Unusual association of diseases/symptoms

A series report of autoimmune hypothyroidism associated with Hashimoto's encephalopathy: an under diagnosed clinical entity with good prognosis

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Summary

Thyroid dysfunctions may be accompanied by numerous neurological and psychiatric disorders. The most well-known is cognitive impairment and depression in hypothyroid patients, as well as an increased risk of cerebrovascular accidents. A separate, although a rare entity, is Hashimoto's encephalopathy. Unlike encephalopathy associated with other conditions, management in Hashimoto's encephalopathy highly responds to steroid treatment and may be associated with normal thyroid profile at presentation. Hashimoto's encephalopathy, while rare, may have been under-recognised since its clinical presentation overlaps several more common disorders, such as depression, seizures or anxiety. We present two cases of hypothyroidism with peculiar presentation. The first case has rapidly progressive neurological dysfunction, normal thyroid function at presentation, normal MRI finding and responds to steroid treatment. The second case has a subacute progressive neurological deterioration with elevated thyroid-stimulating hormone titre at presentation. Both these cases are known hypothyroidism on regular thyroxine replacement therapy with elevated anti-thyroid peroxidase antibodies. We conclude that Hashimoto's encephalopathy can present with a wide spectrum of neurological illnesses in the setting of hypothyroidism. Thyroid status may vary from hypothyroid, normothyroid to even hyperthyroid. This condition usually has an abnormal electroencephalography (EEG) background and usually responds to high dose steroids.

BACKGROUND

We report two cases that illustrate the efficacy of steroid treatment for encephalopathy in the setting of autoimmune thyroiditis and we review the literature. We present this case series as prevalence figures for Hashimoto's encephalopathy are higher than expected when compared to the few cases reported in the literature, which suggests that this condition is presently underdiagnosed. Therefore, it remains important to maintain a high clinical suspicion for Hashimoto's encephalopathy since it is a readily treatable condition that carries a good prognosis unlike many of the other diagnoses it resembles.

CASE PRESENTATION

We present two cases of hypothyroidism with peculiar presentation. The first case has a rapidly progressive neurological dysfunction, normal thyroid function at presentation, normal MRI findings and responds to steroid treatment and the second case has a subacute progressive neurological deterioration and an elevated thyroid-stimulating hormone titre at presentation. Both these cases are known hypothyroidism on regular thyroxine replacement treatment with elevated anti-thyroid peroxidase antibody.

INVESTIGATIONS

In the first case, thyroid peroxidase antibody titre was measured and the result was positive (1200 U/litre). Thyrotropin and free thyroxine (FT4) levels were normal at 1.76 µIU/

litre and 15 pmol/litre, respectively. MRI showed only mild cerebral atrophy. EEG showed near-continuous bilateral temporal and frontal spikes. With this finding, valproic acid treatment was initiated. No clinical or EEG changes were observed after 2 days.

In the second case, the thyroid peroxidase antibody titre result was positive at 746 U/litre. Thyrotropin was raised and free thyroxine (FT4) levels were normal at 26 µIU/litre and 15 pmol/litre, respectively. ECG suggested mild to moderate pericardial effusion.

MRI showed normal study. EEG showed borderline abnormal record, diffusing slowing and delta waves, and no epileptic form focus.

DIFFERENTIAL DIAGNOSIS

Viral encephalitis; metabolic encephalopathies; Creutzfeldt-Jakob disease.

TREATMENT

Both patients were started with prednisolone, rapidly improved and steroid tapered over the next 4–6 months.

OUTCOME AND FOLLOW-UP

Both patients improved on steroid treatment.

DISCUSSION

Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the most common cause of hypothyroidism in iodine-sufficient areas of the world. Thyroid failure is seen in up to

10% of the population and its prevalence increases with age.¹ A very rare condition associated with Hashimoto's thyroiditis is Hashimoto's encephalopathy—a neuroendocrine disorder first described by Brain and colleagues.² Hashimoto's encephalopathy is rare. Very few cases have been reported,^{3–11} mostly in the neurology literature. The pathogenesis of this encephalopathy is unknown. Hypothyroidism can be excluded, since Hashimoto's encephalopathy is seen in the euthyroid state or after the correction of hypothyroidism.^{3–6} Current evidence suggests that the encephalopathy results from an autoimmune process, although the exact mechanism has not been elucidated. Some findings suggest acute disseminated encephalomyelitis as a potential model,⁷ while others favour cerebral angiitis as a paradigm.⁶ Because it is little known and its symptoms are primarily neurological, it is easy to misdiagnosis or overlook and the symptoms frequently lead to mistaken neurological diagnoses. The bulk of evidence points to an autoimmune vasculitis or other inflammatory process, perhaps associated with immune complex deposition, and possibly disrupting the cerebral microvasculature.^{8–12} However, autopsy or brain biopsy studies in a few patients have identified lymphocytic infiltration around small arterioles and venules.^{13–14}

When should the diagnosis of Hashimoto's encephalopathy be entertained? Any neuropsychiatric condition that is not responding to conventional treatment, especially in the setting of probable or known autoimmune thyroiditis, should raise suspicion for Hashimoto's encephalopathy. The presence of goitre on physical examination or a positive family history for thyroid dysfunction, in the proper clinical setting, warrants testing for thyroid function and antithyroid antibody titre. Additional studies such as EEG, MRI and lumbar puncture should be done not only to look for supporting evidence for Hashimoto's encephalopathy, but also to rule out other aetiologies of encephalopathy. Clearly, more common causes of encephalopathy, such as infections, electrolyte imbalance, toxins and neoplasms, must be reasonably excluded before steroid treatment is initiated.

Learning points

- ▶ Increased awareness is the first step in clarifying the nature of this condition.
- ▶ The diagnosis should be considered in patients with potential or known autoimmune thyroiditis with atypical neuropsychiatric manifestations not responding to conventional treatment.

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Competing interests None.

Patient consent Obtained.

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