

# Early operative treatment of anti-N-methyl D-aspartate (anti-NMDA) receptor encephalitis in a patient with ovarian teratoma

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## Summary

**Background:** Anti-N-methyl D-aspartate (anti-NMDA) receptor encephalitis is often accompanied by ovarian teratoma. Early tumor resection is reported to be effective as a treatment. **Case:** A 21-year-old woman presented with anti-NMDA receptor encephalitis which was accompanied by ovarian teratoma. The present case was a very rare case of an early stage of anti-NMDA receptor encephalitis receiving operative treatment before confirming the presence of anti-NMDA receptor antibody. The diagnosis was established postoperatively by identifying anti-NMDA receptor antibody. **Conclusion:** In case of suspecting anti-NMDA receptor encephalitis in a patient with ovarian teratoma, early operative treatment should be considered even before confirming the presence of anti-NMDA receptor antibody.

**Key words:** Anti-NMDA receptor encephalitis; Ovarian teratoma.

## Introduction

Anti-N-methyl D-aspartate (anti-NMDA) receptor encephalitis often occurs in young females [1, 2]. Patients follow a very similar course, gradually improving after progressing through common cold symptoms, a period of psychiatric symptoms, an immobile period, and a hyperactive period [1-3]. This disorder results in a characteristic syndrome that presents with prominent psychiatric symptoms or, less frequently, memory deficits, followed by a rapid decline of the level of consciousness, central hypoventilation, seizures, involuntary movements, and dysautonomia [2, 4]. Definitive diagnosis is possible when anti-NMDA receptor antibody is detected in the cerebrospinal fluid and blood serum [3]. As a therapy, the immunotherapy including corticosteroids, intravenous immunoglobulin or plasma exchange are often effective [2-4].

Anti-NMDA receptor encephalitis is often accompanied by ovarian teratoma [1-6]. In patients with ovarian teratoma, early tumor resection is reported to be effective [1-6]. In most previously reported cases, the ovarian teratoma was removed a few months after neurological symptom presentation [1-6]. Moreover, operation was performed after confirming the presence of anti-NMDA receptor antibody in most cases [1-6]. There is no report that operation was performed before identifying anti-NMDA receptor antibody for patients with an early stage of disease.

The authors present a rare case of an early stage of anti-NMDA receptor encephalitis patient with ovarian teratoma,

who received early operative treatment before confirming of the presence of anti-NMDA receptor antibody.

## Case Report

A 21-year-old woman without a past medical history of interest developed epilepsy 25 days before admission to the present hospital. She visited a local doctor and was initially diagnosed with epilepsy. She was treated with antiepileptic drug such as diazepam, phenytoin, and acyclovir was started for suspicion of herpes simplex virus (HSV) encephalitis. Although the convulsions were under control by treatment and the disturbance of consciousness was improved, the involuntary movement of fingers of left hand was not responding to the treatment. Antiepileptic drug such as carbamazepine, phenobarbital, levetiracetam, and topiramate was added to treatment. She was admitted to the Department of Geriatric Medicine of the present hospital because of persistent symptoms.

The disturbance of consciousness and the involuntary movement of fingers of left hand was observed. No other psychiatric symptoms were observed. Magnetic resonance imaging (MRI) examination of the brain showed no remarkable findings. Single photon emission computed tomography (SPECT) study showed slight hypoperfusion in the left temporal region and the left occipital region. Electroencephalogram (EEG) showed no remarkable findings. On hospital day 8, contrast-enhanced computed tomography (CT) examination of the abdomen and chest demonstrated a right cystic adnexal mass with an internal focus of fat and high-attenuation material, suggesting an ovarian teratoma (Figure 1). Anti-NMDA receptor encephalitis accompanied by teratoma was initially considered the most likely diagnosis. Therefore, anti-NMDA receptor antibody was examined in the blood serum and steroid pulse therapy was initiated. On hospital day 10, she visited the present gynecologist.

Revised manuscript accepted for publication July 7, 2014

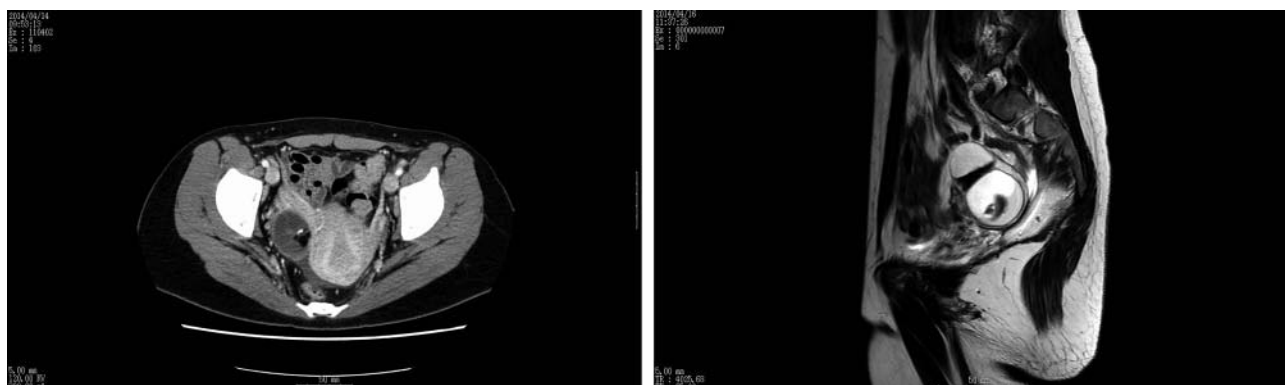


Figure 1. — Left: The image of computed tomography (CT) examination of the abdomen, which demonstrates a right cystic adnexal mass with an internal focus of fat and high-attenuation material. Right: The image of magnetic resonance imaging (MRI) examination of the pelvis, which demonstrates a right cystic adnexal mass with an internal focus of fat and calcification

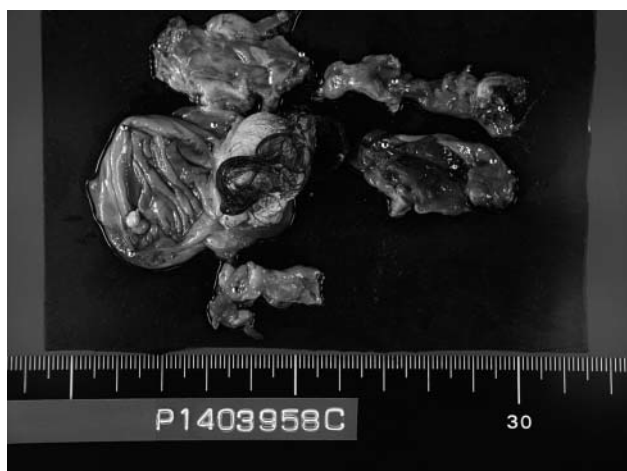


Figure 2. — The macroscopic image of resected specimen. There is a right ovarian tumor (size: 5 x 3 cm) which contains fat tissue and hair.

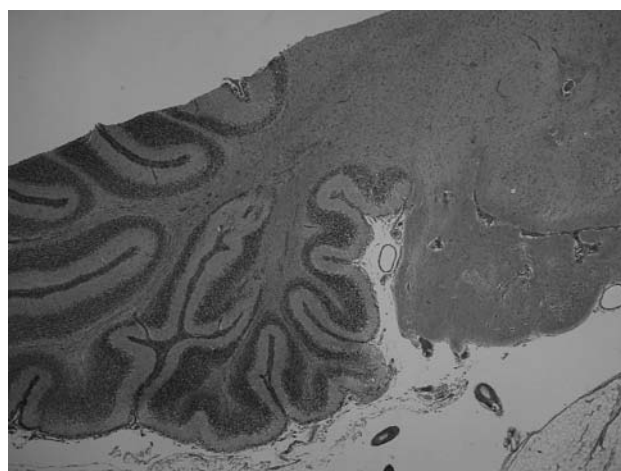


Figure 3. — The microscopic image of tumor cells (Hematoxylin & Eosin), which shows adipose, epithelial, and nervous tissues.

cology outpatient clinic and also underwent MRI examination of the pelvis, which demonstrated a right cystic adnexal mass with an internal focus of fat and calcification, suggesting an ovarian teratoma (Figure 1). Laboratory investigations showed no remarkable findings without slightly elevated liver enzymes. Serum tumor markers were within the normal ranges (CA125: 18 U/ml; CEA: 0.8 ng/ml; CA19-9: 11 U/ml; SCC: 0.6 ng/ml). The cytological examination of cervix showed no abnormality. The authors decided to perform operative treatment of right ovarian teratoma as a treatment of anti-NMDA receptor encephalitis before confirming the presence of anti-NMDA receptor antibody.

On hospital day 11, she underwent a laparoscopy-assisted cystectomy of right ovary. Macroscopically, there was right ovarian tumor (size: 5 x 3cm) which contained fat tissue and hair. The left ovary and uterus were unremarkable (Figure 2). There were no other remarkable findings in the peritoneal cavity.

Finally, the pathological examination showed a mature cystic teratoma, including adipose tissue, epithelial tissue and nervous tissue (Figure 3). The authors confirmed the diagnosis of mature cystic teratoma of right ovary. On hospital day 35, they confirmed

the presence of anti-NMDA receptor antibody and the diagnosis was established postoperatively.

On hospital day 40, the disturbance of consciousness was almost completely cured and the involuntary movement of fingers of left hand improved completely without progression of the disease.

## Discussion

Anti-NMDA receptor encephalitis is an autoimmune and paraneoplastic encephalitis first reported in 2007 by Dalmau *et al.* [1]. They reported clinical data gathered from around the world in 2008 [2]. This type of encephalitis often occurs in young women (approximately 80% of the patients are females and the median age is 23 years) [2]. Patients follow a very similar course, gradually improving after progressing through common cold symptoms such as fever, headache or malaise, a period of psychiatric symptoms, an immobile period, and a hyperactive period [1-3]. This dis-

order results in a characteristic syndrome that presents with prominent psychiatric symptoms or, less frequently, memory deficits, followed by a rapid decline of the level of consciousness, central hypoventilation, seizures, involuntary movements, and dysautonomia [2,4]. Definitive diagnosis is possible when anti-NMDA receptor antibody is detected in the cerebrospinal fluid and blood serum [3].

As a therapy, immunotherapy including corticosteroids, intravenous immunoglobulin or plasma exchange are often effective [2-4]. In non-responders, second-line immunotherapy including rituximab or cyclophosphamide or combined therapy is required [5, 6]. Despite the severe symptoms and prolonged clinical course, 75% of patients achieve complete recovery [2]. The mortality rate is reported to be 7% [2]. On the other hand, anti-NMDA receptor encephalitis is often accompanied by teratomas in various regions such as an ovary [1-6]. Dalmau *et al.* reported that 31% of female patients had a tumor and all tumors were ovarian teratomas [2]. In patients with ovarian teratoma, early tumor resection is reported to be effective [1-6]. In most previously reported cases, the ovarian teratoma was removed in a few months (median: nine weeks) after neurological symptom presentation, sometimes when symptoms had already partially responded to immunotherapy [1-6]. Moreover, surgery was performed in most cases after confirming the presence of anti-NMDA receptor antibody. Although operation was performed before confirming the presence of anti-NMDA receptor antibody in a few cases, these patients were in advanced stage of disease and were transferred to the intensive care unit (ICU). There was no report that operation was performed before identifying anti-NMDA receptor antibody for patients with an early stage of disease. In this report, the authors present a rare case of an early stage of anti-NMDA receptor encephalitis patient with ovarian teratoma, who received early operative treatment before confirming the presence of anti-NMDA receptor antibody.

In the present case, a 21-year-old woman presented with neurological symptom onset 25 days before admission to the present hospital. On hospital day 8, ovarian teratoma was detected by CT and anti-NMDA receptor encephalitis was initially considered the most likely diagnosis. On the same day, anti-NMDA receptor antibody was examined in the blood serum and steroid pulse therapy was initiated and operative therapy was performed three days later. The present authors confirmed the presence of anti-NMDA receptor antibody and the diagnosis was established postoperatively. Iizuka T *et al.* reported that early tumor resection seemed to be the most important factor enabling prompt and full re-

covery from anti-NMDA receptor encephalitis [7]. They also reported that early treatment could shorten the duration of ventilatory support and dyskinesia compared with that of patients without tumor resection [7]. The present case was a case of an early stage of anti-NMDA receptor encephalitis. Considering possibility of worsening of the disease status, the authors performed operative treatment before confirming the presence of anti-NMDA receptor antibody. By early operative treatment, the present patient seemed to recover early and achieve almost complete recovery without progression of disease.

If young female patient with ovarian teratoma presents encephalitis or psychiatric symptoms, anti-NMDA receptor encephalitis should be considered as a diagnosis. Moreover, early operative treatment should be considered even before confirming the presence of anti-NMDA receptor antibody.

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