Recurrence panic attack and bilateral hippocampus lesions as main manifestation in an autoimmune encephalitis associated with primary biliary cirrhosis

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To the Editor: Autoimmune encephalitis (AE) is a group of autoantibodies-mediated central nervous system (CNS) inflammatory diseases with a wide spectrum of neuropsychiatric symptoms.1 Cognitive impairment, epileptic seizures, and mental behavior disorder, along with both limbic and extra-limbic brain structures lesions in radiologic imaging, are the most common manifestation. Of late years, AE has been widely recognized and could be combined with multiple autoimmune diseases; however, little has been described about co-existence of the AE and primary biliary cirrhosis (PBC).

A 27-year-old woman was admitted to our hospital with a 1-month history of memory deterioration and repeating panic attack in February 2019. One month before her presentation, she gradually developed short-term memory loss and exhibited sudden, transient, recurrent sense of panic, accompanied by nausea, dizziness, chest congestion, and limbs tremors. She, therefore, went to the local hospital where she was tested with Hamilton depression (HAMD) and anxiety (HAMA) scale and was diagnosed with moderate depression and obvious anxiety. She then came to us for further diagnosis and treatment. The patient was once diagnosed with autoimmune hepatopathy (AIHT) in the local hospital in May 2018 when she was at her midtrimester and treated with ursodesoxycholic acid (250 mg, q.d., for 1 month). She gave birth to a healthy baby boy by natural labor in September 2018. Her personal and family history was unremarkable. Neurological examination revealed an important impairment of short-term memory. Other cognitive functions were normal.

Blood tests detected moderately elevated alanine aminotransferase (ALT) of 75 U/L (normal range 7–10 U/L), aspartate aminotransferase (AST) of 54 U/L (normal range 13–35 U/L), and markedly increased alkaline phosphatase (ALP) of 295 U/L (normal range 35–100 U/L), and gamma glutamyltransferase (GGT) of 677 (normal range 7–72 μmol/L). Qualitative serum analysis of autoantibodies detected strongly positive anti-mitochondrial antibody M2 (AMAM2), and positive anti-nuclear antibody (ANA), but normal level of anti-neutrophil cytoplasmic antibodies (ANCA), pANCA of 1.40 U/mL (normal range 0–5.00) and cANCA of 1.8 U/mL (normal range 0–5.00). Other antibodies were all normal (Supplementary Table 1, http://links.lww.com/CM9/A159). Blood and urine examination of amino acid and acyl carnitine spectra was normal. Cerebrospinal fluid (CSF) examination had no abnormal findings supporting bacterial, fungal, virus infection, or presence of autoantibodies (Supplementary Table 1, http://links.lww.com/CM9/A159).

Epileptic waves were not tracked in short-term electroencephalogram (EEG) by 3 times or in long-term EEG. T2-weighted and flair magnetic resonance imaging (MRI) displayed symmetric swelling changes and high intensity signals in the bilateral hippocampus region [Figure 1]. According to the laboratory data, PBC was confirmed and administration of ursodesoxycholic acid (500 mg, b.i.d) achieved improvement of her liver function. However, in spite of anti-anxiety and depression therapy with paroxetine (20 mg, q.d.), estazolam (0.5 mg, t.i.d), and olanzapine (2.5 mg, q.d.), the patient’s complain of symptoms could not take a turn for the better. In this point, considering that her clinical symptoms and imaging manifestation were conformed to AE and ruling out of other possible CNS diseases, the diagnosis of AE was finally made. With treatment of intravenous immunoglobulin (0.4 g/kg, q.d., for 5 days), followed by oral methylprednisolone (44 mg, q.d.; with 8 mg decrease every 2 weeks), her panic attack...
was alleviated. At 3-month follow up, the patient’s complaint of panic attack and memory loss resolved, but she refused to review AMAM2 level or magnetic resonance imaging for personal reasons.

This case represents a rare report of AE in a patient with the PBC. The patient showed no typical clinical symptoms suggestive of hepatopathy but only mental behavior disorder, short-term memory loss and panic attack, along with bilateral hippocampus lesions and presence of anti-mitochondrial antibody M2 (AMAM2).

In our case, no previously proven AE-associated antibodies were found in CSF, but AMAM2 was strongly positive in serum. Hu et al has reported the presence of AMAM2 in serum from a patient of systemic lupus erythematosus (SLE) with CNS involvement. Although AMAM2 has been reported to be associated with hepatocellular damage, skeletal muscular impairment and cardiac involvement, specially serving as a biomarker for PBC, it remains unclear whether AMAM2 is a novel AE-related autoantibody or responsible for other CNS-involved diseases, or there were others for the case.

Unfortunately, due to laboratory technique limits, we could not test the presence of AMAM2 in CSF, which need further investigation. Additionally, Il’ichenko et al found that AMAM2-positive PBC is more frequently to have an overlap syndrome. It is still unknown whether there is an overlapping form between AE and PBC. Alonso-Navarro et al had reported a similar case of a PBC patient with limbic encephalitis including Bilateral hippocampal involvement and immunosuppression therapy achieved release of clinical symptoms and imaging changes. To our best knowledge, there are no clear proof of this novel clinical entity – an PBC/AE overlap syndrome, but the coincidence of two diseases of possible autoimmune origin in the same patient would suggest the existence of a relationship between them.

In conclusion, the case report represents a novel clinical entity, an AE associated with PBC, characterized by presence of AMAM2 and symmetric high-intensity lesion of bilateral hippocampus, manifesting as short-term memory loss and panic attack. Whether PBC/AE overlap is a true clinical entity or AMAM2 is responsible for AE can only be figured out by future research.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the work, the patient gave her consent for her images, and other clinical information to be reported in the article. The patient understands that neither her name nor initials will be published, and due effort will be made to conceal her identity, although total anonymity cannot be guaranteed.

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Conflicts of interest
None.

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