
Encefalitis anti-NMDAR atípica en una paciente femenino de 28 años con teratoma de ovario bilateral: reporte de un caso.

Juan Roberto López Vargas* dr.vargas_lopez@outlook.com, Ixchel Guadalupe Rodríguez-Barajas, Luis Vega-Casimiro, Dorian Caballero Espinosa

Hospital General Regional No 72. Tlalnepantla, Estado de México MEXICO

*Corresponding author.

Keywords
Encephalitis, Antibodies, NMDA receptor encephalitis, ovarian teratoma.

Abbreviations
Cerebrospinal fluid (CSF), anti N-methyl-D-aspartate receptor (NMDAR), emergency room (ER), computed tomography (CT), magnetic resonance imaging (MRI), electroencephalogram (EEG).

Introduction
Most frequently recognized causes of encephalitis are infectious; however, an increasing number of autoimmune encephalitis have been identified that can develop with core symptoms resembling infectious encephalitis, and with neurological and psychiatric manifestations without fever or cerebrospinal fluid (CSF) pleocytosis 1. To improve the recognition of these disorders we present the atypical case of a 28-year-old female patient suffering from anti-NMDAR encephalitis associated with bilateral ovarian teratoma.

Case presentation
This is the case of a 28-year-old Mexican Mestizo patient with no significant medical or surgical history, brought in early April 2020 to the emergency room (ER) by her parents for behavioral disorders associating episodes of anxious agitation with phases of decrease of verbal output. Routine lab, CSF studies and head CT were normal, so she was sent home with sertraline. She was brought back to the ER 2 years later, with a history of episodes of anxiety and disorganized thinking with phases of mutism. Within 9 hours, low grade fever, weakness on the right side of the body followed by decreased level of consciousness by stupor appeared. Infectious encephalitis was suspected, and she received empirical antibiotics and acyclovir until the exclusion of infectious causes: CFS, brain IRM, antinuclear antibodies, bacterial and viral PCR panels were negative. In the absence of favorable progress after 3 days of treatment, autoimmune encephalitis was suspected, and she stopped receiving antimicrobials and acyclovir and was empirically started on a 3-day course of methylprednisolone 1gr/day, followed by oral glucocorticoid therapy at 1.0 mg/kg/day of prednisone with a 3-week taper of oral prednisone. After 2 days of the treatment, the patient showed a full recovery of level of consciousness, strength on the right side of the body and no fever but decreased verbal output and memory deficit persisted with no correlation in the electroencephalogram (EEG) patterns. In the presence of prominent psychiatric manifestations and response to immunotherapy, NMDAR encephalitis was suspected. An abdominal-pelvic CT scan and transvaginal ultrasound revealed a probable bilateral ovarian teratoma. A probable diagnosis of anti-NMDAR encephalitis was set. NMDAR antibodies against the GluN1 subunit in the CSF and
serum were positive (Fig. 1 and 2), the definite diagnosis of anti-NMDAR encephalitis with bilateral ovarian teratoma was set. In the presence of an ovarian tumor, its surgical excision is essential since it may be the origin of the autoimmune reaction, so the patient underwent a bilateral oophorectomy, the pathological examination confirmed the diagnosis of a mature teratoma. After 1 day, the evolution was rapidly favorable with gradual return to a normal state of cognitive and neurological functions and the behavioral problems were resolving, with fully recovery at 2 months.

Discussion

Anti-NMDAR encephalitis at onset, about 90% of patients have prominent psychiatric or behavioral symptoms \(^2,3\), distinguishing the disease from a primary psychiatric disorder, viral encephalitis and other autoimmune encephalitis is challenging \(^4\), especially like our case, when weakness on the right side of the body has not been described as a typical symptom and the CSF, EEG studies and brain MRI were normal, nevertheless, these negative results should not be a reason to discount a possible diagnosis of anti-NMDAR encephalitis\(^5,6\), since her speech dysfunction, disorganized thoughts, decreased level of consciousness and memory deficit persisted, raised the suspicion of anti-NMDAR encephalitis. The only specific diagnostic test of anti-NMDAR encephalitis is the demonstration of IgG antibodies against the GluN1 subunit of the receptor in patient’s CSF, NMDAR antibodies are always present in CSF \(^2,4\), emphasizing the importance of neuronal antibody testing to confirm the diagnosis, unfortunately they are not usually available in many centers.

We encourage searching specially for ovarian and other tumors according to age, sex, and probably race \(^7,8,2\) given the favorable evolution on the neuropsychiatric symptoms after removal of the secreting ovarian lesion is described in many cases \(^8\). The impact of tumor excision on the immediate evolution of encephalitis is not demonstrated, but it could improve the effectiveness of medical treatments especially if it is performed early \(^9,10\). When the treatment is well conducted, the clinical course is most often favorable in 80-90 % with a regression in a few weeks of abnormalities of the autonomic nervous system, then very gradually after several months to years of the rest of the symptomatology \(^8,9\).

Conclusion

The diagnosis of NMDAR encephalitis is difficult and time-consuming, and patients may succumb to neurological deterioration, thus necessitating a high index of suspicion and prompt intervention, even in the absence of confirmatory studies.

Declaration of Competing Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/ or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/ or publication of this article.

Informed consent

An informed consent was obtained from the patient before being published this case.

Ethical considerations

This case presentation didn’t need the submission or approval by the local ethics and investigation committee.
References


Fig. 1. Anti-bodies against the GluN1 subunit of the NMDAR
**Fig. 2.** IgG anti-bodies against to neuronal proteins

IgG anti-bodies against neuronal proteins have high-affinity against 31-27 kDa (white arrow) and 80-50 kDa proteins (yellow arrow) than 140-150 kDa proteins (red arrow).

IgG: immunoglobulin G, kDa: Kilodalton, LCR: Translation from Spanish of cerebrospinal fluid, NMDA: N-methyl-D-aspartate.