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Anti-NMDA-receptor encephalitis during pregnancy: A case report and literature review

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Abstract

Anti-*N*-methyl-D-aspartate receptor (anti-NMDA-R) encephalitis is an autoimmune disorder that was first described by Dr Vitaliani in 2005. In 2007, Dalmau *et al.* found anti-NMDA-R antibody expressed both in the hippocampus and prefrontal nerve cell membrane, finally proposing the diagnosis of autoimmune anti-NMDA-R encephalitis. Most of the patients are female (91%), with ages ranging from 4 to 76 years. The average age is 23 years, a birth peak age, although anti-NMDA-R encephalitis is rare during pregnancy. The disorder is characterized by prominent psychosis, dyskinesias, seizures, autonomic disturbance, and central hypoventilation. We report a 24-year-old woman hospitalized at 28 gestational weeks with acute-onset psychosis. Over the course of 3 weeks, her mental status worsened until she fell into a coma. Both serum and cerebrospinal fluid anti-NMDA-R antibodies were found to be positive. At cesarean section, a healthy baby boy was born and a wedge-shaped bilateral ovarian resection was performed. Treatment with corticosteroids, intravenous immunoglobulin, and plasmapheresis can lead to improved outcomes for both mother and baby.

Key words: encephalitis, *N*-methyl-D-aspartate, pregnancy, receptor autoimmune.

Introduction

N-methyl-D-aspartate (NMDA) receptors play crucial roles in synaptic plasticity transmission.[1] NMDA receptors are heteromeric ion channels activated by the simultaneous binding of glutamate in the receptor subunit subtype NR2 and NR1 and glycine (or D-serine) in the subunit subtype NR3. In recent years, in addition to stroke, NMDA receptor dysfunctions have been implicated in neuropsychiatric disorders and severe forms of encephalitis associated with antibodies that directly target the NR1 subunit.[2]

Clinical features of a paraneoplastic neuropsychiatric disorder in ovarian teratoma were first reported by Vitaliani *et al.*[3] Subsequent study further identified autoantigens that are functional heteromers of NDMA receptors in patients with paraneoplastic encephalitis associated with teratomas.[4,5] Indeed, ovarian teratomas have frequently been shown to express NMDA receptors.[6] Case reports and literature reviews have gradually covered most aspects of antibody-mediated pathogenesis in anti-NMDA-receptor (anti-NMDA-R) encephalitis associated with ovarian teratoma. However, the characteristics, syndromes, treatments, and outcomes of anti-NMDA-R encephalitis in pregnant women remain to be explored.

Case Report

A 24-year-old woman presented during the 28th gestational week (GW) with psychiatric symptoms. The patient developed visual and auditory hallucinations. She claimed that people cursed her and that doctors were

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going to kill her and her baby. She was first admitted to the psychiatric ward for observation. Cerebrospinal fluid (CSF) showed slightly elevated total nucleated cells of 5/L with lymphocytic predominance (white blood cell count, 11/μL), with normal protein (24 mg/dL), glucose (59 mg/dL), and lactate (1 mmol/L) concentrations. A complete blood count showed a white cell count of 12.5 $\times$ 10^9/L with neutrophilic predominance. Prolonged video electroencephalogram (EEG) revealed several generalized seizures during sleep, which showed moderate to severe abnormalities (Fig. 1b). The results of brain MRI and magnetic resonance spectroscopy were normal (Fig. 1d). Testing for autoimmune disorders, rheumatologic disorders, Wilson's disease, Huntington's disease, viral infection, and heavy metal poisoning were unremarkable. As the patient's mental status quickly degraded, she was transferred to the Neurology Department for further evaluation and treatment. She developed involuntary tongue thrusting and generalized seizures, accompanied by neck stiffness and episodes of opisthotonus, which lasted for 5 min to 1 h. Eventually she stopped talking and became inactive. Follow-up MRI was performed to exclude brain stroke or other neurologic complications (Fig. 1e). Blood, urine, and CSF samples were culture-negative. Polymerase chain reaction and serological infectious testing of CSF were all negative. The results from peripheral blood smear, antistreptolysin O test, vitamin E evaluation, ceruloplasmin blood test, vanillylmandelic acid test, and anti-DNAse B test were unremarkable. A complete set of thyroid tests showed a decrease in thyroid-stimulating hormone (0.100 ml/L), an increase in reverse triiodothyronine (1.22 nmol/L), an increase in thyroxin (178.30 nmol/L), and an increase in free thyroxine (24.60 pmol/L). Blood electrolytes showed decreased potassium and calcium levels (3.10 mmol/L and 1.93 mmol/L, respectively). Biochemical examination revealed low levels of serum albumin (29.90 g/L), alanine aminotransferase (24 U/L), aspartate transaminase (37 U/L), blood urea nitrogen (4.41 mmol/L), and creatine (47umol/L). Blood gas analysis showed a pH of 7.45, pCO2 of 4.3 KPa, pO2 of 14.7 KPa, bases excess (BE) of −1.3 mmol/L, standard bicarbonate (SB) of 23.9 mmol/L, and HCO3 of 22.2 mmol/L. Antineuronal nuclear antibody-1, -2, and -3, Purkinje cell cytoplasmic antibody-1 and -2, anti-glial/neuronal nuclear antibody-1, antibody to acetylcholine receptor (AChR), ganglionic AChR, N-type calcium channel, P/Q-type calcium channel, and voltage-gated potassium channel were all negative. Toxicology screening was negative. An MRI of the abdomen and pelvis did not reveal any ovarian cyst (Fig. 1c). The patient was treated with fentanyl, lorazepam, propofol, and bromocriptine without any improvement. However, both the CSF and the serum were positive for NMDA antibodies on the 18th day of admission. Based on these findings, the patient was diagnosed with anti-NMDA-R encephalitis. A course of intravenous immunoglobulin (0.4 g/Kg/day) accompanied by methylprednisolone (1000 mg/day) was given daily for 10 days. However, her comatose mental state did not improve and epileptic seizures were observed intermittently. At the 28th day of admission, at 33^{+2} GW, the patient was transferred to the Obstetrics Department because of abnormal fetal monitoring.

The patient had started experiencing repeated episodes of vomiting and nausea 42 days after her last menstrual period and was positive for human chorionic gonadotropin test. She had experienced no vaginal bleeding, fluid flow, poison, or radiation exposure in the early stages of her pregnancy. She had felt fetal movement at 17 GW. She had had no health problems or family history of disease. Ultrasonography, performed regularly, had revealed normal fetal anatomy and appropriate growth for gestational age.

At 33 GW, while the patient was comatose, the non-stress test suggested the fetus was not reactive. An emergency cesarean section was performed after dexamethasone administration to enhance lung maturation. The infant weighed 408 g and Apgar scores were 9 at 1 min, 10 at 3 min and 10 at 5 min. The placenta was 18 cm in diameter and 2.5 cm in thickness. Bilateral ovarian wedge resection was performed. All surgical specimens were confirmed normal by pathologists. After the operation, a gastrostomy tube placement was carried out to provide nutrition and medication to the patient due to her frequent epileptic seizures. Trials of clonazepam, amantadine, haloperidol, carbamazepine, levetiracetam, and valproic acid were used to treat the seizures. Water and electrolyte balance were maintained at perfect levels. Over the next week, the patient was weaned from the ventilator and her consciousness level started to improve progressively. At follow-up, 1 year after the onset of symptoms, she had recovered well and was fully functional. The results of brain MRI were normal (Fig. 1f). The child remains healthy with no obvious adverse effects.

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

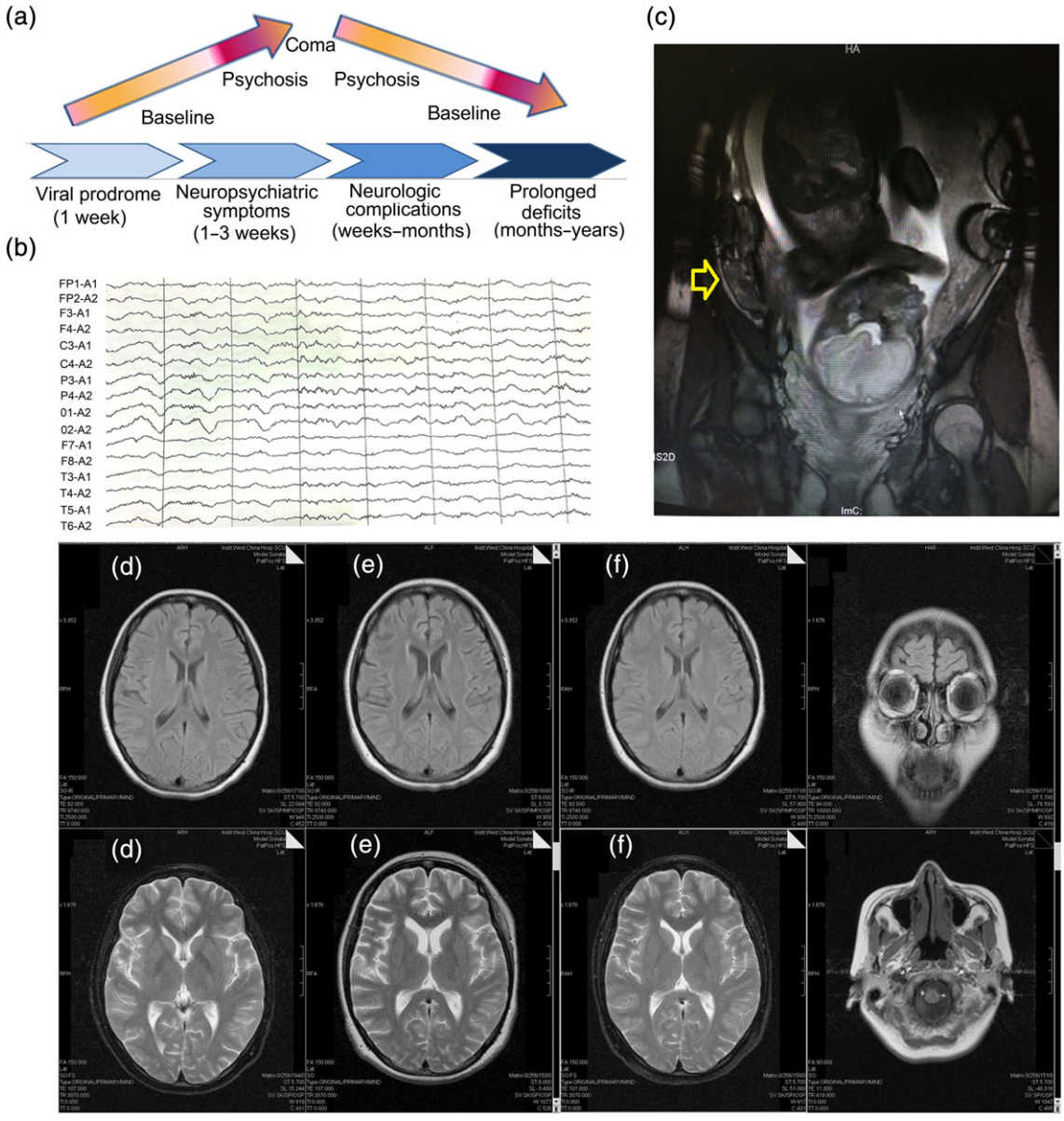

Figure 1 Symptoms and auxiliary examination in a patient with anti-*N*-methyl-D-aspartate receptor (anti-NMDA-R) encephalitis. (a) Four steps of anti-NMDA-R encephalitis. (b) Abnormalities revealed by electroencephalogram (EEG) records. EEG showed slow and disorganized activity in the delta/theta range, sometimes with superimposed electrographic seizures. (c) A magnetic resonance image (MRI) of the abdomen and pelvis did not reveal any ovarian cyst (arrow indicates one side of ovary). (d) The results of brain MRI were unremarkable at the precursor stage (viral prodrome). (e) Follow-up MRI was performed to exclude brain stroke (venous sinus thrombosis) or other encephalitis (neurologic complications). (f) The results of brain MRI were normal during the recovery period (prolonged deficits).

Discussion

Pathogenesis and clinical features

To the best of our knowledge, this is the first case reported in China about a pregnant patient with anti-NMDA-R encephalitis. The case highlights the importance of considering this autoimmune disorder in pregnant women who endure unexplained encephalopathy associated with seizures. The combination of these symptoms can lead to a misdiagnosis as eclampsia.

It has been theorized that the stimulation of ectopic neural tissue against subunits of the NMDA receptor

induces the production of antibodies.[7] Prominent microgliosis and IgG deposits with inflammatory infiltrates have been found in the hippocampus, forebrain, basal ganglia, and spinal cord. There are several main types of autoimmune encephalitis (NMDAR, AMPAR, GABABR, LGI1, and CASPR2). The clinical features of encephalitis associated with NMDA receptor (NR1 subunit) include psychotic symptoms (agitation, paranoia, bizarre behavior, and hallucinations), neurologic symptoms (seizures, dyskinesias, memory loss, and disturbance of consciousness), and autonomic instability.[8] According to a large case series of patients without pregnancy, the ratios of each symptom type (psychotic symptoms, neurologic symptoms, and autonomic instability, separately) are 75%, 25%, and 69%, respectively. However, as of publication, according to retrospective pregnant case materials, these ratios are 100%, 83%, and 71%, respectively.[9]

Auxiliary examination

EEG, CSF, and MRI are the main investigations for final diagnosis. Detection of NMDA antibodies in the patient's serum and/or CSF is considered the gold standard diagnostic test for anti-NMDA-R encephalitis. However, MRI is also used to provide supporting evidence for the diagnosis. MRI often shows increased signal on T2 or fluid-attenuated inversion recovery sequences in the regions of the temporal lobes, cortex, and so forth. Of the 55–59% of anti-NMDA-R encephalitis patients who have ovarian teratoma, most are mature teratoma (93%). The remaining patients are mediastinal teratoma, testicular teratoma, small-cell lung cancer, or neuroblastoma.[10] Pathological examination of tissue sections positive for anti-NMDA-R encephalitis highlight the role of teratomas in this disease. According to the case series to date, four of the 12 cases had ovarian teratoma, and the tumors were always explored by MRI 3 weeks to 4 months after the appearance of neurological symptoms (Table 1).[11–18] Negative results are related to barrier of the gravid uterus, short follow-up time, or poor auxiliary examination. Depending on these factors, ovarian wedge resection and screening for tumor markers are essential for these patients. Empiric surgical oophorectomy in the absence of a confirmed teratoma remains controversial.[19,20]

Timing and manner of terminating pregnancy

The development of anti-NDMD-R encephalitis is divided into four stages (Fig. 1a). In the precursor stage, ~70% of patients experience fever, headache, cough, and weakness as a prodromal viral infection syndrome.[21] The second stage is characterized by neuropsychiatric symptoms, which include anxiety, irritability, delusions, paranoid or bizarre behavior, or phonism/photism. Some patients may experience short-term memory loss. During this stage, most of the patients have seizures (76%) and their consciousness is decreased (88%). Generalized tonic clonic seizures are the main characteristic. One large study described the necessity for an average of 2 months' ventilatory support. The third stage is neurologic complications. Patients present movement abnormalities, dysautonomia, hypoventilation, and seizures. The fourth stage is prolonged deficits, during which patients present executive dysfunction, impulsivity, disinhibition, and sleep abnormalities. Some patients recover stage by stage, while some of them experience severe disability or death. Until now, only nine papers have reported a total of 12 cases of anti-NMDA-R encephalitis complicated by pregnancy. The literature has described four of five cases as delivering healthy babies after patients had gone through severe stage three safely; however, in one case the pregnancy was terminated due to the early stage of pregnancy. Until now, we have been unable to provide strong evidence for the right time to terminate pregnancy in patients with anti-NMDA-R encephalitis. Even though we know most patients can get better after the first three stages, we cannot say that stage four is the best time to terminate pregnancy. In stage four, with recovered consciousness and gradually improved muscle contraction ability, communication among the patient, the doctor, and the other hospital staff will improve and this decreases the risk of post-partum hemorrhage, vaginal tear injury, and fetal intrauterine distress. Balancing the severity of the disease with fetal safety is the main factor in determining the optimum time for delivery.

While most reported anti-NMDA-R encephalitis patients experienced mental and neurological symptoms, in other reports, vaginal delivery was still accomplished (six of 12). According to previous case report data, the indications for vaginal delivery as opposed to cesarean section in anti-NMDA-R encephalitis patients have not been established. In our case, the patient suffered from frequent seizures and muscle stiffness spread from the lower limbs to the upper limbs. Therefore, neurological and obstetric risk assessments suggested that these abnormal activities were adverse to uterine contraction, and were not beneficial to natural vaginal delivery.[22] Elective cesarean section, ultimately, was our preferred selection.

Table 1 Synoptic presentation of data concerning known gestations complicated with anti-*N*-methyl-D-aspartate receptor encephalitis cases

Patient[Ref.]	Age (years)	Gestational age when diagnosed (weeks)	Gestational age when pregnancy was terminated (weeks)	Teratoma	Method of termination	Main treatment	Outcome	Year of publication
Patient 1[11]	32	8	32	Left ovary	CS	MP Plasma exchange Left oophorocystectomy at 32 GW, together with CS	Both mother and baby survived	2012
Patient 2[12]	19	14	38	Left ovary	CS	IVIg MP Left oophorectomy was at 21 GW	Both mother and baby survived	2010
Patient 3[12]	20	8	10	Bilateral ovary	Abortion	IVIg Left salpingo-oophorectomy and removal of both tumors at 10 GW, and the pregnancy was terminated	Discharge on day 87	2010
Patient 4[12]	19	17	37	No ovary cyst found	Delivery	MP	Both mother and baby survived	2010
Patient 5[13]	24	Before pregnancy	35	NR	Delivery	IVIg for precaution	Both mother and baby survived	2012
Patient 6[14]	18	9	34	No ovary cyst found	Delivery	Azathioprine Three courses of IVIg	The patient died shortly after her transfer to another hospital, due to infection, baby survived	2014
Patient 7[15]	24	20	28	No ovary cyst found	CS	One course of pulsed MP One course of IVIg (400 mg/kg) and MP (1 g daily)	Both mother and baby survived	2015
Patient 8[16]	23	First trimester	Miscarriage within 2 days of hospitalization	Left ovary	Delivery	MP Plasmapheresis Rituximab	Discharge on day 87	2015
Patient 9[17]	36	2	Full-term	No ovary cyst found	Delivery	Three days of oral steroids, then 7 days of MP	Both mother and baby survived	2015
Patient 10[1]	26	22	37	No ovary cyst found	Delivery	Five days of high-dose MP, then oral steroids (60 mg for 9 days, then tapered over the next 6 days) Plasmapheresis after 1 month of hospitalization (7 exchanges, one every 2 days)	Both mother and baby survived	2015

(*Continues*)

Table 1 (continued)

Patient[Ref.]	Age (years)	Gestational age when diagnosed (weeks)	Gestational age when pregnancy was terminated (weeks)	Teratoma	Method of termination	Main treatment	Outcome	Year of publication
Patient 11[18]	21	10	40	No ovary cyst found	Delivery	Three-day course of MP (250 mg/day) Two courses of IVIg (20 g/day during 5 days) in 4 weeks	Both mother and baby survived	2015
Patient 12†	24	30	33	No ovary cyst found	CS	IVIg MP Wedge-shaped resection of bilateral ovaries at 33 GW, together with CS	Both mother and baby survived	2015

†Case of this paper. CS, cesarean section; GW, gestational weeks; IVIg, intravenous immunoglobulin; MP, methylprednisolone; NR not reported.

Outcome for mother and baby

This study suggests that patients and babies can have good outcomes after clear diagnosis, immediate treatment, and supportive care of the mother and fetus. Most of the newborns underwent term delivery and obtained high Apgar scores (10/12).[18] Among the 12 pregnant women who have presented with anti-NMDA-R encephalitis during pregnancy, two pregnancies were terminated during the first trimester. Among the 10 other cases, all babies (as in our observation) were reported to be normal with a maximal follow-up of 1 year. Even so, concern for the fetus and newborn is warranted, as studies have shown that NR1 antibodies from patients decrease NMDA-R clusters *in vitro* and *in vivo*.[23] Jagota *et al*. verified that the baby of an anti-NMDA-R encephalitis patient showed NMDR antibody titer at the same level as that of the mother 2 days after birth and this was negative at 1 year. Also, the baby showed cortical dysplasia and developmental delay on brain MRI. Furthermore, involvement of NMDA-R may affect brain development, and glutamatergic dysfunction may play an important role in the genesis of schizophrenia.[14] Early immunomodulatory therapy may hasten recovery.[11–14,18–24] Treatment with corticosteroids, intravenous immunoglobulin (IVIg), plasmapheresis, and removal of a teratoma resulted in favorable outcomes.[12,13,19] McCarthy concluded from experience that plasmapheresis may be superior to other treatment methods, because plasmapheresis not only quickly decreases antibodies in the fetus, but can also be used safely during pregnancy.[11] These treatments have enhanced effectiveness when patients have an underlying tumor that is removed. In patients without tumor, additional second-line immunotherapy treatment has proven essential, such as with a rituximab or cyclophosphamide.[6] The patient in our report did not receive plasmapheresis nor tumor removal and still obtained good results after giving birth, which seemed to accelerate recovery.[25] This, and the predominance of the disorder in young women, bring into consideration a possible role of hormonal factors that should be studied further.

Approximately 75% of patients without pregnancy have full recovery with mild sequelae, while 25% of patients remain severely disabled or even die. Total mortality is estimated to be 4%. To our knowledge, corresponding data for pregnant women is still unknown. The relapse rate in anti-NMDA-R encephalitis is relatively low (~20–25%), and is sometimes triggered by discontinuation of medication, often with substantial and prolonged symptom improvement between episodes.

Periodic screening for an ovarian teratoma, as well as psychiatric and neurocognitive follow-up examination over 2 years, is recommended for such post-encephalitis patients, especially for patients without a tumor.

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Disclosure

No potential conflicts of interest are disclosed.

References

1. Shahani L. Steroid unresponsive anti-NMDA receptor encephalitis during pregnancy successfully treated with plasmapheresis. *BMJ Case Rep* 2015. DOI:10.1136/bcr-2014-208823.
2. Goldberg EM, Titulaer M, de Blank PM, Sievert A, Ryan N. Anti-N-methyl-D-aspartate receptor-mediated encephalitis in infants and toddlers: Case report and review of the literature. *Pediatr Neurol* 2014; **50**: 181–184.
3. Vitaliani R, Mason W, Ances B, Zwerdling T, Jiang Z, Dalmau J. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. *Ann Neurol* 2005; **58**: 594–604.
4. Peery HE, Day GS, Dunn S *et al.* Anti-NMDA receptor encephalitis: The disorder, the diagnosis and the immunobiology. *Autoimmun Rev* 2012; **11**: 863–872.
5. Dalmau J, Tuzun E, Wu HY *et al.* Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007; **61**: 25–36.
6. Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol* 2011; **10**: 63–74.
7. Dalmau J, Gleichman AJ, Hughes EG *et al.* Anti-NMDA-receptor encephalitis: Case series and analysis of the effects of antibodies. *Lancet Neurol* 2008; **7**: 1091–1098.
8. Yu AY, Moore FG. Paraneoplastic encephalitis presenting as postpartum psychosis. *Psychosomatics* 2011; **52**: 568–570.
9. Barry H, Hardiman O, Healy DG *et al.* Anti-NMDA receptor encephalitis: An important differential diagnosis in psychosis. *Br J Psychiatry* 2011; **199**: 508–509.
10. Tuzun E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. *Acta Neuropathol* 2009; **118**: 737–743.
11. McCarthy A, Dineen J, McKenna P *et al.* Anti-NMDA receptor encephalitis with associated catatonia during pregnancy. *J Neurol* 2012; **259**: 2632–2635.
12. Kumar MA, Jain A, Dechant VE *et al.* Anti-N-methyl-D-aspartate receptor encephalitis during pregnancy. *Arch Neurol* 2010; **67**: 884–887.
13. Magley J, Towner D, Tache V, Apperson ML. Pregnancy outcome in anti-N-methyl-D-aspartate receptor encephalitis. *Obstet Gynecol* 2012; **120**: 480–483.
14. Jagota P, Vincent A, Bhidayasiri R. Transplacental transfer of NMDA receptor antibodies in an infant with cortical dysplasia. *Neurology* 2014; **82**: 1662–1663.
15. Lamale-Smith LM, Moore GS, Guntupalli SR, Scott JB. Maternal-fetal transfer of anti-N-methyl-D-aspartate receptor antibodies. *Obstet Gynecol* 2015; **125**: 1056–1058.
16. Chan LW, Nilsson C, Schepel J, Lynch C. A rare case of anti-N-methyl-D-aspartate receptor encephalitis during pregnancy. *N Z Med J* 2015; **128**: 89–91.
17. Lu J, Samson S, Kass J, Ram N. Acute psychosis in a pregnant patient with Graves' hyperthyroidism and anti-NMDA receptor encephalitis. *BMJ Case Rep* 2015. DOI:10.1136/bcr-2014-208052.
18. Mathis S, Pin JC, Pierre F *et al.* Anti-NMDA receptor encephalitis during pregnancy: A case report. *Medicine* 2015; **94**: e1034.
19. Kort DH, Vallerie AM, DeMarco EF, Lobo RA. Paraneoplastic anti-N-methyl-D-aspartate-receptor encephalitis from mature cystic teratoma. *Obstet Gynecol* 2009; **114**: 373–376.
20. Kim J, Park SH, Jung YR, Park SW, Jung DS. Anti-NMDA receptor encephalitis in a pregnant woman. *J Epilepsy Res* 2015; **5**: 29–32.
21. Kayser MS, Dalmau J. Anti-NMDA receptor encephalitis in psychiatry. *Curr Psychiatry Rev* 2011; **7**: 189–193.
22. Chapman MR, Vause HE. Anti-NMDA receptor encephalitis: Diagnosis, psychiatric presentation, and treatment. *Am J Psychiatry* 2011; **168**: 245–251.
23. Hoftman AC, Hernandez MI, Lee KW, Stiehm ER. Newborn illnesses caused by transplacental antibodies. *Adv Pediatr* 2008; **55**: 271–304.
24. Rosenfeld MR, Dalmau J. Anti-NMDA-receptor encephalitis and other synaptic autoimmune disorders. *Curr Treat Options Neurol* 2011; **13**: 324–332.
25. Finke C, Kopp UA, Pruss H, Dalmau J, Wandinger KP, Ploner CJ. Cognitive deficits following anti-NMDA receptor encephalitis. *J Neurol Neurosurg Psychiatry* 2012; **83**: 195–198.