



# A case of Hashimoto's encephalopathy presenting with seizures and psychosis

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Hashimoto's encephalopathy (HE) is a rare, poorly understood, autoimmune disease characterized by symptoms of acute or subacute encephalopathy associated with increased anti-thyroid antibody levels. Here, we report a case of a 14-year-old girl with HE and briefly review the literature. The patient presented with acute mental changes and seizures, but no evidence of infectious encephalitis. In the acute stage, the seizures did not respond to conventional antiepileptic drugs, including valproic acid, phenytoin, and topiramate. The clinical course was complicated by the development of acute psychosis, including bipolar mood, insomnia, agitation, and hallucinations. The diagnosis of HE was supported by positive results for antithyroperoxidase and antithyroglobulin antibodies. Treatment with methylprednisolone was effective; her psychosis improved and the number of seizures decreased. HE is a serious but curable condition, which might be underdiagnosed if not suspected. Anti-thyroid antibodies must be measured for the diagnosis. HE should be considered in patients with diverse neuropsychiatric manifestations.

**Key words:** Hashimoto's encephalopathy, Seizures, Psychosis

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## Introduction

Hashimoto's encephalopathy (HE) is an unusual condition associated with autoimmune thyroiditis. It must be included in the differential diagnosis of non-specific neurological or psychiatric symptoms in a patient with hypothyroidism. However, there are uncommon conditions associated with auto-immune encephalopathy, which are not caused by thyroid dysfunction. Therefore, normal or slightly abnormal thyroid function tests (TFTs) do not exclude the diagnosis. HE is likely to be undiagnosed if not suspected. We report a case of HE in a 14-year-old girl who presented with acute mental changes and seizures, which were complicated by the development of acute

psychosis with normal thyroid function.

## Case report

A 14-year-old girl was admitted to the hospital after becoming acutely drowsy and suffering three generalized, tonic-clonic seizures, each episode lasting more than 10 minutes. Three days before admission, she had a fever of up to 38°C, muscle weakness, polyarthralgia, and an erythematous papular skin rash on both hands. Her history and family history included no psychiatric diseases, seizures, or other medical problems. She was an above-average eighth-grade student. Her initial vital signs were stable, with a body temperature of 36.5°C,

heart rate of 92 beats per minute, respiratory rate of 24 breaths per minute, and blood pressure 91/50 mmHg. She was 163.5 cm tall (75 to 90th percentile) and weighed 59.2 kg (75 to 90th percentile), for a body mass index of 22.1 kg/m<sup>2</sup>. On physical examination, her heart, lungs, liver, and abdomen were normal and she had no palpable goiter. A formal neurological examination did not reveal any focal abnormal findings. The initial laboratory findings were as follows: white blood cell count 8,000/mm<sup>3</sup>, hemoglobin 13.7 g/dL, platelet count 221,000/mm<sup>3</sup>, and C-reactive protein 0.09 mg/dL. Routine biochemical analyses of serum, blood gases, electrolytes, blood ammonia, and lactate were within normal limits. The cerebrospinal fluid (CSF) analysis showed normal pressure and a normal cell count and protein and glucose levels. Cultures of blood and CSF were sterile. Serum and CSF examination for herpes, zoster, enterovirus 71, influenza, Epstein-Barr virus, and mycoplasma were negative. Brain magnetic resonance imaging (MRI) was normal. Electroencephalography (EEG) showed generalized slow waves with diffuse cortical dysfunction, without any epileptiform discharges. In the acute stage, the seizures did not respond to conventional anti-epileptic drugs, including valproic acid (20 mg/kg/day), phenytoin (5 mg/kg/day), and topiramate (100 mg). On the 4th day, she reported visual hallucinations before the onset of seizures; these consisted of a blue circle and unknown men wearing blue shirts in one event and unknown men wearing red shirts in another. She also showed personality changes, mood swings between depressive and maniac states, difficulty with concentration, insomnia, and agitation. The etiology of the acute encephalopathy (i.e., the mental changes, seizures, and psychosis) was not clear. Therefore, we checked her autoimmune status. The serum anti-nuclear antibodies, rheumatic factor, and anti-DNA screening were negative. TFTs were normal (TSH, 4.78  $\mu$ IU/mL, free T<sub>4</sub>, 1.33 ng/dL, and T<sub>3</sub>, 89 ng/dL), but the anti-thyroid antibodies were elevated: the thyroperoxidase antibody titer was 280 IU/mL (normal <100) and the antithyroglobulin antibody was 138 IU/mL (normal <100). Given the indications for Hashimoto's encephalopathy, she was subsequently started on intravenous methylprednisolone therapy, beginning at 1 g intravenously per day for 3 days, followed by prednisone 60 mg orally per day. The patient's clinical improvement was impressive and her neuropsychiatric symptoms resolved. On the 14th day, she was discharged. On follow-up as an outpatient, she had been symptom free for 1 month and her anti-thyroid antibodies level was normal. However, the seizures recurred while tapering the steroid.

## Discussion

Hashimoto's encephalopathy is a steroid-responsive acute or subacute

encephalopathy associated with elevated anti-thyroid antibodies. The evaluation of patients with recent-onset progressive neurologic symptoms and cognitive and psychiatric problems can be challenging. More common causes of encephalopathy should be excluded, such as infection, electrolyte imbalance, metabolic disease, toxins, neoplasm, or the central nervous system involvement of vasculitic syndromes. HE is a rare, but important, cause of encephalopathy, although HE has mainly been described in adults. This is the first report of HE in a pediatric patient in Korea. We describe the clinical features of HE in a 14-year-old girl. Pediatricians should be familiar with the clinical features of HE, as this disease may be treated successfully.

The presenting features of HE vary widely<sup>1)</sup>. Two distinct presentations are described in adults: 1) a vasculitic type with seizures, acute deterioration of consciousness, and stroke-like episodes; and 2) a diffuse progressive type with insidious deterioration of cognitive function leading to dementia, confusion, agitation, restlessness, and hallucinations or inactivity, apathy, and social isolation<sup>2)</sup>. The most common seizure pattern includes generalized tonic-clonic seizures followed by complex partial seizures, with or without secondary generalization. Diffuse slowing of the background is the most common EEG abnormality seen in both children and adults<sup>3)</sup>. Neuroimaging is usually normal. However, MRI may occasionally show bilateral subcortical high signal lesions on the T2-weighted images. Computed tomography and angiography are typically normal. Brain single photon emission computed tomography (SPECT) may show global hypoperfusion<sup>4)</sup>. We present the case of an adolescent presenting with uncontrolled seizures and psychosis. This case reinforces the importance of evaluating thyroid function and anti-thyroid antibodies in pediatric patients who present with ill-defined neuropsychiatric symptoms. Psychiatric symptoms include impaired short-term memory and other cognitive dysfunction in 66 to 90% of cases and depression in 40%<sup>4)</sup>.

It is still debatable whether this is a specific syndrome seen in patients with autoimmune thyroiditis or the coincidence of a rare neurological condition with a common endocrinological disease<sup>4)</sup>. Chong et al.<sup>5)</sup> systemically reviewed all reported cases and concluded that the combination of encephalopathy, high serum anti-thyroid antibodies, and responsiveness to steroids was unlikely to be coincidental; therefore, the condition constituted a new syndrome. Our case shows that the thyroid function tests may be normal. Diagnosing HE in children requires a high index of suspicion, and our case stresses the importance of evaluating anti-thyroid antibodies in pediatric patients, even though thyroid function tests are normal.

Etiologically, HE is a controversial diagnosis, as it lacks a precise pathophysiologic basis. An interesting aspect of our case was related to the changes in the anti-thyroid antibody levels over the course of the patient's steroid treatment. The anti-thyroid antibody level nor-

malized after the patient's clinical course improved. However, the literature contains no evidence for a causative link between thyroid autoimmunity and encephalitis. Ferracci et al.<sup>6)</sup> found that the anti-thyroid antibody levels did not reflect the clinical status. Thyroid autoantibodies are elevated in all patients and this is required for a diagnosis. However, the association of neurological symptoms and anti-thyroid antibody titers is not sufficient for the diagnosis of HE, because the role of the anti-thyroid antibodies in the pathogenesis of encephalopathy remains unclear.

There are no formal studies of the treatment of HE; most reports have shown that glucocorticoids are effective. We recommend the use of high-dose steroids, with intravenous methylprednisolone initially, followed by a prednisone (1 to 2 mg/kg/day, max 60 mg/day) for 6 to 8 weeks. The dose should be reduced gradually with the expected improvement in symptoms over 3 to 6 months. Despite treatment, patients may experience relapses, and adolescents with this condition may experience residual cognitive deficits. Vasconcellos et al.<sup>3)</sup> suggested continuing the steroid treatment for at least 6 months, but normalization or improvement in the EEG and neuropsychological tests are considered better tools for monitoring both the response and the length of therapy. The therapeutic options for relapsing cases (or as an alternative to steroids) include azathioprine, cyclophosphamide, mycophenolate mofetil, methotrexate, intravenous immunoglobulin, and plasmapheresis, alone or in combination<sup>7)</sup>. In treated adults, the prognosis of HE is good, with 90% of the patients in remission after 10 years. By contrast, children tend to suffer from more residual sequelae than do adults<sup>3,4)</sup>.

In conclusion, HE is a rare disease, which is probably underdiagnosed, especially in children. Our observations indicate that a high degree of suspicion is necessary to make the diagnosis of HE. We suggest that HE be considered in any patient with unexplained encephalopathy presenting with uncontrolled seizures and psychosis, as in our case, because it is responsive to steroid therapy and is readily reversible. Therefore, we recommend prompt evaluation of the anti-thyroid antibodies in pediatric patients with an unexplained encephalopathy, even when the standard thyroid function tests are normal.

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