

Hashimoto's encephalopathy presenting as acute cognitive decline in an elderly male

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Core tip: Hashimoto's encephalopathy is a rare form of reversible encephalopathy characterized by the presence of anti-thyroid antibodies in serum and/or cerebrospinal fluid. We suggest that an assessment of thyroid antibodies should be included in anyone presenting with acute cognitive decline in the absence of alternative explanation.

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Abstract

Hashimoto's encephalopathy (HE) is a rare form of reversible encephalopathy characterized by the presence of anti-thyroid antibodies in serum and/or cerebrospinal fluid. The syndrome is more common in women and the presentation varies considerably. Here, we report a case of an elderly male with a history of Hashimoto's thyroiditis, presenting with acute cognitive decline. A diagnosis of HE was established based on the presence of anti-thyroid antibodies in the serum, diffuse electroencephalography changes and lack of an alternative explanation. The patient promptly responded to steroids and was discharged on the 8th day of admission. We suggest that an assessment of thyroid antibodies should be included in anyone presenting with acute cognitive decline in the absence of alternative explanation.

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Key words: Hashimoto's encephalopathy; Hashimoto's thyroiditis; Anti-thyroid antibodies; Electroencephalography; Steroids; Cognitive decline; Immunosuppressants

INTRODUCTION

Hashimoto's encephalopathy (HE) is a rare, poorly understood neurological syndrome associated with autoimmune thyroiditis. The disease has an estimated prevalence of 2.1/100 000^[1]. Since, it was first described by Brain *et al* in 1966, about 113 cases have been reported till date^[2]. HE has a widely variable clinical spectrum with both acute and indolent forms^[3]. However, cognitive decline and seizures are the commonest manifestations of this disease^[2]. Most reported cases are females and the disease seems to peak in the fifth and sixth decades of life^[2]. In this report, we present a case of an elderly male who presented to us with acute cognitive decline along with a brief review of literature. We emphasize the importance of an early diagnosis of this potentially treatable condition.

CASE REPORT

A 76-year-old Caucasian male with history of Hashimoto's thyroiditis presented with complaints of feeling unwell and confusion for 1 d. His past medical history was significant for atrial fibrillation, diabetes mellitus, hyperten-

sion, hyperlipidemia, Hypothyroidism due to Hashimoto's thyroiditis and gastroesophageal reflux disease. He was diagnosed with Hashimoto's thyroiditis 8 years back based on the presence of anti-thyroid peroxidase antibody, anti-thyroglobulin antibody and biopsy showing diffuse lymphocytic and plasma cell infiltration. He was currently taking levothyroxine 100 mcg daily. His other medications included metoprolol and omeprazole. He denied chills, fever, shortness of breath, chest pain and seizure activity. On examination, he was afebrile with a heart rate of 150/min and blood pressure of 78/44 mmHg. He was not oriented to time, place and person. However, no focal neurological deficits were appreciated. The patient did not have a past history of similar symptoms. In the emergency room, he was noted to be in atrial fibrillation with a rapid ventricular response. He was then intubated for his unstable vital signs and transferred to the intensive care unit.

Lab work done revealed CBC and Electrolytes to be normal. Urine drug screen was negative. Cultures of blood and urine were negative. His chest X-ray and arterial blood gas were normal. Cortisol level was within normal range. Electrocardiogram revealed atrial fibrillation but no evidence of recent onset ischemia. Cardiac enzymes were normal. Computed tomography of the chest, abdomen and magnetic resonance imaging (MRI) of the head were negative. Toxicology screen for acetaminophen and alcohol were negative. Cerebrospinal fluid (CSF) analysis was normal except for elevated protein at 229 mg/dL. CSF cultures failed to grow any organisms. Viral serology done for HSV, St. Louis and West Nile virus were negative. TSH was elevated at 11.4 IU/mL (normal 0.3-5 IU/mL). Also, anti-thyroid peroxidase antibody was elevated at 128 IU/mL (normal: < 34 IU/mL). However, T3 and T4 were 1.1 ng/mL (normal: 0.9-1.8 ng/mL) and 7.8 µg/dL (normal: 5.5-11.6 µg/dL), respectively. Anti-thyroglobulin antibody was elevated at 554 IU/mL (Normal: 0-60 IU/mL). Electroencephalography (EEG) revealed continuous slow and generalized pattern along with focal spikes and triphasic waves.

In the intensive care unit, blood pressure was maintained with intravenous fluids and dopamine. Over the next 24 h, the patient had improvement in hemodynamics and was in normal sinus rhythm and was successfully extubated. However he continued to be encephalopathic for the next 36 h. Neurological examination revealed generalized stupor, gross disorientation to time, place and person and absence of any focal neurological deficits.

Our initial impression of hypoxic encephalopathy was refuted because the patient continued to be confused even after the stabilization of hemodynamics. This led us to search for other causes of his confusion. Central nervous system infection was ruled out by normal CSF findings. Any, organic lesion of the brain and stroke were ruled out with normal MRI findings. Other metabolic causes were ruled out with normal urine drug screen, liver and renal function tests. With the background of an abnormal EEG, elevated thyroid antibodies, elevated

CSF protein, unrevealing cerebral MRI and lack of an alternative diagnoses, we suspected the patient to have HE and started the patient on 200 mg of intravenous hydrocortisone every 8 h for 2 d. He showed significant improvement and completely recovered with no neurological deficits in the next 48 h. He was then switched to 60 mg of oral hydrocortisone to be tapered over 3 wk and was discharged on 8th day of admission. At the time of discharge the patient was alert and well oriented to time, place and person. The patient is undergoing regular follow up and is in good health since then.

DISCUSSION

HE is an under-diagnosed, steroid-responsive, reversible encephalopathy associated with high titers of serum anti-thyroid antibodies^[3]. The pathogenesis of this condition is still unclear and is unlikely to be directly related to thyroiditis indicated by the presence of thyroid peroxidase antibodies^[3]. As a result, some authors have advocated a change of nomenclature to "steroid-responsive encephalopathy associated with autoimmune thyroiditis"^[4]. Recent reports have suggested it to be a result of reversible cerebral inflammation mediated by an autoimmune mechanism^[5].

In contradiction to our case, most reported cases are females, probably reflecting the fact that autoimmune thyroiditis has a female predilection^[3]. Castillo *et al*^[5] suggested that as much as 70% of cases of HE are females. The age at presentation is widely variable with an average of 50 years and reported cases ranging from 2 to 84 years^[3,6]. The commonest age group, however, is in the fifth and sixth decades of life^[2]. Our patient, being 76 years of age, is one of the oldest patients reported to have this disease.

The clinical features of HE are known to be extremely variable. It may present acutely, with episodes of cerebral ischemia, seizures and psychosis, or it may present as an indolent form with depression, myoclonus, tremors, cognitive decline and fluctuations in the level of consciousness^[2]. Acute cognitive impairment, as seen in our case, is one of the commonest forms of presentation, seen in approximately 36% of the cases^[4].

The exact pathogenesis for HE is unknown. Autopsy/brain biopsy samples of affected patients have shown perivascular lymphocytic infiltrates, predominantly of the T-cell type, in the meninges and the brain parenchyma^[5]. This, along with the female preponderance of the disease and a good response to steroids, favors an autoimmune etiology. As the majority of patients are euthyroid at presentation, the disease does not seem necessarily to be related to the level of thyroid hormones. Current evidence does not show that antithyroid antibodies interact with neuronal tissues and their levels are not related with the severity of the disease or the response to treatment either^[2]. However, a recent study has shown that thyroid antibodies are associated with other anti-neuronal antibodies such as antibodies to voltage-gated potassium channel and N methyl-D-aspartate receptor; suggesting a possible pathogenetic mechanism of this condition^[7].

Most of the cases of HE are affected by Hashimoto's thyroiditis, which was also seen in our patient^[8]. However, about 19% of cases have Grave's disease, suggesting that the disease is not associated exclusively with Hashimoto's thyroiditis, but also with other autoimmune thyroid diseases^[2]. Most patients have normal levels of thyroid hormones; a few are hypothyroid or hyperthyroid at presentation. Our patient was euthyroid at presentation.

There is no universally agreed diagnostic criterion for HE^[9]. One such criteria suggested by Peschen-Rosin *et al*^[10] encompasses unexplained occurrence of certain neurological symptoms along with three conditions among which are: abnormal EEG, elevated thyroid antibodies, elevated CSF protein, excellent response to steroids and unrevealing cerebral MRI. In our case, a diagnosis of HE was conveniently made by fulfilling this criteria along with an absence of an alternative diagnosis. Elevated levels of anti-thyroid antibodies are the most consistent finding in reported cases, which could be considered as a hallmark of HE^[11]. However, there is no evidence that these antibodies affect neuronal function and their levels do not correlate with the severity of the disease or the response to treatment^[12,12]. Similarly, abnormal EEG findings are found in up to 98% of cases; the most common abnormality being a generalized slowing of waves, as in our case^[13]. Meanwhile, the role of brain imaging in the diagnosis is primarily to exclude other diagnostic possibilities. Brain imaging is normal in as many as 50% of cases, and abnormal findings include cerebral atrophy, diffuse white matter changes and meningeal enhancement^[6]. In our patient, the role of brain imaging (MRI) was to rule out other alternative diagnoses.

HE is known to be one of the reversible forms of encephalopathy. Corticosteroids are the preferred medications for treatment, effective in as much as 98% of the cases^[12]. In our case, rapid clinical improvement was seen following the use of steroids. Other immunosuppressants such as methotrexate, azathioprine, and cyclophosphamide have also been reported to treat HE successfully^[6]. However, sometimes, HE might not be completely cured and relapses may occur. Nevertheless, the overall prognosis remains optimistic, as long as patients receive adequate treatment^[6].

In summary, HE is a rare form of reversible encephalopathy, occurring in patients with or without overt thyroid disease. The presentations are varied but diffuse cognitive decline is a common manifestation. Considering the myriad of neurologic manifestations of this disease and a lack of well-defined diagnostic criteria, the disease appears to be under-diagnosed. Nevertheless, a timely diagnosis

is crucial as it is often completely reversible. Anyone presenting with rapidly progressive cognitive dysfunction with or without a history of thyroid disease, should be considered for a possibility of HE and assessed for the presence of antithyroid antibodies.

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