Steroid-Responsive Encephalopathy Associated with Autoimmune Thyroiditis: Findings on Catheter Angiography Suggestive of Microvascular Vasculitis

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Abstract
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) or Hashimoto’s encephalopathy is a recognized but poorly understood neurological complication of autoimmune thyroid disease. Proposed etiologies include autoimmune demyelination, autoimmune vasculitis, and anti-CNS antibodies. Catheter angiography in a 41-year old woman initially presenting with language difficulty and eventually diagnosed with SREAT demonstrated a focus of arterial hyperperfusion consistent with a microvascular pathology, supporting the theory that the underlying abnormality in SREAT is a small vessel vasculitis. Serial MRI examinations performed during her clinical course demonstrated migratory waxing and waning cortical and subcortical T2 signal abnormalities typical of the disease.

ABBREVIATIONS
SREAT: Steroid Responsive Encephalopathy associated with Autoimmune Thyroiditis; DWI: Diffusion-Weighted Imaging; CSF: Cerebrospinal Fluid.

INTRODUCTION
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) or Hashimoto’s encephalitis is a recognized but poorly understood neurological complication of autoimmune thyroid disease. Patients have elevated anti-thyroid antibodies though the correlation between severity of neurological disease, thyroid hormone status, and antibody titers is unclear [1]. Generally accepted diagnostic criteria include elevated anti-thyroid antibodies and steroid responsive neurological disorders including cognitive impairment, focal neurologic deficit, movement disorders, and/or seizures [2]. The time course is variable with acute, subacute, chronic progressive, and relapsing remitting presentations reported in the literature [2, 3]. The vasculitic type is characterized by acute stroke-like episodes with focal neurological deficits, myoclonus and seizures. The other subtype is diffuse, progressive and associated with insidious onset and progressive mental status impairment [4]. Approximately 50% of patients have normal neuroimaging and the other half demonstrate non-enhancing foci of T2 prolongation in the cerebral white matter [2,3,5,6].

CASE PRESENTATION
A 41-year-old female presented with a two-week history of difficulties with word finding and comprehension of written information as well as a left frontal headache that had resolved a week prior to presentation. Past medical history was significant for hypertension and right-sided vision loss at age 19 secondary to acute zonal occult outer retinopathy. Neurological examination on presentation was unremarkable. MRI without gadolinium performed the day of presentation revealed a focus of increased T2 signal within the cortical and subcortical inferior left temporal lobe. There was no corresponding abnormality on diffusion-weighted imaging (DWI). Additionally, there were scattered subcentimeter foci of increased T2 signal within the
supratentorial deep and subcortical white matter bilaterally. Follow up MRI with gadolinium performed 20 days later demonstrated interval increase in size of the left temporal lesion and no enhancement. The patient’s language difficulties abated approximately one week after her initial presentation. She subsequently developed episodic left upper extremity paresthesias. Follow up MRI performed 65 days after initial presentation demonstrated complete resolution of the left temporal lobe lesion and a new similar appearing process within the right frontotemporoparietal subcortical white matter (Figure 1). She presented to the emergency room 20 days later after two episodes of generalized tonic clonic seizure. MRI performed at that time redemonstrated the right frontotemporoparietal lesion. Catheter angiography performed the following day demonstrated gyral swelling, hyperperfusion and decreased transit time within the right frontotemporoparietal region corresponding to the MRI abnormality (Figure 1). There was no arterial beading, irregularity, focal narrowing or occlusion. Serology demonstrated elevated anti-thyroid peroxidase antibody levels of >1300 U/mL (reference range < 60 U/mL) and elevated anti-thyroglobulin antibody levels of 373 U/mL (reference range < 60 U/mL). Thyroid stimulating hormone level was normal. Anti-nuclear antibody screen was weakly positive. B. Burgdorferi immunoassay was negative. Venereal disease research laboratory test was nonreactive. Cerebrospinal fluid protein (CSF) glucose, lactic acid, angiotensin converting enzyme levels, IgG index and cell count were normal. Oligoclonal bands were not detected. Polymerase chain reaction of the CSF for herpes simplex virus, cytomegalovirus, and varicella zoster virus was negative. CSF cultures yielded no growth. IV methylprednisolone was started for presumed SREAT (250 mg IV Q6hr) and was administered for one day then transitioned to oral steroids. She was seen in follow up one week following discharge and was seizure free but reported continued episodic left upper extremity numbness and tingling. Additional investigation yielded a negative paraneoplastic autoantibody panel and negative aquaporin 4 antibodies. Free T3 was mildly decreased at 2.0 pg/ml (reference range 2.3-4.2 pg/ml). Total T3 was decreased at 45 ng/dl (reference range 60-181 ng/dl). The patient was maintained on oral steroids (prednisone 10 mg daily) and was asymptomatic at most recent outpatient follow up, 3 months following hospital discharge. MRI performed at that time, 237 days from initial presentation, demonstrated complete resolution of the right frontotemporoparietal lesion and a new small lesion within the subcortical right temporoparietal lobe. Given the new lesion, prednisone dosage was increased to 20 mg daily. Subsequent endocrinology evaluation yielded a diagnosis of Hashimoto’s thyroiditis. She has maintained a euthyroid state and has not required supplementation with L-thyroxine.

**DISCUSSION**

While more than 100 patients with SREAT have been reported in the literature, the pathogenesis remains poorly understood. Proposed etiologies include autoimmune demyelination, vasculitis with or without immune complex deposition, and anti-CNS antibodies [5]. Reports of pathologic findings in SREAT are sparse with few descriptions in the literature: lymphocytic perivenular cuffs [1,5], vasculitis of venules and arterioles [7,8], microglial activation [9,10], and primary demyelination [5]. While termed a steroid responsive encephalopathy, the efficacy of steroids is variable, with approximately 50% of patients responding [3]. Ferracci et al have suggested that increased CSF titers of anti-thyroid antibodies may be more specific [11]. Serum anti-thyroid antibodies may be misleading as anti-thyroid peroxidase antibodies are elevated in 10% of healthy adults and no correlation between serum anti-thyroid antibody level and encephalopathy has been shown in SREAT patients [2]. Furthermore, studies have shown CSF anti-thyroid antibodies to be present in some patients with SREAT and absent in healthy subjects [12]. Many patients with SREAT have normal neuroimaging or white matter abnormalities consistent with chronic ischemia [2]. Approximately 50% will have diffuse or focal non-enhancing areas of T2 prolongation in the cerebral white matter and potentially dural enhancement, findings that
The patient provided informed consent for the submission of this manuscript.


could be directly attributable to Hashimoto's thyroiditis itself. While the pathogenesis of SREAT remains unclear, biopsy findings and steroid responsiveness suggest a potential inflammatory vasculitis. Findings of hyperperfusion on catheter angiography are supportive of an underlying microvascular abnormality. As such, further investigation of perfusional imaging abnormalities may provide insight into the pathophysiology of SREAT, potentially impacting treatment in the future.

CONFLICT OF INTEREST

The authors have no competing interests and all have contributed sufficiently to the preparation of this manuscript. The patient provided informed consent for the submission of this work. IRB approval was obtained (IRB # 7661). No funding was provided.

REFERENCES