Endocrine encephalopathy

King W Yong, Steven Soule, Penny Hunt

Abstract

The diagnosis of Hashimoto’s encephalopathy is made when no other cause is found for an acute encephalopathic illness, in the presence of positive thyroid autoantibodies, and is supported by a response to steroid therapy.

A 59-year-old woman developed an encephalopathic illness with mixed aphasia, global weakness and generalised seizures requiring intubation and ICU admission. Extensive imaging and laboratory investigations looking for an underlying cause for the encephalopathy were unremarkable. Thyroid autoantibodies were strongly positive, raising the possibility of Hashimoto’s encephalopathy. Thyroid function testing showed profound primary hypothyroidism.

The patient was commenced on high-dose methyprednisolone, with prompt cessation of seizure activity. Thyroxine replacement was commenced, with the methyprednisolone switched to oral prednisone and slowly weaned. The patient had no further seizures and ultimately made a full recovery.

Hashimoto’s encephalopathy was first described in 1966 in a patient with seizures, disorientation, alternating hemiparesis and positive thyroid autoantibodies. The pathophysiology was thought to be an autoimmune encephalopathy related to the thyroid autoantibodies.

The diagnosis is made when positive thyroid autoantibodies are found in a patient with an unexplained encephalopathic illness, and is supported by a response to steroid therapy. It is a rare condition with a recent review identifying only 121 reported cases.

Case report

A 59-year-old woman, previously well, was admitted with 3 days of abdominal pain. Ascending and transverse colitis, presumed secondary to recent diclofenac usage, was found on CT abdomen on day 1 and subsequent colonoscopy. Her abdominal symptoms gradually improved, however she became acutely confused and incoherent on day 13. She had mixed aphasia and a generalised reduction in power with normal tone and reflexes. She proceeded to a generalised seizure with subsequent status epilepticus, requiring intubation and ICU admission. Recurrent seizures occurred over the next 6 days, despite treatment with three anticonvulsants (valproate, phenytoin and levetiracetam).

Extensive investigations including CT and MRI brain, CSF analysis for HSV, blood cultures, vasculitic screen and HIV serology were all unremarkable apart from mild elevation in CSF protein at 1.43 g/L (0.15–0.40). Plasma sodium ranged between 133 and 145 mmol/L (135–145) over the acute illness and there were no evidence of hypoglycaemia or hypothermia.
Thyroid autoantibodies were found to be strongly positive on day 20—anti-TPO 707 IU/ml (<10), anti-TG 91 IU/ml (<10), raising the possibility of Hashimoto’s encephalopathy. Thyroid function tests on day 21 showed profound primary hypothyroidism—free T4 6 pmol/L (10–24), TSH 180 mIU/L (0.4–4.0)—and endocrinology was consulted.

The patient was commenced on 1 gram methylprednisolone and 50 mcg thyroxine daily on day 21, with prompt cessation of seizure activity, successful extubation and transfer to a medical ward after 2 days. Methylprednisolone was switched to oral prednisone 40 mg daily after 5 days and thyroxine was increased to 100 mcg daily after 2 weeks.

The patient continued to improve, with no further seizure activity and ongoing recovery in neurological function. She was transferred to a rehabilitation facility 39 days after admission, on a reducing course of prednisone and valproate. She returned home on day 49. Prednisone was ceased after 3 months and valproate discontinued at 1 year. She remains well on thyroxine 100 mcg daily in the community 2 years later.

**Discussion**

Hashimoto’s encephalopathy is a rare diagnosis of exclusion, which usually presents with encephalopathic symptoms and seizures, positive thyroid autoantibodies, and characteristically responds to steroid treatment.

Thyroxine replacement alone was shown to improve symptoms in 8 of 47 patients with subclinical or overt hypothyroidism with Hashimoto’s encephalopathy. However, hypothyroidism alone is unlikely to account for the encephalopathy as not all patients respond to thyroxine therapy and patients have variable thyroid function at presentation. If thyroid dysfunction is present, it should be managed no differently to those patients without an encephalopathic illness.

Myxoedema coma may have a similar neurological presentation, with seizure and status epilepticus usually attributed to severe hyponatraemia. We believe Hashimoto’s encephalopathy is a far more likely diagnosis in our patient, given the absence of hypothermia (a cardinal feature of myxoedema coma), the minimally deranged plasma sodium and the prompt cessation of seizure with glucocorticoid and low dose thyroxine therapy.

We commenced thyroxine at a low-dose initially to reduce the risk of exacerbating occult coronary artery disease in our patient. A loading dose of thyroxine was not administered as the clinical presentation was not consistent with myxoedema coma.

An autoimmune pathogenesis for Hashimoto’s encephalopathy is supported by the finding of peri-arteriolar lymphocytic infiltration at brain biopsy, the identification of autoantibodies against the enzyme α-enolase and the steroid responsiveness of the condition.

No CNS antigenic locus has been found for the thyroid autoantibodies and there is no correlation between the symptom severity and the titre of thyroid autoantibodies. The thyroid autoantibodies therefore are thought to be markers of autoimmunity and steroid-responsive encephalopathy associated with antibodies to thyroperoxidase (SREAT) is a designation used by some authors for this condition.
In summary, Hashimoto’s encephalopathy is an unusual condition which should be considered in the encephalopathic patient when more common metabolic, infective and toxic aetiologies are excluded. The disorder is associated with positive thyroid antibodies, variable thyroid function and is typically responsive to parenteral high dose glucocorticoid therapy.

**Author information:** King W Yong, Endocrine Registrar; Steven Soule, Endocrinologist; Penny Hunt, Endocrinologist. Department of Endocrinology, Christchurch Hospital, Canterbury District Health Board, Christchurch

**Correspondence:** King W Yong, RMO Unit, Christchurch Hospital, Private Bag 4710, Christchurch, New Zealand. Fax +64 (0)3 3641473; email: kingwei.yong@gmail.com

**References:**