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Case Report

A case report of Hashimoto's encephalitis in a young patient: a diagnostic challenge

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ABSTRACT

Encephalopathy may arise from intrinsic neurological factors or systemic illnesses. The causes can be diverse, with many being reversible. Therefore, prompt identification of the underlying cause is essential for effective patient management. Hashimoto's encephalopathy, also known as steroid-responsive encephalopathy with autoimmune thyroiditis (SREAT), is characterized by markedly elevated antithyroid peroxidase antibody levels, suggesting an autoimmune origin. The term SREAT reflects its remarkable responsiveness to corticosteroid therapy. Being readily reversible and its response to steroids, Hashimoto's encephalopathy should be taken into consideration when investigating cases of encephalopathies where no definite aetiology is found. Diagnosis involves ruling out other potential causes, including infections, dysglycemia, electrolyte imbalances, myxedema coma, thyroid storm, hypo- and hypercortisolism, among others. This report presents the case of a 25-year-old woman with a history of hypothyroidism who presented with altered consciousness. Following the exclusion of other potential causes, a diagnosis of Hashimoto's encephalopathy was established, and the patient responded well to intravenous steroid treatment, showing marked clinical improvement. This highlights the importance of considering this differential in treating young hypothyroid patients presenting with altered mental status.

Keywords: Hashimoto's encephalopathy, Encephalopathy, Autoimmune thyroiditis, Steroid responsive thyroiditis, Antithyroid antibodies, Hypothyroid

INTRODUCTION

Hashimoto's encephalopathy is an unusual autoimmune-related condition seen in patients with a history of underlying thyroid disorder, mostly characterised by elevated titres of antithyroid antibodies with subclinical hypothyroidism or euthyroid status. Current studies hypothesise that serum antithyroid antibodies (ATAs) might directly act on the antigens that are present in the brain, which are shared by the brain and thyroid; nevertheless, they serve as a good marker for the treatment response.[1] HE presentation varies from altered mental status, confusion, and stroke-like signs to sometimes seizures, ataxia, myoclonus, cognitive impairment, and dementia.[2] Diagnosis is based on clinical findings plus positive Anti-thyroglobulin antibody titres and additionally requires the exclusion of paraneoplastic syndromes and other autoimmune disorders. Given that HE is easily treatable with steroids, it is crucial to consider it in the differential diagnosis.

CASE REPORT

A 25-year-old female came to the emergency room with complaints of altered mental status and lethargy over seven days. According to her family members, the patient exhibited decreased responsiveness, usage of inappropriate words, loss of appetite, and sleep

disturbances over the past seven days. They also noted three episodes of seizure-like activity. The patient was a known case of hypothyroidism for five years and had been on levothyroxine 100 mcg for the past five years. However, she had been non-compliant with her medication for the past twenty days. The family history was unremarkable, with no reported autoimmune conditions.

Upon examination, the patient was drowsy, irritable, but arousable, disoriented to time, place, and person and occasionally obeyed verbal commands. Her Glasgow Coma Scale (GCS) score was 11 out of 15. There was no evidence suggestive of meningeal irritation.

On inspection and palpation of the neck, there was no evidence of goitre. Neurological examination revealed generalised hypertonia and hyperreflexia, along with the presence of Babinski reflex in both lower extremities. Additionally, myoclonus was present. The fundoscopic examination was normal.

To diagnose the aetiology, a complete blood count, basic metabolic panel, coagulation studies were ordered, all yielding normal results ruling out metabolic causes. Blood and urine toxicological screening was negative. TSH was markedly elevated with a value of 52 mIU/mL (normal range -0.5-5 mIU/ml). Anti-thyroid peroxidase (Anti-TPO) and anti-thyroglobulin antibodies (Anti-TG) were elevated.

Autoimmune workup including Anti-Nuclear Antibody titres were inconclusive. An ultrasound of the neck revealed increased vascularity in the thyroid lobes and was suggestive of thyroiditis. Both CT scans and MRI brain scans were conducted to look for evidence of stroke, brain tumours, vasculitis, and infections. The electroencephalogram showed no epileptiform discharges. A lumbar puncture was done and CSF was sent for analysis.

The results are outlined in table 1, the CSF glucose was more than two-thirds of blood glucose, and CSF protein was elevated. CSF analysis for viral RT-PCR for herpes simplex virus, varicella zoster virus, cytomegalovirus, Ebstein barr virus, and other common viral encephalitis was negative. Furthermore, to exclude potential paraneoplastic syndromes, most commonly ovarian and breast cancers in women, ultrasound of the pelvis and breast were performed, both showing no abnormal findings.

Tumour markers such as CA-125 and CA-15-3 were within normal limits, and a paraneoplastic and autoimmune encephalitis antibody panel including antibodies to anti-to, anti-hu, NMDA, AMPA 1, AMPA 2, CASPR (contactin-associated protein 2-VGKC associated), LGI-1 (leucine-rich glioma-inactivated protein 1/VGKC associated), GABA-b receptors yielded negative results.

Table 1: CSF analysis results.

CSF analysis	Results	Reference values
CSF-protein (mg/dl)	55.8	15-45
CSF-LDH (IU/l)	27	≤ 40
CSF-glucose (mg/dl)	53	50-80

Table 2: Diagnostic.

S. no.	Diagnostic
1.	Encephalopathy with seizures, myoclonus, hallucinations or stroke-like episodes
2.	Subclinical or mild overt thyroid disease
3.	Brain MRI normal or with non-specific abnormalities
4.	Presence of serum thyroid antibodies (anti-TPO, anti-thyroglobulin)
5.	Absence of well characterised neuronal antibodies in serum and CSF
6.	Reasonable exclusion of alternative causes

Therefore, following the exclusion of other potential causes, a probable diagnosis of Hashimoto's encephalopathy was considered, supported by the presence of positive anti-TPO and anti-TG antibodies along with elevated TSH levels and normal free T4 levels. According to the standard treatment protocol, the patient was treated with 500 mg of intravenous methylprednisolone for three days. Additionally, she was restarted on 100 mcg of levothyroxine. After 24 hours of treatment, the patient showed significant clinical improvement, and at 72 hours, she showed complete recovery of her CNS functions. Subsequently, she was transitioned to oral prednisone 60 mg (1 mg/kg) once daily and was planned to taper gradually over 2–3 months. She was advised to follow up with endocrinology after 2 weeks and instructed to be compliant with the levothyroxine. Patient attendees were counselled about the relapsing and remitting course of the disease as well as the need for regular follow-up.

DISCUSSION

HE is quite uncommon, with an estimated frequency of 2/100,000. According to epidemiology, females are 4-5 times more likely than males to have HE.[13] Hashimoto's encephalopathy is an autoimmune encephalopathy that is likely underdiagnosed. This is due to limited knowledge of the disease and the diverse range of clinical presentations.

Experimental studies to date have not confirmed a direct correlation between the ATAs and HE. Despite the high concentrations of the antibodies in the serum, little to no concentration has been found in the CSF or histopathological examination of the brain tissue. There is a possible association between anti-TPO antibodies and fibrosis of the thyroid gland, but not with anti-TG antibodies. Thus, these antibodies are considered markers

for autoimmune thyroiditis, not for HE.[3] Other proposed hypotheses include autoimmune vasculitis, cerebral hypoperfusion, and the harmful effects of TRH on the brain, but these lack supportive evidence.[4] Severe hypothyroidisms can lead to cerebral dysfunction, but there is no substantial evidence because most reported cases involve patients in euthyroid states.[5] Our patient exhibited subclinical hypothyroidism, which theoretically could account for the presenting symptoms; however, neurological diagnostics did not provide evidence supporting this correlation.

HE is a syndrome that manifests with a multitude of symptoms, like altered consciousness, disorientation, myoclonus, and seizures.[4] Atypical presentations like psychosis and catatonia with normal neurological findings have also been reported.[6] Seizures occur in the majority of cases of HE. In instances of refractory seizures with either focal or generalized presentation, Hashimoto's encephalopathy should be considered as a potential diagnosis.[7] Due to the lack of specific signs and symptoms in Hashimoto's encephalopathy (HE), its presentation can mimic other central nervous system disorders. Before confirming a diagnosis of HE, it is necessary to exclude conditions such as Creutzfeldt-Jakob disease, rapidly progressing dementia, vasculitis, paraneoplastic and non-paraneoplastic limbic encephalitis, and primary psychiatric illness.[8]

Laboratory investigations show increased anti-TPO and antithyroglobulin antibodies, which are part of the diagnostic criteria for HE (Table 2).[9] The sensitivity and specificity of the antibodies are still unremarkable. There are non-specific antibodies like NAE (against the N-terminal amino acid of alpha-enolase) that are present and are common to Creutzfeldt-Jakob disease (CJD).[10] Most of the patients have normal MRI findings. Few presents with findings such as ischemic lesions, demyelination, oedema, and atrophy in the hippocampus or temporal lobe.[11] EEG findings in our patient were normal, but there can be non-specific findings such as focal spikes or sharp waves and frontal intermittent rhythmic delta activity (FIRDA). CSF studies are mild but usually show elevated protein levels of no more than 100 mg/dl and mild lymphocytic pleocytosis.

All six criteria must be met for the diagnosis of Hashimoto's encephalopathy. Our patient presented with seizures and myoclonus alongside severe hypothyroidism, substantiated by the presence of antithyroid antibodies (ATAs). Normal findings on MRI plus the absence of other neuronal antibodies in the serum and CSF effectively excluded other potential diagnoses. These comprehensive evaluations definitively met the criteria for diagnosing HE. SREAT should be considered only after ruling out other relevant causes like infectious, metabolic, paraneoplastic, autoimmune, and toxic causes.

At present, the most effective treatment for this condition is either intravenous high-dose short courses of methylprednisolone (1 g/day) or oral prednisone 50–150 mg for three to seven days. To prevent recurrence, the dosage of prednisone is gradually reduced over several weeks to months.[12] The treatment response varies among patients, while the majority experience recovery within a timeframe ranging from hours to weeks. In refractory cases, azathioprine is combined with steroids.

Also, plasma exchange and intravenous immunoglobulin are used as alternatives for refractory cases. There is limited data to support the success of methotrexate and cyclophosphamide combination therapy.[13] The prognosis for patients with HE is generally good. Some patients have achieved spontaneous recovery without steroid treatment. Even without treatment, 25% of the patients experienced residual cognitive improvement. Following treatment, the majority of patients remain disease-free, with fewer relapses.[14] In young individuals presenting with altered sensorium, readily reversible causes like SREAT should always be considered.

CONCLUSION

Clinicians should maintain a high level of suspicion for SREAT, as it can present with a wide range of clinical symptoms. Diagnosis is largely one of exclusion, ruling out other infectious, inflammatory, autoimmune, and neoplastic causes, while noting elevated anti-TPO and/or anti-thyroglobulin antibodies. A positive response to steroid treatment strongly supports the diagnosis. Given that the condition is reversible, SREAT should be included in the differential diagnosis of central nervous system disorders, and treatment with steroids should be promptly initiated if SREAT is suspected.

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REFERENCES

1. Chiarello P, Talarico V, Nicoletti A, et al. Hashimoto encephalopathy: A case report and a short revision of current literature. Acta Biomed. 2020;91:34-57.
2. Canevini MP, Sgarzi M, De Sarro G, et al. Antiepileptic drug treatment in children with epileptic encephalopathies: A national consensus survey of the Italian League Against Epilepsy (LICE). Front Neurol. 2019;10:440.
3. Chaudhuri J, Mukherjee A, Chakravarty A. Hashimoto's encephalopathy: Case series and literature review. Curr Neurol Neurosci Rep. 2023;23(4):167-75.
4. Chong JY, Rowland LP, Utiger RD. Hashimoto encephalopathy: Syndrome or myth? Neurology. 2003;60(2):368-74.

5. Olmez I, Moses H, Sriram S. Diagnostic and therapeutic aspects of Hashimoto's encephalopathy. J Neurol Sci. 2013;331(1-2):67-71.
6. Joaquim AF, Gomes JG. Neuropsychiatric manifestations in autoimmune thyroiditis: A case report and literature review. Psychiatry Rep. 2023;5(1):100198.
7. Li J, Li F. Hashimoto's encephalopathy and seizure disorders. Front Neurol. 2019;10:440.
8. Ramalho J, Castillo M. Hashimoto's encephalopathy. Radiol Case Rep. 2015;6(1):445.
9. Ahmed OM, El-Gareib AW, El-Bakry AM, Abd El-Tawab SM, Ahmed RG. Thyroid hormones states and brain development interactions. Int J Dev Neurosci. 2008;26(2):147-209.
10. Ochi H, Horiuchi I, Araki N. Proteomic analysis of human brain identifies alpha-enolase as a novel autoantigen in Hashimoto's encephalopathy. FEBS Lett. 2002;528(1-3):197-202.
11. Waliszewska-Prosół M, Bladowska J, Budrewicz S, et al. The evaluation of Hashimoto's thyroiditis with event-related potentials and magnetic resonance spectroscopy and its relation to cognitive function. Sci Rep. 2021;11(1):2480.
12. Ferracci F, Carnevale A. The neurological disorder associated with thyroid autoimmunity. J Neuropsychiatry Clin Neurosci. 2006;18(1):14-20.
13. Mocellin R, Walterfang M, Velakoulis D. Hashimoto's encephalopathy: Epidemiology, pathogenesis and management. CNS Drugs. 2007;21(10):799-811.
14. Nunez J, Celi FS, Ng L, Forrest D. Multigenic control of thyroid hormone functions in the nervous system. Mol Cell Endocrinol. 2008;287:11-42.

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