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HASHIMOTO'S ENCEPHALOPATHY CASE REPORTS OF HASHIMOTO'S ENCEPHALOPATHY IN TERTIARY CARE HOSPITAL

Neurology

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ABSTRACT

Hashimoto's encephalopathy (HE) is an uncommon syndrome and rare disease, associated with Hashimoto thyroiditis. It is characterized by a acute to chronic loss of cognitive dysfunction ,subacute onset of confusion with altered level of consciousness, stroke like episodes , neuropsychiatric manifestations ,seizures, and myoclonus. HE is believed to be an immune-mediated disorder rather than representing the direct effect of an altered thyroid state on the central nervous system. Hashimoto encephalopathy or Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) and a more general term, nonvasculitic autoimmune meningoencephalitis, are also used to describe this condition. Here we are reporting 3 cases of hashimoto encephalopathy in the tertiary care centre who presented with acute to chronic memory loss , neuropsychiatric disturbances, complex parital seizures visual hallucinations and myoclonus and responded to steroids. A negative microbiological screen of the CSF and serum along with raised CSF protein, elevated serum antithyroid antibodies, characteristic EEG and neuroimaging findings yielded the diagnosis

KEYWORDS

Hashimoto encephalopathy; Hashimoto thyroiditis ; Autoimmune encephalopathy ; Steroid response encephalopathy associated with autoimmune thyroiditis

INTRODUCTION

Hashimoto's encephalopathy (HE) is a rare, but treatable disease[1]. Hashimoto encephalopathy or Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) and a more general term, nonvasculitic autoimmune meningoencephalitis, are also used to describe this condition. It is defined by acute or sub-acute encephalopathy in the presence of elevated titres of anti-thyroid peroxidase (anti-TPO) antibodies, independent of thyroid status and absence of evidence of CSF infection[2,3].Recently, it has drawn attention as a treatable cause of dementia and one of the important differential diagnoses of Creutzfeldt-Jakob disease.It includes various neurological symptoms such as stroke-like episodes , diffuse neuropsychiatric symptoms, seizures, hallucinations and myoclonus which are well responsive to steroids. Here we are reporting 3 different cases of hashimoto encephalopathy who presented with different signs and symptoms of acute to chronic memory loss , neuropsychiatric disturbances, complex partial seizures, visual hallucinations and myoclonus and responded to steroids.

Report of cases

CASE REPORT 1:

44 years Female presented with subacute onset of memory loss for 6 months, patient was apparently normal till 6 months, from 6months onward patient developed gradually progressive memory disturbances, with history of aggressive behavior in form of hitting the neighbours, using bad words, loss of recent memory and remote memory, auditory hallucinations , chronic headache associated with nausea for past 6 months, no history of seizures, no history of loss of consciousness , no history of trauma , no history of weakness of upper limbs and lower limbs , no history of cranial nerve involvement & sensory system involvement, no history of autonomic nervous involvement. CT brain was done elsewhere during her first visit shows left temporal hypo density and no other co morbidities.

Now patient was admitted in our hospital. On physical examination patient was severely obese , her higher mental examination ,MMSE was 10 /30 other systems are with in normal, spinomotor , sensory , cranial nerve examination are normal.

All routine investigations are sent. MRIbrain is with in normal limits .Thyroid profile [FT3- 2.4 pg/mL (normal 2-4.4 pg/mL), FT4- 1.0 ng/dL (normal 0.93-1.7 ng/dL), TSH–43 µIU/mL (normal = 0.27-4.2 µIU/mL)] was sent shows hypothyroidism and antiTPO and anti thyroglobulin was done are severely elevated > 1000 . EEG within normal limits , CSF analysis was done shows elevated protein , absent NMDA receptor antibody . Patient was diagnosed as having hashimotos thyroiditis with hashimotos encephalopathy. She was treated with steroids, methyl prednisolone for 5 days. Patient has improved symptomically.

Case report 2

66 year Male presenting with sudden onset of confusion with auditory and visual hallucinations (complex partial seizures) lasting for 2 to 3 hours intermittently during day or night times for past 2 days, no history of fever, no spino motor system , sensory or cranial system involvement. No past history of seizures or other co morbidities Patient was admitted and all necessary investigations were done,thyroid profile was with in normal limits , anti TPO and anti thyroglobulin are elevated. MRI brain with contrast and EEG were within normal limits. CSF analysis was acellular with sugar- 74 mg/dL and protein- 194 mg/dL. CSF study for HSV , Cryptococcus, Mycobacterium, fungi and other pyogenic organisms was negative and autoimmune antibodies are negative. Patient was treated with steroids for 5 days and patient had improved completely with in 5 days.

Case report 3

55 year male, farmer known case of psychiatric disorder on antipsychotics drugs for past 15 years, presented with neuro psychiatric manifestations, sudden onset of muteness, catatonia, frontal disinhibition not associated with fever and seizures for 1 week. No other co morbidities on physical examination, patient was moderately built and moderately nourished , higher mental functions not able to be elicited ,cog wheel rigidity of both upper limbs and lead pipe rigidity of both lower limbs, catatonia, reduced glabellar tap, with primitive reflexes was diagnosed as drug induced parkinsonism. MRI was done shows bilateral basal ganglia calcification and EEG shows diffuse cortical dysfunction.

Laboratory evaluation showed a free thyroxine (T4) level<3.48 pmol/L, high-sensitivity thyroidstimulating hormone (hsTSH) of 159.7 mIU/L, an antithyroid peroxidase (anti-TPO) antibody value of 1697.78 IU/mL, antithyroglobulin antibody (ATA) level of 157.07 IU/mL, creatine kinase of 14.4 mkat/L, and total cholesterol of 4.69 mmol/L. CSF analysis was acellular with sugar- 50 mg/dL and protein- 110 mg/dL. CSF study for, HSV, Cryptococcus, Mycobacterium, fungi and other pyogenic organisms was negative and autoimmune antibodies are negative. Later with all investigations, it was diagnosed as hashimoto's encephalopathy. Patient was treated

with steroids, methyl prednisolone for 5 days and patient improved symptomically at the time of discharge.

DISCUSSION

The first case of Hashimoto's encephalopathy was reported by Brain et al in 1966[4]. Thrush and Boddie described two cases of autoimmune thyroid disease accompanied by episodic encephalopathy in 1974[5]. Subsequently more number of cases with variable clinical manifestations were reported. The condition is known by many names that refer to different pathophysiological mechanisms: (1) steroid-responsive encephalopathy associated with thyroid auto-immunity: with an emphasis on a good response to steroid therapy(SREAT[6]); (2) non-vasculitic autoimmune inflammatory meningoencephalitis, which covers many different etiologies; (3) Hashimoto's encephalopathy, as most patients have underlying Hashimoto's thyroiditis; and (4) encephalopathy associated with autoimmune thyroid disease, which contains a broad spectrum of conditions, not only Hashimoto's thyroiditis ,but also grave's disease

DEFINITION

A relapsing encephalopathy occurring in association with Hashimoto's Thyroiditis with high titers of anti-thyroid antibodies. Clinically, the condition may present with one or more symptoms. Onset is often gradual and may go unnoticed by the patient and close associates to the patients. Symptoms sometimes resolve themselves within days to weeks, leaving a patient undiagnosed. For many other patients, the condition may result in ongoing problems with a variety of manifestations, often confusing clinicians due to the diffuse nature of symptoms.

Hashimoto's encephalopathy is characterized by numerous neurological and neuropsychiatric symptoms. Signs and symptoms includes personality changes, aggression, delusional behaviour, concentration and memory problems, coma, disorientation, headaches, myoclonus (65% cases), ataxia (65%), partial paralysis, psychosis[8-10], seizures, sleep abnormalities, speech problems (transient aphasia), status epilepticus , tremors. The most common symptoms are seizures, altered consciousness, headache, and hallucinations[11,12]

The pathogenesis of Hashimoto's encephalopathy is still unknown. There is no evidence that the anti-TPO antibody directly causes encephalopathy, but other autoantibodies that are associated with autoimmune thyroid diseases might induce encephalopathy. Some autopsy reports have noted that Hashimoto's encephalopathy may be associated with lymphocytic infiltration and vasculitis in the brainstem or brain gray matter. Several mechanisms, such as autoimmune vasculities, autoantibodies against brain-thyroid antigens, encephalomyelitis-associated demyelination, global cerebral hypoperfusion, a direct toxic effect of thyrotropin releasing hormone and neuronal dysfunction due to brain edema have been proposed for Hashimoto's encephalopathy.

Diagnosis

Peschen –Rosin et al outlined the first diagnostic criteria for Hashimoto's encephalopathy that included patients with unexplained episodes of relapsing myoclonus, generalized seizures, focal neurological deficits or neuro psychiatric disorders.

Diagnosis of Hashimoto encephalopathy can be made when all six of the following criteria have been met

1. Encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes
2. Subclinical or mild overt thyroid disease (usually hypothyroidism)
3. Normal brain MRI [6]or with non-specific abnormalities
4. Presence of serum thyroid (thyroid peroxidase, thyroglobulin) antibodies
5. Absence of well-characterized neuronal antibodies in serum and CSF
6. Reasonable exclusion of alternative causes[7]

In our study, out of 3 patients, 2patients are male and one patient is female , presented with different signs and symptoms, from stroke like episodes to complete mute, catatonic posturing, all these 3 patients has been diagnosed differently and started on treatment, after complete evaluation of these 3 patients with CSF analysis ,MRI brain , EEG and complete thyroid profile. As in our first case, additional clues may be provide by the detection of anti-TPO antibody and ATA, and an increase in protein concentration or IgG level in the CSF without pleocytosis. Computed tomography scans, MRI of the brain and EEG traces are either normal or present with nonspecific findings. The role of imaging studies is mainly to exclude other possible causes of encephalopathy.

Differential diagnosis- The common differential diagnoses include neurological infections, stroke, viral encephalitis, TIA, metabolic, toxic, autoimmune (limbic encephalitis, such as anti NMDA receptor encephalitis and paraneoplastic encephalopathy), demyelinating aetiology like ADEM, dementia, psychiatric illness and Creutzfeldt-Jakob disease (CJD) . Encephalopathy of unclear cause and positive anti-thyroid antibodies and corticosteroid responsiveness yields the clues towards diagnosis of Hashimoto's encephalopathy

TREATMENT

Treatment for Hashimoto's encephalopathy is divided into three categories. The first approach is to use immunomodulatory agents. When Hashimoto's encephalopathy is suspected, corticosteroid treatment is advised as the first- line therapeutic choice. Various regimens of corticosteroid treatment have been proposed. According to the literature, methylprednisolone 1000 mg as an intravenous infusion for 3 to 5 days is recommended.The neurological symptoms usually respond within 1 week, sometimes as quickly as 1 day. In up to 40% of patients, there is no recurrence after the first course of corticosteroid pulse therapy. Occasional steroid resistance and a recurrence of psychiatric symptoms may occur. For patients with a recurrence of symptoms, the effectiveness of corticosteroid therapy remains good. Combination of oral prednisone (1 mg/kg/day) after high-dose corticosteroid can be considered for patients showing frequent recurrence, followed by progressive tapering until the drug is withdrawn after 6 to 12 months, depending on clinical evolution and responsiveness. In patients with a poor response to corticosteroids, combination with azathioprine, cyclophosphamide, methotrexate, intravenous immunoglobulin (IVIG), or plasmapheresis has been suggested.

The second approach is to give thyroxine or an antithyroid drug, as it is beneficial to maintain a euthyroid status for patients with Hashimoto's encephalopathy. Third approach, treatment should be given for other complications: if a seizure occurs, antiepileptic drugs are considered In conclusion, Hashimoto's encephalopathy is an encephalopathy related to autoimmune thyroid diseases. Although the laboratory findings are nonspecific except to prove that the patient has autoimmune thyroid disease, and the imaging findings are used only to exclude specific lesions, early diagnosis and treatment is important as the response to steroid therapy is good.

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