Pin-Point Pupils with Drowsiness as a Presentation of Hashimoto's Encephalopathy Mimicking Pontine Infarction

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Abstract

Purpose: Hashimoto's encephalopathy (HE) is an autoimmune-mediated encephalopathy with various manifestations. Pupil size change has never been previously reported as a presentation of HE.

Case Report: A 65-year-old woman without previous known thyroid disease presented with acute onset of drowsiness and blurred vision. Neurologically, she was drowsy and had bilateral pinpoint-sized pupils without a light reflex, which probably indicated a bilateral pontine lesion. Brain MRI showed two tiny infarctions at the left midbrain and left thalamus, but did not show a pontine lesion, and demonstrated patent vertebral/basilar arteries. Electroencephalography showed intermittent diffuse slowing. She had an elevated protein level (123 mg/dl) in cerebrospinal fluid without pleocytosis. Of note, she had elevated serum levels of anti-TG antibody (282 IU/mL) and anti-TPO antibody (117 IU/mL). Her symptoms improved spontaneously including gradually normalization of her pupil size in 3 days and clear consciousness in 6 days; therefore, corticosteroid was not administered.

Conclusion: This case illustrates that physicians should be aware of the treatable condition of HE as a possible diagnosis in patients with bilateral pinpoint pupils and drowsiness but without corresponding MRI lesions.

Key Words: Hashimoto's encephalopathy, pupil size, pons, thyroid disease

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INTRODUCTION

Hashimoto's encephalopathy (HE), which was first reported in 1966, is diagnosed as encephalopathy with a high serum level of one anti-thyroid antibody, and no evidence of infection or other well-defined cerebral disorders [1,2]. Characteristic serological hallmarks of HE are high level of thyroid autoantibodies, including antithyroglobulin antibody (anti-TG antibody) and antithyroid peroxidase antibody (anti-TPO antibody) [3]. HE is a rare disorder and has a wide range of clinical manifestations such as stroke-like episodes, consciousness disturbance, seizure, psychosis, dementia, tremor and myoclonus [4,5]. These nonspecific presentations of HE may result in the diagnosis being overlooked, particularly when

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the thyroid function of patients with HE actually ranges from hypothyroidism to euthyroid or even the thyrotoxic state [1,3]. Here, we report a case of a patient with HE who had acute onset of disturbance of consciousness and bilateral pinpoint-sized pupils mimicking acute pontine stroke.

CASE REPORT

A 65-year-old woman with diabetes mellitus, hypertension and coronary artery disease had no previous history of thyroid disease. Several years earlier she had two episodes of somnolence which persisted for several days and then improved spontaneously without seeking medical help. This time she presented at the emergency room with drowsiness and blurred vision for several hours. She did not have fever, headache, dizziness, diplopia, unsteady gait or vomiting. She did not use sedative drugs, illicit agents, or eye drops, and was not recently exposed to insecticide or herbicide. On examination, she was afebrile, had a regular pulse of 70 beats/min, and her blood pressure was 139/61 mmHg. She did not have neck stiffness or photophobia. The Glasgow Coma Scale score was E3M6V4. She had bilateral pinpoint-sized pupils without a light reflex, blurred vision in both eyes and normal range of extraocular muscle movement. Muscle power of her four limbs was graded 4-5 symmetrically on the manual muscle power test, and Babinski's sign was negative.

Emergent brain MRI showed two tiny spots with hyperintensity on diffusion-weighted imaging (DWI) and hypointensity on apparent diffusion coefficient at the left medial thalamus and left anterior midbrain, which were compatible with acute ischemic lesions (Figure 1). At the pons, there was no signal change on DWI, T2-weighted imaging or fluid-attenuated inversion recovery (Figure 1). However, these two tiny lesions could not explain her pinpoint-sized pupils. Electroencephalography (EEG) showed intermittent diffuse slow waves at 3-7 Hz, 20-60 μV without epileptiform activity. Blood testing showed a normal white blood cell count, which excluded an active bacterial infection. The results of tests for electrolytes, arterial blood gas, and renal and liver function were also normal. A urine drug screen was negative for opiate. A cerebrospinal fluid (CSF) study showed a high protein level (122.7 mg/dL), white blood cells 0 /μL and a normal glucose level (134 mg/dL); therefore, noninfectious inflammatory encephalopathy was highly suspected. Culture results of CSF were all negative. Her thyroid function was normal. Of note, she had elevated serum levels of anti-TG antibody (282.1 IU/mL; normal range 0~14.4 IU/mL) and anti-TPO antibody (117.0 IU/mL; normal range 0~5.6 IU/mL). Therefore, the diagnosis of HE was made based on clinical symptoms, results of CSF studies, EEG findings and high titers of these two autoantibodies, and with exclusion of other disorders.

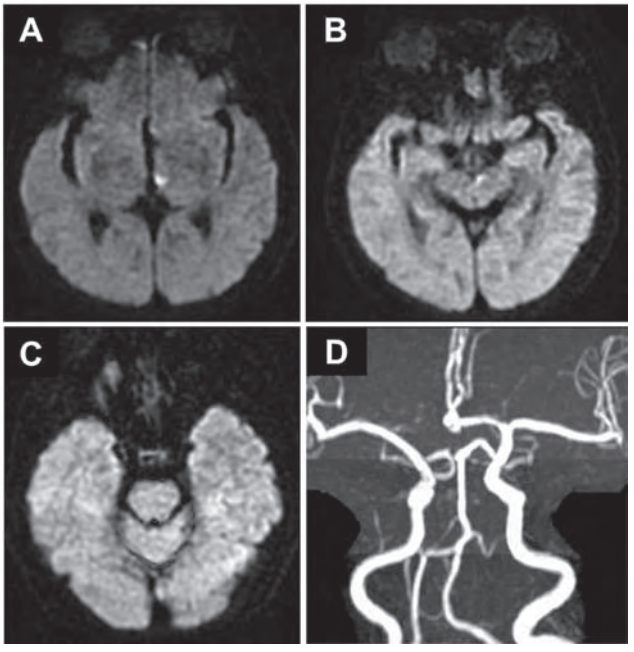

Figure 1. Brain MRI findings of the reported case. There were tiny infarctions at (A) left medial thalamus and (B) left midbrain but (C) without signal change at pons on diffusion-weighted imaging of MRI. (D) MR angiography showed patent vertebral-basilar arteries.

During the days after admission, her symptoms improved spontaneously; she had normal pupil size of 3 mm in both eyes after 3 days and clear consciousness after 6 days. There was also corresponding improvement in her blurred vision. Due to her spontaneous recovery, corticosteroid therapy not administered. Regular follow-up visits were suggested to the patient because of possible relapse in the future.

DISCUSSION

We report the case of a patient with HE who presented with acute onset of disturbance of consciousness and bilateral pinpoint-sized pupils, which was associated with elevated serum levels of anti-TG and anti-TPO antibodies, as well as a high protein level in the CSF. This is the first report of the presentation of bilateral pinpoint-sized pupils in HE. According to the change in bilateral pupil size and alertness of this patient, it would be surmised that the lesion was most likely at the bilateral pons, with involvement of bilateral sympathetic tracts and the ascending reticular activating system[6]. Brain MRI showed two tiny infarcts at the left medial thalamus and left anterior midbrain, without a structural lesion at the pons or stenosis in the vertebral/basilar arteries. The two infarct lesions might be due to occlusion in the thalamoperforating arteries or branches of the artery of Percheron [7]. The patient's altered consciousness might be partially attributed to the tiny infarction at the left medial thalamus [8], but her bilateral pinpoint-sized pupils cannot be linked to the left medial thalamic and left midbrain lesions [9]. A bilateral pontine lesion such as mild ischemia, which was not demonstrated on MRI, was highly suspected. Minor ischemic stroke has been reported to have a high rate of negative findings on DWI of up to 33% [10]. In addition, the two tiny infarctions also could not have been the cause of a high protein level on the CSF study, because the area of breakdown of the blood-brain barrier usually correlates with infarct size [11]. The high protein level without pleocytosis in the CSF study indicated autoimmune encephalopathy, possibly through a vasculitic process.

Other etiologies which should be considered for bilateral pinpoint-sized pupils include drugs or toxins. The patient denied using opiate agents, and a urine drug screen excluded that possibility. Organophosphate intoxication also can lead to pinpoint-sized pupils and disturbed consciousness through a cholinergic effect [12], but this patient did not have such an exposure history or signs indicating organophosphate intoxication, such as increased secretion, bradycardia and hypotension.

The underlying pathogenesis of HE remains under investigation. The diverse MRI features of HE makes it difficult to understand the pathogenesis of the disease, and MRI results are normal or nonspecific in 50% of cases [2]. The clinical presentations of HE can be divided into two distinct types: vasculitic and diffuse [13]. The vasculitic type manifests as repeated episodes of ischemic stroke or stroke-like episodes, and is characterized by multifocal or regional ischemic lesions through hypoperfusion [14,15]. The hypoperfusion lesions on single photon emission computed tomography (SPECT) in patients with HE have been shown to be reversible after steroid treatment [15]. In autopsy studies, perivenular lymphocyte infiltration can appear in the brain, brainstem and meninges [4,16]. On the other hand, the diffuse progressive type presents with dementia or psychiatric symptoms [13,17]. It is believed to be mediated through autoimmunity against common antigens in the brain and the thyroid gland [18]. Several EEG studies revealed that patients with HE who presented with psychosis had generalized slowing on EEG which correlated well with the severity of psychosis and treatment response [19,20]. As for our patient, she presented with a stroke-like episode, so vasculitis may be the dominant mechanism. Brain MRI showed acute infarction at the left thalamus and left midbrain, possibly suggesting that the bilateral pons might also be affected by vasculitis-related hypoperfusion.

Although elevated serum levels of anti-TG and anti-TPO antibodies are used commonly to diagnose HE, there is no evidence that these anti-thyroid autoantibodies are involved in the pathogenesis of HE [2]. In addition, anti-thyroid autoantibodies are present in about 2-20% of general populations [2], which may be coincident with acute or chronic encephalopathy. In recent years, several specific autoantibodies which have been separated from the serum of patients with HE are probably associated with the pathogenesis of HE. For example, anti-neuronal autoantibody, which can react with a 36-kDa antigenic protein in cerebral cortex [21], and an autoantibody which can recognize the amino terminal of alpha-enolase [22]. Detection of anti-thyroid antibodies in CSF is one of the specific ways to diagnose HE [23], whereas, the detection methods for anti-neuronal and anti-alpha-enolase autoantibodies are relatively complex for routine clinical applications.

Hashimoto's encephalopathy is also called "steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT)" because patients with HE usually

have an excellent response to corticosteroid [5]. However, spontaneous recovery was noted in our patient, which has also been reported in some other patients [24]. In that case series reported by Ferracci et al, 4 of the 9 HE patients recovered spontaneously without treatment while another 3 patients did not have treatment response to oral prednisolone [24]. The patients with HE who recover spontaneously might have milder disease severity, and this subgroup may not require immunosuppressive therapy due to the consideration of risk and benefit of steroid treatment.

In conclusion, HE is a type of autoimmune-mediated encephalopathy with various clinical presentations. In patients with acute onset of drowsiness and bilateral pinpoint-sized pupils but without corresponding lesions on brain MRI, this potentially treatable condition should be considered as a possible diagnosis.

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