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Anti-NMDAR encephalitis in a 19 year old female patient with ovarian teratoma: A case report

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ABSTRACT

Background: Anti-*N*-Methyl-D-Aspartate encephalitis is a subcategory of auto-immune encephalitis. It is known for its aggressive presenting symptoms and rapid deterioration, yet it is treatment responsive. It is associated in 50 % to ovarian teratoma.
Case: We report the case of a 19 year old female patient presenting for a psychiatric disorder of sudden onset with rapid deterioration. Neurologic imaging was in favor of encephalitis, and CSF studies revealed Anti NMDA receptors. Further abdominal imaging showed a right ovarian teratoma of 4 cm.
Laparoscopic ovarian cyst resection was done, and corticotherapy, IVIG and anticonvulsants were given. We report complete resolution of symptoms after 7 months.
Conclusion: Anti-NMDA receptor encephalitis with ovarian teratoma is a rare entity with rapid deterioration. Early diagnosis, surgical resection and proper medical treatment are essential for the management of this disease.
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Introduction

Encephalitis is defined as brain inflammation with neurologic symptoms due to inflammation of brain parenchyma. It arises from either an infectious etiology or an autoimmune disorder [1]. The affected patients suffer from psychiatric symptoms with decreased level of consciousness, seizures and autonomic dysfunction, often requiring ventilatory support [2].

Vitalini et. Al first described in 2005 a case series of 4 patients with a pattern of paraneoplastic encephalitis and ovarian teratoma [3]. Later analysis by Dalmau et. Al suggested a model of autoimmune encephalitis associated with antibodies to NR2B and NR2A heteromers of the *N*-Methyl-D-Aspartate receptor (NMDAR) [2]. Case reports progressively increased as of 2007, showing association between auto-immune encephalitis and ovarian teratomas [4].

We present in this article the case of a 19 year old female patient suffering from anti-NMDAR encephalitis associated with a 4 cm ovarian teratoma.

Case presentation

This is the case of a 19 year old French patient of African descent, brought to the ER by her parents for minor headache of 2 days duration with low grade fever. Lab tests were done showing normal WBCs and CRP of 9. She was sent home with pain killers. She was brought back to the ER two days later, with intense headache, insomnia, dysarthria and aggressive behavior. Panels showed no major modifications. Neurology department was consulted, they advised to hospitalize the patient and proceed to an urgent brain MRI.

Brain MRI showed no signal abnormalities on DWI and ADC sequences. No microbleeds or calcifications were seen on T2*. On T2 FLAIR 3D sequence, a small hyperintense lesion was seen over the right medial temporal area, on the coronal view. No abnormal contrast enhancing lesions on T1W images. EEG was not conclusive with diffuse microvoltage activity and no reaction to photic stimulation. EEG repeated two days later showed an epileptic activity with Theta rhythmic waves over the left hemisphere, lasting twenty seconds, followed by flat recording in post ictal phase. CSF analysis showed lymphocytic pleocytosis with normal protein, glucose and gram stain, and negative bacterial and viral PCR panels. Positive oligoclonal bands were seen in CSF as well in serum, with normal IgG index.

Autoimmune encephalitis was suspected. CSF antibody studies showed positive antibodies to the NMDA receptor. Patient was started on antiepileptic drugs, Solumedrol 1 g/day IV for 5 days

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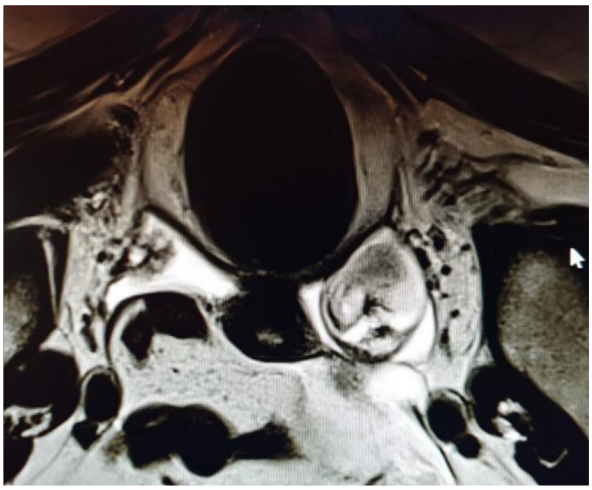

Fig. 1. Pelvic MRI showing right ovarian dermoid cyst.

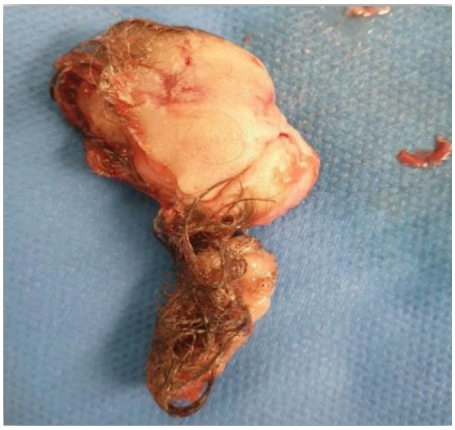

Fig. 2. The ovarian teratoma after surgical resection.

then 1 mg/kg and IVIG (CLAIRIG) 2 g/kg given over 6 days. Pelvic MRI showed a 39*29*32 mm right ovarian teratoma (Fig. 1). Diagnosis of anti-NMDAR encephalitis with ovarian teratoma was set. Gynecology department was notified. The staff decided to proceed with a laparoscopic right dermoid cyst resection (Fig. 2). Patient was stable after the surgery. She was maintained on corticotherapy and anti-epileptic medications with a 3rd dose of IVIG 2 g/kg for 6 days.

Discussion

Encephalitis is the inflammation of the brain parenchyma, a disease resulting in major morbidity and mortality. Etiologies include post infectious processes such as acute disseminated encephalomyelitis, and auto-immune encephalitis [1]. The latter is divided into two categories: the classic limbic paraneoplastic encephalitis (anti-Hu and anti Ma2) and the anti-*N*-methyl-D-aspartate receptor encephalitis [5]. The anti NMDAR encephalitis is characterized by the presence of antibodies against the GluN1 subunit of the NMDA receptor [6]. It is mainly of abrupt onset, with psychiatric manifestations like aggression, psychosis and memory loss, associated to seizures, cognitive decline and coma [5].

Recent studies have shown association between ovarian teratomas and anti-NMDAR encephalitis [4]. Ovarian teratomas or dermoid cysts are germ cell tumors containing multiple tissues of ectoderm, endoderm and mesoderm origins. Less than 3% of dermoid cysts are malignant. Management mainly includes laparoscopic resection and extraction within a bag [7,8].

Diagnosis of encephalitis and searching for the etiology remains complex, and more than 50 % of encephalitis remain of unknown etiology [5]. Diagnostic testing include lumbar puncture, brain MRI and EEG. Diagnostic criteria include one major criterion: patient presenting to medical attention with altered mental status lasting $\geq$24 h with no alternative cause identified, with >2 minor criteria:

Documented fever >38 degrees C° within the 72 h before or after presentation, generalized or partial seizures not fully attributable to a preexisting seizure disorder, new onset of focal neurologic finding, CSF WBC count $\geq$5/cubic mm^3, abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset, abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause [1]. In the case of our patient, symptoms upon presentation, brain MRI, EEG and lumbar puncture were in favor of au autoimmune encephalitis.

After the work of Vitallani et.Al [3] and Dalmau et.Al [2] between 2005 and 2007, a new category of paraneoplastic encephalitis have emerged, associating severe encephalitis with ovarian teratoma in young female patients and anti NMDA receptor antibodies. Once anti-NMADR encephalitis is suspected, an abdominal CT scan is recommended, searching for an ovarian dermoid cyst present in 50 % of patients [4,6]. Treatment includes surgical ovarian cyst resection. Other therapies include immunotherapy like corticosteroids, intravenous immunoglobulin, or plasma exchange [9]. Our patient was put on anticonvulsants after her first seizure (Keppra 500 mg 2*/day, Valium 10 mg every 6 h). Once the

MRI, EEG and CSF analysis were in favor of autoimmune encephalitis, she was started on Solumedrol 1 mg/kg IV. The detection of anti-NMDA receptor antibodies was an argument to introduce IVIG (CLAIRIG) 2 g/kg given over 6 days. IVIG was given over 2 cures before surgery, and 1 cure after surgery. Corticosteroids were maintained after the laparoscopic resection.

According to a systematic review in 2014 [4], improvement with hospital discharge was acceptable after a median of 3 months. Full recovery was noticed in 80 % of patient. Our patient showed minor improvement after 2.5 months, with hospital discharge after 3.5 months. Full recovery was achieved after 7 months.

Conclusion

Anti-NMDA encephalitis associated to ovarian teratoma is a rare entity that carries high mortality and morbidity. The rarity of this category often delays diagnosis, with a mean time to surgery around 74 days in the case of mature teratoma [4]. This pathology needs better understanding and more acknowledgment by neurologists and gynecologists, in order to set early diagnosis and proper management.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] Venkatesan A, Tunkel AR, Bloch KC, Lauring AS, Sejvar J, Bitnun A, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. Clin Infect Dis Off Publ Infect Dis Soc Am 2013;57(October (8)):1114–28.
[2] Dalmau J, Tüzün E, Wu H, Masjuan J, Rossi JE, Voloschin A, et al. Paraneoplastic anti-N-methyl-Daspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol 2007;61(January (1)):25–36.
[3] Vitaliani R, Mason W, Ances B, Zwerdling T, Jiang Z, Dalmau J. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. Ann Neurol 2005;58(October (4)):594–604.

[4] Acién P, Acién M, Ruiz-Maciá E, Martín-Estefanía C. Ovarian teratoma-associated anti-NMDAR encephalitis: a systematic review of reported cases. Orphanet J Rare Dis [Internet] 2014;(October)9. . [cited 2020 Nov 13]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203903/.
[5] Kumar R. Understanding and managing acute encephalitis. F1000Research [Internet] 2020;(January)9. . [cited 2020 Nov 13], Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6993835/.
[6] Guasp M, Dalmau J. Encephalitis associated with antibodies against the NMDA receptor. Med Clínica Engl Ed 2018;151(July (2)):71–9.
[7] Pradhan P, Thapa M. Dermoid Cyst and its bizarre presentation. JNMA J Nepal Med Assoc 2014;52(June (194)):837–44.
[8] Koçak M, Dilbaz B, Ozturk N, Dede S, Altay M, Dilbaz S, et al. Laparoscopic management of ovarian dermoid cysts: a review of 47 cases. Ann Saudi Med 2004;24(5):357–60.
[9] Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol 2011;10(January (1)):63–74.