<Case Report>

Early Intervention of Steroid Therapy Improves Acute Unconsciousness due to Suspected Hashimoto's Encephalopathy: A Case Report

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ABSTRACT

A 68-year-old man was admitted to our hospital with symptoms of dysrhythmia and high fever. He had been administered intravitreal aflibercept, an anti-vascular endothelial growth factor (anti-VEGF) drug, for diabetic retinopathy two days earlier. He was found unconscious and transferred to the intensive care unit (ICU). Computed tomography (CT), magnetic resonance imaging (MRI), and spinal fluid examination revealed no abnormal findings. Hashimoto's encephalopathy was suspected based on findings of low thyroid hormone levels, positive anti-thyroid peroxidase antibodies, and the exclusion of other diseases that present with acute unconsciousness. Although the possibility of encephalopathy due to anti-VEGF antibody therapy was considered, there were no imaging findings of cerebrovascular disorders associated with this therapy. Steroid therapy immediately improved his condition. He was discharged on the 20th day after ICU admission and subsequently transferred to a different hospital on the 77th day. Although autoantibody for anti-NH_2-terminal of α-enolase was negative, Hashimoto's encephalopathy was considered the most likely differential diagnosis from a clinical perspective. When acute loss of consciousness due to autoimmune encephalopathy such as Hashimoto's encephalopathy is suspected, immediate steroid therapy should be considered, rather than waiting for results of time-consuming tests.

INTRODUCTION

Acute unconsciousness can be caused by various diseases such as cerebral or cardiac vascular disorders, arrhythmias, epileptic seizures, and encephalopathy [1]. Hashimoto's encephalopathy (HE) is an autoimmune encephalitis presenting with seizures, myoclonus, hallucinations, and stroke-like episodes with normal or non-specific CSF and brain magnetic resonance imaging (MRI) abnormalities [2]. Patients with HE show positive antithyroid antibodies [thyroid peroxidase (TPO) and thyroglobulin] and respond well to steroids [3]. A recent report showed that half of HE patients were positive for anti-NH_2-terminal of α-enolase (NAE) antibody [4]. We report a case of acute encephalopathy showing rapid improvement after steroid administration, in which HE was considered the most likely differential diagnosis.

CASE PRESENTATION

A 68-year-old male (height 194 cm, weight 127 kg) presented to our hospital with difficulty speaking, dysrhyth-

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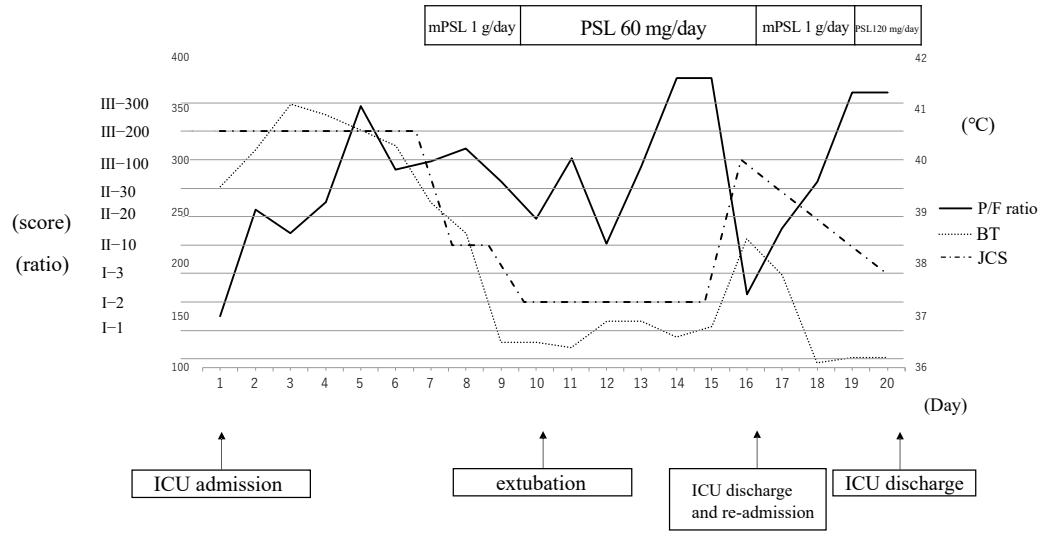

Figure 1 **Clinical course**
mPSL, methylprednisolone: PSL, prednisolone: P/F ratio, PaO_2/FiO_2 ratio: JCS, Japan Coma Scale: BT, body temperature

mia, and fever (**Figure 1**). He had received intravitreal aflibercept, an anti-vascular endothelial growth factor (anti-VEGF) drug, for diabetic retinopathy two days earlier. His medical records revealed a history of ischemic heart disease, diabetes mellitus, and dysrhythmia, as well as treatment for atrial fibrillation five years ago. He was taking metformin hydrochloride for diabetes (last dose was taken two days before), 2-acetoxybennzoic acid and rivaroxaban as anticoagulants, and bisoprolol for heart rate control.

His blood pressure was 187/118 mmHg and body temperature was 39.4 °C. He showed no neurological deficits. Blood test results were as follows: WBC 14,930 /μL (neutrophils 75 %, lymphocytes 17 %), CRP 26.26 mg/dL, glucose 143 mg/L, HbA1c 6.3 %, K 3.8 mmol/L, Na 145 mmol/L, cortisol 19.9 μg/dL, and adrenocorticotropic hormone (ACTH) 30 pg/mL. Computed tomography (CT) scans were negative for evidence of acute cerebral hemorrhage, stroke, or undiagnosed neoplasm. Glucose levels were controlled at 144–202 mg/dL by intravenous administration of insulin in the general ward. Three days after admission, he developed rapid atrial fibrillation (heart rate 200 bpm) and hypotension and lapsed into unconsciousness (Japan Coma Scale (JCS) 300), consequently requiring intubation. He was treated for atrial fibrillation and hypotension, had a prolonged loss of consciousness, and was admitted to the ICU.

Loss of consciousness was prolonged, and an extensive diagnostic workup was performed in the ICU. Specifically, he was negative for new stroke or acute cerebral infection on serial MRI and magnetic resonance angiography (MRA). As the afebrile state lasted during his hospital course, cerebrospinal fluid (CSF) was tested, revealing a mononuclear leukocyte count of 6 /μL. Blood cultures were negative. Tests for herpes zoster virus (HSV), varicella zoster virus (VZV), and cryptococcus were all negative. He had low thyroid hormone levels with FT4 0.58 ng/dL, FT3 1.23 pg/mL, and TSH 0.333 mIU/L, was positive for anti-thyroid peroxidase (anti-TPO) antibodies at 4.8 IU/mL, and had elevated levels of serum creatine kinase (CK) isoenzymes in CK-MM (Macro CK type 1) [5]. These data led to a diagnosis of suspected HE, and steroid therapy was initiated. An initial steroid course elicited an improvement in consciousness. He was extubated on the 10th day, his consciousness recovered (JCS 2), and he was discharged from the ICU on the 16th day. Although he was readmitted to the ICU due to recurrent loss of consciousness after steroid reduction during the night of that day, he soon recovered and was discharged from the ICU on the 20th day. About a month later, results of NAE antibody testing were negative. After splenic artery bleeding was embolized by interventional radiology (IVR), he was transferred to a different hospital 77 days after admission as his condition improved while being administered a lower dose of steroids continuously.

DISCUSSION

This report describes a patient with acute unconsciousness that was considered autoimmune encephalitis, showing rapid improvement after steroid administration. HE was suspected as the most likely cause after excluding other differential diagnoses that could have accounted for the presentation of acute unconsciousness. Autoimmune encephalitis is a neurological disorder with rapid progressive encephalopathy associated with autoantibodies and responds well to immunotherapy [2]. HE is a type of autoimmune encephalitis with elevated anti-thyroid antibod-

ies and normal or non-specific thyroid and MRI abnormalities [3]. Patients with macro CK type 1 are also suspected to be immune-related [5]. The present case had low thyroid hormone levels, positive anti-TPO antibodies, and elevated CK-MM isoenzymes (macro CK type 1), which led to suspicion of autoimmune encephalitis, especially HE. The good response to steroids supports the diagnosis. NAE antibody testing is useful for the diagnosis of HE. The disease specificity of NAE antibody for HE is 91 % and the sensitivity is 50 % [4]. HE cannot be ruled out despite the negative result for the antibody as in the present case. During steroid administration, we paid attention to the occurrence of hyperglycemia, stomach ulcer, osteoporosis, compromised immune system, and mental disorders as steroid-related complications [6].

We did not perform intravenous immunoglobulin therapy and plasma exchange, which are well-known treatment options for acute unconsciousness [7]. This was because of the suspected diagnosis of HE, for which steroids are known to be effective and provide immediate symptom relief. We eliminated various differential diagnoses as the causes of unconsciousness. Hypoglycemia due to side effects of diabetes medication was suspected based on the patient's medical history, but his blood sugar levels were normal. Adrenal crisis and electrolyte abnormalities were ruled out based on his symptoms and laboratory findings [8]. Although cardiac shock was considered, his consciousness did not improve even after stabilization of circulatory dynamics. Anti-VEGF injections were considered the possible cause of acute unconsciousness. There has been a report of cerebrovascular adverse effects due to anti-VEGF injections, which can increase blood coagulability and is associated with the risk of cerebral thrombosis [9–11]. CT scans, MRI, and CSF examination revealed no abnormalities.

CONCLUSION

Acute unconsciousness can be caused by various factors. When acute unconsciousness due to autoimmune encephalopathy such as HE is suspected, steroid therapy should be considered without waiting for results of time-consuming tests.

DISCLOSURE STATEMENT

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