CASE REPORT

Anti-NMDA Receptor Encephalopathy Secondary to an Ovarian Teratoma

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Received: 1/24/2022 Revised: 2/07/2022 Accepted: 2/14/2022 Published: 3/31/2022

Am j Hosp Med 2022 Mar;6(1):2022. DOI: https://doi.org/10.24150/ajhm/2022.002

Keywords: Neurology, Encephalitis, Teratoma, Altered Mental Status

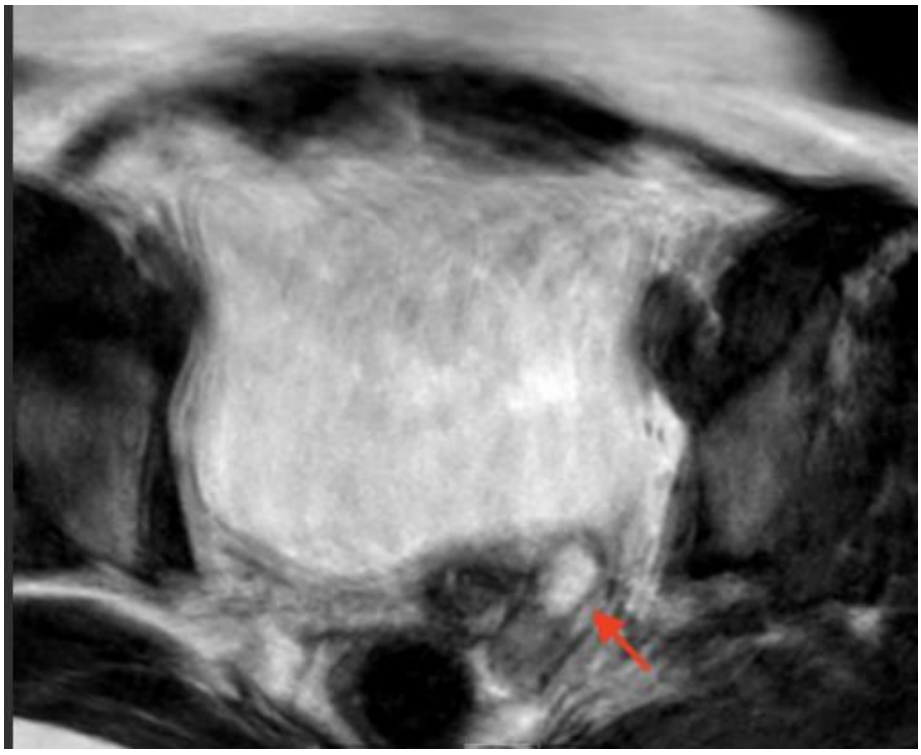

Figure 1: Figure 1: Ovarian Teratoma: red arrow pointing to left adnexal mass.

BACKGROUND:

Anti-N-methyl-D-aspartic acid receptor (anti-NMDAR) encephalitis is a phenomenon commonly associated with ovarian teratomas but often confused with other disease processes that can cause altered mental status. The combined expression of neuronal and lymphocytic tissue in teratomas leads to the creation of autoantibodies that can bind to NMDA receptors in the hippocampus and forebrain regions of the brain.[1,2] This often leads to symptoms mimicking psychosis but other nonspecific symptoms like fevers, seizures, and somnolence may also occur.[3] Because 37% of anti-NMDAR encephalitis cases associated with teratomas occur in patients younger than 18 years of age who often have no other medical problems, diagnosis is difficult and often delayed.[4]

The following case highlights the diagnosis and treatment course of a previously healthy female adult patient who was treated initially for presumptive psychosis and later found to have anti-NMDAR encephalitis.

OBJECTIVE:

To explain the pathophysiology of anti-NMDAR encephalitis and discuss the manifestation of symptoms, methods of diagnosis, and best practices for management.

METHODS:

A previously healthy 29-year-old woman presented to the emergency room displaying symptoms of acute psychosis. The patient's behavior was characterized by incoherent speech, hyper-religiosity, and disorientation to name, time, and location. The patient required frequent medication for agitation throughout her first hospitalization and a psychiatry evaluation suggested that the woman was suffering from an acute manic episode. The patient began to return to her baseline mental status with mood-stabilizing medications and she was later discharged home with her family.

Approximately 5 days after returning home, the patient was brought back to the emergency room by her family with concern that her mental status had worsened despite being adherent to her psychiatric medications. During the subsequent readmission, a broader differential was considered. Head imaging, a lumbar puncture, and an EEG were all performed along with various lab studies to evaluate for infectious, neurologic, autoimmune, and oncologic etiologies of the patient's symptoms, in addition to a possible psychiatric cause. During the patient's second hospital course, her mental status worsened and became characterized by catatonia with dysautonomic features.

RESULTS:

Initial labs for the patient were only remarkable for a slightly elevated white blood cell count of 15.3 and the patient's urine drug screen was normal. The patient's head imaging was negative for any kind of mass or brain lesion explaining the patient's acute changes in behavior and multiple EEGs were negative for status epilepticus or any other type of seizure activity. Initial cerebrospinal fluid (CSF) analysis was only remarkable for lymphocytic pleocytosis, and all CSF viral, fungal, and bacterial studies were negative. Based on the lack of evidence of a CNS infection, neurology suggested performing a CT scan of the patient's abdomen to rule out a paraneoplastic process. Abdominal imaging revealed a 1.2 x 1.4 x 1.4 cm mass in the left adnexa concerning for a teratoma. An anti-NMDA receptor antibody CSF assay was sent to an outside lab and returned weeks later confirming the diagnosis of anti-NMDA receptor encephalitis as the etiology of the patient's symptoms. Because the imaging revealed an adnexal mass, a further paraneoplastic workup for specific paraneoplastic syndromes was not performed but they were considered in the initial differential.

The patient was first treated with surgery to remove the adnexal mass which was confirmed by pathology to be a teratoma and then treated with IVIG infusions, rituximab, and a steroid taper. The patient was hospitalized for approximately 3 weeks during which time her symptoms gradually began to resolve.

Readmission CMP

Lab	Value	Reference Range
Sodium	144	135-145 mmol/L
Potassium	4.2	3.6-5.2 mmol/L
Chloride	105	96-110 mmol/L
Carbon Dioxide	27	24-32 mmol/L
Glucose	**113**	65-99 mg/dL
Calcium	9.4	8.4-10.3 mg/dL
BUN	18.0	7.0-25.0 mg/dL
Creatinine	1.07	0.5-1.10 mg/dL
Total Protein	7.7	6.0-8.0 g/dL
Albumin	4.7	3.4-5.0 g/dL
AST	28	<45 U/L
ALT	29	<46 U/L
Alkaline Phosphatase	80	20-120 U/L
Bilirubin, Total	0.4	<1.3 mg/dL
EGFR	81	>89 mL/min

Readmission CBC

Lab	Value	Reference Range
WBC	**15.3**	4.5-11.0 10^3/uL
RBC	4.55	4.00-5.20 10^6/uL
Hemoglobin	12.7	12.0-16.0 gm/dL
MCV	85.9	80.0 – 100.0 fL
MCH	28.0	26.0 – 34.0 pg
Platelet count	163	150-400 10^3/uL

Assorted Labs

Lab	Value	Reference Range
Creatinine Kinase	**958**	<190 U/L
Procalcitonin	**0.06**	<0.05 ng/mL
Lactic Acid	1.0	0.3-2.0 mmol/L

CSF

Lab	Value	Reference Range
CSF WBC Count	**7**	0-5 μL
CSF RBC Count	**7**	0-5 μL
Glucose	**75**	40 – 70 mg/dL
Protein	22.5	15.0 – 45.0 mg/dL
Culture, CSF with smear	No Growth	
Culture, AFB with smear	No Growth	
Culture, Fungal CSF	No Growth	

Autoimmune Labs

Lab	Value	Reference Range
Anti-nmda receptor	**1:40**	<1:10
Immunoglobulin A	167	75-374 mg/dL
Immunoglobulin E	**641**	≤ 214 kU/L
Immunoglobulin G	**2,904**	680-1,530 mg/dL
Immunoglobulin M	68	47- 188 mg/Dl

Imaging Studies

CT Abdomen Pelvis w/contrast	1.4 cm attenuating with mural nodule left adnexal mass consistent with teratoma
MRI brain w & w/o contrast	Probable left limbic encephalitis Subacute ischemic event and inflammatory process
MRI Pelvis w/contrast	1.7 x 1.3 x 1.3 cm left ovarian teratoma No loco-regional lymphadenopathy Uterus is anteverted and retroflexed

DISCUSSION:

Anti-NMDAR encephalitis affects females more commonly than males by a ratio of 8 to 2 and is commonly associated with teratomas.[4] A prompt CSF analysis is critical to making a diagnosis of encephalitis however specific anti-NMDA receptor antibody testing is usually a send-out lab that may take weeks to result.[5] Although serum anti-NMDA receptor antibody tests exist, they are much less accurate.[6] One analysis of 43 anti-NMDAR patients found that in addition to being positive for CSF anti-NMDA receptor antibodies, 58.1% of patients displayed elevated CSF white blood cell counts and 18.6% had elevated CSF protein levels.[5] The patient, in this case, had a lymphocytic pleocytosis in her CSF analysis in the absence of any other signs of infection. All blood and CNS cultures showed no growth and a CSF viral panel, autoimmune encephalitis panel, and multiple sclerosis panel were also negative.
The most significant positive prognostic factors for anti-NMDAR encephalitis are a prompt diagnosis, the presence of a tumor, and not needing ICU-level care.[7] Because a number of other diagnoses are generally ruled out first, time to diagnosis may be delayed as was the case for the patient in this report.

For anti-NMDAR encephalitis cases associated with teratomas, prompt removal of the mass is generally the first step in treatment.[8] Following this, IVIG infusions can be used to neutralize the anti-NMDAR antibodies remaining in the patient's system along with high-dose steroids.[3,7] In more severe cases, plasmapheresis. has been used as a treatment modality as well as rituximab.[9] Recovery from anti-NMDAR encephalitis is slow ranging from weeks to months but most patients regain total neurological and motor function.

CONCLUSION:

Anti-NMDAR encephalitis is an uncommon but severe cause of encephalitis often associated with teratomas in previously healthy young women. Prompt diagnosis is crucial to improving prognosis and anti-NMDAR encephalitis should be considered in the differential for altered mental status not explained by traditional etiologies.

Notes

Potential conflicts of interest: The author reports no conflicts of interest in this work.

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