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LETTER TO THE EDITOR

Downbeat nystagmus as the initial manifestation of anti-NMDAR encephalitis

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Dear Sir,

Downbeat nystagmus (DBN) is a rare neurological disorder characterized by slow upward drifts and fast downward phases [1]. In most cases no anatomical lesion is identified, whereas Arnold-Chiari malformation or spinocerebellar degeneration may underlie this condition [1]. Anti-NMDAR (N-methyl-D-aspartate receptor) encephalitis rarely causes DBN [2]. Recently, we observed a young lady showing DBN as the sole initial manifestation.

A 21-year-old lady presented with the 5-day history of dizziness that worsened gradually. On examination she had spontaneous DBN, which was occasionally overlapped with ocular flutter-like movement. Smooth pursuit was slightly saccadic, and during horizontal gaze horizontal nystagmus overlapped DBN. Eye movements were otherwise intact. She had no intentional tremor or dysmetria on finger-to-nose and heel-to-shin testing. However, her gait was wide-based and mildly unsteady. The remainder of her examination was normal. However, 4 days later, emotional lability and delirium manifested, gradually followed by involuntary movement (crawl swimming-like, myoclonic), mutism, and hyperpnea/apnea that eventually required mechanical ventilation (Fig. 1). Brain magnetic resonance imaging (MRI) on the admission day showed normal findings throughout the course of disease. Single-photon emission computed tomography (SPECT) on the third day showed decrease cerebral perfusion in the medial frontal cortex. An electroencephalography (EEG) was normal. Routine blood studies showed no abnormalities. Cerebrospinal fluid (CSF) analysis showed mildly increased cell count of 35/mm^3 (mononuclear:polymorphonuclear = 32:3) and normal total protein. Viral antigens were all negative. Although survey for malignancies including ovary and paraneoplastic antibodies including anti-Hu, anti-Yo and anti-GAD was negative, she was suspected to have autoimmune encephalitis. Steroid pulse and high-dose intravenous immunoglobulin (IVIG) therapy was of limited benefit. However, anti-NMDAR antibodies in CSF appeared to be increased significantly. From the 37th day she underwent plasmapheresis, which ameliorated significantly her involuntary movement and mildly her level of consciousness. Repeated CT scans of the pelvis showed a 1.5 cm ovarian mass. On the 69th day she underwent tumor resection, which revealed a 14 mm * 13 mm mature teratoma. This surgery brought her to normal consciousness.

Previously, DBN has been seldom reported in paraneoplastic encephalitis except for anti-Ma2 antibody encephalitis (one case) [3], anti-glutamate acid decarboxilase (GAD) antibody encephalitis (one case) [4], and anti-NMDAR encephalitis (one case) with upbeat nystagmus at the plateau stage under mechanical ventilation [2]. Our patient was unique in that she presented with DBN and dizziness as the sole initial manifestation. Experimental and functional neuroimaging studies indicated that DBN is caused by dysfunction of the vestibulocerebellum (flocculus, nodulus of cerebellar vermis) and, rarely, bilateral paramedian brainstem [1]. Although brainstem and cerebellum are not commonly

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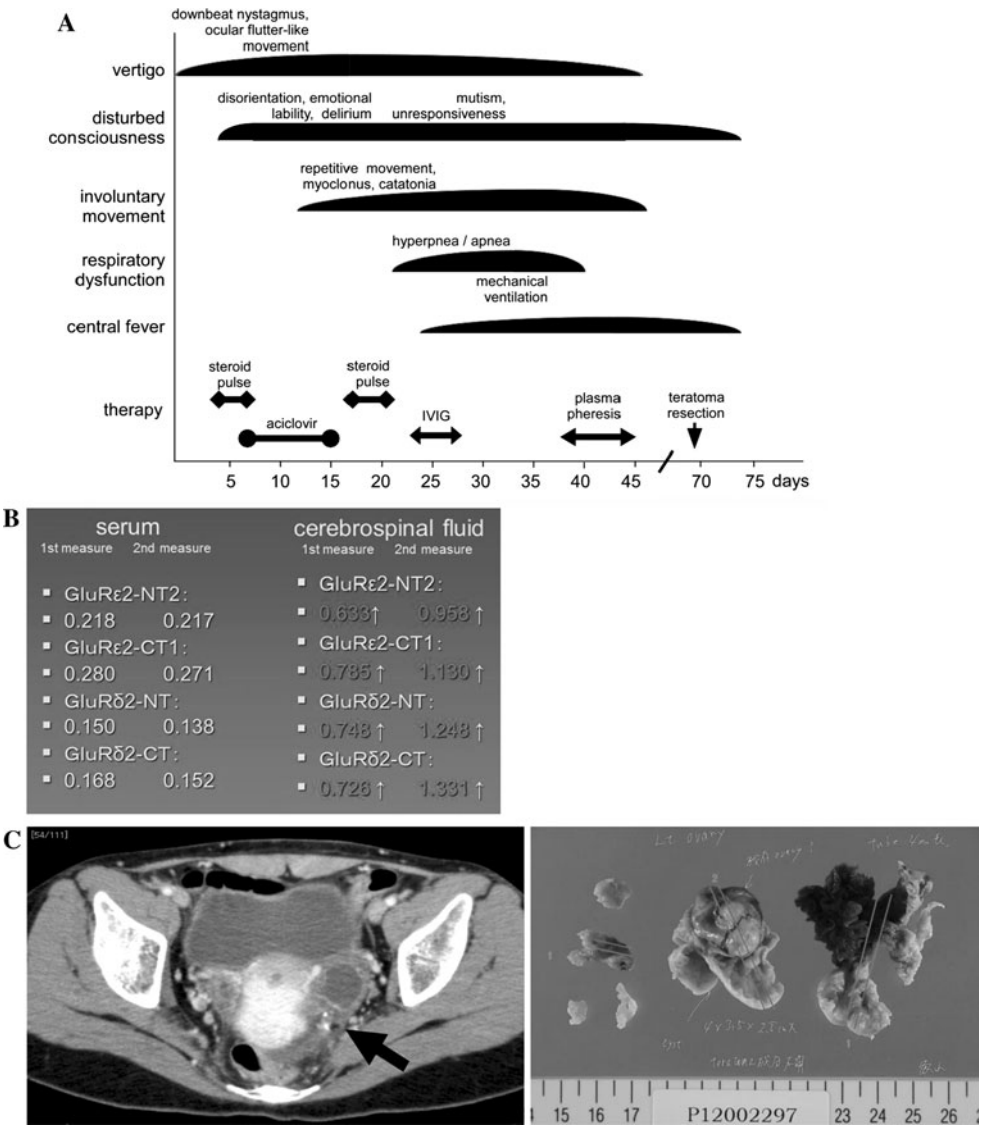

Fig. 1 Clinical pictures of a patient with anti-NMDAR encephalitis. **a** Clinical course. *IVIG* high-dose intravenous immunoglobulin. **b** Antibodies against NMDA receptors (measured at the Mayo Clinic, Rochester, Minnesota). First measure: the first day on admission, second measure: 7 days after admission. *GluRε2* anti-N-methyl-D-aspartate (NMDA) glutamate receptor epsilon 2 subtype, *GluRδ2* anti-NMDA glutamate receptor delta 2 subtype, *NT* N-terminal, *CT* C-terminal. **c** Ovarian teratoma. CT scan (*arrow*) and pathology showing 13 mm*14 mm mature teratoma including tissues of the central nervous system, skin, spin appendage, trachea, etc.

affected sites in anti-NMDAR encephalitis [4], recent studies have shown MRI abnormalities in these areas [5]. Although no discrete lesion was found on MRI scans of our case, above evidences suggest that autoimmune dysfunction might have occurred first in the vestibulocerebellum of our patient. In conclusion, anti-NMDAR encephalitis may present with DBN and dizziness as the sole initial manifestation. DBN of our case suggests that autoimmune dysfunction might have affected firstly the brainstem and cerebellar structures involved in vestibule-oculomotor control.

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