




Case Report

Steroid response encephalopathy associated with autoimmune thyroiditis

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ABSTRACT

Introduction: Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is a rare autoimmune disorder affecting the central nervous system, characterized by a spectrum of neurological and psychiatric symptoms.

Aim: This case study aims to highlight the diagnostic challenges and the successful management of SREAT syndrome in a young woman with autoimmune thyroiditis.

Case study: A 21-year-old woman with documented Hashimoto's thyroiditis and polycystic ovary syndrome was admitted to the Clinic of Neurology following a 5-minute tonic seizure and subsequent confusion state lasting several hours. Initial brain MRI showed no abnormalities, and EEG revealed generalized slowness. Comprehensive laboratory assessments, including a complete blood count, biochemical analysis, and electrolyte panels, all yielded normal results. Further investigation revealed a significantly elevated anti-thyroid peroxidase antibody (anti-TPO) titer exceeding 1000 IU/mL. The suspicion of SREAT syndrome was considered. Pulse therapy with methylprednisolone was associated with rapid recovery. The patient was discharged from the hospital with an oral corticosteroid tapering regimen.

Results and discussion: The administration of pulse therapy with methylprednisolone resulted in a rapid and very good response in the patient, evidenced by the resolution of seizure activity and improvement in confusion. Laboratory investigations, particularly the markedly elevated anti-TPO titer, supported the diagnosis of SREAT syndrome. The subsequent management with an oral corticosteroid tapering regimen maintained the patient's clinical stability.

Conclusions: This case highlights the importance of considering autoimmune encephalopathy in patients with a history of autoimmune thyroiditis presenting with neurological and psychiatric symptoms. Further research is warranted to better understand the underlying pathomechanisms.

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1. INTRODUCTION

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is a rare disease, first described by Brain et al. in 1966 as Hashimoto's encephalopathy. It is characterized by encephalopathy linked to antithyroid antibodies, specifically anti-thyroid peroxidase (anti-TPO) and/or anti-thyroglobulin (TG) antibodies, in the absence of other etiologies.^{1,2} Since its initial description, numerous reports have highlighted the varied neuropsychiatric manifestations of this condition, which is still not fully understood and often leads to misdiagnosis in the field of neuropsychiatric disorders.³⁻⁶

The exact pathomechanisms underlying the condition are not fully understood. It has been observed that while nearly all individuals with SREAT have elevated levels of antibodies against the thyroid gland, a clear causal or linear link between antibody titers and SREAT has not been definitively established. Additional factors considered significant contributors to the pathogenesis of SREAT include disruptions in the blood-brain barrier and metabolism due to diffuse vasculitis and/or disseminated encephalomyelitis (Figure 1).^{7,8} Owing to its diverse clinical presentation, SREAT might often be an underdiagnosed condition that delays treatment and affects prognosis. Symptoms reported include fatigue, migraine headaches, seizures, stupor/coma, dyscognitive disorders, brain fog syndrome, focal neurological deficits, psychosis/delusions/hallucinations, and mood disturbances. Additional symptoms include alternating hemiparesis and cerebellar ataxia.⁹

Behavioral changes were described in 90%–100%, dyscognitive disorders in over 80%, and seizures in 60%–70% of patients with SREAT syndrome. A relapsing and remitting course was described in 50% of cases, an insidious progressive course in 40%, while the remaining 10% lacked a defined course. Elevated levels of antibodies against the thyroid gland represent the most frequently observed laboratory abnormality, with anti-TPO serving as a marker to confirm the diagnosis.¹⁰

The presented case underscores the diagnostic complexities associated with SREAT syndrome, given its potential to mimic a myriad of neurological signs and symptoms. Early diagnosis is key to initiating adequate therapy, crucial for achieving a favorable outcome in cases with SREAT syndrome. Familiarization with this syndrome undoubtedly enhances awareness of the condition and its neurological manifestations, particularly in individuals with autoimmune thyroid disease who may exhibit symptoms correlating with SREAT syndrome.

Currently, there is no universally accepted treatment protocol for SREAT syndrome, but there is a consensus that treatment as soon as possible yields a better prognosis. The most common therapeutic approaches involve the administration of high-dose steroids and non-steroid immunosuppressive drugs. Treatment typically starts at 1–2 mg/kg of prednisone, with subsequent tapering based on symptomatology. The duration of corticosteroid therapy varies widely,

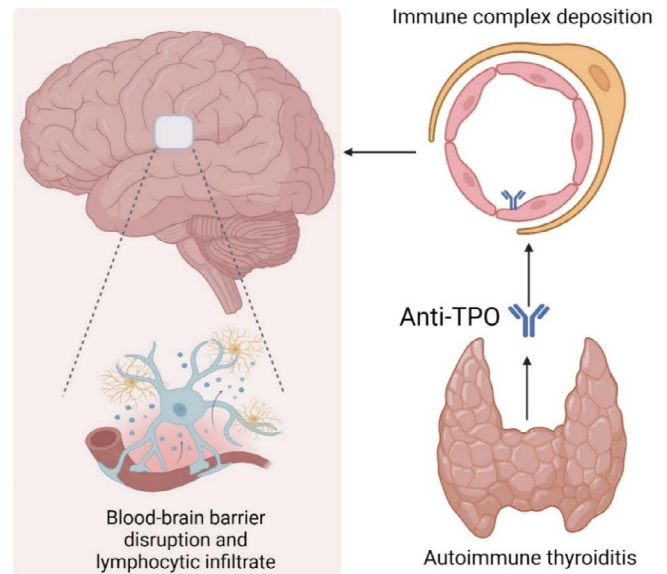


Figure 1. Pathomechanisms of SREAT. Elevated levels of anti-TPO in the bloodstream are linked to the deposition of immune complexes in blood vessels, potentially contributing to the disruption blood-brain barrier and metabolism.

from 4 months to 10 years in many cases.¹⁰ In cases where steroid therapy proves ineffective, potential second-line therapies include intravenous immunoglobulin (IVIG),¹¹⁻¹² non-steroid immunosuppressive drugs such as azathioprine or cyclophosphamide, and plasma exchange.

2. CASE STUDY

Here, we present the case of a 21-year-old woman with a history of Hashimoto's thyroiditis and polycystic ovary syndrome. Before the diagnosis of Hashimoto's thyroiditis, she reported experiencing static tremors, dizziness, and brain fog syndrome. She was prescribed levothyroxine for Hashimoto's thyroiditis. However, despite the administration of thyroid hormone therapy, her symptoms persisted. After six months, her condition deteriorated, culminating in a tonic seizure lasting approximately five minutes. Subsequently, she experienced two days of cognitive dysfunction, confusion, behavioral changes, and mood imbalances.

She was admitted to a Clinic of Neurology in another country and subsequently transferred to an intensive care unit, where she underwent intubation for one week. Upon discharge, she was diagnosed with status epilepticus and Hashimoto's thyroiditis, for which she received antiseizure medication and continued thyroid hormone therapy. Approximately a month later, she experienced another tonic seizure, accompanied by cognitive disorders, prompting her admission to our Clinic of Neurology at the University Clinical Center of Kosovo.

She underwent head MRI and angio-MRI, which showed no evidence of mesial temporal sclerosis, cortical dysplasia,

or abnormal cortical development. Intracranial and extracranial blood vessels were within normal limits without any pathologic changes; however, a hypoplastic right vertebral artery was noted, though it did not impact brain blood flow, as depicted in Figure 2. The EEG revealed generalized slowness, with Delta waves of 2–3 Hz. Comprehensive laboratory investigations, including a CBC, hsCRP, BUN, glucose, creatinine, transaminase, cholesterol, triglycerides, ANA, ANCA, anticardiolipin, Anti-Smith antibody, anti-ACE, electrolyte panels, and autoimmune encephalitis antibodies (NMDA receptor, AMPA receptor, LGI1, mGluR1, GABA_AR, IgLON5, MOG), returned normal results. Further examination revealed a notably elevated anti-TPO antibody titer, exceeding 1000 IU/mL. SREAT syndrome was suspected, and methylprednisolone pulse therapy (1 g for 5 days) was initiated.

Remarkably, the patient's clinical condition improved following the administration of the first corticosteroid dose. After initial hospitalization, she was discharged with an oral corticosteroid regimen. Despite several attempts to discontinue corticosteroid therapy, discontinuation was unsuccessful, leading to relapses of symptoms such as dizziness, brain fog syndrome, and short stages of dyscognition, like memory problems and disorientation. An effort was made to substitute corticosteroids with a nonsteroidal immunosuppressive (azathioprine); however, the patient became pregnant, necessitating the discontinuation of the treatment. Consequently, corticosteroid therapy was resumed. The patient had a normal delivery and gave birth to a healthy child. Currently, she continues to take 5 mg of prednisolone on alternate days and has maintained this treatment regimen for almost 5 years without relapses.

3. DISCUSSION

SREAT syndrome is a rare systemic autoimmune disorder that affects the central nervous system, characterized by a wide array of neurological and psychiatric symptoms. It often poses a diagnostic challenge, especially in differentiating it from autoimmune encephalitis, particularly NMDA receptor encephalitis. Notably, studies have shown that antineuronal antibodies, including NMDA antibodies, are detected in fewer than 20% of SREAT cases.¹³

To confirm the diagnosis of SREAT syndrome, evidence of significant improvement in mental status upon the administration of steroid treatment is essential. In the presented case, the patient exhibited significant recovery of symptoms after receiving the first dose of methylprednisolone. This positive response to corticosteroid treatment in this patient group has led to the alternative designation of 'steroid-responsive encephalopathy' for HE.³ The estimated prevalence of SREAT syndrome is 2.1 per 100,000 patients with neurological symptoms.¹⁴ Owing to the rarity of the disease, diagnosis and treatment initiation are often delayed. In our case, the patient underwent weeks of treatment with antiepileptic drugs without any improvement.

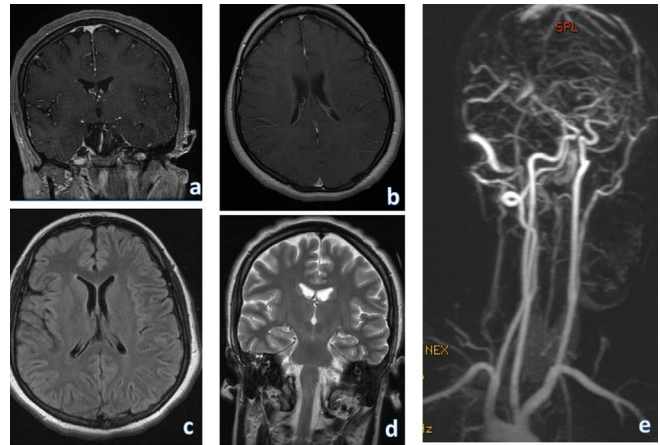


Figure 2. Head MRI and MRA: (A) sequence T1 with contrast coronal; (B) T1 axial; (C) Flair axial; (D) T2 coronal; (E) cervico-cerebral MRA. No evidence of mesial temporal sclerosis, cortical dysplasia or cortical development identified. Intracranial and extracranial blood vessels are within normal limits without any pathologic changes, there is hypoplastic right vertebral artery, but without impact on brain blood flow.

It's important to highlight that the optimal response for seizure control is more likely achieved through immunosuppressive therapy rather than antiseizure therapy. She remained intubated for a full week due to repeated and unresponsive seizures. The initiation of corticosteroid therapy one month after her first seizure was a pivotal moment, leading to rapid improvement.

This case illustrates that a low level of clinical suspicion is common in patients with Hashimoto's thyroiditis who exhibit symptoms associated with SREAT syndrome, emphasizing that early treatment significantly impacts the health and quality of life of patients.

Currently, there is no well-established definitive dosage of steroids, and no universally accepted standard of care exists for this condition. Treatment strategies vary, including the administration of daily oral prednisone with doses ranging from 50 mg to 150 mg, as well as daily high-dose intravenous methylprednisolone. The comparative effectiveness of intravenous steroids versus oral administration remains uncertain. In the case presented, methylprednisolone pulse therapy was administered at a dosage of 1000 mg for 5 days, followed by an oral tapering regimen.

It is evident that a significant majority – ranging from 90% to 98% – of patients with HE treated with steroids exhibit a positive response within weeks to months, often achieving full recovery.¹⁵

The association between Hashimoto's thyroiditis and other autoimmune systemic diseases underscores the classification of SREAT syndrome as an encephalitis associated with systemic autoimmune diseases.^{16,17}

In summary, the objective of presenting a case of SREAT syndrome is to enhance understanding and increase awareness of the myriad symptoms associated with SREAT syn-

drome, as well as the diagnostic challenges and treatment as early as possible for better prognosis for patient. Also to contribute in existing literature by providing documented case study which raise evidence for this issue.

4. CONCLUSIONS

- (1) Low level of suspicion in patients with Hashimoto thyroiditis with symptoms of SREAT syndrome.
- (2) Earlier treatment better prognosis for patients.
- (3) Corticosteroids or non-steroid immunosuppressive have better effect on seizure control then anticonvulsants in patients with SREAT syndrome.

Conflict of interest

None.

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