

Occult Ovarian Teratoma and Neuropsychiatric Manifestations: Recent Advances in Diagnosis, Autoimmune Pathogenesis and Multidisciplinary Management—A Case-Based Review

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Abstract

Occult ovarian teratoma is an uncommon but clinically significant cause of **anti-N-methyl-D-aspartate receptor (anti-NMDA receptor) encephalitis**, a form of autoimmune encephalitis characterized by acute neuropsychiatric symptoms. The disease frequently presents with **first-episode psychosis**, hallucinations, delusions, catatonia, seizures, memory impairment and autonomic instability. Recent evidence has emphasized the importance of identifying autoimmune aetiologies in young women presenting with atypical psychiatric symptoms or rapidly progressive neurological deterioration. This article summarizes current knowledge regarding the epidemiology, autoimmune pathogenesis, neuropsychiatric manifestations, diagnostic approaches and multidisciplinary management of occult ovarian teratoma-associated anti-NMDA receptor encephalitis. The review highlights the role of ectopic neural tissue within mature cystic teratomas in triggering antibody-mediated neuronal dysfunction and discusses advances in cerebrospinal fluid antibody testing, neuroimaging, pelvic imaging, and immunotherapy. Early diagnosis combined with prompt immunotherapy and surgical removal of the teratoma has significantly improved neurological and psychiatric outcomes. Greater awareness among psychiatrists, neurologists, gynaecologists, radiologists, and pathologists is essential to reduce diagnostic delays and improve long-term prognosis.

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Introduction

Occult ovarian teratoma is an important yet frequently overlooked cause of autoimmune encephalitis in young women. Mature cystic teratomas or dermoid cysts, are the most common benign ovarian germ-cell tumors and account for approximately **20% of all ovarian neoplasms**. While most remain asymptomatic, a subset contains mature neural tissue capable of triggering an autoimmune response directed against neuronal surface antigens, particularly the N-methyl-D-aspartate receptor (NMDAR).

The discovery of anti-NMDA receptor encephalitis by **Dalmau and colleagues** transformed the understanding of acute psychosis and encephalopathy. Rather than representing a primary psychiatric illness, many patients were found to have an immune-mediated disorder initiated by an underlying ovarian teratoma. The resulting antibodies disrupt glutamatergic neurotransmission, producing a constellation of psychiatric, neurological, and autonomic manifestations.

Psychiatric symptoms—including anxiety, insomnia, hallucinations, agitation, delusions, and behavioural changes—often dominate the early clinical course and may precede neurological signs by days or weeks.

Over the past decade, advances in antibody testing, neuroimaging, and multidisciplinary care have substantially improved outcomes. Current evidence supports early cerebrospinal fluid antibody testing and pelvic imaging in young women presenting

with first-episode psychosis accompanied by atypical neurological features or poor response to antipsychotic therapy.

To complement the current evidence, we present an illustrative case of a young woman whose initial presentation with acute psychosis and catatonia masked the underlying diagnosis of anti-NMDA receptor encephalitis associated with an occult ovarian teratoma. The case highlights the importance of early multidisciplinary evaluation and reinforces key diagnostic and therapeutic principles discussed in this review.

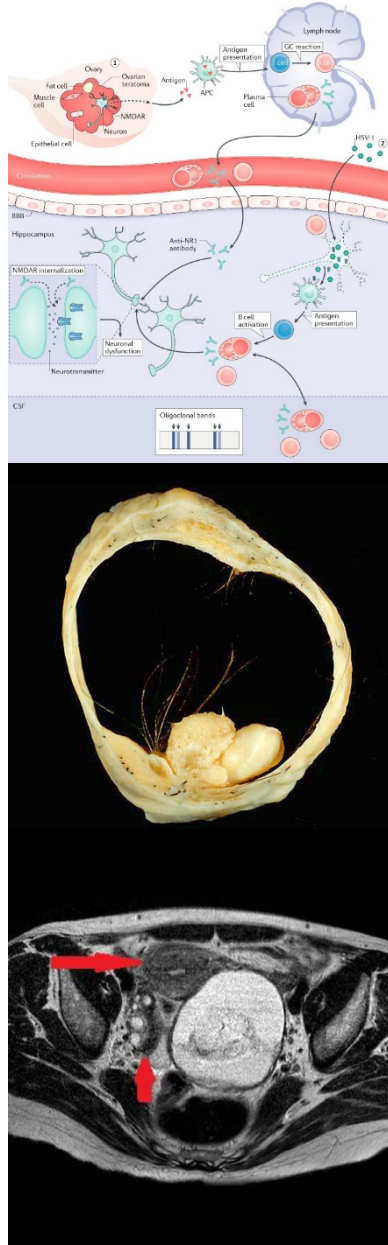
Epidemiology

Anti-NMDA receptor encephalitis is now recognized as one of the most common autoimmune encephalitis in children and young adults. Females account for approximately **80%** of reported cases, with the highest incidence occurring between **18 and 35 years of age**. Among adult women diagnosed with anti-NMDA receptor encephalitis, **up to 56%** are found to harbour an ovarian teratoma, whereas the prevalence is considerably lower in paediatric patients and men.

A recent integrative study estimated that **37.4% of female patients** with anti-NMDA receptor encephalitis have an associated ovarian teratoma, underscoring the importance of pelvic imaging in suspected cases. Mature cystic teratomas comprise nearly **74%** of tumour types associated with the disorder, reflecting the presence of ectopic neural tissue capable of initiating antibody production.

Earlier diagnosis has translated into better clinical outcomes, with studies demonstrating recovery rates exceeding **75–80%** when immunotherapy is combined with prompt tumors resection.

Autoimmune Pathogenesis



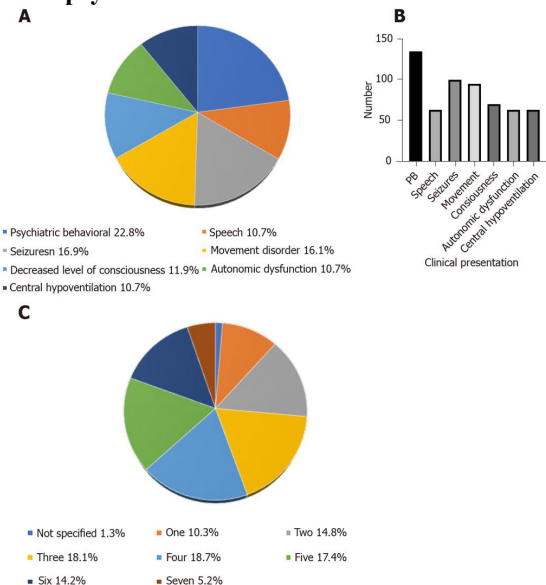
The association between occult ovarian teratoma and anti-NMDA receptor encephalitis is one of the best-characterized examples of a paraneoplastic autoimmune neurological disorder. Mature cystic ovarian teratomas frequently contain differentiated tissues derived from all three germ layers, including **ectopic neural tissue**. This neural tissue expresses N-methyl-D-aspartate (NMDA) receptors that are recognized as foreign by the host immune system, triggering the production of anti-NMDA receptor antibodies.

Following antibody production, disruption of the blood–brain barrier permits circulating immunoglobulin G (IgG) antibodies to enter the

central nervous system and bind to the GluN1 subunit of the NMDA receptor. Rather than destroying neurons, these antibodies induce receptor internalization, reducing synaptic NMDA receptor density and impairing glutamatergic neurotransmission. The resulting dysfunction particularly affects the hippocampus, frontal cortex, and limbic system, explaining the characteristic psychiatric, cognitive, and neurological manifestations.

The clinical progression is typically multiphasic. Patients often experience a viral-like prodrome with fever, headache, or malaise, followed by abrupt psychiatric symptoms. Neurological deterioration subsequently develops with seizures, movement disorders, autonomic instability, and, in severe cases, respiratory failure requiring intensive care. Because psychiatric manifestations precede neurological findings in most patients, diagnosis is frequently delayed until neurological symptoms become prominent.

Neuropsychiatric Manifestations



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Psychiatric Manifestations

Psychiatric symptoms are present in **approximately 90%** of affected patients and include behavioural disturbances, psychosis, mood changes, hallucinations, and cognitive dysfunction besides delusions, agitation and aggression, anxiety and panic attacks, catatonia and insomnia.

Neurological Symptoms

Neurological features usually emerge within days to weeks after psychiatric symptoms and often indicate disease progression.

The most frequently reported symptoms include Seizures, Oromaxillary dyskinesias, speech dysfunction, Aphasia, memory impairment, reduced consciousness, central hypoventilation, autonomic instability and cardiac arrhythmias.

Clinical Red Flags for Psychiatrists

Early recognition is essential because this condition is highly treatable. The following features should raise suspicion for autoimmune encephalitis rather than a primary psychiatric disorder:

- First-episode psychosis in a young woman (18–35 years)
- Rapid progression over days or weeks
- Poor response to antipsychotic medication
- New-onset seizures
- Catatonia or abnormal involuntary movements
- Speech deterioration
- Autonomic instability (tachycardia, blood pressure fluctuations, hyperthermia)
- Reduced level of consciousness

Recent meta-analysis recommends **early cerebrospinal fluid anti-NMDAR antibody testing and pelvic imaging** in patients presenting with these red flags to facilitate timely diagnosis and improve neurological and psychiatric outcomes.

Illustrative Case Presentation

A 30-year-old unmarried woman with no previous psychiatric illness presented with a one-month history of progressive behavioral changes characterized by excessive talkativeness, impulsive spending, paranoid ideation, visual and auditory hallucinations, self-muttering, and second-person auditory hallucinations. She held a master's degree in English, worked as an artist, and had a ten-year history of polycystic ovarian disease (PCOD). There was no significant family history of psychiatric or neurological illness.

Initially diagnosed with an acute psychotic disorder, she was admitted to a neuropsychiatric hospital where her symptoms failed to improve despite treatment. One week later, she developed catatonic features, including mutism, prolonged staring, refusal to eat, and stereotypic movements involving the jaw and both hands. A lorazepam challenge test produced minimal improvement.

Within two days of admission, she developed fever (100.4°F) and generalized seizures, prompting transfer to the neurology service. Brain magnetic resonance imaging (MRI) and routine hematological investigations were unremarkable, whereas serum prolactin was elevated (68.92 ng/mL). Cerebrospinal fluid (CSF) analysis demonstrated positive anti-NMDA receptor antibodies, confirming autoimmune encephalitis. Computed tomography (CT) of the abdomen and pelvis revealed a left ovarian teratoma with partial torsion of the pedicle.

A diagnosis of **anti-NMDA receptor encephalitis secondary to an occult ovarian teratoma presenting with acute psychiatric symptoms** was established. Initial management with lorazepam and broad-spectrum antibiotics failed to improve her neurological status. Subsequently, she received intravenous methylprednisolone pulse therapy for

five days followed by intravenous immunoglobulin (IVIG, 140 g). Following gynecological consultation, laparoscopic ovarian cystectomy was performed. The patient's neurological and psychiatric symptoms improved progressively after surgery, and she was discharged in stable condition with planned multidisciplinary follow-up.

Discussion of the Illustrative Case

This case exemplifies several characteristic features of ovarian teratoma-associated anti-NMDA receptor encephalitis described in recent literature.

1. Initial psychiatric presentation

The patient's illness began with psychosis, mania-like symptoms, hallucinations, and paranoia without obvious neurological deficits.

2. Evolution to catatonia

The subsequent development of catatonia and stereotypic movements represents a recognized progression of autoimmune encephalitis.

3. Development of neurological symptoms

The appearance of fever and seizures within days of psychiatric hospitalization represents the classic transition from psychiatric to neurological disease.

4. Importance of CSF testing

CSF anti-NMDA receptor antibody positivity established the diagnosis, emphasizing that normal neuroimaging does not exclude autoimmune encephalitis.

5. Detection of occult ovarian teratoma

The ovarian teratoma was identified only after neurological evaluation. This illustrates why pelvic imaging should be performed in young women presenting with first-episode psychosis accompanied by atypical neurological features.

6. Multidisciplinary treatment

The patient's favourable outcome following immunotherapy and ovarian cystectomy supports current recommendations advocating early combined medical and surgical management.

Diagnosis

Early diagnosis of occult ovarian teratoma-associated anti-NMDA receptor encephalitis remains challenging because psychiatric manifestations frequently precede neurological symptoms. Delayed recognition may result in prolonged hospitalization, intensive care admission, and poorer neurological outcomes.

The diagnosis relies on a combination of **clinical evaluation, laboratory testing, neuroimaging, and pelvic imaging**.

Histopathology

Definitive diagnosis of the ovarian lesion is established following surgical excision and histopathological examination. Mature cystic teratomas typically contain tissues derived from all three germ layers, including skin, hair follicles, sebaceous glands, cartilage, bone, and neural tissue. The presence of mature neural elements is believed to initiate the autoimmune response responsible for anti-NMDA receptor encephalitis.

Multidisciplinary Management

Successful treatment requires close collaboration among **psychiatrists, neurologists, gynaecologists, radiologists, pathologists, immunologists, and intensive care specialists**. The combination of immunotherapy and prompt surgical removal of the ovarian teratoma has become the standard of care.

Immunotherapy

First-line immunotherapy includes:

- High-dose intravenous methylprednisolone
- Intravenous immunoglobulin (IVIG)
- Plasma exchange

Patients who fail to respond adequately may receive second-line therapies such as:

- Rituximab
- Cyclophosphamide

Supportive management includes seizure control, intensive monitoring of autonomic instability, respiratory support when required, nutritional rehabilitation, and psychiatric symptom management.

Surgical Treatment

Current evidence strongly supports **early surgical removal of the ovarian teratoma**, even in patients with severe neurological impairment. Laparoscopic cystectomy is preferred for benign lesions in women wishing to preserve fertility, whereas oophorectomy may be indicated in selected cases based on age, tumour characteristics, or surgical findings.

A 2024 systematic review reported that **97% of patients underwent surgical resection**, with **62.2% achieving complete neurological recovery** and **34.4% experiencing partial recovery** following combined immunotherapy and surgery.

Future Perspectives

Advances in autoimmune neurology continue to improve the diagnosis and management of anti-NMDA receptor encephalitis. Future research should focus on identifying reliable biomarkers capable of detecting disease during the earliest psychiatric phase before neurological deterioration occurs.

Incorporating autoimmune encephalitis into the differential diagnosis of acute psychosis may facilitate earlier treatment and improve long-term neurological and psychiatric outcomes.

Conclusion

Occult ovarian teratoma-associated anti-NMDA receptor encephalitis represents a rare but highly treatable cause of acute neuropsychiatric illness. Psychiatric manifestations frequently precede neurological symptoms, making early recognition by psychiatrists essential.

Recent advances in cerebrospinal fluid antibody testing, neuroimaging, and pelvic imaging have substantially improved diagnostic accuracy. Early initiation of immunotherapy combined with prompt

surgical removal of the ovarian teratoma remains the cornerstone of treatment and is associated with favourable neurological and psychiatric recovery in the majority of patients.

A multidisciplinary approach involving psychiatry, neurology, gynaecology, radiology, pathology, and intensive care medicine is essential to reduce diagnostic delays, improve clinical outcomes, and minimize long-term disability. Continued research into biomarkers, standardized diagnostic algorithms, and long-term follow-up will further enhance the management of this important neuro-immunological disorder.

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