Case Report

# A case of Steroid Responsive Encephalopathy associated with Autoimmune Thyroiditis: A Diagnostic Dilemma

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## Abstract

We present a case of 42 year-old female, who presented with generalized tonic-clonic seizures with altered sensorium, not responding to antiepileptic medications. She was a diagnosed case of hypothyroidism since last three years and was on replacement therapy. Her systemic examination including the neurological examination did not point to any specific diagnosis. Her routine investigations, brain imaging and CSF analysis were also within normal limits. Thyroid function test revealed raised thyroid stimulating hormone and anti-TPO antibody with normalT4 and T3 levels. Here we considered diagnosis of "Encephalopathy Associated with Autoimmune Thyroid Disease". She was given intravenous methylprednisolone pulse to which she responded dramatically and seizures were controlled. She was discharged on oral anti-epileptics and steroids in a stable condition.

**Keywords:** Thyroid, Seizures, Encephalopathy

## Background

Hashimoto's encephalopathy or *Encephalopathy Associated with Autoimmune Thyroid Disease or SREAT (steroid responsive encephalopathy associated with autoimmune thyroiditis)* is a diagnosis of exclusion. The disease is related to thyroid autoimmunity and does not correlate well with the thyroid functional status. It has a wide range of clinical presentations in form of neuropsychological episodes but convulsive status epilepticus is very rare presentation like in our case. This case highlights the importance of doing thyroid function test and anti TPO antibodies in all patients with unexplained encephalopathy as treatment response is excellent.

## Case Presentation

A 42 year old female, presented to our emergency department with 15 days history of recurrent generalized tonic-clonic seizures, 3 to 4 episodes in a day with three days history of altered sensorium. There was history of urinary incontinence, tongue bite and post-ictal confusion.

The generalised tonic-clonic seizure episodes were followed by altered sensorium. There was no weakness of any limbs. Also there was no history of fever, headache, nausea, vomiting, abdominal pain, loose motion, jaundice, decreased urine output, oral ulceration, joint pain, skin rashes, photosensitivity, decreased appetite, or weight loss. She was a known case of hypothyroidism and was taking 75 mcg of thyroxine for last three years. There was no past history of similar

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episode, head trauma, diabetes mellitus, hypertension, or tuberculosis. No history of recent vaccination or animal bite. Patient was initially admitted in private hospital where she went into status epilepticus and was put on ventilator. She was given intravenous antiepileptic along with other medications. Patient was extubated on third day of admission but seizures did not stop completely even after adding three antiepileptic drugs. The relatives left against medical advice from that hospital and brought her to our hospital.

In our hospital, she was delirious and disoriented to time, place and person. She had no pallor, icterus, cyanosis, clubbing, lymphadenopathy or pedal edema. Jugular venous pressure was not raised. The blood pressure and pulse rate were 110/80 mmHg and 84 beats per minute respectively. There was no thyromegaly. On central nervous system (CNS) examination the Glasgow coma scale was 5 out of 15. The cranial nerves could not be examined. Fundus examination of both eyes were normal. Direct and consensual light reflex with vestibulo-ocular reflex were present and normal. Muscle tone was bilateral symmetrical in all four limbs. The power was 2+/5, and deep tendon reflexes were 2/4 in all four limbs. Bilateral plantar reflex were flexor. There was no neck rigidity. Sensory and cerebellar system examination could not be examined. Other systemic examination like cardiovascular system and respiratory system were normal.

## Investigations

The complete blood count, liver function, kidney function and serum electrolyte were within normal limits. Malaria antigen test was negative.Typhidot-IgM test was negative. Cerebrospinal fluid (CSF) was clear with normal opening pressure, and total leukocyte count of 5 cells (all lymphocyte). The protein and sugar level in CSF were 24 mg% and 88 mg% respectively. CSF serology was negative for Japanese encephalitis virus, herpes simplex virus, and enterovirus.CSF examination by Ziehl Neelsen stain was negative for acid fast bacilli. Adenosine deaminase level in CSF was normal too. Serum ammonia level was in normal range. Serology for HBsAg, anti HCV, HIV and VDRL were also non-reactive. Anti-nuclear antibody was also negative. Non-contrast CT scan of head (figure 1) and MRI brain (figure 2) did not reveal any abnormality.

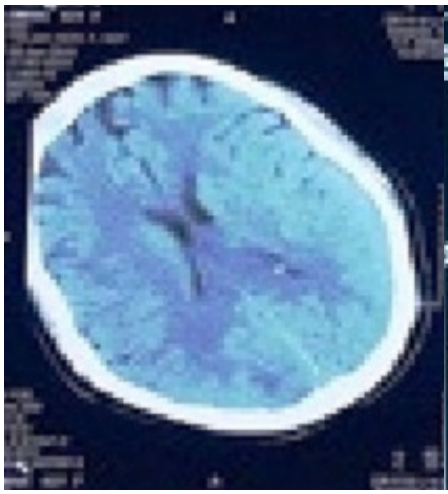

**Figure 1.NCCT head was normal**

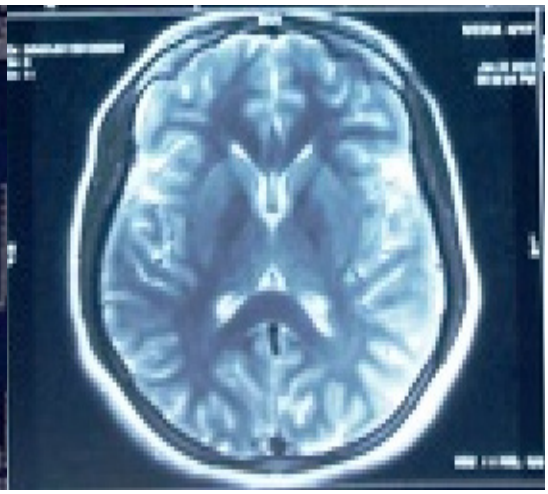

**Figure 2.MRI brain too was normal**

Thyroid function test was done which showed an elevated serum TSH levels of 16.3 µU/ml (normal range 0.5-5.5 µU/ml). The serum T4 and T3 levels were6.35 µgm/100ml (normal range, 5.1-14 µgm/100ml) and 0.8ng/ml (normal range 0.8-2.0 ng/ml) respectively. Anti-thyroid peroxidase antibodies (anti-TPO) level were markedly raised to more than 1300 IU/ml (normal level is less than 34 IU/ml).Electro-encephalography (EEG) showed frequent, generalized, sharp-and-slow wave discharge(figure 3).

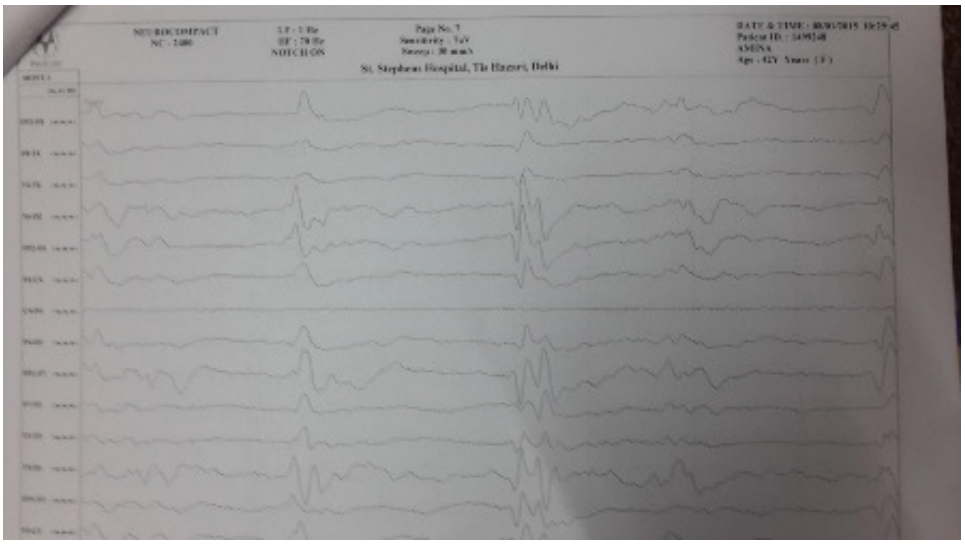

Figure 3.EEG showing low amplitude wave with frequent, generalized, sharp-and-slow waves

## Treatment

The patient was initially started on empirical treatment with injection ceftriaxone, acyclovir, sodium valproate, levetiracetam, sodium phenytoin, and tablet thyroxine. Once we got the report of raised TSH and anti-TPO, intravenous methylprednisolone 1g/day for 3 days was given followed by oral prednisone 1mg/kg/day with a plan to gradually taper off the steroid along with oral anti-epileptic drugs.

## Outcome and follow-up

She responded dramatically after the initiation of steroids. Initially, spontaneous eye opening was noticed on third day, followed by improvement in motor power. Verbal command also improved after 1 weeks. Seizure episodes also stopped during hospital stay. She was discharged with oral prednisolone 40 mg/day along with tablet levetiracetam, clobazam and thyroxine.

On follow-up as an outpatient, she had been symptom-free for 1 month and has only one episode of seizure episode. However, the seizures reoccurred while tapering the steroid dose to 15mg/day in fourth month of follow up. A repeat thyroid function test, which included serum T3, T4 and TSH, done at six months of follow up, was in normal range. The anti-TPO had decreased from more than 1300 IU/ml to 57 IU/ml at six month. She is asymptomatic at dose of 20mg/day of prednisolone, 75 mcg/day of thyroxine along with above antiepileptic drugs.

## Discussion

Hashimoto's encephalopathy was first described in 1966 by Brain and colleagues. [1] It is associated with autoimmune thyroiditis. It is also seen in euthyroid state or after the correction of hypothyroidism. The average age of onset is 47 years (range 14 to 78 years), and approximately 85% of the patients are women. Hashimoto's encephalopathy is always a diagnosis of exclusion. The clinical symptoms are nonspecific, the onset being acute, subacute or chronic with a variable disease course, self-limiting, progressive or relapsing-remitting.[2] While reviewing the literature, we found that the patients with Hashimoto's encephalopathy have presented with manic symptoms, acute psychosis, chronic hallucination, depression, status epilepticus, amnestic syndrome, progressive cerebellar ataxia, dementia, and declining upper brain function.[3-11]The exact pathogenesis is not known for sure, but a few mechanisms have been postulated like autoimmune cerebral vasculitis, toxic effect of thyroid stimulating hormone on the CNS or antibodies-induced neuronal hyper-reaction. There are no specific diagnostic test. The TSH and T4 levels are found to be abnormal in 80% of cases. A positive antithyroid antibody titre is necessary. Majority of the patients will have positive serum anti-TPO while a few may have anti-Thyroglobulin antibodies. However the thyroid autoimmunity does not correlate well with the thyroid functional status.In a review article, 23 to 35% patients had subclinical hypothyroidism, 17 – 20% had overt hypothyroidism, 7% had hyperthyroidism and 18 – 45% were euthyroid. [12]

Biochemical, radiological or cerebrospinal fluid examination may show nonspecific findings. CSF may reveal a mononuclear pleocytosis and elevated protein but glucose level is always in normal range. The titre of antithyroid antibodies can also be measured in the CSF. However, the titres of antithyroid antibodies in the CSF do not correlate with the clinical stage of the disease, and sensitivity and specificity of these finding remain unclear. EEG shows nonspecific, intermittent slow wave activity. MRI brain usually reveals nonspecific findings, such as bilateral subcortical high intensity lesions on T2 images or mild cerebral atrophy. Patients with Hashimoto's encephalopathy respond dramatically to steroid therapy.


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[13]Majority of the patients will achieve remission and will not require prolonged steroid treatment. However, some patients may require lifelong fixed low-dose of steroid to prevent recurrence as in our case. Steroid-sparing agents like azathioprine, cyclophosphamide, chloroquine, and methotrexate may be used in place of steroids if patients do not tolerate or are not responding to steroids.

Our patient presented with recurrent episodes of generalised tonic-clonic seizures without gaining consciousness. There was no history of fever to suggest any infective etiology. Examination did not point to a specific diagnosis either. The biochemical, pathological, microbiological tests and imaging of brain were particularly negative for infectious cause of status epilepticus. However elevated TSH, anti-TPO levels together with typical EEG findings clinched the diagnosis of Hashimoto's encephalopathy. A dramatic response after giving steroid pulse also supported our diagnosis.

## Conclusion

It is important to recognize Hashimoto's encephalopathy in comatose patient with thyroid diseases it is reversible. It should be suspected in any case of coma or cognitive dysfunction which remains undetected despite thorough investigation when other metabolic, infective and structural neurological causes have been excluded. The disease is highly responsive to steroid therapy so timely treatment can salvage the patient.

## Conflict of Interest: None

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