Recurrent hemichorea in a patient with diabetes and anti-phospholipid syndrome: a case report

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To the Editor: Many diseases present with chorea, such as cerebrovascular disease, diabetes mellitus, and systemic autoimmune disorder. The differential diagnosis for chorea is complicated, with many other rarer causes of chorea. Hemichorea is a type of chorea with unilateral involuntary movements. Hemichorea associated with non-ketotic hyperglycemia and high-signal-intensity lesions on T1-weighted brain magnetic resonance imaging (MRI) is recognized as diabetic striatopathy (DS).1,11 The movement disorder and imaging abnormalities typically resolve with the treatment of hyperglycemia. Therefore, the disease is now easy to diagnose with the typical characteristics. However, hemichorea with anti-phospholipid syndrome (APS) has rarely been reported and presents with more highly variable clinical characteristics and imaging findings compared with DS.

A 65-year old female patient presented with a 3-month history of involuntary movements of her left arm and leg. She had a 10-year history of type 2 diabetes mellitus without regular therapy. She had no history of cerebrovascular disease and any other neurological diseases. Her medical history was impressive for the diagnosis of secondary APS in June 2018 because of thrombocytopenia and pulmonary embolism. At that time, the laboratory tests revealed a decreased platelet count of 61 × 10^9/L (normal range: 100–300 × 10^9/L), an increased antinuclear antibody (ANA) titer of 185.36 U/mL (normal range: 0–18 U/mL), a lower complement 3 (C3) of 0.74 g/L (normal range: 0.9–1.8 g/L), an increased anti-cardiolipin antibody-immunoglobulin (ACA-IgG) titer of 91.48 GPL-U/mL (normal range: 0–18 GPL-U/mL), positive anti-b2 glycoprotein-I antibodies (anti-b2GPI) (normal range: negative), a prolonged primary screening test of lupus anti-coagulant (LAC) of 158 s (normal range: 31–44 s), and a prolonged reconfirmation test of LAC of 61 s (normal range: 30–38 s). Computed tomography of the pulmonary artery confirmed pulmonary embolism. Systemic lupus erythematosus (SLE) and secondary APS were diagnosed according to the diagnostic criteria.13 The patient was treated with prednisone and hydroxychloroquine. Considering the risks of bleeding, the patient refused anti-coagulant treatment and took only clopidogrel 75 mg/d orally. The platelet count returned to normal after 3-month treatment, and then the patient ceased all the medications without following her physician’s advice.

The patient had abnormal involuntary movements involving the left upper limb and lower limb in January 2019 during a non-ketoacidotic hyperglycemic episode (random serum glucose 15.22 mmol/L; hemoglobin A1c [HbA1c] 16.8% [normal range: 4.0%–6.0%]). The T1-weighted brain MRI revealed high-signal-intensity lesions in the right basal ganglia region. Her diabetes was successfully controlled with a subcutaneous insulin injection, and the symptoms considerably improved over the following months. However, 3 months later, she suffered a recurrence of her involuntary hemichorea. Therefore, she was admitted to the department for further diagnosis and treatment.

On admission, she exhibited involuntary movements of her left arms and legs. Other nervous system examinations were not remarkable. Her fasting blood glucose fluctuated from 4.8 to 6.9 mmol/L, and post-prandial blood glucose fluctuated from 7.1 to 11.6 mmol/L. HbA1c was 7.5%. Repeated cranial MRI showed right-sided striatopallidal T1-hyperintensities, which showed no significant changes compared with the previous MRI. Cerebrospinal fluid (CSF) tests of cell counts and glucose and protein levels were all within normal ranges, and CSF cytology was also normal (Figure 1).

Her symptoms were poorly controlled with a combination of clonazepam and sulpiride. On the second day of admission, the patient suffered from acute heart failure...
with a dramatically increased pro-B-type natriuretic peptide of 13,024 pg/mL (normal range: 0–300 pg/mL). She was intubated and transferred to the neural intensive care unit. The echocardiographic assessment showed the reduced beat of the left ventricle and the decreased ejection fraction of 41% (normal range: 50%–70%). The chest radiograph showed pulmonary edema. At the same time, the symptoms of involuntary movements worsened dramatically. The serum glucose of the patients was quite stable with random serum glucose of 6 to 10 mmol/L. The common risk factors of heart failure, including infection, excessive fluid, and arrhythmias, were excluded. The immunological markers of the patients were re-evaluated with an increased ACA-IgG titer of 150.1 GPL/mL, positive anti-b2GPI, a prolonged primary screening test LAC of 160 s, a reconfirmation test LAC of 59 s, an increased ANA titer of 145.37 U/mL, and a lower C3 of 0.88 g/L. The results showed that APS related to SLE was still not controlled. With thorough evaluation, it was considered that this AHF was caused by lupus. With diuretic and fluid restriction, methylprednisolone (40 mg/d) was initiated.
The involuntary movement of the patient was completely relieved within 2 days.

DS is a syndrome associated with hyperglycemia, including the classical symptoms of hemichorea, characteristic imaging findings, and reversible clinical manifestations with the correction of hyperglycemia. The underlying mechanism of this syndrome is still unclear. The synergistic effects of hyperglycemia and vascular insufficiency may play an important role in a transient dysfunction of the striatum, causing subsequent chorea. Hyperglycemia causes the depletion of gamma-amino butyric acid, the main inhibitory neurotransmitter. The inflammation induced by hyperglycemia disrupts the blood-brain barrier and causes the occlusive vasculopathy of the arterioles and transient ischemia of vulnerable striatal neurons. Therefore, a prompt correction of hyperglycemia can resolve the symptoms. A meta-analysis of 53 cases of DS showed consistently characteristic hyperintense basal ganglia lesions in the T1-weighted brain MRI of all patients, consistent with the present case, suggesting that the first episode of the hemichorea of the patient was secondary to DS.

Chorea is a rare manifestation of APS, and its prevalence has been estimated to be 1.3%. Chorea is strongly correlated with high plasma titers of anti-phospholipid antibody (aPL). The mechanism of aPL-related chorea is unclear. The high plasma titers of aPL could bind to the endothelium of the brain vessels, disrupting the blood-brain barrier and the phospholipids in the basal ganglia, causing choreic movements. Almost all patients had no characteristic imaging findings with normal brain MRI or small-vessel ischemic changes related to aging, hence not providing additional diagnostic information.

Although DS generally is considered to be fully reversible, some cases demonstrate that DS can result in permanent structural lesions with persistent symptoms because of insulin resistance or delayed treatment. The diabetes of the patient in the present case was medically controlled, and the choreic movement was considerably resolved in the first episode. Interestingly, the recurrence of hemichorea was consistent with medication cession during APS treatment. The underlying comorbidities may play an important role in recurrent hemichorea.

Currently, no diagnostic criteria exist for APS-related chorea. The patient in the present case had persistently elevated serum levels of aPL antibodies. The cerebral angiography and CSF were normal. Her diabetes was well controlled. Besides, the recurrent hemichorea worsened with AHF and was dramatically improved with the use of methylprednisolone. It is believed that recurrent chorea should be diagnosed as APS-related chorea.

This study presented a case of a patient with recurrent hemichorea with diabetes and APS. The first episode of chorea was consistent with the diagnosis of DS, and the second episode was triggered by APS. In patients with chorea, the diagnosis of DS and APS should be considered. The comorbidities might be the underlying causes of chorea.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient’s guardians have given his/her/their consent for his/her/their images and other clinical information to be reported in the article. The patients/patient’s guardians understand that their names and initials will not be published and due efforts will be made to conceal the identity of the patient, although anonymity cannot be guaranteed.

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Conflicts of interest

None.

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