

## BRIEF REPORT

# Autoimmune Anti-thyroid Encephalopathy: A Case of Steroid Responsive Hashimoto Encephalopathy

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## KEYWORDS:

Allergy/Immunology

Anti-thyroid

Encephalopathy

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Hashimoto

Hashimoto encephalopathy (HE) or steroid-responsive encephalopathy associated with anti-thyroid antibodies is a rare diagnosis but may be under-recognized among physicians. Although hyper or hypothyroidism is implied with the name Hashimoto, most of these patients are euthyroid. Nevertheless, most cases respond well with high-dose intravenous or oral steroids. The patient featured, SS, is a 46-year-old female who presented to our family medicine private practice in February for complaints of fatigue, word-finding difficulties, and generalized "mental fog." The patient's initial physical exam revealed prolonged relaxation phase of her bilateral patellar reflexes and poor accommodation in her right eye. The patient also exhibited a deficit in recall, in which she was only able to remember two out of the three objects on the mini-mental status exam. Her MRI showed numerous scattered T2/FLAIR hyperintensities in the cerebral matter, predominantly in the white matter. Her only lab abnormality was a mildly elevated anti-TPO antibody. CSF showed two oligoclonal bands. She was eventually diagnosed with HE eight months after presentation and responded very well to high-dose steroids for 3-4 months before relapsing, which ultimately required another round of steroid treatment. All in all, clinicians should check for the presence of anti-thyroid antibodies even if TSH is normal for patients presenting with either subtle or very profound, otherwise unexplained encephalopathy.

## INTRODUCTION

Hashimoto encephalopathy (HE) or sometimes better classified as steroid-responsive encephalopathy associated with anti-thyroid antibodies (SREAT) is a rare disorder<sup>1-3</sup> that may be under-recognized, especially with primary care physicians. The first case of HE was diagnosed in 1966 and the existence of this disorder remains a topic of debate.<sup>4</sup> There are several theories to suggest that the pathophysiology stems from auto-immune complex mediated vasculitis, demyelination, and several more.<sup>3</sup> Although Hashimoto is in its name, these patients are euthyroid in a majority of cases.<sup>1,3</sup> Patients present with very varying clinical signs and symptoms, but a majority of cases improve with a brief course of high-dose steroids.<sup>1-5</sup> Because of this, it is important to make this difficult diagnosis.

The clinical manifestations of autoimmune disorders make up a large part of a primary care physician's practice, and vague symptoms such as fatigue and decreased concentration represent large and sometimes complicated differential diagnoses. Because of this, it can be difficult to decide where to start in the workup. Even worse, the history and physical exam may not be overwhelmingly helpful. The purpose of this article is to enlighten primary care physicians about this interesting diagnosis and to ensure that they consider this with otherwise unexplained encephalopathy. This case represents a case of HE with a very subtle presentation.

## CASE PRESENTATION

A 46-year-old female with no major past medical history presented as a new patient in our family medicine office in February with complaints of fatigue, progressive short term memory loss and word-finding difficulties for about one year. She first noticed the problem when she was deployed for the Air Force for four months from the prior year. Her symptoms fluctuated from day to day,

## CORRESPONDENCE:

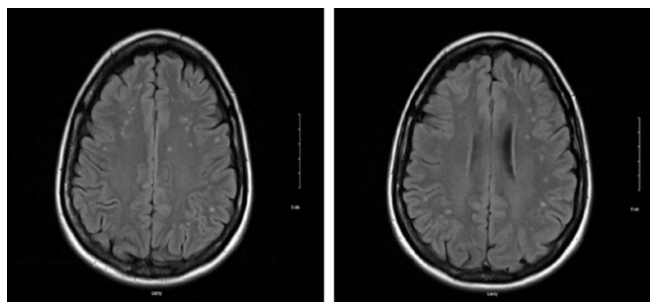
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where cognition would be unpredictably worse on certain days. The patient had not seen a primary care provider for several years prior, as she stated that she had been healthy. The patient denied any head traumas, concussions, forgetting major events, falls, numbness, tingling, or weakness. She was adamant that she sleeps well, exercises regularly and eats a balanced diet. Her surgical history included a tubal ligation. She does not smoke tobacco, drink alcohol or use any illicit drugs. Her family history includes atrial fibrillation and hypertension in her mother. On physical exam, SS displayed prolonged relaxation phase of her bilateral patellar reflexes and poor accommodation in her right eye. The patient also exhibited a deficit in recall, in which she was only able to remember two out of the three objects registered earlier in the mini-mental status exam. The rest of her exam was completely normal.

Impressions of her MRI suggested numerous scattered T2/FLAIR hyper-intensities in the cerebral matter, predominantly in the white matter (*Figure 1*). These were later classified to be non-specific, but according to the reading radiologist it can be seen in the setting of migraines, chronic small vessel ischemia, demyelinating disease, Lyme disease, vasculitides, prior insults such as infection, inflammation or trauma, as well as other etiologies. Lab work was all within normal limits. The Lyme panel only revealed one reactive KD 23 IgM. On follow up visit two weeks later, SS stated that there was no improvement to her memory or other symptoms and was sent to neurology at a tertiary care center nearby in Philadelphia. Repeat Lyme titers revealed reactive KD 23 IgM, KD 23 IgG and KD 41 IgG bands.

#### FIGURE 1:

Numerous scattered punctate T2/FLAIR hyper-intensities in the cerebral matter, predominantly subcortical white matter



At her initial neurology visit in April, SS displayed slowed mental searching capabilities and errors in delayed recall. Her deep tendon reflexes were also noted to be hyperactive with slowed relaxation. Labs including ammonia, heavy metals, lipids, sedimentation rate, CBC, coags, vitamin D, and hemoglobin a1c were all within normal limits, but her thyroid peroxidase antibodies were elevated at 23 IU/mL (almost 2.5 times normal). Her cerebral spinal fluid (CSF) was analyzed for Lyme, oligoclonal bands, cytology and protein electrophoresis. The fluid was positive for two oligoclonal bands, mildly low albumin and mildly high gamma globulin. At the patient's follow up visit one month later, SS started complaining of bilateral hip and knee pains. Consequently, she was sent for rheumatology workup as well as a neuropsychological (NP) evaluation. She was

also seen by ophthalmology for visual evoked potential test to officially rule out multiple sclerosis.

Rheumatology had a low clinical suspicion of primary rheumatological disease. Regardless, SS was sent for x-rays of her cervical spine, hips and knees as well as extensive blood work, which was not available at the time of this write-up. Per the patient, this lab work was normal. X-rays of the hips and knees were normal, but the cervical spine showed degenerative disc changes at C5-C6. NP evaluation showed mild cognitive disorder with the largest deficits in auditory and visual attention, and executive and visuospatial functions. Recommendations included consideration of starting a psychostimulant as well as implementing compensatory strategies for memory, staying active, exercising, participating in psychotherapy like cognitive behavioral therapy, practicing mindfulness and a repeat NP evaluation in one year. SS did not tolerate the psychostimulant for more than two weeks, stating that she didn't like the way it made her feel. She felt like the medication made her feel jittery. In the interim, SS was evaluated by infectious disease in July who recommended a three week trial of doxycycline. She reported that her bilateral arthralgias did not improve and even worsened one week after stopping them.

The patient was seen by endocrinology in September. A thyroid ultrasound showed an inflamed thyroid gland and SS was subsequently started on 12.5 mcg of levothyroxine daily. Her repeat anti-TPO at this time was 587 IU/mL. The diagnosis of HE was made by neurology at this time. It was decided to treat the patient with a four-day course of high-dose solumedrol. After admission, she was discharged with a prednisone taper over one month. Repeat anti-TPO level during admission was 531 IU/mL. On follow up visit, SS reported resolution of her cognitive difficulties and was working again without issues. She still reported intermittent arthralgias in her knees and neck. She was re-evaluated by NP several weeks after her hospitalization, which showed resolution of her prior attention deficits.

The patient recently followed up with neurology, where she reported feeling well cognitively. She was able to work and think clearly without difficulty. Unfortunately, SS stated that her word-finding difficulties and "mental fog" returned in February of the following year. She was treated with five days of high-dose burst steroids and reports that her above symptoms, including her memory, almost completely resolved one week after.

## DISCUSSION

Although rare, the diagnosis of Hashimoto Encephalopathy may be underdiagnosed and should be on the radar of any primary care doctor for any patient with symptoms resembling encephalopathy such as change in mental status, memory problems, "mental fog," and word-finding difficulties. The prevalence is about 2.1 in 100,000 patients.<sup>1-3</sup> HE predominantly affects women like other autoimmune disorders with a ratio of men to women of about 1:4, and has an average age of 52.<sup>1</sup>

HE is a steroid-responsive encephalopathy that is associated with autoimmune thyroiditis or more commonly with anti-thyroid peroxidase or anti-thyroglobulin antibodies. Average anti-TPO

antibody titers in the serum at the time of diagnosis is 900 IU/mL. The presence of antibodies has shown in the cerebral spinal fluid. Furthermore, serum antibody titers are always positive in the serum when CSF is positive for antibodies.<sup>1</sup> The clinical syndrome can vary from case to case but it usually lies on a spectrum ranging from stroke-like focal neurological deficits to a diffuse pattern that can cause impairments such as dementia, altered mental status, word-finding difficulties, hallucinations, confusion, etc.<sup>1-3,5</sup> Of note, a large percentage of patients with HE often suffer from altered cognitive functioning, seizures, and myoclonus. HE can present chronically with waxing and waning phases or acutely like delirium or rapidly progressive dementia.<sup>3</sup> Although Hashimoto is in the name of this disorder, hypo or hyperthyroidism is not a necessary criterion for the diagnosis. Most patients are euthyroid when the diagnosis is made. There also appears to be no correlation between the anti-thyroid level and the severity of the disease. Regardless, the presence of anti-thyroid antibodies is paramount to make this diagnosis.<sup>3</sup>

The pathophysiology of the disorder is not well understood, but some theories suggest autoimmune vasculitis or deposition of immune complexes as the cause of the signs and symptoms.<sup>3</sup> Another widely accepted explanation includes immune-mediated demyelination where anti-thyroid or TPO antibodies attacks neurons in the same way they destroy the thyroid gland.<sup>1</sup> Patients often get near or complete resolution of their symptoms with high-dose steroids, even after years without treatment.<sup>1-3,5</sup> Immunomodulation with IV immunoglobulins, azathioprine, rituximab, plasma exchanges, or hydroxychloroquine also appears to be helpful in a handful of cases. Some of these above treatments were combined with steroids, but outcomes did not appear to differ.<sup>1</sup> To further complicate diagnosis and treatment, symptom relapse has been shown, as was evident with our above patient.

Brain MRI is sometimes negative, but up to 52% of cases have shown either cortical atrophy or nonspecific T2 signal abnormalities at the subcortical white matter. HE can also have non-specific findings on EEG in over eighty percent of cases. In many reported patients, EEG changes improved or resolved after proper treatment.<sup>1</sup>

As with any encephalopathy, it is important to rule out all other causes. The differential diagnosis in the above case with a physical exam and MRI findings included Lyme disease, multiple sclerosis, rapidly progressive dementia, stroke/transient ischemic accident, occult anxiety or depression, heavy metal toxicity, thyroiditis, or attention deficit hyperactivity disorder. With any syndrome including delirium or rapid dementia, other diagnoses such as Creutzfeldt-Jakob disease, infectious meningoencephalopathies, paraneoplastic encephalitis, tertiary syphilis, vitamin deficiencies, degenerative dementia, and cerebral vasculitis should be ruled out. To rule out all of these diagnoses, it is recommended to get a lumbar puncture, MRI with contrast, labs such as complete metabolic panel, complete blood count, urinalysis with culture, urine drug screen, ammonia, liver function tests, thyroid function, inflammatory markers, Lyme disease immunoglobulins, heavy metals such as lead and mercury, vitamin b12, and syphilis screen to rule out other causes of change in mental status, and an EEG.<sup>3</sup>

There were some limitations to this case report. As with many other private practice offices, patient information can be somewhat difficult to obtain from bigger, academic facilities and/or local specialists. To mitigate this weakness the patient featured in this report was contacted to corroborate the clinical course and to fill in any holes that may have presented themselves. It would have been particularly helpful to have data on the presence of anti-thyroid antibodies in her CSF because her HE diagnosis would have been made much quicker. It also appeared that the patient did not get an EEG study. It is unknown why this was never ordered. After a review of the literature, it is unclear which treatments are most efficacious for relapses. This should be a topic for further research. Regardless, the patient's diagnosis was made via a very systematic and logical clinical approach. In conclusion, clinicians should check for the presence of anti-thyroid antibodies even if the TSH is normal for patients presenting with either subtle or very profound, otherwise unexplained encephalopathy.

#### **AUTHOR DISCLOSURES:**

No relevant financial affiliations

#### **INFORMED CONSENT:**

The entirety of the case was reviewed with SS in our private practice office and she gave informed consent to publish this case report.

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