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LETTER TO THE EDITOR

Anti-NMDAR encephalitis preceded by dura mater lesions

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Dear Editors,

Limbic encephalitis is characterized by psychosis, memory loss, and seizures. It is sometimes caused by autoimmune mechanisms, including anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis. Anti-NMDAR encephalitis is typically a multistage disorder. After a prodromal event, psychiatric symptoms develop, followed by seizures, suggesting cortical involvement. Subsequent subcortical involvement is observed in most patients leading to movement disorder, and reduction in consciousness. The signal changes in brain magnetic resonance imaging (MRI) have been reported in the cerebral parenchyma such as the hippocampi, cerebellar or cerebral cortex, frontobasal and insular regions, basal ganglia, and brainstem [1]. Herein, we present a case with anti-NMDAR encephalitis preceded by dura mater lesions in brain MRI.

A 50-year-old man with no medical history and head contusion suddenly developed tonic–clonic seizure. Brain MRI showed signal changes in the dura mater of the occipital areas (Fig. 1a, b). A day later, he developed status epilepticus (SE) and was sedated with propofol. Cerebrospinal fluid (CSF) examination showed normal cell counts and elevated concentration of total protein (48.0 mg/dl) and IL-6 (51.0 pg/ml). The laboratory investigations for herpes simplex viruses and human herpesvirus-6 were negative. Antinuclear antibody, thyroid antibodies, onconeuroal antibodies (Hu, CV2, Ma2, Ma1, Yo, Ri, amphiphysin), and glutamic acid decarboxylase antibodies (GAD-ab) were negative. Although high-dose intravenous methylprednisolone (1,000 mg/day for 3 days) led to recovery from SE, he exhibited cognitive impairment (15/30 on the Mini-Mental State Examination), psychomotor agitation, nystagmus, rigidity, postural tremor, and ataxia. Brain MRI on the 14th hospital day showed signal changes in cerebellum and cingulate gyrus with improvement of lesions in the dura mater (Fig. 1c). No additional treatment led to complete recovery from the neurological deficit within 2 months after disease onset. Antibodies to NR1/NR2B heteromers of the NMDA receptor (anti-NMDAR antibody), examined by a cell-based assay as described previously [2], were positive in serum and CSF obtained upon admission. Despite an extensive oncologic workup such as whole-body CT and fluorodeoxyglucose-positron emission tomography (FDG-PET), there was no evidence of tumor. He has not had relapsing episodes of encephalitis for 26 months. Repeat FDG-PET every 6 months showed no tumor.

Anti-NMDAR encephalitis was originally considered as having paraneoplastic syndrome in young women with ovarian teratoma [1]. However, recently it has become clear that patients with anti-NMDAR encephalitis are not always women and paraneoplastic [3–5]. Brain MRI abnormalities have been reported in the cerebral parenchyma such as the hippocampi, cerebellar or cerebral cortex, frontobasal and insular regions, basal ganglia, and brainstem [1]. Abnormalities in medial temporal lobes are

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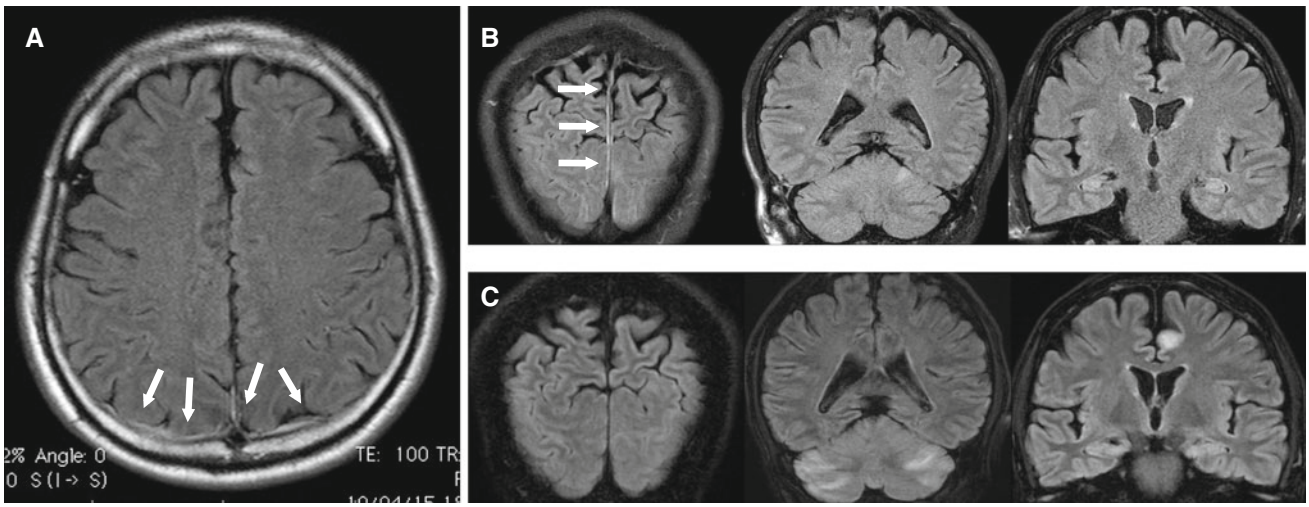

Fig. 1 Brain MRI (FLAIR images) of case (**a**–**c**). Initial brain MRI showed high-intensity lesions in the dura mater of the occipital areas (**a**, **b**). Two weeks later, brain MRI showed high-intensity lesions in cerebellum and the cingulate gyrus with improvement of lesions in the dura mater (**c**). *Arrows* indicate abnormal lesions in dura mater

most reported [1, 4]. In present case, the marked dura mater lesions on brain MRI were observed at the onset. Later, brain MRI abnormalities expanded into the cerebellum and cingulate gyrus. Irani et al. analyzed two main stages in anti-NMDAR encephalitis. The early stage is characterized by neuropsychiatric symptoms and seizures with cortical MRI changes, whereas the late stage is characterized by movement disorder and reduction in consciousness, with subcortical MRI changes [4]. The dura mater MRI signal changes have not been reported previously. In present case, it is likely that the dura mater MRI signal changes show the initial site of inflammation in the central nervous system. Dura mater, where the blood–brain barrier is absent, may be one of the initial sites of inflammation in anti-NMDAR encephalitis, followed by the early and late stages as described by Irani et al. The dura mater abnormalities on brain MRI may be useful diagnostic findings and may provide us with a clue to elucidate the pathogenetic mechanisms of anti-NMDAR encephalitis. In anti-NMDAR encephalitis, seizures develop at early stages of the disease [3, 4]. SE is unusual, but described and developed at early stages of the disease. The frequency and intensity of the seizures decrease as the diseases evolve. In present case, the dura mater lesions may induce seizure and SE as the initial symptoms. Future investigation of the dura mater abnormalities on brain MRI associated with anti-NMDAR encephalitis in large number of cases is necessary.

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