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LETTER TO THE EDITOR

Anti-*N*-methyl-D-aspartate receptor encephalitis with acute disseminated encephalomyelitis-like MRI features

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Sir,

In anti-NMDAR (anti-*N*-methyl-D-aspartate receptor) encephalitis, MRI is usually normal or demonstrates non-specific lesions in the grey matter [1]. We report the case of a patient with anti-NMDAR encephalitis in whom the MRI features were suggestive of acute disseminated encephalomyelitis (ADEM).

A 34-year-old patient presented with a 1-month history of recurrent psychomotor agitation, incoherent speech, loss of judgement, insomnia and aggressiveness associated with progressive walking difficulties. The patient could not maintain prolonged contact with the examiner, although she was conscious. She was disoriented both spatially and temporally. Her speech was grossly disorganized, and she had recurrent blockings, distractibility, echolalia and neologisms. Delusions of persecution were evident. She experienced alternating episodes of agitation and slowness and in-between scenes of explosive laughter and echopraxia. Neurological examination showed a mild dysarthria, a marked cerebellar ataxia and an asymmetry in finger-to-nose and heel-to-knee manoeuvre. There was a moderate left hemiparesis. Proprioceptive sensation was affected in both lower limbs. Deep tendon reflexes were brisk bilaterally on all limbs with a bilateral Babinski response. Bladder dysfunction was present. The patient was wheel-chair dependent. Neither seizures nor movement disorders were observed. The rest of the clinical exam was unremarkable.

Brain and spinal MRI were suggestive of an ADEM, showing widespread and multifocal white matter lesions, a right frontal contrast-enhancing lesion and a longitudinally extensive transverse myelitis (Fig. 1). Cerebrospinal fluid (CSF) analysis demonstrated 19 leucocytes/mm^3 (90% lymphocytes) with numerous oligoclonal bands. Protein was 47 mg/dl and glucose was 40 mg/dl. Viral serology was negative as well as PCR for HSV, HZV, EBV, CMV and enteroviruses in the CSF. Bacterial cultures including atypical germs and mycobacterium tuberculosis were all negative. Extensive autoantibody testing was negative (including anti-DNA, anti-nuclear, anti-Ro, anti-La, anti-phospholipids, anti-aquaporin 4 and classical onconeural antibodies such as anti-Hu, Yo, Ri, CV2/CRMP5, Amphiphysin and Ma2), except for anti-NMDAR antibodies, which were detected at a high level in the CSF. Pelvic ultrasound, chest, abdominal and pelvic computerized tomography were normal, as were pelvic MRI. Intravenous polyvalent immunoglobulins and steroids had only a mild effect on both psychiatric and neurological symptoms. Therefore, rituximab was administered. The patient received two 1 g infusions at a 2-week interval followed by

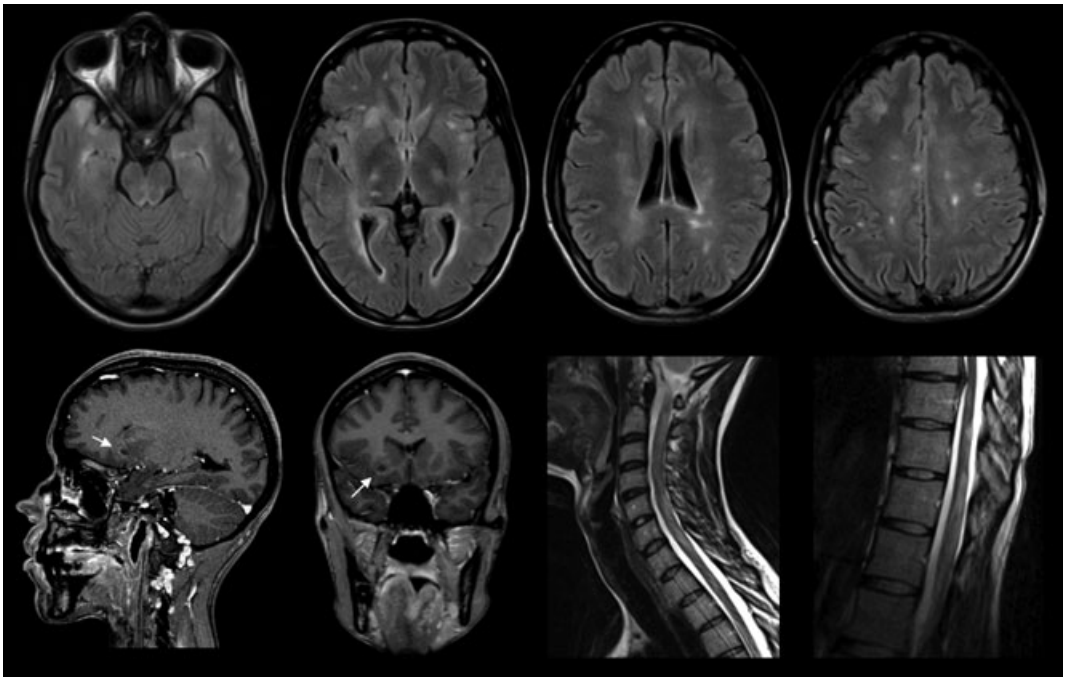

Figure 1 Top: multiple and disseminated white matter lesions on FLAIR-weighted imaging; bottom left: right frontal contrast-enhancing lesion on T1-weighted imaging after administration of gadolinium (arrow); bottom right: cervical (left) and lumbar (right) extensive myelitis on T2-weighted imaging.

6 monthly maintenance infusions (375 mg/m^2), which resulted in a dramatic improvement of her neurological and psychiatric symptoms. Upon her most recent visit, 18 months after the first symptoms, the patient was ambulatory despite moderate ataxia and was maintaining euthymia. No delusions were present. Brain and spinal cord MRI showed a mild reduction in white matter lesions but no post-contrast enhancement.

In our patient, the MRI features and the neurological symptoms were suggestive of ADEM, but the prominent psychiatric symptoms prompted us to search for anti-NMDAR antibodies. As it is unlikely that anti-NMDAR antibodies were responsible for the extensive white matter lesions, our case suggests that there might be an overlap between anti-NMDAR encephalitis and demyelinating diseases, potentially involving other immunological mechanisms. Consistent with this hypothesis a case of anti-NMDAR encephalitis associated with a clinical and radiological presentation of seronegative neuromyelitis optica has recently been reported [2]. In the largest published series of patients with encephalitis and anti-NMDAR antibodies, one patient with multifocal white matter lesions has also been reported [1]. Further studies are needed to more precisely describe the incidence and the characteristics of anti-NMDAR/demyelinating overlap syndromes. In conclusion, our case demonstrates that anti-NMDAR antibodies should be assessed in patients with encephalitis and psychiatric symptoms, even when the MRI is suggestive of demyelinating disease.

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Disclosure of conflict of interest

The authors have no conflict of interest to declare.

References

1. Dalmau J, Lancaster E, Martinez-Hernandez E, *et al.* Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol* 2011; **10:** 63–74.
2. Kruer MC, Koch TK, Bourdette DN, *et al.* NMDA receptor encephalitis mimicking seronegative neuromyelitis optica. *Neurology* 2010; **74:** 1473–1475.