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A Case of Hashimoto Encephalopathy Presented with Seizure

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ABSTRACT

Hashimoto encephalopathy (HE) is a steroid-responsive but relapsing neuropsychiatric disorder associated with high titers of anti-thyroid antibody with or without thyroid dysfunction. Though numerous neurological manifestations are often associated with thyroid disorder, this entity is less documented. We are reporting a case of HE in a 63 year old female presenting with sudden onset focal seizure following an attack of mild fever. Other causes of vascular, infective, metabolic, autoimmune and toxic encephalopathy were excluded. MRI of brain revealed oedematous gyri of left medial temporal lobe with diffuse age related brain atrophy. Patient's thyroid function tests were normal but anti-thyroid peroxidase (anti-TPO) antibody was significantly raised. EEG showed diffuse slow wave pattern. After suspecting diagnosis of HE, Intravenous methylprednisolone (one gram) given for five days. Patient regained consciousness slowly over a period of one week. HE must be kept in mind in comatose patients when other metabolic, infective and structural neurological causes have been excluded. Proper and timely treatment can salvage the patient.

KEYWORDS

Introduction

Hashimoto's encephalopathy (HE) is an uncommon relapsing neuro-endocrine disorder more common in women which is associated with Hashimoto thyroiditis (HT) with high titers of anti-thyroid antibodies. The disorder is reported rarely in India as well as world literature. Clinical presentation of this relapsing-remitting disease include seizures, stroke-like episodes, cognitive decline, neuropsychiatric symptoms and myoclonus.

Case Report

A 63 year old Hindu female from Ahmedabad city presented with sudden onset focal seizure involving right upper and lower extremities followed by unconsciousness for two days with preceding history of mild grade fever. She was a known patient of hypothyroidism and diabetes and having history of ischemic stroke 3 years back which was recovered. Her family history was unremarkable.

On the day of admission, patient was completely comatose. Glasgow Coma Scale (GCS) score was 3/15. Her pulse rate was 82/min, regular. Blood pressure was 136/90 mm of Hg. Respiratory rate was 22/min. Pallor, cyanosis and icterus were absent. On neurological examination, pupils were symmetrical and bilaterally reacting normally to light. There was no facial asymmetry. Light reflex, doll's eye reflex and gag reflex were normal. Neck rigidity was absent. Planter reflex was flexor. Deep tendon reflexes were preserved. There was no thyroid swelling in the neck. Examination of other systems revealed no abnormality.

During routine investigation, blood picture revealed hemoglobin 10.8 gm/ dl, total leucocyte count (TLC) 12900/cu mm, with neutrophil 88%, lymphocyte 10% and eosinophil 2%. Biochemical tests revealed random blood sugar 109 mg/dl, serum urea 22mg/dl, creatinine 0.69mg/dl, sodium 136 mEq/l and potassium 5.4mEq/l. Hepatic profile, ECG, Chest X-ray and Bed-side 2-D Echo was normal. Ultrasonography of abdomen was normal. Initially IV Antibiotic (Ceftriaxone and Vancomycin) was given and we started further investigations to find out the cause of encephalopathy. Arterial Blood Gas analysis revealed no hypoxia. Magnetic resonance image (MRI) of brain revealed oedematous gyri of left temporal lobe which was hyperintense in T2W and FLAIR images with age related cerebral and cerebellar atrophic changes. Electro-encephalography (EEG) revealed characteristic diffuse slowing (without any focal epileptiform discharge) suggestive of encephalopathy. Other investigations to rule out different causes of encephalopathy depicted in table.

After investigation clinically Hashimoto encephalopathy suspected and intravenous methylprednisolone (1g daily for five days) started along with antibiotics and she responded dramatically. Initially the eye opening returned and gradually motor response also improved. On fifth day of steroid therapy, spontaneous eye opening was present. On eighth day the motor function improved to withdrawal on pain stimulus and over-all GCS score improved to 10/15. Patient was discharged with oral steroids in tapering doses.

Investigations	Result
RPR	Non-reactive
Widal	Non-reactive
HbsAg	Non-reactive
Malaria antigen	Negative
C-Reactive Protein	Negative (<0.6 mg/dl)
HIV	Non-reactive
HbA1C	6.4 %
RA Factor	Negative
ESR	39mm hg
S. Ammonia	12micromol/L (Normal)
Dengue Ns-1 Antigen	Negative
ANA	Negative
CSF Examination	Protein – 29.12 mg% (15-45) Glucose – 90.43 mg% (40-70) Total cells 10/cmm (Up to 10) No organism and AFB seen.

Thyroid Profile	
TSH	2.1641 microIU/mL (0.49-4.67)
Total T3	0.82 ng/mL (0.79-1.49)
Total T4	7.21 microgram/dL (4.5-12.0)
Anti TPO Antibody	360 U/mL (up to 60)

Discussion

HE was first described by Brain et al in 1966.[1] Other names for this disorder include steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) and non-vasculitic autoimmune meningo-encephalitis (NAIM). Average age of onset for HE is 47 years (range 14 to 78 years) and majority of patients are women. Presence of goiter or a positive family history for thyroid dysfunction may be present. Two types of clinical presentation are commonly observed. First type is acute stroke-like presentation with transient focal neurologic deficits which was present in our patient. It may be associated with speech problems (transient aphasia), focal or generalized seizures and status epilepticus. Second form is of insidious onset, progressing to dementia, psychosis and coma over several weeks without any focal neurologic deficits. Associated features include lack of concentration, sleep abnormalities, headaches, tremors, myoclonus and ataxia. Differential diagnosis for the disorder includes Alzheimer's disease, cerebrovascular accidents (CVA), Creutzfeldt-Jakob disease, HIV and other viral encephalitis.

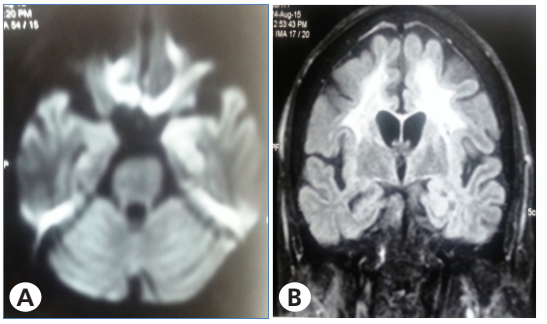
Exact pathogenesis of HE is unknown. It is considered to be an autoimmune encephalopathy because of its higher prevalence in females, fluctuating course, association with other autoimmune disorders and improvement with corticosteroid therapy. It is associated with anti-TPO and anti-thyroglobulin (anti-TG) antibodies, but the precise role of antithyroid antibodies is still unclear. No shared antigen has been identified between thyroid gland and brain.[2] Antithyroid antibody titers also do not correlate with disease severity. Thyroiditis and encephalopathy may represent two concurrent autoimmune diseases. Presence of other auto-antibodies, such as anti-parietal cell antibody or anti-intrinsic factor antibody has also been reported in patients with HE. Alpha-enolase (isoenzyme of enolase, a glycolytic enzyme) has been identified as an auto-antigen for the disease.[3]

Patients of HE may have subclinical, overt hypothyroidism or patients may be euthyroid.[4] Liver enzymes and ESR may be elevated. Serum ammonia level may be elevated especially in presence of hypothyroidism.[5] In our patient ammonia, thyroid function and liver function tests were normal. CSF may reveals elevated protein level with occasional mononuclear pleocytosis.[6] Normal CSF examination may be present in up to 25% of cases. EEG shows diffuse or generalized slowing or frontal intermittent rhythmic delta activity. Prominent tri-phasic waves, focal slowing, epileptiform abnormalities, photo-paroxysmal and photomyogenic responses may be seen. EEG features usually revert to normal after steroid therapy. Anticonvulsant therapy does not improve epileptiform abnormalities and even worsen EEG features. MRI may be normal or reveal nonspecific findings, such as diffuse cerebral atrophy, focal mesio-temporal, basal ganglia or white matter abnormalities. Cerebral angiograms and Doppler ultrasound of cerebral vessels are usually normal.

Patients with HE respond dramatically to steroid therapy. Initial dose varies between 50 mg and 150 mg of oral prednisolone daily, slowly tapered over weeks to months depending on clinical course of the disease. High dose intravenous methylprednisolone (1 gm / day) may also be given for initial three to seven days followed by oral prednisolone tapering therapy. Rapid improvement can be observed within three days but significant clinical improvement may take average four to six weeks. Most patients stay in remission even after discontinuation of treatment. In some patients, treatment may be required lifelong. Azathioprine, cyclophosphamide, chloroquine, methotrexate may be used as steroid sparing agent. Periodic intravenous immune globulin and plasma exchange are other therapeutic options.[7] Our patient had sudden onset focal seizure followed by unconsciousness with initial examination revealing focal neuro-deficit. Infective causes were ruled out (malaria, enteric fever and meningo-encephalitis). Magnetic resonance image (MRI) of brain revealed hyperintense gyri of left temporal lobe in T2W and FLAIR images which was due to posi-ictal oedema. Presence of anti-TPO antibody in high titer, charasteric EEG finding with Dramatic response to steroid clinched the diagnosis of HE.

Conclusion

HE is probably under reported as a cause of altered sensorium. Very high level of awareness is needed to diagnose this uncommon entity because of its rarity, variety of presentations and high chance of misdiagnosis. It is important to recognize HE as it is potentially reversible and treatment is cheaper. It should be suspected in any cause of coma or cognitive dysfunction which remains undetected despite through investigation or when any neuropsychiatric condition is not responding to conventional therapy especially in the setting of probable or known autoimmune thyroiditis. The disease is highly responsive to steroid. However, more common causes of encephalopathy, such as infections, electrolyte imbalance, toxins and neoplasms must be excluded before steroid therapy is initiated.



MRI Brain of patient A. T2 weighted diffusion transverse scan shows hyperintensities in left medial temporal lobe. B T2 wighted coronal scan shows hyperintensity in left temporal lobe with periventricular hypodensities.

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