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LETTER TO THE EDITOR

Brainstem and vestibulocochlear nerve involvement in relapsing–remitting anti-NMDAR encephalitis

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Background

Since first reported in 2007, anti-*N*-methyl-*D*-aspartate receptor (NMDAR) antibodies have become an increasingly recognized cause of autoimmune encephalitis (AIE). Usually, the disease is mono-phasic. The main symptoms include progressive psychosis, memory impairment, movement disorders, seizures, dysautonomia and decreased level of consciousness [1]. Brainstem symptoms are rarely noticed. We reported a case of relapsing–remitting anti-NMDAR encephalitis, wherein presented with dizziness and hearing loss related to brainstem and right vestibulocochlear nerve injury in relapse.

Case

In September 2013, 10 days after cough and expectoration with mild fever, a 16-year-old female became alert to light and sound and suffered from optical and auditory hallucination, hypochondriac idea of epilepsy, as well as a decline in concentration, calculation capability and memory. Her electroencephalogram (EEG) revealed diffuse slowing waves. Routine blood tests, cerebrospinal fluid (CSF) examinations and brain magnetic resonance imaging (MRI) showed no notable alteration. The patient was diagnosed with viral encephalitis and treated with antiviral and antipsychotic agents. Dexamethasone 10 mg daily was administered and tapped gradually. The patient experienced a period of reduced consciousness and then complained of shortness of breath and hyperhidrosis. However, she gradually returned to baseline conditions in 1 month and was asymptomatic between December 2013 and February 2014 while using antipsychotics and prednisone 10 mg per day.

In March 2014, after a few days of cough and expectoration, she complained of blurred vision as well as tinnitus and hearing loss in the right ear. She then felt vertiginous and could not walk stably. On admission, her temperature was 100.9 °F. Neurological examinations revealed right supertemporal and left supernasal visual-field defects, coarse horizontal nystagmus in both eyes, and hearing loss in the right ear. During hospitalization, the patient again complained of shortness of breath and hyperhidrosis. Routine blood and CSF tests were still unremarkable. Oligoclonal bands were negative in the CSF. Brain MRI scan revealed abnormal areas in the left temporal lobe, left hippocampus and parahippocampal gyrus, right cerebellum and right brachium pontis. Notably, the right vestibulocochlear nerve was hyperintensified on T2 flair images (Fig. 1a–d).

Considering the likelihood of AIE, high doses of methylprednisolone were administered. After anti-NMDAR antibodies 1:1 positive were detected in the CSF, anti-NMDAR encephalitis was confirmed. Bilateral cystic adnexal masses were identified using computerized tomography (CT) scan (Fig. 2). The patient gained near-complete recovery, experiencing only horizontal nystagmus and slight unsteady gait on discharge. For maintenance, methylprednisolone was gradually tapped to 8 mg every other day and azathioprine 50 mg per day was added. No sign of relapse has been found so far (Fig. 1e, f).

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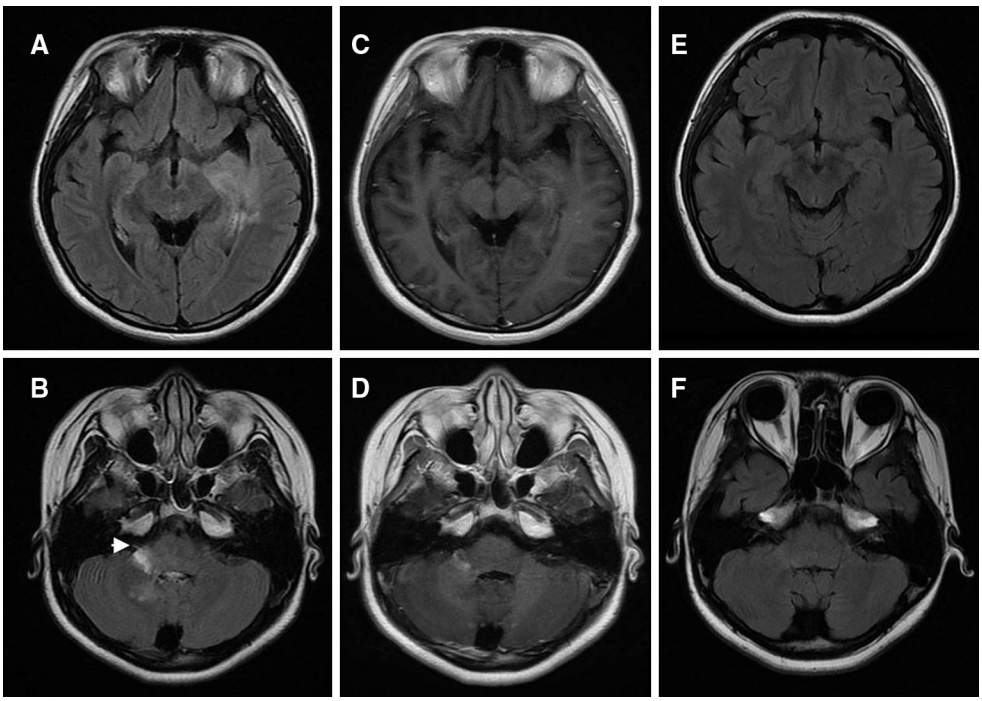

Fig. 1 Magnetic resonance images of the patient in relapse before and after immunotherapy. **a**, **b** Before immunotherapy, hyperintensified lesions were observed in the left temporal lobe, left hippocampus and parahippocampal gyrus, and the right cerebellum and right brachium pontis on T2 flair. The right vestibulocochlear nerve was also involved, as indicated by the *arrow*. **c**, **d** T1 contrast demonstrated slightly enhance in the abnormal regions. **e**, **f** Three months after immunotherapy, the hyperintensified lesions returned to normal

Fig. 2 Cystic adnexal masses revealed by computerized tomography, as indicated by *arrows* on both sides

Discussion

We reported the first case of relapsing–remitting anti-NMDAR encephalitis presenting with typical symptoms of psychotic disorders and cognitive impairment in the first episode but dizziness and hearing loss related to brainstem and cerebellar as well as vestibulocochlear nerve injury in the second episode.

The patient was admitted for dizziness and hearing loss; however, after reviewing her medical history, a special "viral encephalitis" was noticed. It was characterized by limbic system symptoms that lacked signs of meninges involvement, shared common features, such as suspected hypoventilation and autonomic dysfunction with the present illness, and was responsive to steroids. We believed the patient suffered from AIE with a relapsing–remitting course. Detected anti-NMDAR antibody in the CSF led to the diagnosis of anti-NMDAR encephalitis.

Relapses occur in approximately 25 % of anti-NMDAR encephalitis cases. The typical manifestation in relapse is mild symptoms consistent with the first episode [1]. To our knowledge, our case is the first one which presented with different symptoms in the two episodes. Consistent with the distribution of NMDARs, neuro-inflammation has been proved to affect the pons and cerebellum in anti-NMDAR encephalitis by PET/SPECT [2]. Nevertheless, brainstem symptoms are rare in clinical practice. Only one other case with ophthalmoplegia accompanied by flaccid paraplegia has been reported. In that case, ophthalmoplegia was more likely to be a part of Miller-Fisher syndrome during the course of anti-NMDAR encephalitis [3, 4]. Our patient complained of hearing loss and vertigo. Brain MRI indicated inflammatory alteration in the right vestibulocochlear nerve and the circular region. NMDAR expression is

proved in the cochlear nuclei [5]. The abnormal signal in the right vestibulocochlear nerve could be secondary to the cochlear nuclei and vestibular nuclei insults. Both cases were relapsing–remitting. We speculated that brain stem and cerebellum involvement may be associated with a higher probability of relapse.

The first-line immunotherapy for anti-NMDAR encephalitis, including steroids, intravenous immunoglobulin and plasmapheresis, could prevent disability and relapses. However, the recommendation for chronic immunotherapy is still undetermined. Our patient responded well to high-dose steroids, but relapse still occurred after infection despite low-dose steroid maintenance, which implies that the immunotherapy regimen should be carefully considered.

Conclusion

Occasionally, the presentation of anti-NMDAR encephalitis is atypical and incomplete, thereby increasing the difficulty for correct diagnosis. Our experience indicates that dizziness and hearing loss could be components of the disease and highlights the involvement of cranial nerves and the brainstem.

Compliance with ethical standards

Conflict of interest The authors state that they have no conflict of interest.

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