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Hashimoto's Encephalopathy: Is it a Rare Condition or a Masquerading One?

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Abstract:

Hashimoto's encephalopathy is an uncommon neurological disorder of unknown etiology, found in association with thyroid autoimmunity. This is a case of a 60 year old Indian lady who had an episode of acute onset encephalopathy. High levels of antithyroid antibodies were found in her serologic studies. Her cerebrospinal fluid analysis was near normal. Magnetic resonance imaging showed a lacunar infarct in pons and vasculitis. Her electroencephalographic studies were consistent with Hashimoto's encephalopathy. Hashimoto's encephalopathy is a poorly understood syndrome, which is often under recognized because of its heterogeneous neurological symptoms. Hence, it is important to have an insight regarding the clinical manifestations and treatment of this rather uncommon condition.

Key words: Brain Diseases, Electroencephalography, Hashimoto Disease, Magnetic Resonance Imaging, Lacunar Stroke.

Introduction

Hashimoto's encephalopathy (HE) is a rare neurological disorder. Due to the presence of high titres of antithyroid antibodies, this condition is presumed to be associated with thyroid autoimmunity. Brain vasculitis and autoimmunity directed against common brain-thyroid antigens have been proposed as the most likely etiological pathway. These patients can present with unexplained seizures resistant to anticonvulsive therapy, confusion, headaches, hallucinations, stroke-like episodes, impaired cognitive function, behavioural and mood disturbance, ataxia, and presenile dementia. The thyroid functions may be normal or decreased in these patients but serologic studies will reveal the presence of high antithyroid antibody levels, especially against thyroperoxidase. Cerebrospinal fluid (CSF) analysis, magnetic resonance imaging (MRI) brain and electroencephalographic (EEG) studies can further aid in its diagnosis. These patients may have a subacute or acute onset, with dramatic recovery following corticosteroid therapy.

Case Report

The patient being reported in this case is a 60 year old unmarried lady, a retired government officer. She was diagnosed to have schizophrenia

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at the age of 24, but was on irregular treatment and follow up. Over a period of one year, her relatives have noticed a mild difficulty in walking and dressing, poor hygiene, increased irritability, amnesia and disorientation.

On the day of presentation, she was found unconscious in her bed with uprolled eyes and tongue bite, surrounded by vomitus. She was brought to the emergency department in unconscious state. Her vitals showed a heart rate of 70 beats/ minute, blood pressure of 160/100 mmHg, respiratory rate of 22 breaths/minute and temperature 99°F. Her oxygen saturation was 94% in room air. On neurological examination, her Glasgow Coma Scale (GCS) score was E1V2M1. Her pupils were bilaterally symmetrical and reacting to light. Deep tendon reflexes were normal and plantars bilaterally flexor. Mild tremors were present over her left upper limb. There was no neck stiffness. Respiratory system examination revealed minimal right sided crepitations, while her cardiovascular and abdominal examinations were normal. Her computed tomography (CT) brain did not show any abnormalities. Her chest X-ray showed mild right sided aspiration pneumonia and ECG was normal. Her complete blood count showed elevated total counts with neutrophilia. Her sugar levels, renal and liver functions and electrolytes were normal. Her thyroid functions revealed TSH of 4.10 IU/L, FT3 2.43 pg/mL and FT4 1.1 ng/dL. A probable diagnosis of cerebrovascular accident with seizures and hypoxic encephalopathy and aspiration pneumonia was made, and the patient was started on antiplatelet drugs, statins, antiepileptic drugs, mannitol and intravenous antibiotics.

On day 2, MRI brain was taken which revealed lacunar infarct in left pontine region and vasculitis. Her CSF analysis showed mildly elevated proteins and normal counts and glucose levels. On day 3, patient became conscious and her GCS showed mild improvement to E2V3M1. Her viral markers i.e. HIV, HBsAg, anti HBs and anti HCV were negative. Her antinuclear antibody titre, anti-double stranded DNA, anti neutrophil cytoplasmic antibodies (p-ANCA and c-ANCA) were normal. Over the next two days, her total counts became normal. However, there was no further improvement in her neurological status.

Her EEG showed a slow background with theca waves. Based on the history, clinical presentation and investigations, the possibility of HE was considered and antithyroid peroxidase antibody was sent, which was well elevated (852 IU/mL). The patient was started on oral prednisolone 1 mg/kg/day. On day 8, patient showed dramatic improvement. She became conscious and started obeying simple commands. Over the next three days, she was able to walk and was discharged on day 12 on tapering dose schedule of prednisolone.

Discussion

HE is a rare neurological disorder of unknown aetiology. This term was coined for the first time by Shaw in 1991. He had come across 5 cases with symptoms such as seizures, frequent episodes of alternating hemiparesis and disorientation. They also had high protein levels in the CSF and EEG abnormalities. These patients were hypothyroid with positive antithyroid antibodies [1]. The disorder is more common in females, with female to male ratio being 4:1. It is commonly seen during the fourth decade of life, but can appear in children as well [2-4].

Two major patterns of clinical manifestations have been reported: i) 25% of patients exhibit a stroke-like pattern of multiple recurrent episodes of focal neurologic deficits with a variable degree of cognitive dysfunction and impaired consciousness, and ii) 75% present with

a diffuse progressive pattern of slow cognitive decline with dementia, confusion and hallucinations [2,5]. However, a third pattern was recently described by Watemberg *et al.* as "relapsing-remitting manner including cognitive deterioration and psychiatric illness" [6]. These patients may experience focal or generalized tonic-clonic seizures or even status epilepticus. Other features include myoclonus, tremors, hypereflexia, psychosis, visual hallucinations and paranoid delusions [2,3,5].

The exact mechanism of HE remains unknown. The most probable mechanisms include disseminated encephalomyelitis and/or autoimmune general cerebral vasculitis [1,6,7]. As a result of impaired cerebral perfusion and metabolism, a wide range of symptoms have been described [8]. The diagnosis of HE requires the presence of elevated levels of antithyroid antibodies. In some cases, the diagnosis is supported by the presence of Hashimoto's thyroiditis while in others there may not be any concomitant thyroid disorder. However, neither the clinical stage of the disease nor the severity of the neurological symptoms have any relation with the concentration of these antibodies. These antibody titres may be elevated in CSF [2,3,9].

A new autoimmune antigen, amino terminal of alpha-enolase (NAE), was found in the brain of HE patients. A high level of antibodies against this antigen was also found in these patients. These antibodies were not detected in patients with other neurological diseases [10]. Studies have confirmed the high specificity of NAE in HE, and together with antithyroid antibodies, it can be a useful diagnostic marker for HE [11,12]. CSF analysis, EEG and MRI brain studies do not show consistent findings which can aid in the diagnosis of HE. Lymphocytic pleocytosis and elevated protein levels may be seen in the CSF analysis of HE patients [2,5]. A nonspecific slow background activity, focal spikes or sharp waves and transient epileptic activity are some of the EEG abnormalities [5,13]. The MRI brain of these patients can be normal or may show ischemic lesions, demyelination, vasogenic edema or atrophy [14].

Due to the cocktail of symptoms, HE can masquerade a vast number of conditions like stroke or transient ischemic attack, cerebral vasculitis, carcinomatous meningitis, toxic metabolic encephalopathy, paraneoplastic syndromes, Creutzfeldt-Jakob disease, degenerative dementia and psychiatric diseases [2,3]. Once the diagnosis of HE is confirmed, corticosteroids form the mainstay of treatment [15]. Intravenous immunoglobulin has also been tried in certain cases [16]. Unlike myxodema coma, HE does not respond to thyroxine replacement [17]. The long-term prognosis is variable. Most of the patients respond to the treatment; while others show a relapsing or progressive pattern [2,3].

Conclusion

HE is a rare disorder probably because of the low awareness of the disease or due to its masquerading features. Hence, while dealing with a patient presenting with unexplained encephalopathy, the possibility of HE should be considered, especially in the presence of high antithyroid antibody levels. Since the disorder is autoimmune in nature, initiation of corticosteroid therapy shows dramatic recovery.

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