Hashimoto’s encephalopathy in a pregnant female: A diagnosis in disguise

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INTRODUCTION

Hashimoto’s encephalopathy (HE) is a very rare condition characterized by various clinical features consisting of psychiatric manifestations, seizures, and focal neurologic deficits. HE, a rare autoimmune disease with unknown origin, is referred to as nonvasculitic autoimmune encephalopathy/meningoencephalitis, Hashimoto’s thyroiditis, or steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT).[1] The condition is more frequently found in females than in males, with a ratio of 5:1. It is also possible that there are many more undiagnosed cases. Because it is little known and its symptoms are primarily neurological, it is easy to misdiagnose or overlook and the symptoms frequently lead to mistaken neurological diagnoses.[2] Therefore, for all patients with unexplained acute- or sub-acute encephalopathy, or atypical psychiatric manifestations, especially patients who have autoimmune thyroid disease, HE must be included in the differential diagnosis.[3] If treatment is delayed due to misdiagnosis, it often becomes fatal, and therefore physicians should have a high degree of suspicion and awareness for this condition. Here, we present a case highlighting that of a 21-year-old previously healthy woman diagnosed with HE at 6 months of gestation.

CASE REPORT

A 21-year-old female who was carrying 6 months of the first pregnancy was admitted to our department with a history of hiccupping for 1 month, urinary retention for 3 days, gait instability for 3 weeks, and weakness of limbs.

While Hashimoto’s encephalopathy (HE) is quite rare, it is also likely that there are many more undiagnosed sufferers. Because it is little known and its symptoms are primarily neurological, it is easy to misdiagnose or overlook and the symptoms frequently lead to mistaken neurological diagnoses. We report a case of a 21-year-old female diagnosed with HE at 6 months of gestation. She was successfully treated. HE is a neuropsychiatric disorder of exclusion. As a good response can be obtained with corticosteroid therapy, early diagnosis and treatment is very beneficial for patients. To the best of our knowledge, there is no such report in the literature.

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accompanied with dyspnea for 2 days. Furthermore, her younger brother noticed self-talking behavior, paranoid ideas, and intermittent crying in her. She had an earlier history of hiccupping, nausea, and vomiting, which were ameliorated with symptomatic treatment. The patient had no prior personal or family psychiatric history. She had neither history of fetal wastage nor any past history of medical disorder. Her husband was unemployed, alcohol dependent, and was hardly present at home. One day before hospitalization, the patient experienced limb weakness, dyspnea, cough and hoarseness, and discontinuous unconsciousness. Physical examination was otherwise normal except fluctuating psychomotor agitation, emotional liability, impulsivity, and anxiety. The patient had incoherent speech, persecutory delusions, auditory hallucinations, and was disoriented in time and space. She was not known to be taking any medications nor did she suffer from substance abuse. Neurological examination revealed dysarthria, nystagmus, weakened extremities, muscle strength graded 3, hyperreflexia in all limbs, and positive Babinski sign on both sides. Pulse was 110/min regular and blood pressure was 120/78 mmHg. As a consequence, oral resperidone 2 mg daily and intravenous (IV) lorazepam were introduced. After 24 h, the symptoms worsened, and she presented with permanent auditory hallucinations, as well as aggressive behavior, stereotypic gestures, and psychomotor instability.

Electroencephalography (EEG) showed widespread slowing of background activity without sharp waves suggestive of encephalopathy. Brain magnetic resonance imaging was normal. Cerebrospinal fluid (CSF) examination showed the concentration of protein to be 0.4 g/L and cell count of $5 \times 10^6$. The concentration of glucose, sodium, and chloride was normal. CSF cultures were negative. Thyroid function tests were performed which revealed the following: free triiodothyronine 2.37 pmol/L, free thyroxine 8.04 pmol/L, thyroid-stimulating hormone 18.39 µIU/ml, and antithyroid peroxidise antibody (TPO) Ab 686.9 U/mL. Ultrasound imaging result of thyroid revealed heterogeneous gland without any signs of inflammation. No other abnormality was found from further testing including blood test for regular autoimmune disorders; serological tests for herpes simplex virus, cytomegalovirus, viral hepatitis B and C, human immunodeficiency virus, syphilis; as well as blood sampling for Vitamin B12 and ceruloplasmin.

The patient was diagnosed with HE given the association of high concentrations of antithyroid antibodies and the presence of an otherwise unexplained neuropsychiatric condition. Although medication with resperidone 2 mg daily was initiated and eventually lorazepam was on going, no clinical amelioration was observed. She was treated using IV immunoglobulins (0.4 g/kg/day) for 5 days. Simultaneously, she was treated using methylprednisolone (500 mg/day) for 5 days. It was quickly followed by a dramatic improvement of the clinical picture. Within 72 h, the patient was again oriented in time and space, and auditory hallucinations, as well as neurological symptoms, disappeared. A follow-up EEG returned normal. Although the patient had a fetal wastage, she continued methylprednisolone at a dose of 16 mg/d after discharge and maintained treatment with gradually reduced dose and stopped within a year. There was no recurrence of symptoms.

**DISCUSSION**

HE is a rare autoimmune disease associated with a prevalence of 2.1/100,000, with a female-to-male ratio of 5:1 and the mean age of onset between 45 and 55 years. It is relapsing-remitting and sometimes progressive encephalopathy occurring in association with Hashimoto’s thyroiditis.

The pathogenesis of HE 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. Several mechanisms such as autoimmune vasculitis, autoantibodies against brain thyroid antigens, encephalomylitis-associated demyelination, global cerebral hypoperfusion, a direct toxic effect of thyrotropin-releasing hormone, and neuronal dysfunction due to brain edema have been proposed for HE.

HE is suspected whenever the symptoms of acute- or sub-acute encephalopathy are associated with high serum levels of antithyroid antibodies. Because it lacks specific markers and is a clinically heterogeneous syndrome, HE remains an elusive nosologic entity. Clinical manifestations include confusion, coma, stroke-like episodes, seizures, psychosis, dementia, myoclonus, and myelopathy. As in our case the pregnant female came with intractable hiccupping which gradually progressed to stumbling and urinary incontinence along with the predominance of psychiatric symptoms and the presence of multiple risk factors, our initial diagnosis was psychosis. However, treatment resistance made us suspect an organic etiology. HE was very probable in our case after giving high titers of antithyroid antibodies and rapid normalization of her clinical symptoms and EEG once treatment was introduced. It must be noted that neither abnormal brain imaging nor the presence of antithyroid antibodies in the CSF is necessarily required for HE diagnosis. In addition, the thyroid status may vary from normal to pathological among patients with HE. Our patient had a fetal wastage.
at 6 months which could be due to thyroid autoantibody positivity and such women are likely to have an increased miscarriage rate which could lead to fourfold increase in the incidence of placental abruption. A number of etiologies have been hypothesized as the cause of relationship between spontaneous termination of pregnancy and autoimmune thyroid antibodies. These include (1) the existence of a subtle degree of hypothyroidism, (2) thyroid antibodies reflecting an autoimmune imbalance in the pregnant female, and (3) thyroid autoantibodies acting directly on the placenta. One study showed a marked reduction in miscarriages when thyroid antibody women were treated.

Due to its variety of clinical symptomatology, this condition may be difficult to diagnose at initial presentation and this may mimic stroke, rapidly progressive dementia, Creutzfeldt–Jakob disease, and paraneoplastic or viral encephalitis. This poses a diagnostic challenge and requires extensive workup to rule out toxic, metabolic, vascular, and infective causes. It is often called investigation of negative encephalopathy.

EEG studies, while always abnormal (98%), are usually nondiagnostic. The most common findings are diffuse or generalized slowing or frontal intermittent rhythmic delta activity. Prominent triphasic waves, focal slowing, epileptiform abnormalities, and photomyoclonal responses may also be seen. These findings are nonspecific and may be seen in toxic, metabolic, and postanoxic encephalopathies.

Most patients respond to high-dose steroid therapy, and therefore it is called SREAT. Initial treatment is with oral prednisolone or high-dose IV solumedrol for 7 days along with thyroid hormone treatment for concurrent thyroid disorder. Alternative therapies including immunosuppressants may be effective along with immunomodulation with periodic IV immunoglobulins and plasma exchange. None of the treatments have been studied in controlled trials, and therefore there are no clear guidelines for their use.

CONCLUSIONS

As psychiatric symptoms may be prominent in encephalopathy, they could potentially be misleading and point to psychiatric disorder. However, an organic etiology should always be considered, especially in the absence of any mental disorder history. HE is a difficult diagnosis, especially when thyroid hormone status is normal. This case is unusual as it the first report of a patient with first-time pregnancy presenting with HE. The present case also highlights the importance of early establishment of multidisciplinary diagnostic approach with psychiatrist, obstetrician, and neurologist and prompt initiation of steroid therapy in the successful management of HE.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Zhu Y, Yang H, Xiao F. Hashimoto’s encephalopathy: A report of three cases and relevant literature reviews. Int J Clin Exp Med 2015;8:16817-26.
2. Pathak LK, Vijayaraghavan V. Hashimoto’s encephalopathy: A diagnosis in disguise, case report and review of literature. J Med Cases 2014;5:643-5.
3. Chang JS, Chang TC. Hashimoto’s encephalopathy: Report of three cases. J Formos Med Assoc 2014;113:862-6.
4. Schiess N, Pardo CA. Hashimoto’s encephalopathy. Ann N Y Acad Sci 2008;1142:254-65.
5. Lalanne L, Meriot ME, Ruppert E, Zimmermann MA, Danion JM, Vidaillhet P, et al. Attempted infanticide and suicide inaugurating catatonia associated with Hashimoto’s encephalopathy: A case report. BMC Psychiatry 2016;16:13.
6. De Vivo A, Mancuso A, Giacobbe A, Moleti M, Maggio Savasta L, De Dominici R, et al. Thyroid function in women found to have early pregnancy loss. Thyroid 2010;20:633-7.
7. Negro R, Formoso G, Mangieri T, Pezzarossa A, Dazzi D, Hassan H, et al. Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: Effects on obstetrical complications. J Clin Endocrinol Metab 2006;91:2587-91.
8. Jacob S, Rajabally YA. Hashimoto’s encephalopathy: Steroid resistance and response to intravenous immunoglobulins. J Neurol Neurosurg Psychiatry 2005;76:455-6.