

An Unusual Cause for Altered Sensorium - A Case Report

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Abstract: Hashimoto's encephalopathy is an autoimmune disorder, with high titres of antithyroid peroxidase antibody, usually with a clinically and biochemically normal thyroid function. Here we present a case of Hashimoto's encephalopathy in a 34yr old man, who presented with acute onset of cognitive impairment on a background of psychiatric illness. Initially a probability of neuroleptic malignant syndrome and CNS infection were entertained, but finally patient had high titres of anti thyroid peroxidase antibodies. Hence, we should ascertain different differentials, and a high level of suspicion is required to diagnose Hashimoto's encephalopathy, unlike other autoimmune disorder. Though more common among female population, it should be encouraged as a differential even in male.

Keywords: Hashimoto's, Encephalopathy, Autoimmune

1. Introduction

Hashimoto's encephalopathy is a term used to describe an encephalopathy of presumed autoimmune origin characterised by high titres of antithyroid peroxidase antibodies. In a similar fashion to autoimmune thyroid disease, Hashimoto's encephalopathy is more common in women than in men. It has been reported in paediatric, adult and elderly populations throughout the world. The clinical presentation may involve a relapsing and remitting course and include seizures, stroke-like episodes, cognitive decline, neuropsychiatric symptoms and myoclonus. Thyroid function is usually clinically and biochemically normal. Hashimoto's encephalopathy appears to be a rare disorder, but, as it is responsive to treatment with corticosteroids, it must be considered as part of investigation for suspected encephalopathies. Diagnosis is made in the first instance by excluding other toxic, metabolic and infectious causes of encephalopathy with neuroimaging and CSF examination. Neuroimaging findings are often not helpful in confirming the diagnosis. Common differential diagnoses when these conditions are excluded are Creutzfeldt-Jakob disease, rapidly progressive dementias, and paraneoplastic and nonparaneoplastic limbic encephalitis. In the context of the typical clinical picture, high titres of antithyroid antibodies, in particular antithyroid peroxidase antibodies, are diagnostic. These antibodies, however, can be detected in elevated titres in the healthy general population. Treatment with corticosteroids is almost always successful, although relapse may occur if this treatment is ceased abruptly. Other forms of immunomodulation, such as intravenous immunoglobulin and plasma exchange, may also be effective. Despite the link to autoimmune thyroid disease, the aetiology of Hashimoto's encephalopathy is unknown. It is likely that antithyroid antibodies are not pathogenic, but titres can be a marker of treatment response. Pathological findings can suggest an inflammatory process, but features of a severe vasculitis are often absent. The links between the clinical pictures, thyroid disease, auto-antibody pattern and brain pathology await further clarification through research. It may be that Hashimoto's encephalopathy will be subsumed into a group of nonvasculitic autoimmune inflammatory meningoencephalopathies. This group may include disorders such as limbic encephalitis associated with voltage-gated potassium channel antibodies. Some authors

have suggested abandoning any link to Hashimoto and renaming the condition 'steroid responsive encephalopathy associated with autoimmune thyroiditis' to better reflect current, if limited, understanding of this condition.

2. Case Report

A 34 yrs old male, chronic alcoholic for 10 yrs presented with altered sensorium and fever for 1 day. On examination, he was febrile, confused and not oriented to time, place and person, restless movement of all 4 limbs were present. Neck stiffness was present and B/L plantar withdrawal. Initial Labs showed increased TC 15000 and CPK 15573 levels. CT brain and CSF analysis was done to rule out CNS infection, which turned out to be normal. On the 3rd day of admission, the patient's sensorium worsened and patient was intubated electively in view of worsening sensorium. In view of persistent fever, spasticity of the muscles, past history of psychiatric drug usage and altered sensorium, clinical diagnosis of neuroleptic malignant syndrome was thought of and patient was initiated on T. Bromocriptine. Mentation did not improve and the disease had a relapsing and remitting course. CPK levels declined to 473 on day 5 of admission. The patient was pulsed with inj. methyl prednisolone 1000mg for 5 days and anti-thyroid peroxidase and anti-thyroglobulin antibodies, volume gated potassium channel was done. Anti-TPO and anti-thyroglobulin turned out to be positive and a diagnosis of HASHIMOTOS ENCEPHALITIS was made and patient improved clinically with pulsing of steroids.

In this patient, since his thyroid profile was normal, Hashimoto's encephalitis was not considered initially. Common conditions like alcohol dependant syndrome, meningitis, neuroleptic malignant syndrome were considered with a background history of psychiatric drug usage and high CPK levels.

3. Discussion

As a rare steroid responsive neuropsychiatric syndrome, HE is associated with the serologic evidence of anti-thyroid antibodies when other causes of encephalopathy are excluded. The clinical manifestations of HE include cognitive impairment, various types of epileptic seizures,

dystaxia and tremor, sleep disturbance and headache.[1] In this case, this male patient suffered from mild cognitive impairment as well as limbs dystaxia and had a relapsing and remitting pattern of the illness. Recently, HE has received extensive attention due to its treatability and unclear pathogenesis. In China, Hashimoto's encephalopathy is still not fully recognized because of its complex clinical manifestations and absence of specific biomarkers. The previous research demonstrated that cognitive impairment (84.6%) and psychiatric symptoms (38.5%) were the most frequent symptoms, however, seizures (30.8%) and myoclonus (7.7%) were relatively infrequent in thirteen consecutive patients with HE.[2] Therefore, presenting symptoms of HE may be quite variable.

The diagnosis of HE should be considered in patients presenting with the characteristic neuropsychiatric manifestations excluding other causes of encephalopathy. Generally, high levels of anti-thyroid antibodies in serum or CSF are important and helpful in the diagnosis of HE. They have no alteration in the CSF and/or imaging tests compatible with infectious, vascular, or neoplastic etiology, and response well to immunosuppressive therapy.[3] Non-specific electroencephalogram abnormalities are presented in the vast majority of patients, and brain MRI may display abnormalities in 49%, such as cerebral atrophy, focal cortical abnormality, diffuse subcortical abnormality and non-specific subcortical focal white matter abnormality.[4] In this male patient, the analysis of CSF as well as serum inflammation biomarkers was normal, indicating the exclusion of intracranial infection. Although the elevated CSF protein is common in HE, this change depends on the severity of the illness. His brain MRI showed normal pattern. Neuroimaging results have no reliable diagnostic value in HE.

In the context of the typical clinical picture, high titres of antithyroid antibodies, in particular TPOAb, are diagnostic.[5] Recently, Blanchinet *al.*[6] reported that TPOAb from Hashimoto's encephalopathy patients could bind cerebellar astrocytes in HE patients but not in Hashimoto thyroiditis patients. This may support the role of TPOAb in the pathogenesis of Hashimoto's encephalopathy. TPOAb is present in 95-100% and TGAAb in 73% of patients with HE. Elevated serum level of TPOAb may be related with vasculitic type Hashimoto's encephalopathy and elevated serum levels of TPOAb and TGAAb may be with diffuse progressive type of HE. However, the elevated titres of these antibodies can be tested in the healthy population. Therefore, the role of those antibodies and their pathophysiology are unknown. In addition, corticosteroid treatment is successful in most cases, which can further support the diagnosis of HE. Furthermore, other common causes of encephalopathy should be ruled out, such as intracranial infection, metabolic disease, electrolyte imbalance, poisoning or toxins, neoplasm, and the central nervous system involvement of vasculitic syndromes. With the aid of a detailed medical history and related auxiliary examination (such as CSF and MRI), it is easy to rule out these diseases.

Regarding treatment for HE, the patient's symptom

improved significantly and rapidly after initiation of corticosteroid treatment, and eventually achieved a long-term stable remission. Clinical improvement with corticosteroid therapy is usually observed in the first 4-6 weeks. This positive response has been considered to be part of the definition of HE, but does not occur in all patients.[7] Other therapies such as plasmapheresis and immunosuppressant medications have been successfully used in patients non-responsive to corticosteroids. It was reported that only a few HE patients have been treated with Intravenous immunoglobulins.[8] Moreover, since the antithyroid antibodies could not be used as relapse markers of encephalopathies, the question of the continuation of the immunomodulatory of immunosuppressive drugs remains an open debate.[9]

In conclusion, HE is a rare disease associated with encephalopathy and autoimmune thyroiditis. Our research suggests that a high degree of suspicion is necessary to diagnose HE, especially in those patients with high levels of antithyroid antibodies and presented with unexplained encephalopathy, such as seizures and cognitive dysfunction, as in our case. Corticosteroid treatment is successful for HE in most cases, however, clinicians should be aware that relapses can occur early or even late after tapering of steroid use; therefore, a long follow-up period should be recommended.

4. Conclusion

Hashimoto's is a rare clinical syndrome, which has complete recovery with immunosuppressive therapy. When evaluating a case of suspected encephalitis the possibility of Hashimoto's encephalopathy has to be encouraged. If CSF and neuro imaging are non-contributory to the diagnosis of encephalitis, evaluation of Hashimoto's has to be done with thyroid function and anti-TPO antibodies. These patients have to be followed on a regular interval to watch for relapsing symptoms.

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