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CASE REPORT

A Woman with Psychogenic Non-epileptic Seizures and Pelvic Mass

Teng-da Xu[1]*, Sheng-yong Xu[2], and Jia-yuan Dai[2]

[1]Department of Health Management & Emergency Medicine, [2]Department of Emergency Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

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MOST cases of encephalitis are caused by viruses but a few have an immunological basis, such as paraneoplastic encephalitis, with specific antibodies identified. One recently characterized encephalitis caused by antibodies is anti-N-methyl-D-aspartate (NMDA) receptor encephalitis. It is a form of paraneoplastic limbic encephalitis associated with ovarian teratoma and has recently been described.[1, 2] The NMDA receptor mediates excitatory neurotransmission. It is important for synaptic plasticity, and thus for higher function such as learning and memory. This disorder results in prominent psychiatric symptoms followed by a rapid decline of the level of consciousness, central hypoventilation, seizures, involuntary movements and dysautonomia.[1, 2]

Despite the severity of symptoms and prolonged clinical course, most patients recover if the disorder is promptly recognized and treated.[3] 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 who we later discovered had an ovarian tumour (see image sequence).

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*Corresponding author Tel: 86-10-69159866, E-mail: xutd@pumch.cn

CASE DESCRIPTION

A 21-year-old Chinese woman was presented to the emergency department with intermittent psychogenic seizure. Over the course of approximately four weeks she developed delirium, catatonia, repeated oral dyskinesia, dyspnea and hypoxemia. Her medical history was unremarkable, other than one month of mild depression and anxiety. She had no history of infection or exposure to neuroleptic drugs. She had no family history of epilepsy. Physical examination showed she had a low grade fever (37.8°C), hyperhidrosis, autophagia, and repeated oral dyskinesia. Her consciousness level fluctuated from somnolence to stupor.

Routine laboratory tests were within the normal range. Cerebrospinal fluid (CSF) showed no marked change.

Extensive serum tests were 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, were negative. The patient underwent chest X-ray, brain and spinal magnetic resonance imaging (MRI), including fluid-attenuated inversion recovery (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. Her electroencephalographic (EEG) showed diffuse high voltage and slow waves. Serum and CSF anti-NMDA receptor antibodies were positive.

Abdominal ultrasound and computed tomography (CT) revealed a pelvic mass (Figs. 1, 2). Bilateral ovarian cystic teratoma were found at laparoscopy (torsion of the left side cyst was 6 cm in diameter, the right one was 1 cm), and the biopsy confirmed to be mature cystic teratoma containing brain tissue. After laparoscopic resection of tumor, neuropsychiatric symptoms and respiratory condition improved. This patient was finally diagnosed with anti-NMDA receptor encephalitis triggered by an ovarian teratoma.

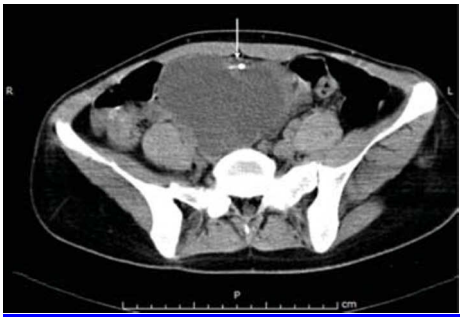

Figure 1. Computed tomography shows calcific components in the pelvic mass (arrow).

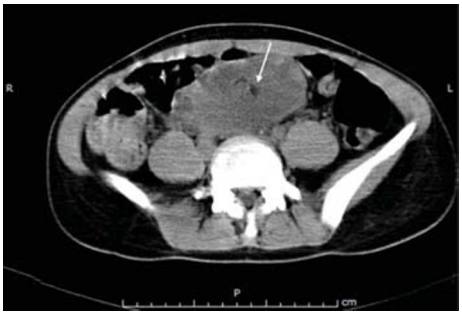

Figure 2. Computed tomography shows fat intensity components within the pelvic mass (arrows). The wall of this mass is partially calcified. Computed tomography images demonstrate a mature cystic teratoma.

DISCUSSION

Anti-NMDA receptor encephalitis has been recently described in the neurology literatures.[1-3] The pathogenesis remains unknown. Recent studies suggested that it may relate to antibodies-mediated encephalitis.[1, 2] The diagnosis was based on the presence of anti-NMDA receptor antibody in the CSF. Combined therapy including tumour resection and immunotherapy is recommended.[3, 4]

The patient first presented to the emergency department with intermittent psychogenic seizure. Initially, viral encephalitis was suspected, but viral tests were negative. Studies for other infective and metabolic encephalopathies were also negative. The prominent orofacial and limb dyskinesias are noted, in retrospect, to be typical for anti-NMDA receptor encephalitis rather than other limbic encephalitides.

This disorder usually develops in young women with ovarian teratoma, who typically present with neuro-psychiatric symptoms. Most cases develop seizures, followed by disturbed consciousness, central hypoventilation frequently requiring mechanical ventilation, dyskinesias and autonomic dysfunction.

The largest published case series to date by Dalmau *et al*[1] included 100 patients with anti-NMDA receptor encephalitis. This reported that 90% of the patients were women, with a median age of 23 years (range, 5-76 years). Many patients have non-specific prodromal symptoms of fever, fatigue, and headache in the preceding 2 weeks, as seen in this patient. This suggests that an infectious process may trigger an immunological response. The majority of patients (77%) reported by Dalmau *et al*[1] presented to psychiatrists because of prominent anxiety, paranoia or hallucinations, while 23% presented with memory loss or seizures, with or without psychiatric manifestations. One characteristic feature of the disease is severe refractory movement disorder, as was seen in our patient. These movements are repetitive, persisting even during depressed consciousness and may lead to self-injury. Autonomic instability such as blood pressure fluctuations, arrhythmias, hyperthermia and diaphoresis may occur. Many patients have central hypoventilation and require prolonged ventilation support. Our patient also exhibited disturbed consciousness, dyskinesias and autonomic dysfunction. Iizuka *et al*[2] have grouped the symptoms of anti-NMDA receptor encephalitis into five characteristic phases—prodromal, psychotic, unresponsive, hyperkinetic, and gradual recovery phase.

Most patients have lymphocytic pleocytosis and elevated protein in their CSF. Epileptiform activity on EEG was seen in only 21% of patients as reviewed by Dalmau *et al*[1];

the usual finding noted on EEG being generalized or predominantly frontotemporal slow waves. Increased signal on fluid-attenuated inversion recovery or T2 sequences on MRI occurred in 55% of patients, involving the mesial temporal lobes, cerebral cortex, cerebellum, brainstem and basal ganglion (in decreasing order of frequency), but these findings were non-specific and correlated poorly with patients' symptoms. Contrast enhancement of the MRI abnormalities was uncommon, transient, and faint.

To establish the diagnosis, NMDA receptor antibodies by definition must be detected in the CSF, but are sometimes also detected in the serum. Titres in the CSF are higher than in the serum and appear to correlate with clinical activity. No false positives to the test have been reported to date. Sixty percent of patients have an underlying tumor, most commonly an ovarian teratoma, but other tumors, such as testicular teratoma and small cell lung cancer, have been found.[5] Most of these tumors are benign and may not be detected on positron emission tomography scanning, requiring ultrasound, CT or MRI for detection. The heterogeneous appearance of the tumor, with fat and calcification inside, seen on the CT scan of our patient suggested an ovarian teratoma, and this was confirmed by histological study.

Paraneoplastic limbic encephalitis is characterized by short-term memory impairment, temporal lobe seizures, and psychiatric symptoms. Patients with encephalitis associated with voltage-gated potassium channel antibodies have neuromyotonia and hyponatraemia. This patient did not have demonstrable evidence of limbic dysfunction. The wide range of abnormal movements, which are semi-arrhythmic in character, with prominent orofacial involvement, persistence during depressed consciousness and resistance to treatment, together with psychiatric symptoms, autonomic features and central hypoventilation, distinguish anti-NMDA receptor encephalitis from other paraneoplastic encephalitis.

The cause of alter mental status and dyskinesias is not always clear in the acute setting, unfortunately most of these patients have potentially life threatening. As a result, comprehensive assessment and the development of treatment strategies should be considered (Fig. 3). Treatment

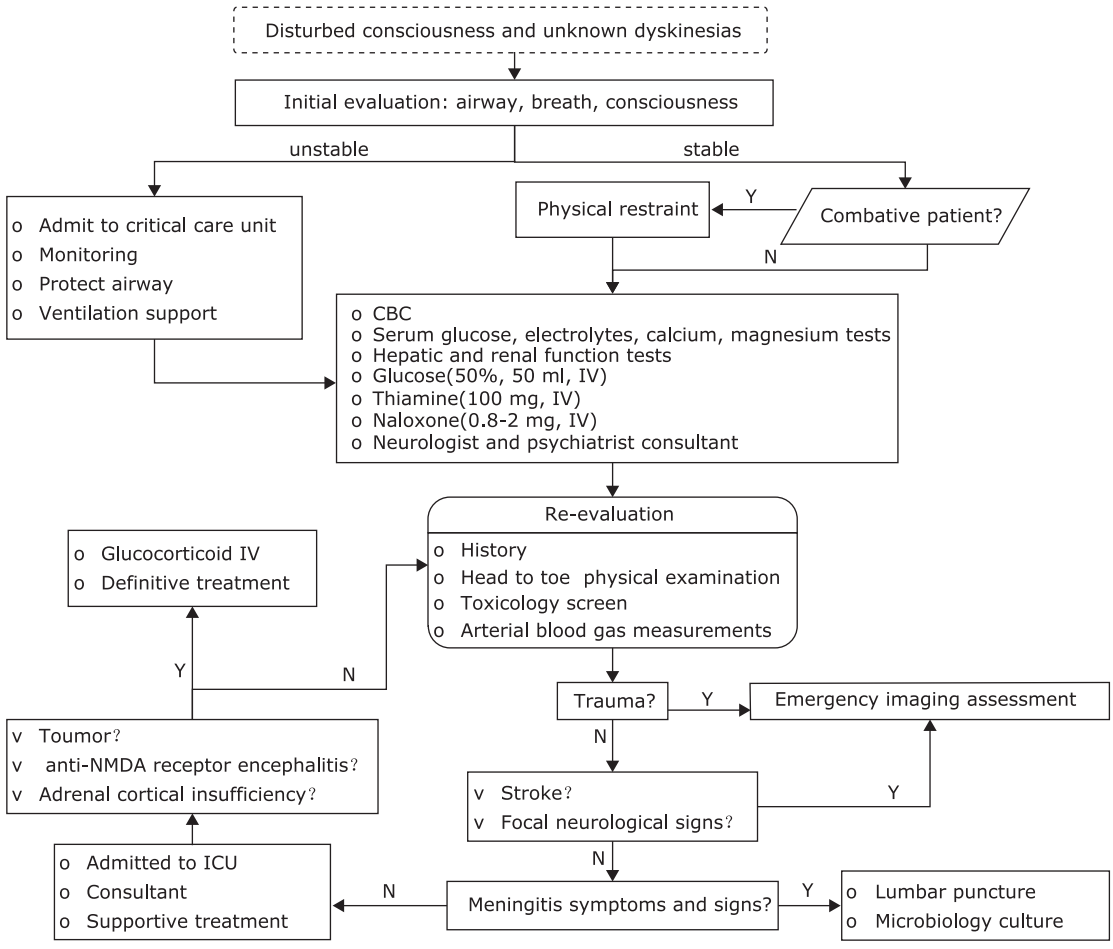

Figure 3. Algorithm of disturbed consciousness and dyskinesias patient treatment in acute setting.
CBC: complete blood count; IV: intravenously; ICU: intensive care unit; Y: yes; N: no.

of anti-NMDA receptor encephalitis is best achieved by combined tumor removal with immunotherapy. Immunomodulatory agents, including corticosteroids, intravenous immunoglobulin, plasma exchange, cyclophosphamide, azathioprine and the monoclonal antibody rituximab have been used.[6, 7] The outcome is better for those who undergo tumor removal, especially if this is completed within months of neurological symptom development, with the antibody titer decreasing after surgery. Without surgery or with late tumor treatment, the clinical course may be fatal or prolonged.[4] Despite its rarity, clinicians should bear this potentially lethal but curable disease in mind.

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