Ovarian teratomas typically present with pelvic symptoms; however, teratomas causing neuropsychiatric symptoms may occur if they contain brain tissue. N-methyl-d-aspartate (NMDA) receptor encephalitis usually occurs in young, otherwise healthy women. Frequently, the diagnosis of NMDA receptor encephalitis is delayed because of the nature of the symptoms, with resulting delays in treatment and worse long-term neurologic outcomes. The present case emphasizes the importance of evaluating the whole patient in the presence of apparently localized symptoms and an unremarkable history.

Report of Case
A 33-year-old nulligravid woman started having musical hallucinations and generalized malaise, and 24 hours later she became disoriented and nonsensical. Her boyfriend brought her to the emergency department, where she grew paranoid and aggressive, requiring restraints. She was admitted to the hospital with a diagnosis of acute schizophrenia and given valproic acid, risperidone, haloperidol, and lorazepam before she was transferred to a psychiatric hospital.

The patient’s medical, surgical, and obstetrical histories were unremarkable. Her menses were regular but with dysmenorrhea. According to her family, she did not have any psychiatric history but had a sister with bipolar disorder. She worked as a construction worker and lived with her significant other. She denied use of illicit substances, tobacco, or alcohol. She did not

Gynecologic teratomas commonly present with pelvic symptoms. The authors report a case of teratoma causing acute psychosis, encephalopathy, and sudden-onset seizures in a previously healthy 33-year-old woman. After common organic causes were excluded, investigation revealed an immature teratoma containing brain tissue on her left ovary. Anti–N-methyl-d-aspartate receptor encephalitis was diagnosed and, with excision and medical management, her symptoms resolved and she was discharged home in stable condition. Encephalopathy is not commonly attributed to gynecologic causes, but anti–N-methyl-d-aspartate receptor encephalitis may be caused by ovarian teratomas with a neuronal component. Thorough gynecologic examination should be performed on any female patient presenting with new-onset psychosis, encephalopathy, and seizures, especially in the absence of other organic or structural causes. Thus, it is important to look at the whole patient and not just the symptoms.
The patient was given high-dose steroids on HD 13, with 1 g of solumedrol administered intravenously. Owing to deteriorating mental status on this day, a midline laparotomy with left salpingo-oophorectomy was performed. The mass was smooth, intact, and without excrescences. It contained cystic components as well as skin, hair, brain, bone, and cartilage (Figure 2). Staging was not performed because of the emergent nature of the case. The abdominal and pelvic regions showed no other pathologic findings. Endometriosis implants were noted but not excised. The final pathologic results confirmed the frozen section diagnosis of immature teratoma (Figure 3), and the antibody titers confirmed the suspicion of anti-NMDA receptor encephalitis.

After the solumedrol dose was completed, 0.4 mg/kg of intravenous immunoglobulin was started, but the course was discontinued because of mental status deterioration. She was given plasmapheresis through a Quinton catheter in the groin on HD 22, which improved her psychosis and agitation. Owing to swallowing difficulties, on HD 30 a percutaneous endoscopic gastrostomy tube was placed, and enteral feeding was initiated. By HD 41, she was transferred to inpatient rehabilitation and discharged 7 days later. She was scheduled to receive 3 courses of bleomycin-etoposide-platinum chemotherapy, and she continued to take anticonvulsant medication. If neuropsychiatric deterioration were to recur, she would have received second-line chemotherapy with cyclophosphamide and rituximab at 750 mg/m² monthly for 4 to 6 months and 375 mg/m² weekly for 4 weeks, respectively.

Discussion

Teratoma presenting with encephalitis is an uncommon but well-described condition in the psychiatric and medical literature. It was first reported in 1997 and formally defined in 2007 after the anti-NMDA receptor antibody was discovered. At least 500 cases have been reported, affecting both sexes but predominantly females (80%), with ages ranging from infancy to the 90s. Most patients take any prescription medications; however, a bottle of OxyElite (USPlabs LLC) diet pills was found at her house, and her family reported that she had taken weight loss medications in the past. Her family was unsure whether she had taken a diet pill before the onset of symptoms.

By the third day in the psychiatric facility, the patient’s neurologic status worsened and generalized seizures developed. She was transferred to the community teaching hospital for further evaluation. Her examination results were unchanged, and a computed tomographic (CT) scan of the head did not reveal any abnormality. A neurologist evaluated the patient for these new-onset seizures and added levitiracetam to her regimen. Further encephalopathy workup with serum toxicity screening, blood alcohol level, thyroid stimulating hormone, and syphilis antibodies was performed along with an autoimmune workup, testing for levels of vitamins and herpes antibodies, and lumbar puncture. The aforementioned test results were all normal. The lumbar puncture specimen was clear, with 100% lymphocytosis, a white blood cell count of 13/mm, 0 monocytes, a protein level of 19 mg/dL, and a glucose level of 65 mg/dL.

Because of the lack of response to the standard treatments for patients with encephalitis and seizures, by hospital day (HD) 9, a diagnosis of anti–NMDA receptor encephalitis was suspected. A CT scan of the abdomen and pelvis was ordered because of the association of anti–NMDA receptor encephalitis with teratomas, and a serum antibody titer was concurrently sent to an outside laboratory to confirm the diagnosis. The CT scan showed a complex left ovarian mass measuring 9.2 × 8.7 × 10 cm with differing densities (Figure 1). No ascites, omental caking, or other findings consistent with malignancy were noted. Gynecologic consult was requested, and the mass was confirmed on pelvic examination. Tumor marker levels were: α-fetoprotein, 25 ng/mL (reference range, <9 ng/mL); lactate dehydrogenase, 167 U/L (reference range, 100-200 U/L); CA-125, 35.6 U/mL (reference range, <35 U/mL); and β human chorionic gonadotropin, 0.6 mIU/mL (reference range, <2.9 mIU/mL).
patients with a diagnosis of anti–NMDA receptor encephalitis are aged between 18.5 and 24 years,\textsuperscript{2,6-11} with associated teratoma in 60% of those who are female.\textsuperscript{9,12}

Symptoms start with a nonspecific prodrome, such as mucocutaneous blisters,\textsuperscript{7} headache, or fatigue. Patients are afebrile\textsuperscript{2} and present within weeks with neuropsychiatric symptoms. Roughly 77% are initially evaluated by psychiatrists\textsuperscript{9} and receive diagnoses of bipolar disorder or schizophrenia.\textsuperscript{2,13} Symptoms include hallucinations, psychosis, memory disturbances, disinhibition, dyskinesia, autonomic dysfunction with flushing, tachycardia, arrhythmia, hypersalivation, catatonia, central hypoventilation, and diaphoresis.\textsuperscript{1,11,12}

The outcome depends on the speed of diagnosis, time to operation, and nosocomial complications.\textsuperscript{8} Excision of a teratoma yields improvement in 80% of patients.\textsuperscript{1} Permanent neurologic sequelae remain in 11.5%,\textsuperscript{11} and the mortality rate has been reported to be as high as 7%,\textsuperscript{1} which is independent of teratoma type.\textsuperscript{11}

Teratomas with anti-NMDA receptors are related to immune infiltrates in the brain;\textsuperscript{14} antibody deposits have been found in the brain on autopsy.\textsuperscript{15} The disease typically shows lymphocytic pleocytosis on cerebrospinal fluid (CSF) evaluation\textsuperscript{14} early in the disease and oligoclonal bands in advanced stages.\textsuperscript{16} Neuronal components in a teratoma typically trigger the immunologic reaction,\textsuperscript{15} although not all teratomas have neuronal components.\textsuperscript{17} The disease may be diagnosed by antibody titers, which are highest with confirmed malignancy\textsuperscript{10} and can be tested in blood, CSF, or tumor specimens. Normal antibody titers have a level less than 1:10 in the serum and less than 1:1 in the CSF.\textsuperscript{4} Levels should be monitored for improvement.

Symptom duration ranges from weeks to years, usually with rapid onset. Primary management involves tumor excision, high-dose steroids, intravenous immunoglobulins, or plasmapheresis.\textsuperscript{2} Tumor excision is linked to recovery time. If the aforementioned treatment methods fail, second-line therapy with rituximab and cyclophosphamide can be administered.\textsuperscript{2} Neurologic recovery is reported to be 80% by a median of 24 months, and typically after lengthy hospitalization and multidisciplinary treatment approaches.\textsuperscript{1} Relapse is possible in 12% of patients.\textsuperscript{1} The differential diagnoses for anti-NMDA receptor encephalitis includes drug toxicity, metabolic dysfunction, psychosis, seizures, viral encephalitis, autoimmune encephalitis, neuroleptic malignant syndrome, vasculitic diseases, Hashimoto encephalopathy, other infection, or a space-occupying brain lesion.\textsuperscript{5,12}

Emergent surgical intervention is recommended after neurologic stabilization, with best outcomes when
Management of the current case included rapid development of a differential diagnosis and concurrent anti-NMDA receptor antibody testing, pelvic structure evaluation, and first-line treatment initiation. This process could have been expedited if a pelvic examination had been performed on admission, although nothing in the reported history suggested a pelvic pathologic condition. Further investigation into OxyElite found that the diet pills had been recalled because of reports of nonviral hepatitis and 1 death, but no reported associations with encephalitis were noted.

The operation performed 3 days after the teratoma diagnosis was one of the earliest reported excisions, which we believe contributed to the patient’s recovery. Tumor markers had been tested to rule out other pelvic pathologic condition; endometriosis may have contributed to CA-125 elevation, as well as any of the components in the mass. Because of the emergent surgical procedure, surgical staging was not performed.

Postoperative management was complicated by inadequate analgesia; the patient required sedation with a fentanyl drip. A Foley catheter was maintained for a total of 20 days postoperatively for sedation, infection prevention during plasmapheresis, and prevention of further skin breakdown and fungal infection. She did develop 2 urinary tract infections, which were managed with ceftriaxone sodium.

The patient’s nutritional status was suboptimal; she had received nothing by mouth because of seizures preoperatively, and intermittently tolerated oral intake after sedation was discontinued. Enteral tube feedings were suggested, but the patient was too agitated. Total parenteral nutrition was contraindicated owing to the plasmapheresis. Multiple swallow studies were performed; however, the results were inconsistent because of the patient’s variable levels of alertness. She lost 10 kg during hospitalization.

Immature teratomas require full staging, but the patient’s family was amenable to incomplete staging with the possibility of reoperation or chemotherapy.
They understood the recurrence risks and were reassured that the patient’s childbearing potential would not be affected by the unilateral salpingo-oophorectomy. All appropriate follow-up appointments were scheduled for the patient upon discharge.

Conclusion

In a young female patient with acute encephalopathy or psychosis, it is important for physicians to evaluate for any organic causes of mental status changes, including gynecologic causes. Not all young women with encephalopathy will have an associated teratoma, but it is an important differential diagnosis to consider.

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References


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