Hashimoto Encephalopathy Presenting with Acute Psychosis and Inappropriate Secretion of Antidiuretic Hormone: A Rare Case Responding to Steroid Therapy

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Patient: Male, 72-year-old
Final Diagnosis: Hashimoto’s encephalopathy
Symptoms: Psychosis
Clinical Procedure: —
Specialty: Neurology • Psychiatry

Objective: Unusual clinical course

Background: Hashimoto’s encephalopathy (HE) is an autoimmune encephalopathy that can involve various symptoms including psychosis. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) may be a complication in some neurological diseases. However, the simultaneous occurrence of subacute psychosis and SIADH as the manifestation of HE, observed in the present case, has rarely been reported.

Case Report: A 72-year-old man was hospitalized with a 4-month history of abnormal behaviors, including talkativeness, stopping consumption of coffee and cigarettes, hoarding garbage, and sleep disorders. On physical examination, increased and incoherent speech with flight of idea and delusion were observed. The Mini-Mental State Examination score was 28/30. Laboratory findings included hyponatremia due to SIADH and a positive result for anti-thyroid and anti-NH2 terminal of alpha-enolase antibodies. Cerebrospinal fluid examination revealed only elevation of IL-6. Brain magnetic resonance imaging was unremarkable; however, (I-123)-iodoamphetamine single-photon emission computed tomography showed extensive hyperperfusion involving the brainstem and bilateral frontal and medial temporal lobes. Electroencephalography showed generalized slow waves, but there were no epileptiform discharges. After 2 courses of high-dose intravenous methylprednisolone followed by oral prednisolone, his symptoms improved. Based on the findings of clinical features and steroid responsiveness, he was diagnosed with HE. Oral prednisolone and antipsychotic drugs were decreased without a relapse and he was discharged to his home.

Conclusions: Although psychosis complicating SIADH is rare, HE should be considered in the differential diagnosis because of its treatment efficacy.

Keywords: Autoimmune Limbic Encephalitis • Hashimoto’s Encephalitis • Hyponatremia • Psychotic Disorders • Sleep Disorders, Intrinsic

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Background

Hashimoto’s encephalopathy (HE) is an autoimmune disease that presents with various symptoms in an acute or chronic course [1]. Despite its treatable pathogenesis, diagnosing HE can be difficult or delayed, particularly in cases in which psychiatric symptoms are predominant.

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) can be observed in some neurological diseases [2]. Regarding autoimmune encephalitis with psychiatric symptoms, anti-leucine-rich glioma-inactivated 1 (LGI 1) antibody-positive encephalitis is known to accompany SIADH [3].

In HE, it is reported that limbic encephalitis (LE) subtype cases, associated with anti-NH2 terminal of alpha-enolase (NAE) antibody, complicated hyponatremia [4], but the details of the disease course and the cause of hyponatremia were not described. Moreover, psychosis and SIADH as comorbidities have not been reported in HE to the best of our knowledge.

We present the case of a patient with HE who manifested simultaneous occurrence of subacute psychosis and SIADH and had a good outcome with treatment. Because HE is treatable, treatment opportunities should not be missed, even in atypical cases.

Case Report

Four months before his hospitalization, the 72-year-old man began exhibiting subtle yet unusual behavior. Initially, there was a marked increase in his speech, which, over time, grew progressively disjointed and incoherent. Soon after, another peculiarity surfaced: he stopped drinking coffee and smoking cigarettes, and he frequently screamed during night-time sleep. He then developed abnormal behavior: he hoarded garbage, took customer’s items from work to his home, and came to our outpatient clinic. His medical history included mild hypertension. He took no medication or supplements and had no family history of autoimmune or neurological disease.

On admission, he was awake and alert, although hyperactive, and he had incoherent speech with flight of ideas and delusions. His blood pressure was 162/83 mmHg, pulse was 74 beats per minute, and body temperature was 37.4°C. Except for the above-mentioned speech problems, general physical and neurological examinations revealed no abnormalities, including evidence of dehydration or hypervolemia. His Mini-Mental State Examination and Frontal Assessment Battery scores were 28/30 and 12/18, respectively, and the latter was impaired.

Laboratory assessments unveiled hyponatremia, with a sodium (Na) level of 127 mEq/L (average: 135-145 mEq/L) and a reduced hematosmolality of 264 mOsm/kg (standard:

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Figure 1. Magnetic resonance images (MRI) of the brain without contrast agent on admission. (A) Axial T2-weighted MRI of the brain without contrast agent. (B) Coronal fluid-attenuated inversion-recovery (FLAIR) MRI of the brain without contrast agent. These images show no significant abnormal signal intensity in the brainstem, limbic system, and cortex.
275-310 mOsm/kg. Other notable findings included creatinine at 0.81 mg/dL (average: 0.7-1.1 mg/dL), a slightly elevated early morning cortisol level of 22.6 µg/dL (average: 4.5-21.1 µg/dL), and an antidiuretic hormone level of 0.9 pg/mL. Urinalysis indicated sodium levels at the upper limit, 88 mEq/L (average: 40-90 mEq/L), and osmolality at 700 mOsm/kg (range: 50-1300 mOsm/kg), all consistent with SIADH.

Thyroid functions were within normal limits. However, there was an extraordinary elevation in anti-thyroglobulin (Tg) antibodies, surpassing 4000 IU/mL (normal: <28 IU/mL), and the anti-thyroid peroxidase (TPO) antibody was elevated at 185 IU/mL (normal: <16 IU/mL).

Evaluation of the cerebrospinal fluid (CSF) showed no deviations from normal, except for an increased IL-6 level at 29.6 pg/mL (normal: <4.3 pg/mL). Tests for CSF anti-leucine-N-methyl-D-aspartate antibody, herpes simplex virus DNA, serum onconeural antibodies (encompassing a range from anti-ampiphysin to Tr antibodies), and a Mycobacterium tuberculosis IFN-γ screening yielded negative results.

Further diagnostic tests, including trunk computed tomography, did not detect any malignancies, and the fecal occult blood test came back negative. A brain MRI scan did not identify any significant anomalies (Figure 1). However, subsequent (I-123)-iodoamphetamine cerebral blood flow SPECT revealed pronounced hyperperfusion, especially in the brainstem, cerebellum, and in, frontal and medial temporal lobes (Figure 2). Electroencephalogram recordings also documented the presence of generalized slow waves. Changes in the patient’s clinical course and serum Na levels are shown in Figure 3.

We initially assumed he had anti-voltage-gated potassium channel (VGKC) antibody-associated encephalitis or HE. The first course of high-dose intravenous methylprednisolone (1 g/day for 3 days) was started on day 13 of hospitalization, but there was no change.

In serum and CSF, anti-VGKC antibodies, including anti-LGI 1 and anti-contactin-associated protein 2 antibodies, were later found to be negative, although serum NAE antibody was positive. Thus, we suspected HE and started a second course of high-dose methylprednisolone on day 33, followed by oral prednisolone 50 mg/day (1 mg/kg/day) for 1 month. One day

Figure 2. Cerebral blood flow (I\(^{123}\))-iodoamphetamine single-photon emission computed tomography (SPECT) before and after steroid therapy. Panel (A) was taken in the acute phase of the disease without steroid treatment. Panel (B) was taken after 5 months when his symptoms had already improved. In comparison with Panel (B) retrospectively, Panel (A) suggests extensive cerebral hyperperfusion, including the brainstem and frontal and medial temporal lobes.
after the start of oral therapy, the patient became irritated and aggressive; therefore, we sedated him with dexmedetomidine for 1 week. During sedation, we started antipsychotic drugs to control his psychiatric symptoms, which had been worsened by high-dose steroid.

On day 40, the serum Na level recovered to 136 mEq/L. On day 48, he began conversing coherently, and the abnormal behavior disappeared the following week. Prednisolone was gradually decreased at a rate of 5 mg/2 weeks. Based on this steroid response, he was diagnosed with HE.

A follow-up CSF examination showed IL-6 decreasing to 4.7 pg/mL on day 106. Anti-Tg and anti-TPO antibodies gradually decreased. By encouraging fluid intake for constipation, the serum Na level decreased to 124 mEq/L and recovered to 134 mEq/L by restricting fluid intake to less than 800 mL/day without salt loading. Antipsychotic drugs and oral prednisolone were tapered without relapse, and he was discharged on day 122.

Discussion

HE is characterized by positive anti-TPO antibody and diverse symptoms. The diagnostic criteria for HE, also known as steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), advocated by Castillo et al have been widely used, which emphasis the good response to steroid therapy [5]. However, anti-TPO antibody is not specific, with 13% of the general population known to be positive [6], and the concept of HE itself has become controversial in recent years due to the extremely wide variety of clinical manifestations. Anti-NAE antibodies have been reported to be specific for HE; however, other reports had refuted this [7,8] and there is no certain and specific biomarker.

Some diagnostic criteria for HE have been proposed [5,8,9]. These criteria differ in terms of symptoms (especially detail of psychiatric symptoms), necessity of thyroid dysfunction, cut-off value of anti-TPO antibody titer, and response to treatment. This lack of uniformity indicates that there are no established diagnostic criteria for HE. One point common to all the criteria is the exclusion of alternative diseases, including vascular and metabolic diseases, which is crucial for the diagnosis of HE.

Our case fulfills 1 of the proposed diagnostic criteria [5]. On the other hand, our case met all but 1 of the other proposed criteria (lower anti-TPO antibody titer than the cut-off value [8], and normal thyroid function [9]). Nevertheless, the diagnosis of our case as HE is reasonable based on sufficiently excluded alternative diseases with a wide range of neuronal antibodies searches and imaging studies.

In this case, psychosis such as flight of ideas and delusions was outstanding. Around 10% of HE cases present isolated psychiatric symptoms [1,8]. The detail symptoms vary from being incoherent [10] to psychosis (mutism, catalepsy, echopraxia, and catatonia) [11] and are not disease-specific. Therefore, it is important to consider HE when diagnosing psychiatric patients.
This case is unique in that the patient had psychosis and SIADH as comorbidities. As another cause of hyponatremia seen in neurological disease, cerebral salt-wasting syndrome (CSWS) is associated with a decreased body fluid volume due to urinary sodium excretion, and thus improves with fluid loading, which contrasts to SIADH [2,12]. Our patient’s hyponatremia was relieved after steroid treatment and was aggravated again by fluid loading then improved by fluid intake restriction; hence, we considered the pathogenesis as SIADH.

There are a few reports focusing on the complications of hyponatremia in HE. One reported hyponatremia existed in 40% of patients with LE-subtype HE, although its mechanism and detailed course were not described [4]. In the present case, screaming during sleep was observed and disappeared after treatment. As a limitation, we could not perform polysomnography because of his severe psychiatric symptoms. Hence, we could not confirm whether his sleep disorder was a rapid eye movement sleep behavior disorder (RBD). LE can complicate RBD in relation to the limbic system and brainstem dysfunction [13-15]. Our case fulfills diagnostic criteria for definite autoimmune LE [9], and it can be inferred that SIADH is derived from dysfunction of the limbic system and brainstem. The abnormal findings of brain perfusion SPECT observed in our case — hyperperfusion including the brainstem and medial temporal lobe — improved after steroids treatment along with sleep disorders and SIADH. This supports our hypothesis above.

Conclusions

We report an uncommon instance of HE manifesting with psychiatric disturbances and SIADH, effectively managed with steroid therapy. Given its responsiveness to treatment, it is essential to consider HE in the differential diagnosis, even in cases with atypical presentations.

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Declaration of Figures’ Authenticity

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References: