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Case Report

Encephalopathy of Autoimmune Origin: Steroid-Responsive Encephalopathy With Associated Thyroiditis

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ABSTRACT

Background/Objective: Our objective is to highlight the importance of identifying symptoms of steroid-responsive encephalopathy with associated thyroiditis (SREAT), especially in the setting of intermittent cognitive dysfunction, and to inform that SREAT can develop even in patients with a history of partial thyroidectomies.
Case Report: We present a case of a 51-year-old woman with a long-standing history of hypothyroidism presenting with acute onset myoclonus, involuntary tremors, fatigue, malaise, and palpitations for two weeks, with intermittent lapses in cognitive function. The patient's workup is completely within normal limits, including her cognition, except for elevated thyroid stimulating hormone levels and markedly elevated levels of antithyroid peroxidase antibodies, despite the fact that she previously had a partial thyroidectomy.
Discussion: SREAT is an autoimmune condition characterized by cognitive dysfunction, elevated thyroid autoantibodies, and therapeutic response to corticosteroids. SREAT is primarily considered a diagnosis of exclusion. A crucial feature is the hallmark of significant improvement in symptoms when glucocorticoids are administered. There is a significant correlation between patients with elevated antithyroid peroxidase antibodies and new-onset SREAT. Although total thyroidectomy has been reported as a definitive treatment of SREAT, response to corticosteroids is the "sine qua non" in diagnosing this condition.
Conclusion: Hashimoto's thyroiditis can lead to a rare complication called SREAT, presenting with various neurologic symptoms. Prompt glucocorticoid treatment is vital, and a positive response confirms the diagnosis. Total thyroidectomy may be necessary for definitive SREAT treatment. More research is needed for alternate treatments and an understanding of the pathophysiology of SREAT.

Introduction

Steroid-responsive encephalopathy with associated thyroiditis (SREAT), also known as Hashimoto's encephalopathy, refers to an autoimmune condition characterized by elevated thyroid autoantibodies with cognitive dysfunction responsive to corticosteroids.[1] SREAT presents as an autoimmune-mediated inflammatory disease with vasculitis and rapid progression of neuropsychiatric symptoms that are reversible with corticosteroids.[2,3] SREAT may present with acute or subacute encephalopathy with clinical features of myoclonus, seizures, and stroke-like or psychiatric manifestations.[4] Electroencephalogram findings associated with SREAT reveal generalized slowing with focal temporal or frontal deceleration. Magnetic resonance imaging (MRI) commonly shows generalized cerebral atrophy, restricted diffusion, increased T2, and flair white matter.[4] Biopsies of postmortem brains with SREAT demonstrated vasculitis or lymphocytic infiltration in cerebral small vessels, which suggests that the pathophysiology of SREAT consists of

Abbreviations: EEG, Electroencephalogram; MRI, magnetic resonance imaging.

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reversible cerebral inflammation and vasculitis mediated by an autoimmune mechanism.[3] Here, we present a patient with intermittent symptoms of palpitations, fatigue, sudden episodes of forgetfulness, impulsiveness, and intense paranoia that occurred years after a partial thyroidectomy. All investigative workup on presentation showed negative results except for an elevated thyroid stimulating hormone (TSH) level, with resolution of her neuropsychological symptoms after initiation of steroid therapy, in accordance with the diagnostic criteria of SREAT. Interestingly, patients with SREAT, regardless of preexisting thyroid disease, tend to have normal T3/T4, with normal or near normal levels of TSH.[5] Our patient is unusual because her TSH levels were moderately elevated, possibly because of partial medication nonadherence.

Case Report

A 51-year-old woman with a medical history of coronary artery disease, hyperlipidemia, and hypothyroidism (since 1992 after a partial thyroidectomy for a benign nodule) presents with progressive symptoms of fatigue, malaise, and palpitations with involuntary muscle jerking, muscle shaking, and a history of unprovoked falls for 6 to 8 weeks. Two weeks before the presentation, she had 5 separate visits to different emergency departments for similar debilitating episodes of forgetfulness, intense episodes of feeling overwhelmed, paranoia, and impulsive changes of mind. One episode involved the patient starting her car to visit her family and then suddenly deciding to walk to their house while leaving the car running in her driveway. A similar episode occurred 4 months before, which lasted several weeks and spontaneously resolved. She has no prior psychiatric history but has a history of missing doses of her NP thyroid medication (desiccated thyroid). A few days before presentation, the repeat TSH level was 28 mIU/L and the dose of thyroid replacement was increased from 75 mg/d to 90 mg/d. She denied fever, chills, shortness of breath, or COVID-like symptoms. A physical examination showed myoclonus and muscle shaking. Workup for infectious, metabolic, and toxic causes showed normal results. Although myxedema crisis was considered, the patient's vital signs were without bradycardia, hypotension, hypothermia, decreased respiratory rate, or increased pulse pressure, making this differential unlikely. A head MRI did not show any evidence of acute hemorrhage, infarction, abnormal enhancement, or intracranial masses. The ventricles appeared normal in size and the major vascular structures were unremarkable; thus, an intracranial etiology was ruled out. An electroencephalogram was not completed at this time. The antithyroid peroxidase (TPO) antibody titer was 2112 IU/mL (reference range is <34 IU/mL) (Table). SREAT was the presumed diagnosis and prednisone 60 mg/d was started. The patient's symptoms of fatigue, cognitive dysfunction, myoclonus, muscle shaking, and palpitations were resolved within a few days; the dose was then tapered off over 6 weeks. The patient remains asymptomatic after 4 months of follow-up, and she has not returned for evaluation since this time.

Discussion

Antibody-mediated disorders of the central nervous system can be severe or life-threatening, however, with the potential for reversibility with appropriate treatment. SREAT was first described in 1966 as a rare constellation of neuropsychiatric symptoms.[6-8] SREAT is primarily a diagnosis of exclusion and heavily relies on a marked improvement of symptoms on administration of corticosteroids.[8,9] The 4 major criteria needed to diagnose SREAT are as follows: (1) altered consciousness with changes in cognitive ability; (2) new or worsening psychiatric symptoms; (3) elevated serum TPO-Abs levels (≥0.5 U/mL) or other antithyroid antibodies, such as antithyroid microsomal or antithyroglobulin (TG) antibodies; and (4) exclusion of infectious, toxic, metabolic, or tumorous etiologies that can further explain symptoms.[5,8,9]

In the case of our patient, primary encephalopathy symptoms included altered mental status, paranoia, and myoclonus. All investigative workup upon presentation showed negative results except for an elevated TSH, and importantly, her neuropsychological symptoms wholly resolved after initiation of steroid therapy, making the diagnosis of SREAT very likely.

The most recent estimated prevalence of SREAT is 2.1 per 100 000 patients with a median age of onset of 56 years, with increased prevalence in women.[9] Patients with SREAT have a history of premorbid thyroid disease, such as our patient.[8,9] One study demonstrated that out of 11 patients with diagnosed SREAT, 10 had a preexisting thyroid disease. Of those 10, 6 had confirmed Hashimoto's thyroiditis, 1 had Graves' disease, and the remaining had unspecified hypothyroidism. Patients with SREAT tend to have normal T3/T4, with normal or near normal levels of TSH.[5] Our patient is unusual because her TSH levels were moderately elevated because of partial medication nonadherence.

Elevated TPO antibody titers are a hallmark of diagnosis (our patient presented with a TPO antibody level of 2112 IU/mL, significantly higher than the average newly presenting SREAT 900 IU/mL]); however, their role in SREAT pathogenesis is debated. Laurent et al[1] reported that 251 patients with SREAT had elevated titers of antithyroid antibodies, with 69% of patients having both elevated TPO antibodies and anti-TG antibodies, 34% with only elevated TPO antibodies, and only 7% with isolated elevation of anti-TG antibodies. Although elevated TPO or other antithyroid antibodies are a cornerstone criterion for the diagnosis of SREAT, antithyroid antibodies are frequently found in asymptomatic patients with studies reporting elevated levels in 13% of 265 healthy individuals and 27% of women aged >60 years.[1] This suggests that elevations in TPO antibodies could be an incidental finding.[9,10,11]

Highlights

- Steroid-responsive encephalopathy with associated thyroiditis (SREAT) is a very rare complication of Hashimoto's thyroiditis
- The four major criteria that need to be met for diagnosing SREAT are as follows: (1) altered cognitive ability; (2) new or worsening psychiatric symptoms; (3) the presence of elevated serum antithyroid peroxidase Abs levels (≥0.5 U/mL) or other antithyroid antibodies; and (4) the exclusion of infectious, toxic, metabolic, or tumorous etiologies that can further explain these symptoms.
- Once SREAT is suspected, treatment with glucocorticoids should be started without delay, and a response to the treatment can confirm the diagnosis
- The disease can reoccur, and definitive treatment of SREAT is a total thyroidectomy
- SREAT can occur, rarely in those with partial thyroidectomies

Clinical Relevance

Steroid-responsive encephalopathy with associated thyroiditis is an autoimmune condition characterized by cognitive dysfunction, elevated thyroid autoantibodies, and therapeutic response to corticosteroids. It is generally a diagnosis of exclusion, is rare, and most commonly occurs in the setting of Hashimoto's thyroiditis.

Table
The patient's thyroid function tests over the course of several years

Thyroid function test results														
		December 14, 2020	December 28, 2020	January 13, 2021	February 3, 2021	April 12, 2021	June 25, 2021	September 12, 2021	February 23, 2022	April 15, 2022	June 7, 2022[a]	October 17, 2022[a]	December 13, 2022[a]	February 2, 2023[a]
TSH	0.450-4.500 uIU/mL	2.020	1.420	0.306 (L)	0.257 (L)	6.770 (H)	8.580 (H)	10.700 (H)	0.20 (L)	13.800 (H)	2.27	20.300 (H)	0.018 (L)	0.009 (L)
T4-Free Direct	0.82-1.77 ng/dL	1.25	…	…	1.09	0.74 (L)	0.80 (L)	0.74 (L)	…	…	…	0.76 (L)	2.43 (H)	1.69
T3 Free	2.0-4.4 pg/mL	3.0	…	…	…	2.6	…	…	…	…	…	…	…	…
T4 Free	0.60-2.50 ng/dL	…	1.79	…	…	…	…	…	1.18	1.16	0.64	…	…	…
T3, Total	97-169 ng/dL	…	…	…	…	…	104	91	352 (H)	…	141	…	…	…
Thyroid peroxidase Ab	0-34 IU/mL	…	…	…	…	…	>600 (H)	…	…	2112.0 (H)	581 (H)	>600 (H)	>600 (H)	…

Abbreviations: Ab = antibodies; (H) = indicates levels higher than the standard normal range; (L) = indicates levels lower than the standard normal range; TSH= thyroid stimulating hormone.
On April 25, 2022, the patient began therapy with a tapering dose of oral prednisone over 6 months.
[a] Indicates values after initiating prednisone treatment.

However, some reports suggest a correlation between TPO antibodies and the severity of the clinical presentation of SREAT.[7] Yuceyar et al[12] identified a patient with relapsing episodes of SREAT that were definitively treated with a total thyroidectomy, reducing the TPO antibody levels permanently. Although more research is needed, the combination of elevated thyroid antibodies with cognitive dysfunction and new psychiatric symptoms that respond to steroid treatment must be present to solidify the diagnosis of SREAT.[5]

Currently, there are no reports in the literature of SREAT developing in patients after partial thyroidectomy, such as in our patient, making this a unique presentation of this disease. The ability of SREAT to develop in those with partial thyroidectomies, with complete resolution after a total thyroidectomy, as previously reported, may suggest that antithyroid antibodies play a part in the pathogenesis and the severity of the disease; however, more research in this area is needed.

The prognosis of SREAT is generally favorable because symptoms tend to dissipate with the administration of glucocorticoids in 90% of patients with SREAT.[9] However, those with more severe symptoms, such as coma, had a worse prognosis and were more prone to relapsing episodes of SREAT. In addition, those with sole elevations of anti-TPO antibodies were found to have a more favorable outcome. Although treatment with steroids has been proven to be effective in reducing neurologic symptoms, no established guidelines or treatment regimens, including the use of other immunosuppressants have been created.[9]

Various autoimmune disorders are associated with psychiatric disorders with indirect evidence using the Danish National Registry showing that a personal history of any autoimmune disease was associated with a 45% increase in risk for schizophrenia. *N*-Methyl-D-aspartate receptor hypofunction caused by immunoglobulin antibodies is associated with the development of schizophrenia and psychoses.[13] A study out of Italy showed cases of tic and obsessive-compulsive disorders occurring after streptococcal infections were associated with a significant increase in antistreptolysin O titers.[14] With the introduction of new immunologic techniques and the expansion of immune neuropsychiatric research, evidence is accumulating that at least a subset of psychiatric disorders has an autoimmune basis.[13] In a large meta-analysis in Germany of patients with increased TPO titers, the authors found that approximately 23.8% of patients with autoimmune thyroiditis (AIT) experience depression, and approximately 41.6% of patients with AIT experience anxiety disorders.[15]

Conclusion

AIT is strongly associated with depression and anxiety disorders. Thus, screening for psychiatric symptoms is necessary. SREAT is a very rare complication of Hashimoto's thyroiditis. Typical presentations include myoclonus, cognitive changes, stroke-like symptoms, and characteristic MRI findings. However, the patient's presentation may not always be consistent with the above picture. Once SREAT is suspected, treatment with glucocorticoids should be started without delay, and a response to the treatment can confirm the diagnosis. The disease can reoccur, and the definitive treatment of SREAT is a total thyroidectomy. Further research on the underlying pathophysiology of SREAT and alternate treatment regimens for glucocorticoid nonresponders is needed.

Disclosure

The authors have no multiplicity of interest to disclose.

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