltage-gated potassium channel (VGKC) complexes are often associated with limbic encephalitis, should be suspected in children with seizures, amnesia, and

medial temporal lobe inflammation. These patients do not usually have an underlying neoplasm and their response to immunotherapy is well, with remarkable and sometimes complete recovery (8).

Case Presentation

A 4-year-old boy was admitted with febrile convulsion in our center, Ali Asghar children hospital, Tehran, Iran in April 2017. His disease was presented with nonspecific upper respiratory tract infection 5 days' prior of hospitalization. He had fever (40 °c), recurrent focal tonic-clonic seizures and intermittent agitation. Anticonvulsants including phenytoin and phenobarbital was tried. A probable diagnosis of encephalitis was considered, influenza, enterovirus and herpes viridae DNA PCR tests sent and empirical treatment with acyclovir, ceftriaxone and vancomycin started. In initial tests there was leukocytosis (white blood cell=16200/ μ l with 62% polymorphonuclear cells and 35% lymphocyte. C-reactive protein was negative. Cerebrospinal fluid (CSF) examination revealed just high WBC (620 white cell/ul, 60 red cell/ul), protein 47 mg/dL and sugar 59 mg/dL). Brain MRI and electroencephalogram (EEG) were performed. EEG was minimally abnormal and brain imaging didn't show any abnormal findings.

On the second day of hospitalization, he had severe malaise and fever did not stop. Therefore, replacing antibiotics by Rifampin and Meropenem asked for the patient.

On the fourth day of hospitalization, the patient extremely had restlessness and showed signs of psychosis. He did not recognize his parents and then choreoathetosis and slurred speech developed. He was screaming loudly and signs of agitations were apparent as well. With doubt of swim flu, treatment with oseltamivir and intravenous immunoglobulin (IVIG) was started.

On the fifth day, his impatience became a little better, but had fever and diarrhea, so supportive treatment was performed. PCR results was negative for all viruses. With the psychiatry service recommendation, risperidone and clonazepam was prescribed.

On the tenth day of hospitalization the agitation increased and also he had low grade fever and tonic-colonic seizures, and became lethargic. So emergency neurology consultation was done, and second EEG showed "delta wave activities and a

probable diagnosis of autoimmune encephalitis was considered. Carbamazepine and methylprednisolone was started, IVIG continued, acyclovir discontinued and CSF sample was sent for autoimmune encephalitis panel. In spite of methyl prednisolone pulsing doses, symptoms of patients were not improved. With suspicion to the Wilson disease and vasculitis so, serum for measuring of the ceruloplasmin, copper, CANCA, PANCA, C3, C4, CH50, ANA, Anti DNA was sent. Abdominal, pelvic and testicular ultrasonography was performed for ruling out the masses and organomegaly. All results were in normal limits. Finally, with impression of autoimmune encephalopathy, plasmapheresis was begun and after third session of treatment, signs and symptoms of the patient including fever and psychological problems were dramatically diminished. Just slurred speech and movement disordered were still noticed. The patient was discharged after five sessions of plasmapheresis with a good condition. During recent year of follow up, he did not have any neuropsychiatry problem.

Discussion

Autoimmune encephalitis is a group of disorders associated with antibodies directed against the surface proteins and synaptic receptors. It has wide symptoms including seizure, behavioral changes, psychosis, catatonia and abnormal movements (9). In this case we have seizure and behavioral changes.

Some viral infections may lead to breaking immune tolerance and because antibodies enter CNS by increasing the permeability of the blood-brain barrier. Sometimes a tumor that produces antigen against neuronal cell, likely contributes in triggering the immune response. However, in many of autoimmune encephalitis disorders, the blood brain barrier is intact and the autoantibodies may be synthesized inside the CNS. The diagnosis of NMDAR encephalitic is basically perceive from NMDAR antibodies in CSF or serum, also cited that the sensitivity of antibodies in CSF is 100% (9,10). However, in our case the result of autoantibodies in his CSF was negative.

Anti-NMDA receptor encephalitis is a disorder mediated by antibodies to the NR1 subunit of the receptor (10). Since its original description 8 years ago, NMDAR- antibody encephalitis has been increasingly recognized throughout the world. Children account for 40% of all cases. The prodromal stage in children is likely to present as with some nonspecific symptoms like fever, headache and nausea and then psychotic phase starts with, behav-

ioral changes such as temper-tantrums, hyperactivity and self-injurious behavior. In children, recurrent seizures, including status epilepticus happen more than adults (7). In this study, the major symptoms include fever, tonic-clonic seizures, agitation, malaise, and lethargy.

Diagnosis of autoimmune encephalitis is made by clinical features, antibodies against NMDA receptors in serum and/or CSF, CSF- pleocytosis, and EEG showing diffuse delta activity with paroxysmal discharge (10). Although identification of antibodies in the CSF may further support pathogenicity in these children (11) in our patient, CSF antibodies panel was negative but EEG showed generalized delta waves.

Brain MRI of the patients may be normal or it may show bilateral medial temporal lobe hyperintense signals, almost involving the hippocampus in children with autoimmune encephalitis (12), in this study the child had normal MRI.

Corticosteroids, IVIG and plasma exchange are considered first line therapy for Anti-NMDA receptor encephalitis (13). Second line therapy includes rituximab, cyclophosphamide or both (13-15). Our patient had a good response to plasmapheresis.

NMDAR-antibody encephalitis is associated with ovarian teratomata in up to 60% of women aged 18 years or more. It also rarely happens in young boys as testicular teratomata (16). Therefore, our case was examined for teratomata and nothing were found.

Antibodies to voltage-gated potassium channel (VGKC) complexes are often associated with limbic encephalitis, presenting with seizures, amnesia, basal ganglia changes, focal epilepsies but usually at very low levels, and medial temporal lobe inflammation (17). In this study, our case's CSF antibodies level was negative.

Indeed, most of the children with VGKC encephalitis have normal or non-specific brain MRI findings. Likewise, our case's MRI finding was normal.

Studies about autoimmune encephalitis in Iran are rare. Tavasoli et al. (18) in a case study of 7 years old boy, autoimmune encephalitis was considered because of the refractory course and abnormal movements; but ruled out, as the CSF antibodies panel was negative and response was not seen to high dose of methylprednisolone and IVIG administration. In this study, although CSF antibodies panel was negative, patient responded to plasmapheresis.

Conclusion

The case was reported here suggest that autoimmune encephalitis can be treated with plasmapheresis. In this patient, CSF antibodies panel was negative and EEG had abnormal pattern. However, the latter is not enough to specifying autoimmune encephalitis. Despite that the patient's para-clinics do not approved autoimmune encephalitis, the process of treatment should start immediately when the signs and symptoms of patient are roughly revealed the autoimmune encephalitis. Further research with sufficient case studies are needed to make comprehensive conclusion worldwide.

Conflicts of interest: Authors declared none.

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