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Case Report

# Laparoscopic Cystectomy of Ovarian Teratoma in Anti-NMDAR Encephalitis: 2 Case Reports

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**ABSTRACT** We present 2 case reports of anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis that was successfully treated via laparoscopic ovarian cystectomy. In both cases, resection of an ovarian teratoma resulted in eventual full recovery. Although adnexectomy has been reported for tumor resection in anti-NMDAR encephalitis, we chose ovarian cystectomy to preserve ovarian function. The efficacy of cystectomy is equivalent to that of adnexectomy. This suggests that ovarian adnexectomy may not be necessary in anti-NMDAR encephalitis with ovarian teratoma. Journal of Minimally Invasive Gynecology (2011) 18, 135–137 © 2011 AAGL. All rights reserved.

*Keywords:* Anti-NMDAR encephalitis; Laparoscopic cystectomy; Treatment

That neurons can be the target of an autoimmune attack mediated by antibodies is still not well-acknowledged by the medical community [1]. In recent years, the description of antibodies against neuronal surface antigens in patients with paraneoplastic disease has bolstered the concept that antibodies against central nervous system antigens can be pathogenic [2]. Paraneoplastic encephalitis associated with ovarian teratoma has recently been reported with development of antibodies to the NR1 heteromers of the *N*-methyl-D-aspartate receptor (NMDAR) [3]. Although teratomas are among the most common ovarian benign neoplasms, accounting for 10% to 20% of all ovarian tumors [4], little is known about the prevalence and relationship between teratomas and anti-NMDAR encephalitis. Pivotal roles of NMDAR include synaptic transmission and remodeling, dendritic sprouting, and hippocampal long-term potentiation that is part of a paradigm of memory formation and leading [5]. Anti-NMDAR encephalitis is a highly characteristic syndrome that generally affects young women, is treatment responsive, and associated with tumors that can be benign [6]. Iizuka et al [6] reported that anti-NMDAR encephalitis and acute juvenile female nonherpetic encephalitis are the same. In this disorder, no association has yet been made with infections and cancer; however, inasmuch as most patients develop a prodromic viral-like illness, a postinfectious immune-mediated cause has been postulated. Resection of the tumor is likely important to attain final recovery or sustain the improvement that can be achieved soon after immunotherapy [3]. Herein, we present a case report of cystectomy of an ovarian teratoma in 2 patients that contributed to recovery from anti-NMDAR encephalitis.

## Case Reports

### *Case 1*

A 27-year-old woman without a medical history of interest suddenly developed psychosis and hallucinations. She was admitted to our hospital because of suspected meningitis and encephalitis. Empiric therapy was started immediately with intravenous ceftriaxone, acyclovir, and glycerol. Intravenous haloperidol was administered to control schizophrenialike symptoms. Initially, it was suspected that these neurologic symptoms were caused by herpes encephalitis.

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However, these therapies did not promptly restore normal status. The initial blood cultures were negative, and analysis of cerebrospinal fluid (CSF) for herpes simplex viruses 1 and 2 yielded normal findings. Systemic examination ruled out infection, collagen disease, schizophrenia, and malignancy. The neurologic symptoms gradually improved without specific therapy. From these results, it was suspected that the patient had acute juvenile female nonherpetic encephalitis. Abdominal ultrasonography revealed a right-ovarian mass. Pelvic magnetic resonance imaging revealed a teratoma measuring 4 cm in greatest diameter. A laparoscopic ovarian cystectomy was performed without intraoperative spillage of cyst contents. The clinical symptoms resolved completely about 2 weeks postoperatively. At histologic examination, the final diagnosis was mature cystic teratoma. There was no recurrence within 2 years after the operation.

### *Case 2*

A 26-year-old woman with no medical history of interest had headache and fever (temperature, 39.5°C) for a few days. She was alert, and focal neurologic signs were absent; however, she reported neck stiffness. Initial CSF examination demonstrated 1280 cells/μL, an elevated protein concentration (150 mL/dL), and decreased glucose concentration (41mg/dL). The patient was admitted to our hospital because of suspected meningitis. Empiric therapy was started immediately with intravenous ceftriaxone, acyclovir, and glycerol. The patient's condition improved, with no neurologic sequelae. However, on day 7 of hospitalization, she was disoriented to place and person, and had schizophrenialike symptoms. On day 12, she had a generalized tonic-clonic seizure. However, further examination ruled out infection, collagen disease, and malignancy. Pelvic computed tomography revealed a right-ovarian mass. These findings suggested the possibility of a teratoma with anti-NMDAR encephalitis, and high-dose intravenous immunoglobulin therapy was administered for 5 days. Ten days later, all neurologic symptoms were dramatically improved. No recrudescence developed throughout a month, and the patient was discharged home. Samples of serum and CSF were positive for anti-NMDAR antibodies, and titers were determined using serial dilutions of serum and CSF. From these results, anti-NMDAR encephalitis was diagnosed, and the patient underwent laparoscopic ovarian cystectomy a month after discharge from the hospital. Pelvic magnetic resonance imaging revealed a teratoma measuring 1 cm in greatest diameter. During the operation, laparoscopic ultrasonography was performed to confirm the tumor location. The examination was performed using 10-mm diameter, 7.5-MHz transducers (Hitachi Medical Corp., Tokyo, Japan). Intraoperative spillage of cyst contents did not occur. At histologic examination, the final diagnosis was mature cystic teratoma. There was no recurrence within 3 months after operation.

## Discussion

Despite the severity of symptoms and prolonged clinical course of anti-NMDAR encephalitis, patients usually recover if the disorder is recognized and appropriately treated [3]. However, because some patients demonstrate transient improvement with empiric use of corticosteroid therapy, intravenous immunoglobulin therapy, or plasma exchange, they may be discharged from the hospital without a final diagnosis, and subsequently deteriorate or die if the ovarian mass is not removed [3]. Therefore, search for and removal of a teratoma should be performed after the diagnosis of anti-NMDAR encephalitis. As reported by Iizuka et al [6], despite the presence of the tumor, the immune response is not maintained. However, the severity of this disorder, which may result in death or severe complications, and the reported response to tumor resection and immunotherapy strongly support the use of these treatments [6]. In addition, in previous reports, the surgical method of choice was generally adnexectomy [3,7,8]. Gynecologic surgeons should seriously consider offering patients the option of ovarian conservation. This is particularly crucial because anti-NMDAR encephalitis with ovarian teratoma primarily affects young women. Therefore, ovarian cystectomy is more reasonable than adnexectomy for removal of ovarian teratomas associated with anti-NMDAR encephalitis. More cases with longer follow-up are needed to confirm the prognosis.

Immunohistologic studies revealed that this patient's antibodies reacted with areas of the tumor that contained nervous tissue and demonstrated NMDAR expression [7]. The discovery of NR1-related antibodies in the serum and CSF in anti-NMDAR encephalitis provides a potential diagnostic test for the disorder. High titers of antibodies are significantly associated with the presence of ovarian teratoma. However, antibody titers, primarily those in the CSF, vary according to the clinical outcome [9]. A teratoma that expresses NMDARs is considered to contribute to the breakdown of immune tolerance. This supports the concept that cystectomy is effective for treatment of anti-NMDAR encephalitis.

In conclusion, we believe that the most appropriate treatment for anti-NMDAR encephalitis with ovarian teratoma is early cystectomy. As more cases accumulate, better understanding of the onset mechanism will emerge, and more appropriate management will result.

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