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A CASE REPORT ON HASHIMOTO'S ENCEPHALOPATHY

Naga Lakshmi Netuluri[1]*, Naveen Kumar Naik Ramavathu[1], Venkata Rohit Kumar Chandolu[2], Bhuvana Boppudi[2], J. N. Suresh Kumar[3] and Ch. Siva Rama Krishna[4]

[1]V. Pharm. D Students, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopeta, Guntur (Dist), Andhra Pradesh, India, 522601.

[2]Assitant Professors, Department of Pharmacy Practice, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopeta, Guntur (Dist), Andhra Pradesh, India, 522601.

[3]Department of Pharmaceutics, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopeta, Guntur (Dist), Andhra Pradesh, India, 522601.

[4]Department of Neurology, Guntur City Hospital, Guntur, Andhra Pradesh, India, 522601.

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***Corresponding Author**
Naga Lakshmi Netuluri
V. Pharm. D Students, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopeta, Guntur (Dist), Andhra Pradesh, India, 522601.

ABSTRACT

Introduction: Ashimoto's encephalopathy (HE), also known as steroid- responsive encephalopathy, is associated with autoimmune thyroiditis and presents with encephalopathy and elevations in anti-thyroid antibodies without brain tumor, stroke, or infection of the central nervous system. It is a rare clinical entity, which presents with unspecific neurological symptoms. The syndrome is more common in women, and is associated with autoimmune antithyroid antibodies. Presentation varies considerably; there may be episodes of cerebral ischemia, seizure, or psychosis, or there may be depression, cognitive decline, and periods of fluctuating consciousness. Because the symptoms respond so well to immunosuppressive treatment, prompt diagnosis and management are important.[3] **Case Presentation:** Here we report a 55 year old female patient was admitted in hospital with Neurological symptoms of vertigo associated with drowsiness and altered mental status. She had history hypertension and NIDDM from past 11 years. Diagnostic workup revealed high anti-thyroid peroxidase antibody, slight increase in thyroid stimulating hormone levels and CSF analysis, radiologic findings showed no abnormalities and it was negative for other possible aetiologies. Treatment with steroids induced significant improvement for altered mental status.[5] **Conclusion:** Hashimoto's encephalopathy is a diagnosis of exclusion. This unusual disorder

is often under-recognized because of the multiple and protracted neurocognitive manifestations; therefore, it is important to be aware of the clinical manifestations to make a correct diagnosis.

KEYWORDS: Ashimoto's encephalopathy manifestations to make a correct diagnosis.

INTRODUCTION

Hashimoto's encephalopathy, also known as steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is a neurological condition characterized by encephalopathy, thyroid autoimmunity, and good clinical response to steroids. It is associated with Hashimoto's thyroiditis.[9] It was first described in 1966. It is sometimes referred to as a neuroendocrine disorder, although the condition's relationship to the endocrine system is widely disputed. It is recognized as a rare disease by the NIH Genetic and Rare Diseases Information Center.[1] Up to 2005 there were almost 200 published case reports of this disease. Between 1990 and 2000 43 cases were published. Since that time, research has expanded and numerous cases are being reported by scientists around the world, suggesting that this rare condition is likely to have been significantly undiagnosed in the past. Over 100 scientific articles on Hashimoto's encephalopathy were published between 2000 and 2013.[2]

Definition: Hashimoto's encephalopathy (HE) is a rare relapsingneuroendocrine disorder It is associated with Hashimoto' sthyroiditis (HT) with high titers of anti-thyroid antibodies. Thedisorder is reported rarely in India as well as world literature.

Sign and Symptoms

The onset of symptoms tends to be fairly gradual and to occur over 1–7 days. Symptoms of Hashimoto's encephalopathy may include

- Personality Changes
- Aggression
- Delusional Behaviour
- Concentration And Memory Problems
- Coma
- Disorientation
- Headaches

Jerks In The Muscles (Myoclonus – 65% Cases), Lack Of Coordination (Ataxia – 65% Cases), Partial Paralysis On The Right Side, Psychosis, Seizures (60% Cases), Sleep Abnormalities (55% Cases), Speech Problems (Transient Aphasia – 80% Cases), Status Epilepticus (20% Cases), Tremors (80% Cases).[10]

Risk Factors: The specific risk factors are unknown. They do not appear to be a strong indication that HE affects any particular ethnic group or age group.[7]

Pathogenesis: The mechanism of pathogenesis is not known but it has been hypothesized to be an autoimmune disorder, similar to Hashimoto's thyroiditis as its name suggests. But Very little is known about the pathology of Hashimoto's encephalopathy. Post-mortem studies of some individuals have shown lymphocytic vasculitis of venules and veins in the brain-stem and a diffuse gliosis involving gray matter more than white matter.[6] As mentioned above, autoantibodies to alpha-enolase associated with Hashimoto's encephalopathy have thus far been the most hypothesized mechanism of injury.[6]

Diagnosis: Diagnostic investigation is usually unspecific and there is no direct correlation between thyroid hormone levels or anti-thyroid antibody titers and the clinical presentation.[4]

a) Cerebrospinal Fluid Findings

- Raised protein (25% cases)
- Negative for 14–3–3 protein
- May contain anti-thyroid antibodies
- Magnetic resonance imaging abnormalities consistent with encephalopathy (26% cases)
- Single photon emission computed tomography shows focal and global hypoperfusion (75% cases)
- Cerebral angiography is normal.

b) Laboratory and Radiological Findings

- Increased liver enzyme levels (55% cases)
- Increased thyroid-stimulating hormone (55% cases)
- Increased erythrocyte sedimentation rate (25% cases)

c) Thyroid Hormone Abnormalities Are Common Findings

- subclinical hypothyroidism (35% cases)
- overt hypothyroidism (20% cases)

- hyperthyroidism (5% cases)
- euthyroid on levothyroxine (10% cases)
- euthyroid not on levothyroxine (20% cases)

d) Differential Diagnosis

- Alzheimer's disease
- Cerebrovascular accidents (stroke)
- Creutzfeldt–Jakob disease (CJD)
- Epilepsy
- (including basilar, hemiplegic, and retinal types)
- Other forms of autoimmune encephalitis, including forms of limbic encephalitis such as anti-NMDA receptor encephalitis
- Schizophrenia
- Spontaneous cerebrospinal fluid leak
- Viral encephalitis
- Transient ischemic attack

Treatment

1. Because most patients respond to steroids or immunosuppressant treatment, this condition is now also referred to as steroid-responsive encephalopathy.
2. Initial treatment is usually with **Oral prednisone (50–150 mg/day)** or high-dose IV Methylprednisolone (1 g/day) for 3–7 days. Thyroid hormone treatment is also included if required.
3. Failure of some patients to respond to this first line treatment has produced a variety of alternative treatments including Azathioprine, Cyclophosphamide, Chloroquine, Intravenous Immunoglobulin and plasma exchange. There have been no controlled trials so the optimal treatment is not known.
4. Seizures, if present, are controlled with typical antiepileptic agents.[8]

CASE DISCUSSION

Here we report a case on 55 year old female patient was admitted in the hospital with neurological complaints of sudden fall due to vertigo associated with drowsiness. She was found to be with altered mental status. She had past medical history of hypertension, Non-Insulin Dependent Diabetes Mellitus since 11 years. She has been on regular medication for both hypertension and type 2 diabetes mellitus but her blood sugar levels were not under

control. After second day of admission in hospital she was given Inj. H. mixtard 30/70 BID and tablets Glycomet-SR500 mg BID and there is significant improvement in fasting blood sugar levels and is under moderate control. She had no prior history of thyroid disorder or migraine. Her familyhistory was unremarkable. On the day of admission her vitals reveals her blood pressure as 100/60 mm of Hg, respiratory rate as 28 cycles per minute and pulse rate was 88 beats per minute. There was no thyroid swelling in the neck. Examination of other systems revealed no abnormality. She has been advised to undergo MRI of brain with diffusion and the results reported to be no abnormality detected in brain. Her cerebrospinal fluid analysis for was shown to benormal. Her laboratory investigation states that her thyroid stimulating hormones were found to be elevated. Her testosterone levels were within normal limits. Initial blood picture revealed hemoglobin 10.5 gm/dl, total leucocyte count (TLC) 12600/ cu mm, with neutrophil 81%, Case Report lymphocyte 15% and eosinophil 2%. Biochemical tests revealed fasting blood sugar 218 mg/dl, serum urea 26mg/dl, creatinine 1.1mg/dl, sodium 154 mEq/l and potassium 4.2mEq/l. test for hepatitis surface antigen was negative. Thyroid profile revealed T3 01.06 ngm/ ml (normal 0.8-2.0ngm/ ml), T4 7.94µgm/100 ml (normal 5.1-14.1 µgm/100ml) and TSH 4.72 µU/ml (normal 0.27-4.2 µU/ml). Since then she had been on levothyroxine 100 mg as starting dose and further the dose was reduced to 50 mg on second day and 25 mg on third day and continued the same dose. HIV serology was non-reactive.

Anti-thyroid-peroxidase (ant-TPO) antibody was found positive with high titer (258 IU/ml, normal <34 IU/ml). Electro-encephalography (EEG) revealed characteristic diffuse slowing suggestive of encephalopathy. In view of these neurologic symptoms, associated with high titers of anti- thyroid antibodies and the exclusion of other possible causes of encephalopathy, the patient was diagnosed with HE. We started methylprednisolone 500mg IV 1 pint over 31 hours for first day and continued it for next 3 days with a maintenance dose of 500mg in 00 ml NS, which resulted in a significant improvement in her clinical condition after the second day of treatment, and which was maintained with prednisone 1mg/kg/day and azathioprine 1 mg/kg/day. We developed an index of disease activity and tested for cognitive improvement and observed a good improvement in mental status. Along with this medication she has also been given the cognitive enhancers like piracetam injection thrice a day. The patient condition was improved with improved cognitive function and her memory and mental status. As the patient improved with steroid therapy she had been not given the alternative medication including azathioprine, cyclophosphamide, chloroquine, methotrexate, periodic

intravenous immunoglobulin and plasma exchange and this patient condition could be referred to as steroid responsive encephalopathy along with cognitive enhancers that showed clinical improvement in patient condition.

Laboratory reports	Day 1	Day2	Day3	Reference values
CSF for ADA	2.4	-	-	<10 (-)U/L >10 (+)U/L
Thyroid Stimulating Hormone	4.72	0.82	-	0.27-4.28 µIU/ml
HBA1C	12.5	-	-	Non-diabetic-6.5% Good control-6.5-7.0% Moderate control 7.0-8.0% Poor control-8.0%
Fasting blood sugar	218	260	166	70-110mg/dl
Anti thyroperoxidase antibodies	258	-	-	Negative-<34 Positive->34

CONCLUSION

Very high level of awareness is needed to diagnose HIM 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. This syndrome may become unrecognized fora long period of time; therefore, it should be kept in mind when evaluating a patient with cognitive dysfunction and high titers of ant thyroid antibodies. It should be suspected in any cause of cognitive dysfunction which remains undetected despite through investigation or when any neuropsychiatric condition is not responding to conventional therapy especially in the case of known autoimmune thyroiditis. The disease is highly responsive to steroid therapy. However, more common causes of encephalopathy, such as infections, electrolyte imbalance, toxins and neoplasms must be excluded before initiation of steroid therapy.

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