A case of Hashimoto’s encephalopathy misdiagnosed as viral encephalitis

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Source of support: This research was supported by the Science and Technology Planning Project of Guangdong Province, China (2009B060700040 to Y.P.)

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Patient: Male, 61
Final Diagnosis: Hashimoto’s encephalopathy
Symptoms: Neuropsychiatric or neurological manifestations
Medication: Steroids and immunoglobulins
Clinical Procedure: Immunoglobulin combined with corticosteroid therapy
Specialty: Neurology

Objective: Mistake in diagnosis
Background: Hashimoto’s encephalopathy is a rare autoimmune syndrome characterized by various neuropsychiatric or neurological manifestations and associated with Hashimoto’s thyroiditis, responsive to steroids. Until now, misdiagnosis and delay of treatment of Hashimoto’s encephalopathy are very common because of the diversity of the symptoms.

Case Report: This recent case of a 61-year-old man presented with unconsciousness, spasms and a previous misdiagnosis as viral encephalitis. Response to anti-viral and steroid therapy was unsatisfactory, but treatment with immunoglobulin combined with corticosteroid therapy achieved rapid and complete recovery.

Conclusions: Any patient presenting with acute or subacute unexplained encephalopathy should be considered Hashimoto’s encephalopathy, even if the thyroid function is normal. Thyroid antibody testing should be performed because this may be the most important clue to diagnosis. As soon as the diagnosis is made, steroid therapy is the first choice. If the steroid therapy does not lead to immediate improvement, IVIG is an effective alternative treatment.

Key words: Hashimoto’s encephalopathy • Hashimoto’s thyroiditis • antithyroid antibodies • corticosteroids • intravenous immunoglobulins

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Background

Hashimoto's encephalopathy (HE), first described in 1966 [1], is an uncommon disease that has a wide clinical spectrum with various neuropsychiatric or neurological signs such as: myoclonus, tremor, pyramidal tracts signs, stroke-like episodes, and psychiatric symptoms. Elevated serum antithyroid antibodies and a dramatic response to corticosteroids are the main characteristics of Hashimoto’s encephalopathy. However, because of these myriad symptoms, clinical misdiagnosis is frequent and accurate diagnosis is often difficult. Although excellent response to steroids is characteristic, some patients are non-responsive and require other treatments such as plasmapheresis or administration of azathioprine or cyclophosphamide have been occasionally tested. Immunoglobulin has been reported as an effective therapy in Hashimoto's encephalopathy non-responsive or partially responsive to corticosteroids.

In this case report, we discuss the difficulties and significances in making the correct diagnosis and giving timely effective treatments to improve the patient's prognosis.

Case Report

A 61-year-old man presented with fatigability and cold sensitivity in May 2007 and was diagnosed with hypothyrosis and discharged on thyroxine in a community hospital. One month later, the patient stopped Thyroxine therapy against medical advice. Two years later, his symptoms gradually progressed and still did not take thyroxine regularly. On June 2010, he developed a gradual onset cognition dysfunction, impaired short-term recall, and slow reaction. Ten months later, both hands had postural tremor and worsening of gait was noticed. After an attack of generalized tonic-clonic seizure, he was taken to another community and assisted for more than a few feet.

An extensive evaluation was performed, which included MRI, EEG, CSF, chemistry, and immunological studies. The lesions on MRI had partly narrowed compared with the previous scan from the outside hospital (Figure 2). EEG revealed nonspecific moderate diffuse slowing (into the delta and theta range). A hearing examination showed both drum chambers were normal except for left air conduction, which was dramatically decreased. Examination of the CSF showed an elevated protein level of 0.89 g/L, but the glucose and cell count were all normal and microbiology examination was negative. Serum studies showed a sedimentation rate of 36 mm (normal: 0–20 mm) and negative HIV by ELISA. The free T4 level was 6.58 pmol/L, free T3 was 1.81 pmol/L, TSH was elevated at 34.57 µIU/ml, (normal range, 0.55–4.78 µIU/ml). Thyroid peroxidase antibodies (Anti-TPO) were extremely elevated in serum, with a titer of more than 1:1300 and thyroglobulin antibody (anti-TG) with a titer of more than 1:500. Other studies, including ANA, p-ANCA, c-ANCA, protein electrophoresis with immunofixation, rheumatoid factor, liver function tests, and viral serologies (EBV, Hepatitis A, B, C viruses) were all negative or within normal limits. Based on the clinical picture, elevated anti-microsomal Abs, and no other discernible cause, a diagnosis of Hashimoto’s encephalopathy was presumed. The patient started to receive intravenous Methylprednisolone (500 mg daily for 5 days) and immunoglobulins (0.4 g/kg body weight daily for 5 days). The 5-day course of high-dose, intravenous steroids and immunoglobulins resulted in apparent resolution of the patient’s symptoms. The steroid was reduced gradually, 250 mg daily for 3 days, 100 mg daily for 3 days, followed by prednisone 60 mg orally per day. He improved steadily throughout the hospitalization and was discharged with oral prednisone 60 mg daily.

Figure 1. Initial MRI showing diffusely increased signal intensity within the periventricular white matter bilaterally on T2 images (Left: Axial scan; Right: Coronal scan).

General physical exam was unremarkable. During his neurological exam, he was alert but had impaired attention and phonism, and was incoherent. His cranial nerve, motor, and sensory examination was normal. His reflexes were accentuated and symmetrical and gait was moderately ataxic, with grossly impaired tandem walking. He was unable to walk unassisted for more than a few feet.
Two months later, our patient returned for his follow-up medical appointments with a dramatic remission of symptoms. Serum and CSF anti-microsomal Ab titer were within normal limits. The MRI scan showed the foci growing downwards dramatically (Figure 3).

Discussion

Hashimoto’s encephalopathy, first described in 1966 [1], is a rare autoimmune syndrome characterized by various relapsing-remitting encephalopathy, steroid responsiveness, and associated with elevated serum anti-thyroid antibodies. The clinical presentations of HE are various, but frequently involve stroke-like symptoms, myoclonus, tremulousness, delirium, hallucinations, and seizures [2,3]. Females are more often affected than males (3.6:1), with a mean age of onset of 41 years [4]. Because the symptoms respond so well to immunosuppressive treatment, prompt diagnosis and management are important.

We present the case of a man with progressive impaired cognition function and uncontrolled seizures. Even without proof of viral infection, based on the clinical features and the moderate elevated protein in the CSF, viral encephalitis was diagnosed in the community hospital. Anti-viral treatment combined with steroid therapy failed to achieve dramatic improvement, which was commented on by the patient. The extensive examinations in our hospital found elevated serum and CSF anti-thyroid antibodies and the possibility of viral infection was excluded. However, the MRI scan at the second evaluation in our hospital showed that the lesions narrowed to some extent compared with the outside hospital scan. Therefore, we concluded that our patient was showing the partial responsiveness to steroids characteristic of an established case of HE and further immuno-modulatory therapy was required. Most reports have shown that glucocorticoids are effective in treatment of HE. A systematic review of 85 published HE cases found clinical response in 98% of patients treated with glucocorticoids [3]. However, there are steroid-resistant cases or initial steroid-responsiveness followed by steroid-resistant HE. It has been reported that therapy with intravenous immunoglobulins (IVIG) should be considered in patients with HE that is completely or partially resistant to steroids [5]. Fortunately, our patient responded dramatically well to the consequently applied IVIG combined with the steroid therapy. This case reinforces the importance of having HE in mind and evaluating anti-thyroid antibody titers in patients who present with ill-defined neuropsychiatric symptoms.

Before consideration of Hashimoto’s encephalopathy, we should rule out any probable causes of encephalopathy, such as infections, electrolyte imbalance, toxins, and neoplasms. A diagnosis of encephalopathy is based on the clinical features and elevated serum thyroperoxidase antibody titer, particularly antithyroid peroxidase antibody (also referred to as antimicrosomal antibody) and antithyroglbulin antibodies. Antithyroid antibodies are present in 5% to 20% of the general population, and this percentage normally increases with age and in females. Therefore, high titers (usually 100 times normal), as found in our patient, are necessary for the diagnosis of HE [6]. The pathophysiology of encephalopathy remains unclear. Anti-thyroid antibodies may play a role in the pathogenesis of encephalopathy, as when the anti-thyroid antibody levels of our case normalized with improved clinical course. However, the anti-thyroid antibody level does not reflect the clinical status, as many patients are euthyroid and approximately 10% to 25% of the healthy population has elevated anti-thyroid antibodies titers [7]. Diffuse slow wave of the background is the most common EEG abnormality seen in HE and nonspecific EEG abnormalities are seen in 90% to 98% of patients [6,7]. In our case, the brain MRI lesions decreased as the patient improved gradually, so we suggest that the MRI scan may act as an indicator to reflect the clinical status in some HE cases.

Conclusions

Any patient presenting with acute or subacute unexplained encephalopathy should be considered as having Hashimoto’s...
encephalopathy, even if the thyroid function is normal. Thyroid antibody testing should be performed because these may be most important clue to the diagnosis. As soon as the diagnosis is made, steroid therapy is the first choice of treatment. If the steroid therapy does not lead to immediate improvement, IVIG is an effective alternative treatment.

Acknowledgment

I would like to thanks to Kristen Hogue in Tennessee, USA for revising the article. This research was supported by the Science and Technology Planning Project of Guangdong Province, China (2009B060700040 to Y.P.).

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