CASE REPORT JSLS

Paraneoplastic Limbic Encephalitis Cured with Resection of an Adnexal Mass

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ABSTRACT

Background: Paraneoplastic syndromes are a heterogeneous collection of disease manifestations caused by underlying neoplasms, which can include adnexal masses.

Case: We report a case of paraneoplastic limbic encephalitis consisting of confusion, agitation, and aggression, which subsequently progressed to a comatose state, in the presence of an adnexal mass. It was cured with resection of a mature teratoma with focal immature components.

Conclusion: Female patients who present with symptoms of limbic encephalitis should be thoroughly screened for malignancy. Gynecologic consultation is an important component of the diagnostic workup when an adnexal mass has been identified. Paraneoplastic limbic encephalitis is a serious condition, yet it has a good prognosis if treated promptly with surgical resection of the adnexal mass.

Key Words: Adnexal mass, Paraneoplastic limbic encephalitis, Ovarian teratoma.

INTRODUCTION

Paraneoplastic syndromes are a heterogeneous collection of disease manifestations caused by underlying neoplasm.[1] This syndrome may involve the central nervous system, peripheral nervous system, or neuromuscular junction. Limbic encephalitis (LE) is a paraneoplastic syndrome involving the central nervous system.[2] The classic symptoms of LE include short-term memory impairment, seizures, confusion, irritability, depression, sleep disturbances, and psychiatric disturbances, with onset ranging from days to 12 weeks.[3] Paraneoplastic limbic encephalitis (PLE) is associated with a number of tumors, with ovarian teratomas accounting for 3% to 4% of cases.

The presence of immature features can be as high as 50% to 60% in ovarian teratomas associated with PLE. In contrast, in the general population, the majority of ovarian teratomas are mature, with only 3% possessing immature features.[4] PLE should be suspected in patients with LE who have an adnexal mass. Gynecologic consultation and prompt surgical management are essential to prevent permanent neurologic sequela, as illustrated in this case report.

CASE REPORT

A 29-year-old Caucasian multiparous female with a past medical history of epilepsy and vitamin B12 deficiency, and no prior history of mental illness, presented with complaints of confusion, agitation, and aggression. Shortly after the development of these symptoms, she was placed on a voluntary 72-hour hold at an outside hospital for psychotic behavior. Polysubstance abuse was initially suspected as the cause of her behavior; however, the patient denied any history of substance abuse and a urine drug screen was negative. She was discharged to home, but was readmitted several days later to the medicine service at the same hospital with similar complaints of confusion, agitation, and aggression. At that time, she also complained of mild abdominal pain, and an abdominal CT scan was obtained revealing a heterogeneous enhancing mass (15cm x 15cm x 12cm) arising from the right ovary, which contained fat, calcium, fluid, and septations. No further workup of this ovarian mass was performed at

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the outside hospital, as the mass was suspected to be a mature ovarian teratoma. A lumbar puncture revealed lymphocytic pleocytosis, making viral meningitis the working diagnosis. The patient was treated with acyclovir, vancomycin, and ceftriaxone. Over the next 3 days, the patient's mental status continued to decline; she would not follow simple commands and had no withdrawal to painful stimuli. However, she was breathing spontaneously and did not require mechanical ventilation. At this time, 8 days after her initial presentation, she was transferred to our facility for further evaluation and treatment of presumed viral encephalitis. A brain MRI with gadolinium showed no abnormality. An EEG was interpreted as severe encephalopathy with no epileptiform discharges. A CT scan of the abdomen and pelvis was repeated, confirming the presence of a mass (17cm x 13cm x 11cm) arising from the right ovary. The left ovary was unremarkable. There was no evidence of omental caking, ascites, or lymphadenopathy. Over the next few days, the patient remained comatose and showed no improvement in her neurologic examination; she was noted to have decorticate posture, with extension of her neck and clonus of all 4 extremities. Given the patient's clinical syndrome of acute psychosis with no prior history of psychiatric illness, inflammatory CNS findings, and coma, in the presence of a known ovarian mass, PLE was considered. At this time, the gynecology service was consulted.

On pelvic examination, the uterus was of normal size with a freely mobile 17-cm to 20-cm midline pelvic mass. Tumor markers, including CA125, CEA, AFP, and beta-hcg were obtained and were all within normal limits. The patient was taken to the operating room and underwent a unilateral salpingo-oophorectomy via mini-laparotomy as described by Rhodes et al.[5] The left ovary was examined and was noted to be within normal limits. Her postoperative course was uncomplicated. She was extubated less than 24 hours after her surgery. She remained in the intensive care unit briefly, where she was continued on intravenous fluids and tube feedings. Antibiotics were discontinued after her CSF and blood cultures were found to be negative for infectious etiologies. She was given 5 days of intravenous immunoglobulin to aid in clearing the presumed autoantibodies mediating her encephalopathy. Over the next several days, she progressively improved and was discharged home on postoperative day 11. The final pathologic diagnosis revealed the mass to be an ovarian teratoma with focal immature elements, without capsular penetration. No nonteratomatous germ cell tumor elements were identified. The patient was without any neurologic sequela at her 1-month postoperative visit.

DISCUSSION

Of all ovarian malignancies, germ cell tumors comprise only 5%. These tumors are usually unilateral and are primarily seen in adolescents. Ovarian teratomas typically present as an asymptomatic unilateral pelvic mass or abdominal pain.[6] Immature teratomas may contain tissue from all 3 embryonic germ cell layers with at least one of them lacking full differentiation. Neuroepithelial tissue usually is the origin of this immature tissue.[7] In the rare case that a teratoma is associated with PLE, the majority of women are not aware of having gynecological pathology, similar to our patient. Thus, awareness of paraneoplastic syndromes is important for various practitioners, including both neurologists and gynecologists.

Limbic encephalitis is a paraneoplastic syndrome affecting the central nervous system, which has a subacute onset of days up to 12 weeks. The classic symptoms of LE include short-term memory impairment, seizures, confusion, irritability, depression, sleep disturbances, and psychiatric disturbances. If left undiagnosed, patients with LE may develop progressive unresponsiveness (catatonia-like stage), central hypoventilation, autonomic instability (fluctuations in blood pressure, temperature, and cardiac rhythm), orofacial dyskinesias, and limb choreoathetosis (involuntary movements of the face and extremities) and dystonia. Further, intensive care support and ventilation may be required for several weeks or months.[8] LE can even lead to death when removal of the occult tumor is delayed.

The following tumors are most commonly associated with PLE: bronchial carcinoma (50% to 59%), with the majority being small cell lung cancer; testicular tumors (6% to 20%); breast cancer (3% to 8%); Hodgkin's lymphoma; ovarian teratoma (3% to 4%); and thymoma (2% to 5%). The presentation of LE precedes the diagnosis of malignancy in approximately 60% of cases, with the median interval between diagnosis of LE and underlying cancer being 3.5 months.[3] Thus, when PLE is suspected, a careful history and physical examination along with a thorough evaluation for the above tumors is essential.

A patient with symptoms of LE, with a malignancy that develops within 5 years of the diagnosis of the neurological disorder, meets diagnostic criteria for the diagnosis of PLE. Often onconeural antibodies against neural antigens that are expressed by the tumor can be identified.[2] Recent literature has found that patients without antibodies have a better response to treatment compared with patients with antibodies.[3] Therefore, laboratory assessment for

these onconeural antibodies not only serves as a diagnostic modality but also aids in predicting prognosis.

Gynecologists play a very important role in the management of PLE, as prompt tumor resection is the cornerstone of treatment for cases of PLE with an associated ovarian teratoma, and appears to have the best effect on neurological outcome.[3] In our case, the patient improved dramatically after the teratoma was resected and eventually had complete recovery. Ultimately, any woman who presents with symptoms of LE should be screened for cancer. Further, a gynecologic consult is an integral part of the workup of suspected PLE when an adnexal mass is identified.

CONCLUSION

Female patients who present with symptoms of LE should be thoroughly screened for malignancy. Further, gynecologic consultation is an important component of the diagnostic workup when an adnexal mass has been identified. Paraneoplastic limbic encephalitis is a serious condition, yet it has a good prognosis if treated promptly with surgical resection of the adnexal mass.

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