

Anti-NMDA receptor encephalitis: a video case report

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ABSTRACT – This report concerns a 26-year-old Italian woman who was given the diagnosis of anti-NMDAR encephalitis after the incidental identification of an ovarian tumour. Neuropsychiatric symptoms and hyperkinetic movements are very commonly seen as initial symptoms of paraneoplastic encephalitis. Interestingly, our patient showed stereotypical movements predominantly located to lower limbs, mimicking a psychogenic seizure. This latter feature further extends the clinical spectrum of dyskinetic movements of anti-NMDAR encephalitis. [*Published with video sequences*]

Key words: NMDA receptor antibodies, ovarian teratoma, paraneoplastic encephalitis, psychogenic seizure



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Anti-NMDA receptor (NMDAR) encephalitis, a form of paraneoplastic limbic encephalitis associated with ovarian teratoma, has been recently described (Dalmau *et al.*, 2007; Iizuka *et al.*, 2008). This disorder results in a characteristic syndrome that presents with prominent psychiatric symptoms preceding a rapid decline of the level of consciousness, central hypoventilation, seizures, involuntary movements and dysautonomia (Dalmau *et al.*, 2007; Iizuka *et al.*, 2008; Sansing *et al.*, 2007). Recently, Iizuka *et al.* proposed a progressive clinical course over five phases: prodromal, psychotic, unresponsive, hyperkinetic (mainly orolingual dyskinesias such

as lip licking or chewing) and gradual recovery. Despite the severity of symptoms and prolonged clinical course, most patients recover if the disorder is promptly recognised and treated (Seki *et al.*, 2008; Vitaliani *et al.*, 2005). Neuropsychiatric disorders are very frequently seen as initial symptoms of paraneoplastic encephalitis especially in young women, thus recognition of this new entity and diagnostic testing can prevent inappropriate hospitalization in psychiatric units. We present the sequence of movements mimicking a psychogenic seizure observed in a patient whom we later discovered had an ovarian tumour (*see video sequence*).

Case study

A 26-year-old woman presented at the emergency room because of epileptic status with generalised tonic-clonic seizures, fever (40 degrees), dysarthria, dysphagia and temporal and spatial disorientation. Her medical history was unremarkable, other than one-month of mild depression and anxiety. She was admitted to our neurology department and her neurological examination showed temporo-spatial disorientation without focal neurological signs. She had no family history of epilepsy, nor history of infections or exposure to neuroleptic drugs. The interictal and ictal electroencephalographic (EEG) examinations showed a diffuse slow background activity with periodic lateralized epileptiform discharges (PLEDS) over the left hemisphere (*figure 1A*). Routine laboratory analysis was normal as well as the cerebrospinal fluid examination. The extensive serum tests resulted negative for viral, bacterial and fungal infections. Reactivity with a comprehensive panel of paraneoplastic antibodies, anti-HU, anti-YO, anti-Ri, antibodies to herpes simplex virus (HSV), human herpes virus (HHV)-6 and HHV-7 and with voltage-gated

potassium channels, was negative. The patient underwent chest X-ray, brain and spinal MRI, including FLAIR and post-gadolinium sequences. Brain MRI showed small areas of T2-weighted and FLAIR hyperintensity close to the occipital horn and lateral ventricles bilaterally without post-gadolinium enhancement. During the admission, the patient's clinical condition suddenly deteriorated. She became aphasic and versive motor focal seizures appeared over the left side with secondary generalisation, refractory to antiepileptic treatment. Two weeks later, central hypoventilation and a decreased level of consciousness complicated the clinical picture and the patient was transferred to the emergency unit and treated with mechanical ventilation, corticosteroids and intravenous immunoglobulins (IgG 0.4 grams per kg daily for five following days). After one week, the respiratory condition improved, the patient was partially conscious and seizures were very well controlled with two antiepileptic drugs (350 mg of phenytoin and 400 mg of topiramate). However, prolonged periods of psychomotor agitation lasting 20 to 60 minutes and resisting to benzodiazepines and neuroleptics appeared, while the respiratory symp-

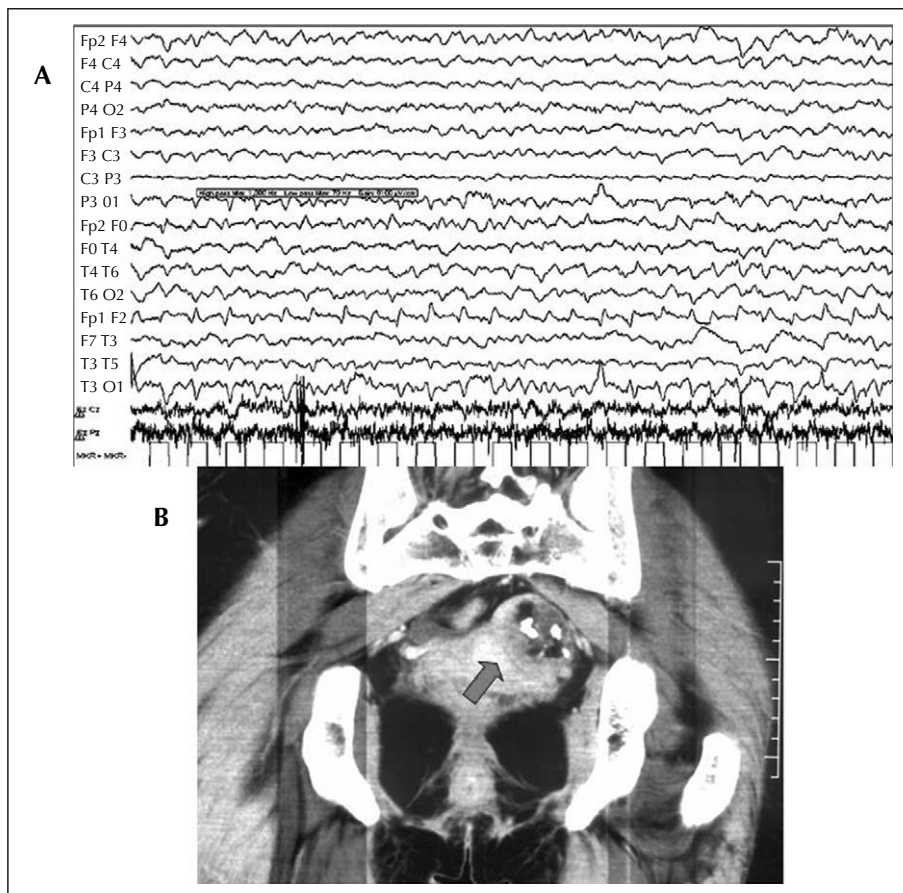


Figure 1. **A)** Ictal EEG recording showing diffuse slow background with periodic lateralized epileptiform discharges (PLEDS) over the electrodes Fp1, F7, T3 and T5. **B)** Computed tomography of the patient showing a 3 cm cystic ovarian lesion (arrow).

toms and epileptic seizures disappeared. A video-EEG recording (see *video sequence*) showed erratic and violent movements, screaming, vocalisation, stereotypical hyperkinetic movements such as cycling or kicking, giving the impression of a psychogenic seizure, whereas the ictal EEG showed no frank epileptiform activity. Nevertheless, these episodes gradually became rarer and the patient was discharged six weeks after admission. She was treated with a combination of antiepileptic drugs (300 mg/day of phenytoin and 400 mg/day of topiramate) and antidepressants (1 mg/day of risperidone and 100 mg/day of sertraline). Seven months later, the patient progressively discontinued antiepileptic medications because of seizure freedom but incidentally, an ovarian mass was radiologically detected with a CT scan of the pelvis (*figure 1B*). The tumour was surgically removed and the biopsy of the tumour confirmed the radiological diagnosis of a mature cystic teratoma. The patient was treated with surgery alone and she was not investigated for tumours before the encephalitis appeared. Furthermore, she was not treated with immunotherapy and ten months after the tumour resection showed no sign of relapse.

Given the patient's history and the result of the CT of the pelvis, the patient was readmitted and a brain MRI scan and NMDAR antibody analysis were performed because of the similarity with previous Japanese cases (Iizuka *et al.*, 2008) and those of Dalmau *et al.* (2008). The repeated brain MRI scan was normal but serum NMDA NR1/NR2B antibodies were positive. The presence of NR1/NR2B antibodies and their association with encephalitis associated with ovarian teratoma confirms the diagnosis.

Discussion

This is the first reported Italian case of a woman with paraneoplastic anti-NMDAR encephalitis. Video-EEG monitoring allowed to differentiate seizures from abnormal movements suggesting events of psychogenic nature. Our patient did not show frequent oro-facial dyskinesias but essentially psychomotor agitation associated with cycling and pedalling movements and loud vocalisations. We suggest that dyskinetic leg movements should be

recognised as part of the hyperkinetic phase of this syndrome, as also reported by Dalmau *et al.* (2008) and not only dyskinesias and dystonic posturing located on the face, as proposed by Iizuka *et al.* (2008).

This syndrome should be suspected in young woman presenting with febrile epileptogenic encephalopathy, transient aspecific MRI hyperintensities and psychiatric symptoms. Because it is potentially fatal, the rapid diagnosis of this syndrome is important since early treatment with antiepileptic drugs, intravenous immunoglobulins and corticosteroids associated with tumour removal can be curative (Iizuka *et al.*, 2008; Vitaliani *et al.*, 2005; Dalmau *et al.*, 2008). □

Disclosures.

None.

Legend for video sequence

The video shows erratic and violent movements, screaming, vocalisation and stereotypical hyperkinetic movements at lower limbs.

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