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CASE REPORT

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# Hashimoto's encephalopathy masquerading as affective illness: a case report

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## Abstract

**Background:** Hashimoto's encephalopathy (HE) is a rare but controversial syndrome showing a variety of neurological and psychiatric manifestations associated with autoimmune thyroiditis.

**Case presentation:** We present a case of 46-year-old hypertensive female who developed acute onset of behavioral symptoms mimicking affective disorder (mania). Investigations revealed high levels of anti-thyroid peroxidase antibodies with elevated thyroid-stimulating hormone. EEG and MRI findings were consistent with those seen in Hashimoto's encephalopathy. She showed excellent response to high dose corticosteroids that helped in making the diagnosis of Hashimoto's encephalopathy.

**Conclusions:** Hashimoto's encephalopathy is an extremely important, though rare, diagnosis. It should be suspected and screened for in patients with encephalopathy of unknown origin because responses to treatment are usually excellent.

**Keywords:** Hashimoto's encephalopathy, Affective illness, Anti-thyroid peroxidase antibodies, Corticosteroids

## Background

Hashimoto's encephalopathy [HE] is a neurological disorder of unknown cause associated with thyroid autoimmunity. The disorder was first outlined by Brain et al. in 1966 [1]. HE is mostly seen in adults with a female preponderance in the ratio of 4:1 to 5:1 [2]. The prevalence of this syndrome has been estimated to be about 2.1 per 100,000 [3]. Female predominance, auto antibodies, relation with other autoimmune diseases, fluctuating clinical course, and response to immunosuppressive therapy, all suggest an autoimmune nature of the disease. The clinical manifestations of HE vary from stroke-like attacks, memory lapses, ataxia, seizures myoclonus, tremor, sleep abnormalities, gait difficulties, and cognitive impairment to psychiatric manifestations [4, 5]. Peschen-Rosin et al. [6] described the criteria for the diagnosis of Hashimoto encephalopathy as unexplained episodes of relapsing neurologic symptoms and at least 3 of the following: abnormal EEG; positive anti-TPOAb; elevated CSF protein; excellent response to steroids; and normal head MRI findings. The disorder has also been called SREAT (steroid responsive encephalopathy associated with autoimmune thyroiditis) [7, 8]. The exact etiology of Hashimoto's encephalopathy is still uncertain. The major mechanisms speculated in pathogenesis of HE include vasculitis, autoimmunity and deregulatory influence of some hormones excessively produced in response to hypothyroidism. We could find only isolated case reports of HE in the literature and most of such cases had neurological manifestations rather than psychiatric. Our case is unique as the patient presented with pure psychiatric symptoms. Also, there were some atypical features and newer symptoms developed during her hospital course which made us to think on alternative lines and evaluate the patient further.

## Case presentation

The patient is a 46-year-old female with a history of hypertension, who presented with a 1 week history of excessive and irrelevant speech, irritable mood, use of

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abusive words against her family, suspiciousness that people are plotting against her, agitation, and decreased need for sleep. Her family reported a history of fever before admission. The patient had no past history of any psychiatric illness and no family history of affective disorders.

On general appearance and physical examination, the patient was agitated, talking excessively, was oriented to time, place and person, with heart rate of 86/min, blood pressure of 140/90, respiratory rate of 15/min, temperature of 36.7 °C and oxygen saturation of 97% on room air. There were no focal sensory or motor deficits. Cranial nerves were intact and pupils were bilaterally symmetrical and reacting normally to light stimulus. There were no signs of meningeal irritation. Superficial and deep tendon reflexes were intact. Strength was 5/5 in proximal and distal muscles of upper and lower extremities bilaterally with normal tone and bulk. There were no abnormal movements. Sensory examination was normal. Both planters were down going. She was not taking any medications at the time of her admission.

In mental status examination, the patient had increased psychomotor activity, elevated mood, excessive talkativeness, flight of ideas, elevated self-esteem, hyper-religiosity, and poor insight.

The patient underwent psychometric assessment using young mania rating scale and the score was recorded as 35 which identified the current illness as a manic episode.

Her baseline laboratory evaluation showed total White blood cells of 58,000 with 62% neutrophils, hemoglobin of 8.7 gm/dl with microcytic hypochromic picture and platelets of 3.37 lakh/µl. Serum sodium was 137, serum potassium 4.2, and random blood glucose level was 116 mg/dl. Her serum thyroid-stimulating hormone level was 8.89 mIU/L with free triiodothyronine (T3) and thyroxine (T4) levels of 1.33 pmol/L and 4.1 pmol/L respectively suggestive of subclinical hypothyroidism.

The patient was treated with mood stabilizer, sodium valproate and anti-psychotic drug, and olanzapine. The patient showed no significant improvement in her signs and symptoms after 2 weeks. The patient developed transient episodes of disorientation associated with inappropriate agitated behavior and sleep disturbances during hospital stay. These episodes used to last for about 2–3 h and occurred almost every day. Patient was started on 600 mg of carbamazepine in two divided doses and risperidone 6 mg, which she received for almost 10 days with no response. Electro-convulsive therapy (ECT) was finally planned. The patient received five sessions of modified ECT (m-ECT) but her condition deteriorated and she started to develop delirious episodes post her m-ECT. M-ECT sessions were put on hold and extensive workup was done to rule out any organic cause. Her dose of risperidone was tapered to 2 mg and clonazepam 0.5 mg was added so that her delirious episodes may settle. Her attendant also gave history of memory lapses and confusion in patient but, on several mental status examinations, her memory was found to be intact. Her Mini Mental Status Examination score was 27/30 which is normal.

Magnetic resonance imaging (MRI) was done which revealed bilateral periventricular white matter hyperintensities with multiple T1 /T2 hyperintense foci found in bilateral cerebral and cerebellar hemispheres, basal ganglia region, and brainstem suggestive of microhemorrhages.

Electroencephalogram (EEG) showed background rhythm consisting of alpha activity with intermittent central theta discharges. A second repeat EEG was done to rule out seizure episodes during hospital stay and that showed occasional generalized slowing.

Thyroid peroxidase antibody titer was positive at 130 IU/ml with negative serum autoimmune encephalitis panel, ANA, and anti-dsDNA. ESR was raised to 73 mm/h, C-reactive protein (CRP) was 0.6 mg/dl, triple serology was negative, and serum ammonia was 47 µg/dl. Examination of CSF was normal. CSF Acid fast bacillus, bacterial stain, cultures, and viral panel including HSV1 were negative. Also, CSF electrophoresis was negative for oligoclonal bands.

Keeping in view, no response to conventional treatments for mania, high titers of anti-TPO antibodies, raised TSH, normal MRI brain, normal CSF analysis, intermittent slowing on EEG, negative screen for autoimmune disorders, treatment was started for Hashimoto's encephalopathy.

The patient was treated with high-dose methyl prednisolone 1 gm/day (intravenous pulse steroid therapy) for 3 days. It was given as an infusion over 1 h and vitals were monitored. The treatment induced a rapid improvement in her mental status and behavioral changes. The course of pulse therapy was followed by oral prednisolone 30 mg/day for 3 weeks followed by 20 mg/day for 4 weeks. No treatment was given for subclinical hypothyroidism.

After 6 weeks of follow-up, patient was doing well on 20 mg of prednisolone, 600 mg/day of carbamazepine, and 2 mg of risperidone. Her dose of prednisolone was further tapered to 20 mg alternate days while risperidone was stopped and only carbamazepine was continued. Her anti-TPO, thyroid profile, CBC, and ESR were repeated and the results showed anti-TPO level of 43.77 IU/ml, free T3 2.76 pmol/L, free T4 4.69 pmol/L, and TSH 1.78 mIU/L. Hemoglobin was 9.5 gm/dl and erythrocyte sedimentation rate 37. There was thus a significant decline in titers of autoimmune markers after treatment.

## Discussion

HE is considered a diagnosis of exclusion and relevant toxic, infectious, metabolic, neoplastic, and other neuronal antibody syndromes have to be excluded before making a diagnosis and initiating treatment. Our patient's symptomatology, negative metabolic, infectious and autoimmune encephalitis workup and presence of anti-thyroid peroxidase antibodies with elevated TSH were appropriate for making a diagnosis of Hashimoto's encephalopathy. The patient was treated with high-dose methyl prednisolone 1 gm/day (intravenous pulse steroid therapy) for 3 days. The treatment induced a rapid improvement in her mental status and behavioral changes. The episodes of delirium also stopped. Her suspicious behavior and agitation improved to a significant degree. We observed a slightly higher reading in her blood pressure during pulse steroid therapy. Other than this, there were no side-effects. The course of pulse therapy was followed by oral prednisolone 30 mg/day followed by gradual taper. The pathophysiology of Hashimoto's encephalopathy is thought to be autoimmune molecular mimicry. It is hypothesized that antibodies targeted against thyroid tissue also react with antigens present in brain, thereby high serum levels of anti-TPO, anti-thyroglobulin, and anti-TSH are seen in HE [3]. We also found high titers of anti-TPO antibodies in our patient along with elevated TSH levels which reduced significantly after steroid therapy.

The currently accepted treatment modality for HE is the use of corticosteroids in addition to the treatment of any concurrent dysthyroidism. We did not treat subclinical hypothyroidism of the patient and her symptoms resolved with steroids only. The reduction in TSH on repeat testing was likely due to steroid effect. Generally, the symptoms improve or completely resolve over a few months. The majority of cases respond to glucocorticoid treatment with initial high dose pulse methylprednisolone infusion given daily for 3–7 days, followed by oral prednisolone 1–2 mg/kg/day for 6 to 8 weeks [9]. The dose is afterwards gradually reduced. Cases not responding to steroids are treated with second line therapies which include plasma exchange, and intravenous immune-globulins (IVIG) therapy. Immunosuppressive drugs like cyclophosphamide, azathioprine, and mycophenolate mofetil are added in more resistant cases or as steroid sparing agents. In a study done by Tran et al., plasma exchange therapy resulted in profound improvement of the patients' symptoms [10].

The treatment of patients of HE such as our case remains a challenge and literary guidance is scarce. These patients present with a diffuse encephalopathy with mostly mental status changes and sometimes without any alteration in level of consciousness. Their symptoms are a combination of affective disturbances, psychosis, and varying cognitive and intellectual impairments. These patients are thought to have anti-neurotransmitter receptor encephalopathy with disruption of synaptic transmission. This is the rationale for using anti-depressants for depression, mood stabilizers for affective illnesses, and anti-psychotics for psychosis. We also did the same in our patient and continued carbamazepine as mood stabilizer in her in addition to oral corticosteroids [11].

## Conclusions

HE frequently presents with a myriad of neurocognitive symptoms with normal findings on routine clinical examination in the majority. The disorder may go unnoticed for a long time. Hence, this syndrome should be kept in mind when evaluating a patient with cognitive dysfunction and high titers of anti-thyroid antibodies because responses to treatment are typically excellent.

#### Abbreviations

HE: Hashimoto's encephalopathy; EEG: Electroencephalogram; TPO: Thyroid peroxidase; CSF: Cerebrospinal fluid; TSH: Thyroid-stimulating hormone; HSV: Herpes simplex virus.

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#### Authors' contributions

Dr. Arjuman Fayaz provided case information and wrote major sections of the manuscript. Dr. Yuman Kawoos edited the manuscript and wrote the discussion. Dr. Irfan Ahmad Shah helped in finalizing the diagnosis in this case and management plan of the patient. Dr. Yasir H. Rather finally approved the manuscript and provide his expertise in management. All authors read and approved the final manuscript.

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## Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

We obtained written informed consent from the patient and her attendant regarding publishing this data maintaining confidentiality of the patient in all respects.

#### Competing interests

The authors declare that they have no competing interests.

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## Publisher's Note