Hashimoto Encephalopathy; A Great Masquerader: Report of Two Cases

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Abstract

Hashimoto encephalopathy (HE) is a constellation of syndrome of acute or subacute encephalopathy which is associated with elevated anti-thyroid antibody titers. It is a rare disorder associated with Hashimoto thyroiditis. We hereby present two such cases in a 35-year-old female and a 64-year-old male, both presenting with altered sensorium. In both the cases there were increased anti-thyroid peroxidase and anti-nuclear antibody titers. Both the cases were managed with high dose steroid and supportive management to which they showed good clinical response. The aim of presenting this report is an endeavor to highlight a rare cause of altered sensorium and cognitive decline in patients suffering with autoimmune thyroiditis. Though the exact pathophysiology of this disorder is not known, the use of steroids and thyroid hormone supplementation has reduced morbidity.

Keywords: Hashimoto Encephalopathy; Hashimoto Thyroiditis; Altered Sensorium; Steroids

Abbreviations


Introduction

HE is rare neurological disorder for which the exact cause is unknown though central nervous system vasculitis and autoimmune antibodies directed against brain-thyroid antigens has been postulated as the possible etiology [1]. HE may present as a sudden catastrophic vasculitic type or a more progressive sub-acute type associated with amnesia, confusion, cognitive dysfunction or even seizures [2]. It is believed to be an immune related disorder [3,4] rather than the direct effect of thyroid hormone on central nervous system. HE is also known by other less common terms like SREAT which suggests patient’s responsiveness to steroids [5] and a more common term NAM.
**Case Report**

**Case 1:** A 35-year-old female (Figure 1) presented with altered sensorium, reduced verbal output, reduced food intake, dysarthria, bladder incontinence of one week duration. There was history of myoclonic jerks and intermittent episodes of confusional state, inappropriate irritability with few amnesic episodes for last 6 months. Clinical evaluation revealed a GCS of E2M4V2. She was hemodynamically stable and had non pitting-pedal edema. However, there was no pallor, icterus, neck rigidity or rise in JVP. Neurologically she was moving all four limbs, had generalized hyper-reflexia with flexor plantar; CBC, LFTs, RFTs were normal. CSF was clear, sugar 80 mg/dl, protein 72 mg/dl. No increase in WBCs and RBCs was seen while dengue and Widal tests were negative.

![Figure 1: Case 1, 35-year-old female on presentation.](image)

TSH was 54.51 uIU/ml (0.4 - 6), T3 0.72 ng/ml (0.6 - 1.8), T4 9.10 ug/dl (5.6 - 13.7), TPO was 280.5 uIU/ml (normal < 30 uIU/ml) while ANA titre was positive. EEG and MRI brain showed normal study. In view of the clinical profile and raised TSH and TPO antibodies, patient was managed as a case of HE with oral loading Eltroxin 400 ug followed by 125 ug daily and parenteral hydrocortisone 100mg every eight hourly. Patient showed remarkable response to therapy and her condition improved within a week.

**Case 2:** A 64-year-old male (Figure 2), a known case of hypertension and type-2 diabetes mellitus on regular medication presented with altered sensorium. There was history of ataxia, diminution of vision for last one month. The patient had tendency to fall on either side while walking and had difficulty in walking in a straight line. Evaluations were suggestive of cortical blindness. Gradually, his sensorium deteriorated and he started speaking irrelevant and developed social disinhibition in the form of urinating in public and using abusive language. There was history of myoclonic jerks.

Investigations revealed normal CBC, LFTs, RFTs and blood sugar profile. His thyroid profile was normal. However his anti TPO was 432.5 uIU/ml. MRI and MRA brain were normal. ANA titres were raised. USG neck showed a normal thyroid gland. The possibilities considered were posterior circulation stroke, HE or Creutzfeldt Jacobs disease. Patient was started on antiplatelet drugs, intravenous methyl prednisolone, insulin and other supportive drugs. Patient’s condition gradually improved.

Discussion

HE is a rare neurological disorder with an estimated prevalence of 2/100,000 people [6] for with the exact mechanism is yet unknown [1]. The disease primarily affects females in fifth and sixth decade. It may present as a sudden catastrophic vasculitic type or a more progressive sub-acute type associated with amnesia, confusion or cognitive dysfunction. However, most of the evidence suggests it to be an autoimmune vasculitis or an inflammatory process involving deposition of immune complexes in cerebral microvasculature [7]. It may result from antibody mediated neuronal injury mostly against the amino terminal end of the enzyme alpha enolase [1,7]. Brain biopsy reveals lymphocytic infiltration around small arterioles and venules [2,8]. As in other autoimmune disorders, the prevalence of HE is four times more common in females than males [9].

There are various patterns of presentation of HE. It can present as an acute stroke-like syndrome with focal neurologic deficits or a more insidious presentation [5,10] with a varying degree of cognitive dysfunction and alteration of consciousness [1,3]. It may present with a slowly progressive cognitive impairment with dementia and confusion. Some cases have a more fulminant presentation in which rapid deterioration to coma occurs [11]. Elevated serum levels of TPO Ab and or Tg Ab form an essential laboratory feature of HE. However, the rise in antibody titre is not directly proportional to the neurological damage [1].

These antibodies were detected both in serum and CSF. Antibodies against the amino terminal end of the enzyme alpha enolase have been identified as a biomarker for HE. These autoantibodies are against an antigen of thyroid and brain. In the brain these antigens are

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found in the endothelial cells suggesting autoimmune vasculitic mechanism. Thyroid hormone levels are not diagnostic. Only 20% of cases have overt hypothyroidism [1,2,10]. CSF is abnormal in 80% of cases, mostly as an increase in protein levels [11]. Electroencephalography reveals nonspecific findings usually demonstrating nonspecific slowing of background activity.

Neuroimaging generally shows multifocal bilateral cortical and subcortical abnormalities [12]. Although usually non-contributory, the diagnosis of HE requires the fulfillment of the following criteria: (1) encephalopathy manifested by cognitive impairment, hallucinations, delusions, myoclonus, generalized tonic-clonic or partial seizures and focal neurologic deficits, (2) presence of serum thyroid antibodies against TPO or Tg, (3) euthyroid status (4) no evidence of infection, toxic or metabolic or neoplastic process, paraneoplastic disease, (5) normal neuroimaging and (6) positive response to steroid. All these conditions were seen in both our cases.

Conclusion

The presentation of HE can be easily confused with any illness associated with a syndrome of delirium, confusional state or rapidly progressive dementia like Creutzfeldt- Jakob disease, ADEM, meningoencephalitis carcinomatous meningitis, toxic encephalopathy, paraneoplastic encephalitis, degenerative dementia, cerebral vasculitis, stroke or transient ischemic attack or basilar or hemiplegic migraine. Sporadic case reports and few case series [13] have described this disorder with an aim to elucidate its clinical and therapeutic implications. The mainstay of management remains corticosteroid treatment and thyroid supplementation. The dose of oral prednisone ranges from 50 mg to 150 mg daily [10]. High-dose intravenous methylprednisolone has also been tried in a few patients, however, no additional benefit has been found in these patients. However, oral thyroid supplementation and conservative management with antiepileptics and antipsychotics without steroids have let to satisfactory treatment of HE in few patients [14]. Intravenous immunoglobulins (IVIG) might represent an efficacious treatment modality for the steroid-resistant or steroid-refractory HE cases [15].

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Ethical Approval

Written informed consent to publication was obtained from the patient.
The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.
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Conflict of Interest

Nil.

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Bibliography


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