



BMH Med. J. 2017;4(1):38-40 **Case Report**

Autoimmune Encephalitis : A Case Report

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Abstract

Background: The etiology of encephalitis are numerous and extensive investigations for infectious agents and other causes are often negative.

Case characteristics: Five year old girl presented with abnormal / aggressive behaviour and seizures. Investigations revealed Anti-NMDAR positive encephalitis.

Outcome: The child improved with immunosuppressant; along with speech and behavioural therapy.

Message: In any child presenting with prominent psychiatric symptoms, we should rule out a possibility of autoimmune encephalitis.

Introduction

Auto immune encephalitis comprises an expanding group of clinical syndromes that can occur at all ages. These disorders are associated with antibodies against neuronal cell surface proteins and synaptic receptors involved in synaptic transmission, plasticity, or neuronal excitability [1].

Case report

Four year 8 months old female child presented with history of abnormal behavior of about 1 month duration, comprising of screaming and night mares, usually within 1-2 hours of sleep associated with urinary incontinence. She was reluctant to play with peers after the onset of symptoms and was lethargic during daytime. The child later developed one episode of focal seizures and intermittent gait abnormality (with circumduction of right foot). She had history of neonatal hypoglycemia (mother had gestational diabetes mellitus), managed in NICU and resolved within 5 days. Developmental history was normal. Examination findings were normal. MRI Brain was normal and EEG showed bilateral epileptiform dysfunction, more on left side. The child improved with antiepileptics and was sent home. One week later the child presented with excessive talkativeness, reduced communication and aggressive behavior. CSF study done was normal. Further investigations revealed a positive reaction to NMDA type of glutamate receptor antibody in serum. USG and MRI pelvis did not show any obvious ovarian mass lesions. The child was started on

corticosteroids and immunosuppressant, with which she improved. She had residual speech impairment for which speech therapy was initiated and on follow up after 1 month her speech and behaviour had improved.

Discussion

Autoimmune encephalitis are mostly severe in nature and potentially fatal, but has good response to immunotherapy [1]. The age of presentation ranges from less than 1 year to 70 years of age, but most frequently children or teenagers are affected. Causes include idiopathic, post-infectious, paraneoplastic, genetic predisposition and possible immunodeficiency.

The clinical presentation is variable and may be mild with only a few symptoms or mimick a psychiatric disorder with delayed diagnosis of encephalitis. More complex symptomatology may be present and it can also have a fulminant course with a fatal outcome [2].

Anti-N-Methyl-D-Aspartate Receptor Encephalitis is a type of autoimmune encephalitis, first described by Joseph Dalmau et al (2007), characterized by antibodies targeting the NR1 subunit of NMDA receptor [1]. It is considered to be the second most common cause of autoimmune encephalitis. In a study from UK, 23% of patients were under 18 years of age [3]. Studies have established the cellular mechanisms through which antibodies of patients with anti-NMDAR encephalitis cause a specific, titer-dependent, and reversible loss of NMDARs [4]. Complement-mediated mechanisms do not appear to play a substantial pathogenic role. In contrast, there are copious infiltrates of antibody-secreting cells (plasma cells/plasmablasts) in the CNS of these patients. The demonstration of these cells provide an explanation for the intrathecal synthesis of antibodies and has implications for treatment [5]. Onset of anti-NMDAR encephalitis may occur during an acute mycoplasma infection or following Guillain-Barre Syndrome [6]. NMDAR antibodies of the immunoglobulin (Ig) subtypes IgA, IgG, or IgM have been reported in 13 of 44 patients (30%) in the course of herpes simplex encephalitis, suggesting secondary autoimmune mechanisms [7]. IgA-type NMDAR (NR1) may be a feature of schizophrenia [8]. A paraneoplastic origin has also been reported [9].

The disease evolves in stages and is characterized by a prodromal stage with fever (phase 1). Later in phase 2, the child manifests usually with prominent psychiatric symptoms like anxiety, aggression, labile affect, mood variations, memory deficit, catatonic features and sleep disturbances. Within a few days or weeks, decreased level of consciousness, seizures and movement disorders tend to develop. Later autonomic symptoms develop but are usually rare in children [1].

Investigations reveal abnormal brain MRI in approximately 35% of cases, characterized by non specific cortical and subcortical T2 FLAIR signal abnormalities. CSF shows moderate lymphocytic pleocytosis (in 80% of cases) and occasionally increased protein synthesis. EEG is abnormal in virtually all patients, and usually shows focal or diffuse slow activity in the delta and theta range along with epileptiform discharges. A characteristic EEG pattern called "extreme delta brush" occurs in 30% adults and in few children. The diagnosis is established by demonstrating NMDAR antibodies in CSF or serum [1].

Although anti-NMDAR encephalitis has a mortality rate of 7%, 80% of cases have substantial or full recovery. Recovery is usually slow and may take upto 2 years. The last symptoms to improve are social interactions, language and executive functions. Relapses occur in 24% of cases [5].

The differential diagnosis include viral encephalitis, neuroleptic malignant syndrome, acute psychosis and drug abuse.

Treatment strategies include intravenous immunoglobulins, corticosteroids, or plasmapheresis. However, because these treatments fail in 50% cases, other modalities like rituximab,

cyclophosphamide have been found helpful.

Conclusion

Anti-NMDAR autoimmune encephalitis is one of the most common causes of autoimmune encephalitis. With early detection and immunotherapy, 80% of patients show full recovery.

Bibliography

1. Thais Armangue, Joseph O Dalmau. Autoimmune Encephalitis. In: Kliegman R, Stanton B, St Geme J, Schor N, Behrman R. Nelson textbook of Pediatrics. 20th ed. Philadelphia: Elsevier; 2016. pp.2905-07.
2. Somnier F. Autoimmune encephalitis - History and current knowledge. Available from: <http://www.ssi.dk/~media/Indhold/DK%20-%20dansk/Diagnostik/DiagnostiskHaandbog/Autoimmune%20encephalitis%2058.ashx> Accessed 24 December 2016.
3. Logesh Lingappa, Sirisharani Siddaiahgari. Autoimmune and Paraneoplastic Encephalitis and Encephalopathies. In: Gupta P, Menon P, Ramji S, Lodha R. PG Textbook of Pediatrics. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2015. p.2173-74.
4. Hughes E, Peng X, Gleichman A, Lai M, Zhou L, Tsou R et al. Cellular and Synaptic Mechanisms of Anti-NMDA Receptor Encephalitis. *Journal of Neuroscience*. 2010;30(17):5866-5875.
5. Martinez-Hernandez E, Horvath J, Shiloh-Malawsky Y, Sangha N, Martinez-Lage M, Dalmau J. Analysis of complement and plasma cells in the brain of patients with anti-NMDAR encephalitis. *Neurology*. 2011;77(6):589-593.
6. Gable M, Gavali S, Radner A, Tilley D, Lee B, Dyner L et al. Anti-NMDA receptor encephalitis: report of ten cases and comparison with viral encephalitis. *Eur J Clin Microbiol Infect Dis*. 2009;28(12):1421-1429.
7. Pruss H, Finke C, Holtje M, Hofmann J, Klingbeil C, Probst C et al. N-methyl- D -aspartate receptor antibodies in herpes simplex encephalitis. *Annals of Neurology*. 2012;72(6):902-911.
8. Tsutsui K, Kanbayashi T, Tanaka K, Boku S, Ito W, Tokunaga J et al. Anti-NMDA-receptor antibody detected in encephalitis, schizophrenia, and narcolepsy with psychotic features. *BMC Psychiatry*. 2012;12(1):37.
9. Dalmau J, Gleichman A, Hughes E, Rossi J, Peng X, Lai M et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *The Lancet Neurology*. 2008;7(12):1091-1098.