

## A Rare Cause of Confusion:

# Steroid-Responsive Encephalopathy Associated with Autoimmune Thyroiditis

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### ABSTRACT

An 81-year-old female patient required numerous admissions for symptoms of confusion, visual hallucinations, myoclonus and seizures, which were treated as stroke, infections and viral encephalitis with some improvement after treatment but with recurrence that caused her to be readmitted to hospital. On the last admission, she was found to have very high antithyroid antibodies and a diagnosis of Hashimoto's encephalopathy was made, with an overwhelming response to steroids.

### LEARNING POINTS

- Hashimoto's encephalitis is a rare autoimmune disease that is frequently underdiagnosed.
- Exclusion of other pathologies together with a triad of encephalopathy, raised thyroid peroxidase and response to steroids is required for diagnosis.

### KEYWORDS

Confusion, encephalopathy, anti-TPO antibodies

### INTRODUCTION

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), or Hashimoto's encephalopathy (HE), is a rare disorder. Its diagnosis can be difficult on initial presentation as it can mimic many common pathologies. Commonly observed manifestations include confusion, tremor, myoclonus, stroke-type events and seizures. Presentation may follow a progressive, relapsing/remitting or self-limiting course. The pathogenesis is uncertain, although association with raised thyroid autoantibodies has been observed. Whether this is a cause-effect relationship or a marker of the disease process is unknown.

We report the case of an 81-year-old female Caucasian patient with a widely fluctuating course with symptoms of confusion, tremor and gait disturbances. Her condition was misdiagnosed as a few different pathologies before a final diagnosis of SREAT was made, following five medical admissions in a period of 6 months.

### CASE REPORT

An 81-year-old female Caucasian patient presented in August 2012 with confusion, tremor, anomia, aphasia, visual disturbance, drowsiness and reduced mobility that had developed over 1 week. In the hospital, she was diagnosed with transient ischaemic attack (TIA). Brain computed tomography (CT), carotid Doppler, chest X-ray, electrocardiogram and bloods (full blood count; urea and electrolytes; erythrocyte sedimentation rate) were all normal and she was treated with aspirin and fenofibrate.

In September 2012, she presented again after collapsing at home. She was clinically aphasic with mild hemiparesia and tremor. She was diagnosed with partial left anterior circulation stroke. A brain CT scan was again normal and as she improved, she was discharged after 3 days on clopidogrel, statin and ACE inhibitors.

She was admitted again 3 weeks later. This time she was unwell and confused, with speech disturbances. In view of positive urinalysis, she was treated for a urinary tract infection with antibiotics.

In October 2012, she presented with similar but more debilitating symptoms and a diagnosis of viral encephalitis was considered. A cerebrospinal fluid (CSF) examination revealed a high protein level of 3.5 g/l and normal white cell count. Inflammatory markers were normal, as were thyroid-stimulating hormones, antineutrophil cytoplasmic antibodies, antinuclear antibodies, Extractable Nuclear Antigen (ENA), paraneoplastic antibodies and brain MRI. A CT of the thorax/abdomen/pelvis showed a single thyroid nodule. NMDA receptor, VGKC, GAD and Purkinje antibodies were all negative. An electroencephalogram (EEG) was consistent with encephalopathy. She improved initially with

aciclovir but deteriorated after discontinuation, as viral polymerase chain reaction was negative for herpes simplex/zoster. The course of acyclovir was completed and she was allowed to go home.

The patient's last admission was in November 2012, when she presented with drowsiness, confusion, delusions, hallucinations and reduced mobility. Sporadic Creutzfeldt–Jakob disease (CJD) was suggested, but a repeat EEG failed to show any specific abnormalities. During this time, her symptoms fluctuated but generally became more progressive. Lewy body dementia was postulated, but after anticholinesterase inhibitors were initiated, she had generalized seizures and so they were withdrawn.

At this point, she was so incapacitated that discharge to a nursing home was planned, however the results of anti-thyroid antibodies requested earlier on admission came back with an anti-thyroid peroxidase (TPO) antibody of 1260 units/ml ( $n < 75$ ) and a diagnosis of HE was made.

She was started on prednisolone 40 mg OD and she had a dramatic recovery on Day 3 of treatment. Six weeks post-discharge, she had recovered her cognitive and functional baseline.

She has remained stable on steroids, with mild relapse when stopped, needing a maintenance dose of 10 mg. The plan is to change to azathioprine for long-term immunosuppression.

## DISCUSSION

SREAT or HE is a rare disorder that has widely variable presentation and can mimic much more common pathologies. The diagnosis of SREAT was based on a triad of classical clinical manifestations (cognitive impairment/encephalopathy), raised thyroid antibodies, response to steroid therapy, plus the earlier exclusion of other more common diagnoses. The particular diagnostic difficulty in this case was the apparent response to earlier treatments and the validity this added to the proposed diagnoses. With hindsight, this can be attributed to the relapsing/remitting nature of the disease.

The prevalence of HE has been estimated to be 2.1/100,000<sup>[1]</sup>, with a male/female ratio of 1:4 and mean age of 44 years old. There are two main subtypes: *relapsing/remitting and progressive*<sup>[2]</sup>. Symptoms are diverse and include:

- Neurological features: seizures, impaired level of consciousness, ataxia, tremor, cognitive impairment, stroke-like events, myoclonus.
- Psychiatric features: Hallucinations, delusions, paranoia.

The pathogenesis of HE is unclear, but the histological finding of perivascular lymphocytic infiltration<sup>[3]</sup> and response to steroids suggest an autoimmune disorder. Elevated antithyroid antibodies are considered necessary for the diagnosis, anti-TPO antibodies (86%) but also antithyroglobulin (46–48%)<sup>[2,4]</sup> but his role in the pathogenesis of HE is not clear. The level of these antibodies does not correlate with disease severity, but the majority (85%) normalize after treatment<sup>[2,4]</sup>. In our case, the thyroid peroxidase level was elevated to 1260 and after treatment reduced to 429. The brain MRI in was normal in our case, as it is in the majority of cases. In the majority of cases, CSF has raised protein levels and EEG is abnormal. It is important to exclude other causes for encephalopathy. Differential diagnosis includes Alzheimer's disease, cerebrovascular accident, CJD, infectious and limbic encephalitis and vasculitis<sup>[5]</sup>.

Glucocorticoids are the main treatment, showing response in 96% in one literature review<sup>[2]</sup>. Second-line treatments are intravenous immunoglobulin and plasmapheresis<sup>[2]</sup>. In cases where long-term immunosuppression is required, azathioprine, methotrexate and cyclophosphamide can be used<sup>[6]</sup>.

Our patient highlights the importance of considering HE as a differential diagnosis in patients presenting with confusion/encephalopathy.

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