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ORIGINAL COMMUNICATION

Anti-NMDA receptor encephalitis with associated catatonia during pregnancy

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Abstract Anti-NMDA-R encephalitis has been described as a cause of acute psychosis in young females. It is rare during pregnancy. We describe a primigravida 32-year-old woman with acute onset psychosis during the first trimester. Eight weeks after becoming pregnant, the patient became psychotic with associated catatonia and autonomic disturbance. Serum anti-NMDA-R antibodies were found. She responded to plasma exchange. At caesarean section, a healthy baby boy was born and a benign mature cystic teratoma was removed from the left ovary. Catatonia associated with psychosis may occur in pregnancy secondary to anti-NMDA-R encephalitis. Prompt and aggressive treatment can lead to a good outcome for both baby and mother.

Keywords Autoimmune encephalitis · NMDA receptor · Catatonia · Pregnancy

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Introduction

Anti-NMDA-R encephalitis is increasingly being recognized as a cause of acute psychosis, especially when associated with autonomic disturbance and seizures [1, 2]. A small number of cases have been reported to have occurred during pregnancy [3, 4]. It has also been reported to occur in the post-partum setting [5]. We describe a case diagnosed during the first trimester, with subsequent aggressive treatment leading to a satisfactory outcome for both mother and baby.

Case report

A 32-year-old woman presented during the eighth week of pregnancy with acute urinary retention and constipation. This was preceded by 6 weeks of new daily persistent headache. She was admitted to the obstetric hospital and within 24 h developed visual and auditory hallucinations. She was transferred to a psychiatric ward and a neurology consult was sought. She was noted to be elated, agitated, hallucinating, talking incessantly, repeating phrases, and paranoid. Her 'dead aunt' was visible to her above the bed and 'people were going to take her baby to do experiments'. Over the next week, she became increasingly paranoid with periods of elation interspersed with a reduced level of consciousness. Physically, she was noted to have a tachycardia, fever, and labile blood pressure. Level of alertness fluctuated, and forced eye closure and neck rigidity developed. Subsequently, intermittent stereotypic movements of the right hand were noted along with catatonia or 'waxy flexibility' (Video). Deep tendon reflexes were brisk and plantars were flexor.

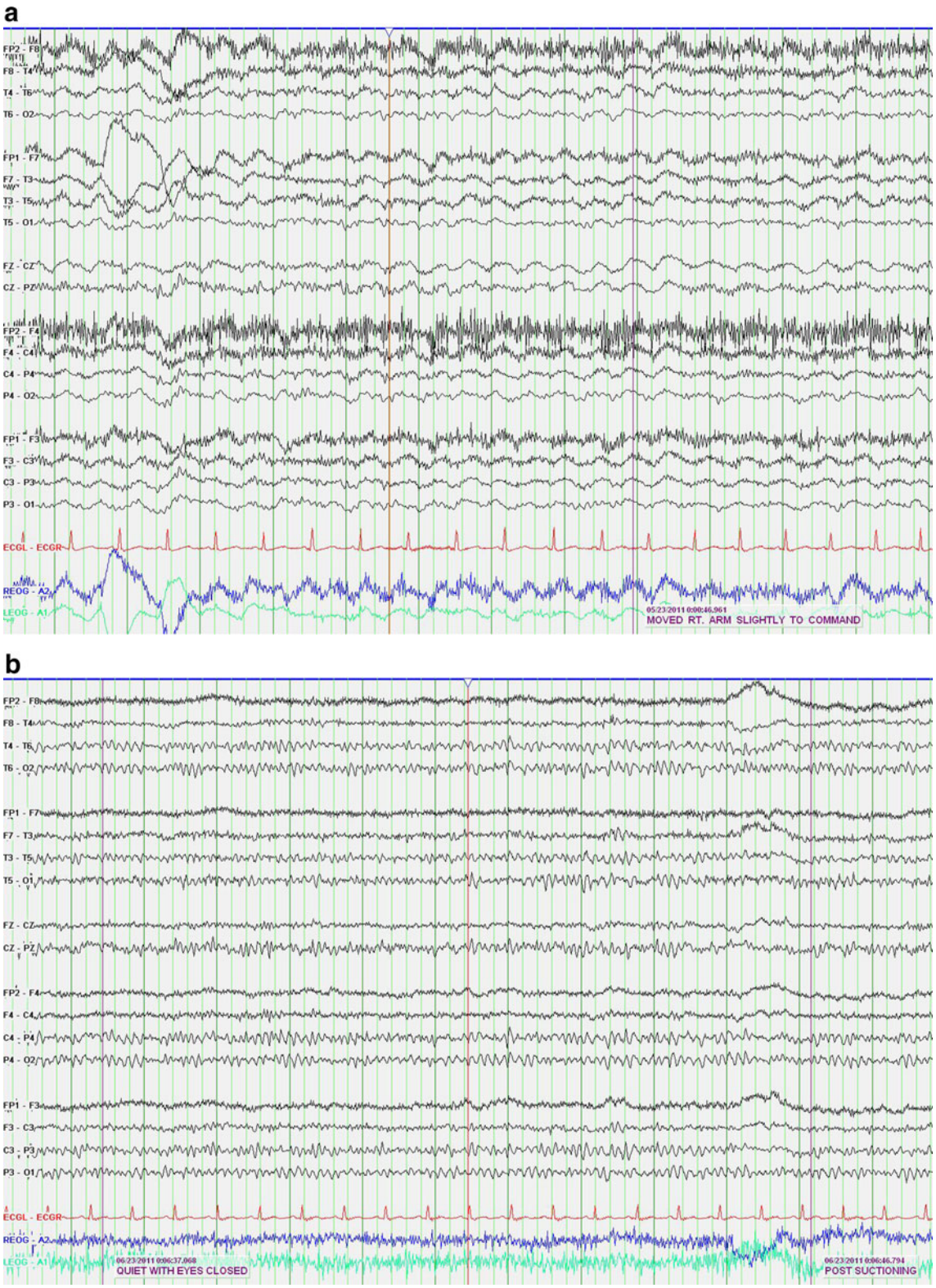

Fig. 1 EEG examinations recorded at diagnosis (**a**) and pre discharge (**b**)

Initial laboratory investigations revealed a mild anemia with normal inflammatory markers, thyroid function tests, and creatine kinase. Brain MRI was unremarkable. EEG examination revealed diffuse slowing, delta > theta (Fig. 1a). CSF examination revealed a normal opening pressure, with a protein of 726 mg/l (normal 150–450 mg/l),

the remainder of the constituents being normal. Pelvic ultrasound revealed a viable fetus without visible ovarian masses. Clinical suspicion of anti-NMDA-R encephalitis led to immediate commencement of high-dose IV steroids (1 g of methylprednisolone for 5 days followed by a slow oral taper). Her condition deteriorated further and she was transferred to intensive care. Plasma exchange was commenced, prior to the antibody being detected, leading to marked clinical improvement and complete resolution of her encephalopathy over a period of 8 weeks. Serum antibodies were subsequently detected against the NMDA receptor. She had a total of 23 1.5 PV (1 plasma volume = 3 l) exchanges. A short period of asystole was recorded in intensive care, not requiring specific treatment. Further imaging with MRI of pelvis and transvaginal ultrasound failed to identify an ovarian mass. Whole-body MRI examination was normal. Laparoscopy was considered, but not performed owing to her clinical improvement. Azathioprine was added. Olanzapine was necessary at night to treat agitation and hallucinations. She was antibody-negative (serum) by 13 weeks of gestation, 4 weeks following admission. Repeat EEG examinations during her hospital stay did not reveal any epileptiform activity and returned to normal prior to discharge (Fig. 1b), 12 weeks post admission.

At week 32 she went into labor and a decision to perform a Caesarean section was made. A healthy baby boy was born. During the Caesarean section, careful examination revealed a left ovarian mass (2.5 × 1.2 × 2 cm). Histology confirmed a cystic teratoma. The baby was not tested for antibodies post partum. The patient remains well.

Comment

NMDA-R encephalitis in the context of pregnancy is a rare disorder. Early diagnosis is essential [6], as the condition responds to immunomodulatory therapy [2]. Prompt treatment should be initiated in such circumstances, paying attention to any cardiac rhythm disturbance that may occur. Psychotropic medication may also be necessary. To date, published data have suggested that outcome may be favorable for such pregnancies [3, 4].

This case demonstrates that plasma exchange may be efficacious when started in a timely manner. We elected to commence and persist with plasma exchange treatment as it is generally regarded as the most rapid way to remove pre-formed disease-causing antibodies. Our local experience with other patients severely affected with anti-NMDA-R encephalitis is that treatment with plasma exchange is superior to treatment with intravenous immunoglobulins. None of these patients were rendered antibody-negative when intravenous immunoglobulin was used. Plasma exchange can be used safely in pregnancy; however, should hypotension occur, this can decrease fetal perfusion [7]. Additionally, in the latter half of pregnancy, careful positioning of the patient is necessary to avoid compression of the inferior vena cava [7]—clearly this may be difficult if psychotic symptoms persist and the patient's ability to cooperate is compromised. There is no data available on the consequences of prenatal exposure of the developing brain to NMDA-R antibodies. IgG transport from mother to fetus begins as early as 13 weeks; however, the largest amount of IgG transport occurs in the third trimester [8]. The NMDA-R is known to be expressed in utero, albeit at lower levels than in adults [9]. Significant cognitive deficits may persist in those who have survived anti-NMDA-R encephalitis [10]. Hence, we aimed to render our patient antibody negative as quickly as possible, in the interests of both maternal and fetal health.

NMDA-R encephalitis is strongly, but not invariably, associated with ovarian pathology, particularly dermoid tumors. Half of the cases reported in pregnancy had associated ovarian teratomas [3, 4]. Radiological diagnosis of ovarian lesions is more difficult during pregnancy, due to the presence of the gravid uterus. Therefore, diagnostic laparoscopy should be considered if there is a high index of suspicion.

This patient responded well to plasma exchange administered during pregnancy. Her second set of exchanges were continued until she was deriving no further clinical benefit. She remained serum antibody negative up to the point of delivery, and remains so. There were no cognitive deficits evident in the mother prior to discharge. NMDA-R encephalitis in pregnancy may have a good outcome for both mother and baby.

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical standards The patient described has given written consent for the use of patient identifiable video material.

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