Ovarian teratoma induced anti N-methyl-D-aspartate receptor antibody encephalitis

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Case

A 44 years old healthy female, was brought in to ED by her brother for disturbed behaviour for 48 hours. Two weeks prior, the patient had an upper respiratory tract infection.

Organic screen; CT brain, lumbar puncture, chest Xray, blood investigations and urine drug screen were all normal. The patient was admitted under psychiatric team for management of acute psychosis with antipsychotics. Despite treatment, she was deteriorating; agitated, catatonic, had auditory hallucinations, gait disturbances, and stool/ urine incontinence. ECT was done, after which she developed hypothermia and became unstable. Medical and neurology team started investigating organic causes again. Repeat MRI and CT brain were unremarkable, EEG showed generalised slowing, ultrasound pelvis and PET scan were normal. Patient started on Methylprednisolone and IVIG awaiting the Anti NMDAR antibody results. The patient was still deteriorating with fluctuating GCS requiring ICU admission. Anti NMDAR antibodies were positive in CSF. Rituximab was then started, and the patient started to improve after the first dose.
Repeat pelvic ultrasound one year later showed a 1.5 cm right ovarian dermoid cyst. Right oophorectomy was performed, and histology showed benign dermoid cyst.

Background

This paraneoplastic syndrome is described as Anti-N-methyl-D-aspartate receptor antibody encephalitis; autoimmune encephalitis that presents mainly with neuropsychiatric symptoms.

Mortality rate: 4-7%

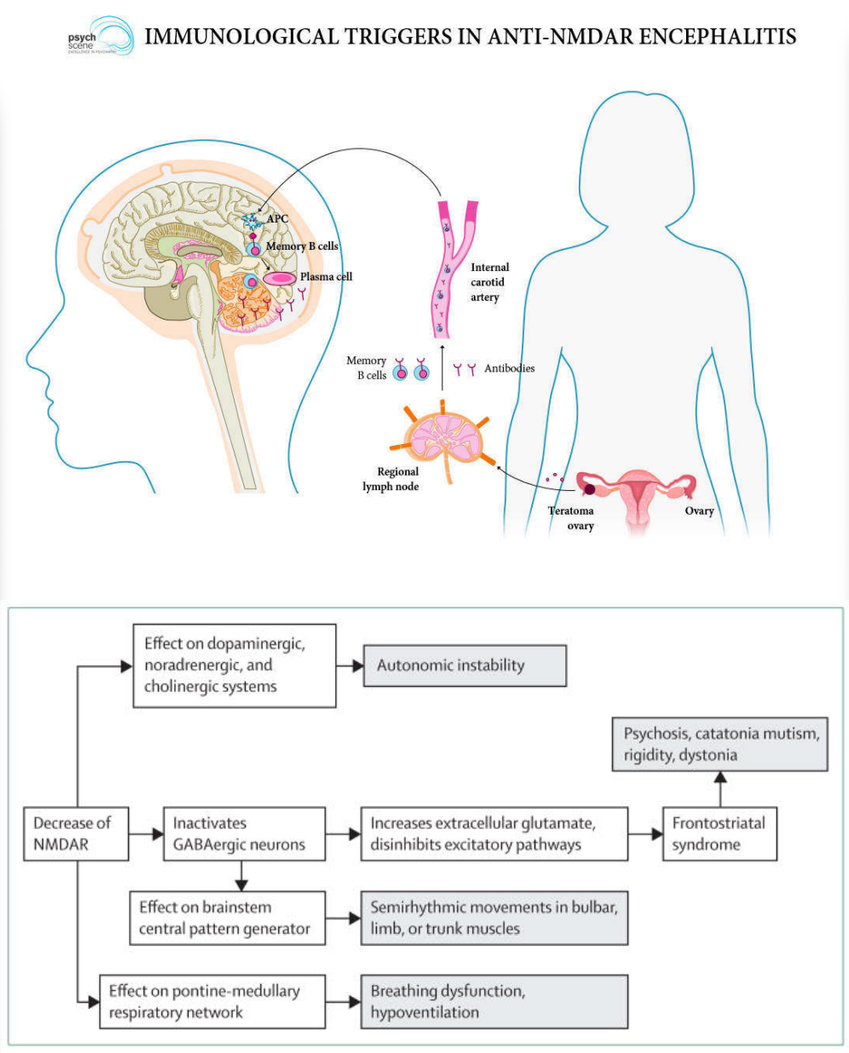
Age group: 18 - 80 years old

Prognosis:
Early diagnosis and treatment are associated with better outcomes. 75% of patients have a full recovery, but 12-24% of cases have relapses usually due to a recurrence of the teratoma.

Pathophysiology:
In 94% of cases, it is associated with ovarian teratomas containing nervous tissue. However, it can be associated with extra-ovarian teratomas such as; neuroblastoma, lymphoma, lung, breast, thymic, testicular, and ovarian carcinoma.

NMDA receptor antagonists are believed to function by blocking the NMDA receptor in the presynaptic GABA neurons of the thalamus and frontal cortex, leading to disinhibition of postsynaptic neurons resulting in excitotoxicity.

Patients' antibodies cause a titre-dependent, reversible decrease of synaptic NMDAR by a mechanism of crosslinking and internalisation.



Clinical picture

1. Non-specific prodrome: A viral illness, gastroenteritis (2 weeks prior to psychiatric symptoms)

2. Psychiatric symptoms: Agitation, bizarre and disinhibited behaviour, delusions and auditory and visual hallucinations, Catatonia

3.Cognitive dysfunction: Short-term memory loss

4. Motor dysfunction: Typical epileptic seizures, dyskinetic movements

5. Autonomic instability: Hypoventilation, cardiac dysrhythmias.

Investigation:
1. Anti NMDA receptor antibodies in CSF or serum

2.CSF may show mild lymphocytic pleocytosis, normal or mildly increased protein concentration, and CSF-specific oligoclonal bands.

3.MRI brain is normal in 50% of cases and the other 50% show T2 hyperintensities in hippocampi, cerebellar and cerebral cortex, basal ganglia, brainstem, frontobasal and insular regions.

4. EEG shows generalised slowing, especially in the catatonic phase. In 2012 a unique pattern was identified; the extreme delta brush pattern, which is characterised by beta bursts riding on delta waves.

5. MRI, CT or USS of the pelvis are all helpful to look for the teratoma.

Treatment

1. First line: corticosteroids, intravenous immunoglobulins or plasma exchange. Removal of any identified teratomas.

2. Second line: immunosuppression using Rituximab or cyclophosphamide. Used in patients with no teratoma found, or patients who have a late diagnosis.

3. Antipsychotics can be used but can complicate the picture. Benzodiazepines are used for catatonic symptoms.

Reference

1. Dalmau J, Tüzün E, Wu HY, et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol. 2007;61:25–36.
2. Gable MS, Gavali S, Radner A, et al. Anti-NMDA receptor encephalitis: report of ten cases and comparison with viral encephalitis. Eur J Clin Microbiol Infect Dis. 2009;28:1421–1429.
3. Seki M, Suzuki S, Iizuka T, et al. Neurological response to early removal of ovarian teratoma in anti-NMDAR encephalitis. J Neurol Neurosurg Psychiat. 2008;79:324–326.
4. Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol. 2008;7:1091–1098.
5. Dalmau J, Lancaster E, Martinez-Hernandez E, et al. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol. 2011;10:63–74.
6. Zhang, T., Duan, Y., Ye, J., Xu, W., Shu, N., Wang, C., … & Liu, Y. (2018). Brain MRI Characteristics of Patients with Anti-N-Methyl-D-Aspartate Receptor Encephalitis and Their Associations with 2-Year Clinical Outcome. American Journal of Neuroradiology, 39(5), 824-829.