

[CASE REPORT]

Anti-*N*-methyl-d-aspartate Receptor Encephalitis Caused by a Teratoma Arising From the Retroperitoneum

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Abstract:

Anti-*N*-methyl-d-aspartate receptor (NMDAR) encephalitis is an autoimmune encephalitis, and 46% of women with anti-NMDAR encephalitis have tumors, of which 94% are ovarian teratomas. Patients with anti-NMDAR encephalitis rarely have extra-ovarian teratomas, particularly extra-ovarian mature cystic teratomas arising from the retroperitoneum. We herein report a 27-year-old woman who was diagnosed with anti-NMDAR encephalitis caused by a teratoma arising from the retroperitoneum. In patients with anti-NMDAR encephalitis, it is important to perform a systemic search, including for extra-ovarian teratomas. Plasma exchange significantly improved the patient's clinical symptoms.

Key words: NMDAR encephalitis, autoimmune encephalitis, teratoma, extra-ovarian teratoma

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Introduction

Anti-*N*-methyl-d-aspartate receptor (NMDAR) encephalitis is a type of autoimmune encephalitis that was first reported in 2005 (1). Dalmau et al. revealed anti-NMDAR as a cause of encephalitis in 2007. Tumors have been detected in 50% of women with anti-NMDAR encephalitis. Of the NMDAR encephalitis-causing tumors, 96% and 2% are ovarian and extra-ovarian teratomas, respectively (2). Mature extra-ovarian cystic teratomas in the retroperitoneum are particularly rare.

We herein report a 27-year-old woman who was diagnosed with anti-NMDAR encephalitis caused by a teratoma arising from the retroperitoneum.

Case Report

A 27-year-old woman presented to our hospital with cold-like symptoms, including a headache, fever, and vomiting. A week later, she developed psychiatric symptoms, such as

hallucinations and delusions. She was unable to communicate with her husband, tried to jump out of the window, and pointed a knife at her husband because she perceived him to be an attacker. On day 10, the patient was hospitalized for treatment. She had no remarkable medical or family history of disease.

Upon admission, she was unable to obey our commands with a Glasgow Coma Scale score of 10 (eye response to pain, localized motor response to pain, and inappropriate words as a verbal response). She was unable to talk to us and continued to speak to herself. Her blood pressure, heart rate, and respiratory rate were 141/81 mmHg, 67 beats/min, and 18 breaths/min, respectively. Her oral temperature was 37.7°C. Her pupils were mid-sized, isochoric, and light-reactive. Her cranial nervous system was normal, without obvious facial paralysis or sensory deficits. She did not have any paralysis, sensory loss, incoordination of the extremities, or involuntary movement.

Brain magnetic resonance imaging (MRI) did not reveal any obvious abnormal lesions (Fig. A). An electroencephalogram did not indicate any extreme delta brush, epileptiform

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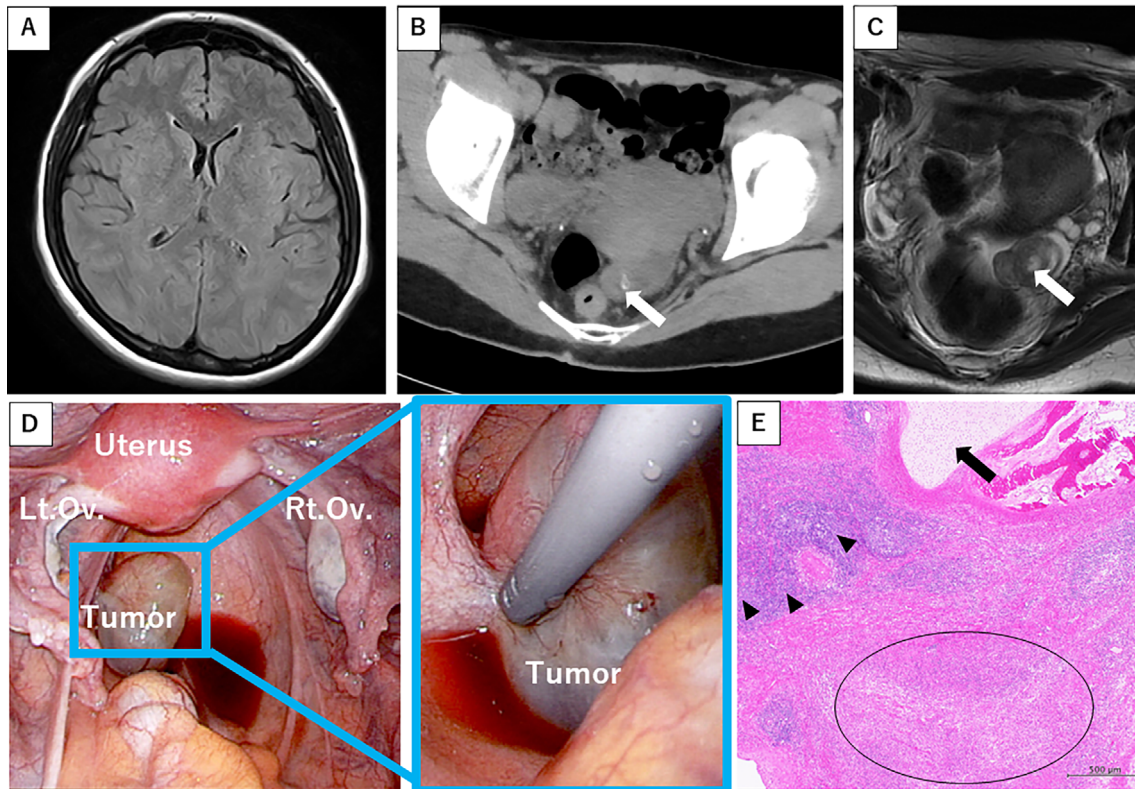


Figure. (A) Brain MRI fluid-attenuated inversion recovery showed no definitive lesion. (B) Pelvis CT scan, indicating a mass lesion with calcification in Douglas' pouch. (C) Magnetic resonance imaging (MRI) of the pelvis, revealing a mass lesion in Douglas' pouch. (D) On laparoscopy, the tumor was identified as originating from the peritoneum of Douglas' pouch, with bilateral ovaries exhibiting no evidence of pathology. (E) The mass in the pelvic region contained T cells (arrowheads), cartilage components (arrow), and nerve cells (circle).

discharges, slow waves, or ictal findings. A cerebrospinal fluid (CSF) analysis revealed a pressure of 115 mmH₂O, 14/μL white cells (predominance of mononuclear cells), 29 mg/dL proteins, 68 mg/dL glucose, and 0.64 IgG-index. Polymerase chain reaction for herpes simplex virus and varicella zoster virus yielded negative results. The CSF culture and cytology results were negative. Blood test results were negative for antinuclear antibodies, MPO-ANCA, PR3-ANCA, anti-thyroid peroxidase, anti-GAD, and anti-MOG antibodies. IgG-oligoclonal bands were not detected in the CSF or serum. Pelvic computed tomography (CT) revealed a mass with calcification in the Douglas' pouch (Fig. B). T2-weighted MRI of her pelvis also showed a mass lesion with an internal enrichment component in the Douglas' pouch (Fig. C). T1-weighted MRI could not be acquired because of severe body movements. We suspected the mass lesions in the Douglas' pouch to be teratomas based on her clinical symptoms and pelvic CT and MRI findings. Anti-NMDAR antibodies were detected in both serum and CSF (detected by commercial indirect immunofluorescence). Therefore, she was diagnosed with anti-NMDAR encephalitis with suspected extra-ovarian teratomas in the retroperitoneum.

As first-line immunotherapy, she was administered intravenous methylprednisolone (1 g/day) for 5 days starting from day 10. However, this treatment did not improve the

symptoms. Laparoscopic pelvic tumor resection under general anesthesia was performed on day 16. The tumor was identified as originating from the peritoneum of the Douglas' pouch, with bilateral ovaries exhibiting no evidence of pathology (Fig. D). The size of the tumor was 2.2 cm × 3.2 cm × 3.7 cm. Immunohistochemical results demonstrated focally positive staining for CD3, CD20, CD56, CD138, NSE, Ki-67, and GFAP and were entirely negative for CD30, S-100, Neurofilament, AE1/AE3, Chromogranin A, Synaptophysin, Calretinin, ER. The pelvic mass contained abundant fat. The pathological finding of the tumor was a retroperitoneum-derived mature cystic teratoma containing T cells, cartilage components, and nerve cells (Fig. E).

Postoperatively, the patient was extubated without respiratory problems. However, her condition did not improve significantly after surgery. She experienced apnea and reduced oxygen saturation on day 21 and required intubation and mechanical ventilation. After treatment with secondary intravenous methylprednisolone (1 g/day) for 5 days, her respiratory condition improved, and she was able to be extubated. However, she had prolonged impaired consciousness and psychiatric symptoms, including suicidal ideation, drowsiness, and anxiety. Therefore, as second-line immunotherapy, we performed plasma exchange therapy five times from day 29. After two rounds of plasma exchange on day 32, her

Table. Clinical Feature of Cases of Anti-NMDAR Encephalitis with Extra-ovarian Teratoma.

Age (sex)	Position of teratoma	Symptom	Treatment	Outcome	Reference
27 (M)	Anterior mediastinum	Fever, hallucination, convulsion, apnea	Operation IVMP PLEX	Improved	(9)
28 (F)	Anterior mediastinum	Headache, agitation, fluctuations in responsiveness	Operation IVMP IVIG	Improved	(10)
15 (F)	Thyroid	Fever, headache, abnormal behavior, hallucination, irritability	Operation IVMP IVIG PLEX	Improved	(11)

consciousness improved, and she no longer suffered from suicidal ideation. Based mainly on the evolution of the patient's level of consciousness, it was concluded that the patient's symptoms had improved with plasma exchange.

The patient was discharged on day 45 with no abnormal neurological findings after five rounds of plasma exchange. The patient did not receive maintenance immunotherapy.

Discussion

We encountered a 27-year-old woman who was diagnosed with anti-NMDAR encephalitis caused by a teratoma arising from the retroperitoneum. The patient was successfully treated using plasma exchange.

Few studies have reported extra-ovarian teratomas in anti-NMDAR encephalitis. Dubey et al. reported that the prevalence of anti-NMDAR encephalitis was 0.6/100,000 (3). Anti-NMDAR encephalitis is reportedly associated with tumors in 38% and 46% of all cases in women. Among the tumors found in women with anti-NMDAR encephalitis, 94% and 2% were ovarian and extra-ovarian teratomas, respectively, reportedly in the anterior mediastinum and thyroid. A PubMed search revealed two reported cases of anterior mediastinal teratoma and one case of thyroid teratoma (Table). Furthermore, 4% comprised other tumors caused by lung, breast, testicular, ovarian, thymic, and pancreatic cancer (4). Therefore, this case study is the first to report an anti-NMDAR encephalitis-induced retroperitoneal teratoma.

Mature cystic teratomas are benign tumors that account for 10-15% of ovarian tumors. Mature cystic teratomas arising outside the ovary are extremely rare (0.4%) (5) and are rarely found intracranially in the mediastinum or retroperitoneum. Therefore, we consider this case to be a valuable one of anti-NMDAR encephalitis caused by an extraovarian teratoma arising from the retroperitoneum.

Tumor resection and immunotherapy have been reported as anti-NMDAR encephalopathy treatments (4). Of the 501 patients with anti-NMDAR encephalitis who were followed for at least 4 months in previous studies, 197 (39%) displayed teratomas, 189 (38%) of which underwent tumor resection. Overall, 461 (92%), 134 (27%), 10 (2%), and 29 (6%) patients received first-line immunotherapy, second-line

immunotherapy, tumor resection without immunotherapy, and no treatment, respectively (4). The treatment algorithm proposed in 2011 included intravenous methylprednisolone, intravenous immunoglobulin, and plasma exchange as first-line treatment, with cyclophosphamide or rituximab alone or combined as second-line treatment (6). In the present case, plasma exchange led to improvement in consciousness and psychiatric symptoms. According to Zhang et al., the plasma exchange group (n=33) showed clinical improvement at 1 and 2 months compared with the non-plasma exchange group (n=24) among patients with severe refractory antibody-associated autoimmune encephalitis, including anti-NMDAR encephalitis (n=51) (7). According to the American Society for Apheresis, plasma exchange is recommended for patients with anti-NMDAR encephalitis (category I, grade 1 C) (8). Based on the results described above, plasma exchange may also be useful as a first-line treatment for anti-NMDAR encephalitis.

Conclusion

We herein report a case of anti-NMDAR encephalitis due to a teratoma originating from the retroperitoneum. It is important to perform a systemic search, including for extra-ovarian teratomas, for patients with anti-NMDAR encephalitis. Plasma exchange significantly improved the present patient's clinical symptoms.

The authors state that they have no Conflict of Interest (COI).

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