CASE REPORT

A rare case of anti-N-methyl-D-aspartate receptor encephalitis during pregnancy

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Abstract

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis was first described as a severe form of encephalitis by Dalmau et al in 2006. This is an autoimmune disorder usually associated with paraneoplastic mechanism that manifests as neuropsychiatric disorder affecting mainly women of child-bearing age. Nevertheless anti-NMDA receptor encephalitis is a rare condition during pregnancy. To date, there have been only four reported cases during pregnancy.

We report a case of a 23-year-old primigravida in first trimester pregnancy with altered mental status and multiple neurological symptoms related to anti-NMDA receptor encephalitis. To the best of our knowledge, this is the first reported anti-NMDA receptor encephalitis during pregnancy in Australasia.

Anti-NMDA receptor encephalitis has been increasingly reported over the last decade, predominantly in young women harbouring ovarian teratomas. Removal of the tumour and immunotherapy often result in recovery. In all syndromes, deficits may be reversible despite the duration or severity of symptoms. This also holds true in patients who fall ill during pregnancy. The current literatures show that anti-NMDA receptor encephalitis can have good outcome for both the mother and new-born.

Case report

A 23-year-old primigravida in first trimester pregnancy presented with 3-day history of fever (38°C), acute confusion, disinhibited behaviour, auditory hallucinations and generalised body shaking without loss of consciousness. She had history of multiple suicide attempts but no previous history of psychosis or illicit substance use. At the time of onset, she also experienced extreme social stressors with recent demise of her grandfather.

The pregnancy unfortunately ended with miscarriage within 2 days of hospitalisation. She was treated initially as herpes simplex virus (HSV) encephalitis with poor response. A week after admission, she developed decrease level of consciousness with Glasgow coma scale of 6 requiring intubation and admission into intensive care unit (ICU). She also experienced increasingly dysautonomic symptoms and frequent limb dyskinesia. These symptoms were difficult to control despite high dose of sedatives (propofol, remifentanil, midazolam and isoflurane).

Cerebrospinal fluid (CSF) analysis showed leucocytosis 3.74 × 10^6/L, 94% lymphocytes, glucose 3.5 mmol/L (normal range: 2.8–4.4 mmol/L), protein 0.57 g/L (normal range: 0.15–0.45 g/L).

General culture, HSV DNA, varicella zoster virus (VZV) DNA and enterovirus RNA were negative. CT brain showed normal brain parenchyma. Brain MRI without contrast showed abnormal signal within the right hippocampus, cerebellar hemispheres and cerebellar vermis, which were hyperintense on T2 and FLAIR imaging. It was not associated with diffusion restriction.

Initial electroencephalogram (EEG) showed rhythmic slow delta waves of 2.5–3.5 Hz over both hemispheres. Repeat EEG showed widespread bilateral rhythmic and semi-rhythmic delta activities which were predominantly frontal.

Autoimmune encephalitis was considered after 12 days of hospitalisation. Serum NMDA antibody was positive confirming diagnosis of anti-NMDA receptor encephalitis. CSF was not tested. Initial pelvic and transvaginal ultrasound were unremarkable. A pelvic CT scan showed 2 cm right ovarian teratoma, which was subsequently removed. She was also treated with methylprednisolone.
plasmapheresis and rituximab. She received prolonged intensive care treatment for over 4 months requiring intubation and tracheostomy.

Five months post oophorectomy, she showed reduced general psychomotor status requiring walking stick to mobilise and slow language function. She continued to make good recovery and steady improvement. One and half years later, she is independent with mobility and able to converse in short sentences.

**Discussion**

Anti-NMDA receptor encephalitis is increasingly recognised as a multistage illness that progresses from psychosis, memory deficits, seizures, language disturbance to autonomic instability. Diagnosis of anti-NMDA receptor encephalitis is based on identification of antibodies in serum or CSF. The disorder predominantly affects young adults, particularly women (80%) of child-bearing age. The antibody subtypes (IgG1, IgG3) can cross the placenta raising concern about effects on the fetus during pregnancy.¹ Our patient’s serum showed presence of NMDA receptor antibody. CSF was not tested.

Gresa-Arribas et al suggests that the sensitivity of NMDA receptor antibody testing is higher in CSF than in serum.⁶ The antibody titres in CSF and serum correlate with clinical outcome with higher levels in patients with poor outcome or teratoma than in patients with good outcome or no tumour.

There are four reported cases of anti-NMDA receptor encephalitis during pregnancy to date. All the cases had ovarian teratomas. In two cases, the pregnancies went to term with delivery of healthy babies. In one case, emergency caesarean section was performed at 32 gestation weeks with delivery of a healthy baby and the fourth case with termination of pregnancy in a patient with recurrent bilateral ovarian teratomas.¹

Previous case reports reported accelerated recovery after delivery or termination of pregnancy. Our patient miscarried in first trimester and she underwent prolonged recovery period which included 4 months of ICU stay.

The majority of cases with anti-NMDA receptor encephalitis are associated with neoplasm, especially germ cell tumour. Analysis of 400 patients confirms that the tumour is less likely to be detected in younger patients (age < 25 years).² In our patient, the initial pelvic and transvaginal ultrasound did not yield any abnormal findings.

Pelvic CT showed evidence of a right ovarian tumour. Prior to detection of the ovarian tumour, she was treated with methylprednisolone, plasmapheresis and rituximab. The current literature shows that patients who are treated with tumour resection and immunotherapy respond faster to treatment in comparison to patients without tumour who receive similar immunotherapy.

Recovery from anti-NMDA receptor encephalitis occurs slowly. Social behaviours and dysexecutive symptoms are usually the last to improve, preceded by several months of hospitalisations and rehabilitation. One and half years post-discharge, our patient is functioning well in the community and she is planning to resume her job as a caregiver.

This case highlights the importance of including anti-NMDA receptor encephalitis in differential diagnosis in young patients with acute psychosis. Early diagnosis and treatment can improve outcomes for this severe disease.

**Competing interests:** Nil.

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References


