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Original

A case of Hashimoto's encephalopathy preceded by recurrent episodes of neurological disturbances

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Abstract

A 72-year-old woman with autoimmune hepatitis, Hashimoto's disease, diabetes mellitus and liver cirrhosis was admitted to our hospital with disturbance of consciousness. Her medical state was stabilized by medications. The high level of serum anti-thyroid antibodies suggested Hashimoto's encephalopathy, thus steroid therapy was started. The patient's serum anti- NH_2-terminal of alpha-enolase (NAE) antibody test was strongly positive. After prednisolone therapy, the patient's consciousness level gradually improved, and she was discharged on hospital day 170 after rehabilitation. This case suggests that due to the various patterns of onset of Hashimoto's encephalopathy, anti-thyroid antibodies in cases of unidentified disturbance of consciousness and neurological disturbances should be evaluated.

Key words : Hashimoto's encephalopathy, anti-NH_2-terminal of alpha-enolase (NAE) antibody, disturbance of consciousness, autoimmune disease

Introduction

Hashimoto's encephalopathy is an autoimmune disease that shows positivity for anti-thyroid antibodies and various clinical manifestations. Patients with Hashimoto's encephalopathy benefit from immunomodulatory therapy such as steroids. We herein report a case of Hashimoto's encephalopathy with rapid progression after recurrent episodes of neurological disturbances and disturbance of consciousness.

Case Report

Since the age of 51, the patient had been treated for autoimmune hepatitis, Hashimoto's disease, diabetes mellitus, and liver cirrhosis with an unidentified age of onset. Her medical condition was stabilized by treatment with prednisolone (5 mg/day) and levothyroxine (50 μg/day). She showed difficulties in standing up from January 2012, and urinary and bowel incontinence and slow, involuntary movement of the fingers of both

繰り返す神経学的異常所見と共に症状が進行した橋本脳症の 1 例
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Table 1. The laboratory Data

WBC	9,100/μL	Na	131 mEq/L	RF	34.4 IU/ml
RBC	433×10^4/μL	K	3.8 mEq/L	ANA	92.5
Hb	13.8 g/dL	Cl	98 mEq/L	MPO-ANCA	19.9 U/ml
Ht	41.6%	CRP	3.0 mg/dL	anti-SS-AAb	>256x
Plt	8.4×10^4/μL	NH_3	18 μg/dL	anti-TGAb	1,530 IU/ml
		Glu	133 mg/dL	anti-TPOAb	71 IU/ml
AST	42 U/L	HbA1c	6.7%		
ALT	38 IU/L				
LDH	138 IU/L	TSH	1.38 μIU/mL		
γGT	43 IU/L	fT3	2.42 pg/mL		
TP	7.6 g/dL	fT4	1.25 ng/dL		
Alb	2.9 g/dL				
BUN	11 mg/dL				
Cr	0.78 mg/dL				

RF : rheumatoid factor, ANA : anti-nuclear antibody, MPO-ANCA : myeloperoxidase anti-neutrophil cytoplasmic antibody, anti-SS-A Ab : anti-Sjogren's syndrome A antibody, anti-TG Ab : anti-thyroglobulin antibody, anti-TPO Ab : anti-thyroid peroxidase antibody

hands developed in August 2012, and she had began experiencing daytime sleepiness from December 2012 ; in mid-December, she was found lying on the floor with the fingers of both hands woven together, and was admitted to the hospital with disturbance of consciousness.

On hospital day 1, she was unconscious with a blood pressure of 162/92 mmHg, and temperature of 37.8°C. She demonstrated neck stiffness, a positive Kernig sign, and tonic arms.

The patient's laboratory data are shown in Table 1. Mild liver damage was found without NH_3 elevation. Plasma glucose levels and thyroid function were normal. Autoimmune antibody test results were as follows : rheumatoid factor, 34.4 IU/mL ; anti-nuclear antibody, positive ; myeloperoxidase anti-neutrophil cytoplasmic antibody, 19.9 U/mL ; anti-Sjögren's syndrome A antibody, >256x ; anti-thyroglobulin (TG) antibody, 1,530 IU/mL ; and anti-thyroid peroxidase (TPO) antibody, 71 IU/mL. Notably, her anti-thyroid antibody titers were high, and her anti-NH_2-terminal of alpha-enolase (NAE) antibody titer was strongly positive. A lumbar puncture revealed clear cerebrospinal fluid with a normal cell count and protein level.

On hospital day 2, the electroencephalography (EEG) showed a slow α wave basic rhythm (8 Hz) with θ and β waves without epileptic discharges. Brain magnetic resonance imaging (MRI) showed lacunar infarcts and bilateral deep white matter lesions (Figure 1). Brain single photon emission computed tomography (SPECT) showed no areas with hypo-perfusion.

Anticonvulsant therapy was ineffective, and her state of consciousness gradually worsened and fluctuated. We observed no signs of meningoencephalitis, hepatic encephalopathy, or symptomatic epilepsy. These findings together with the elevated level of anti-thyroid antibodies suggested Hashimoto's encephalopathy, and on hospital day 9, we started the patient on methyl-prednisolone pulse therapy and 40 mg/day oral prednisolone. After the steroid therapy, the patient's level of consciousness gradually improved, and the anti-thyroid antibody titers decreased by half within the first 2 weeks. We gradually decreased the prednisolone dose by 5 mg/week to 10 mg/day on hospital day 32. After rehabilitation, the patient was discharged home on hospital day 170 (Figure 2).

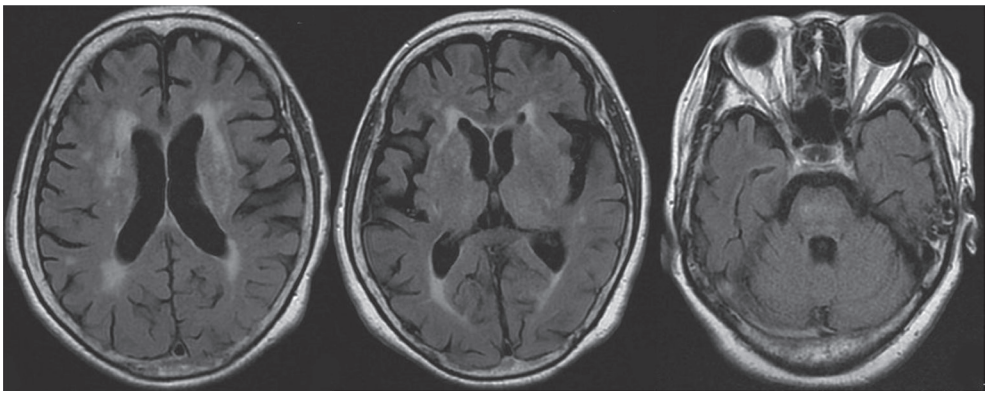

Figure 1. Fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) showed high intensity areas in the bilateral deep white matter and the periventricular and pons areas.

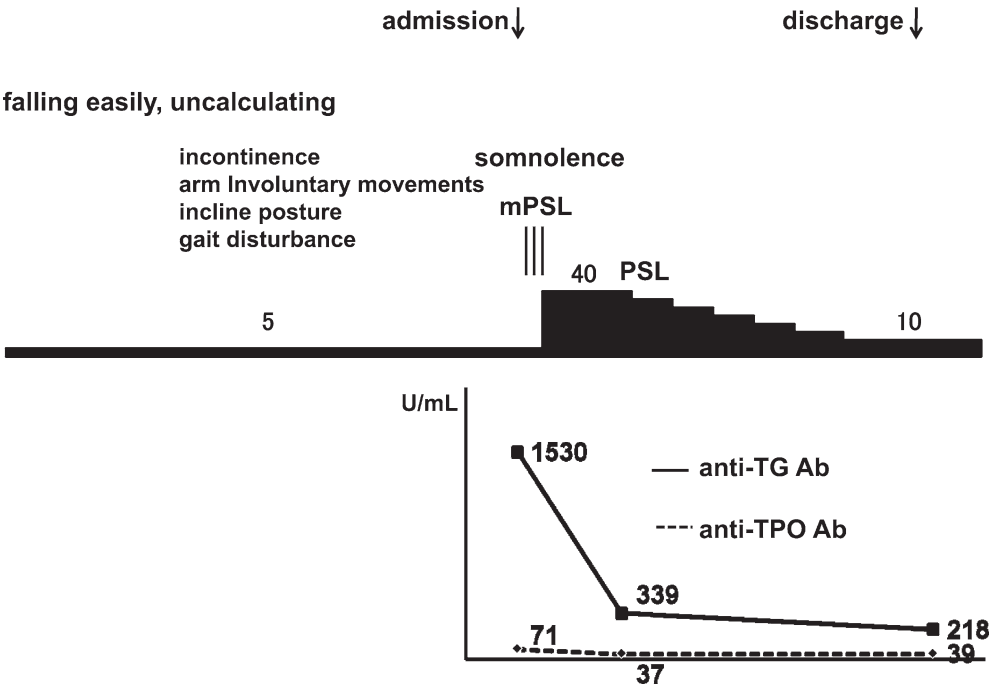

Figure 2. Timeline of clinical events following admission. After recurrent episodes of neurological disturbances, the patient was admitted to our hospital due to disturbance of consciousness. Methyl-prednisolone pulse therapy and oral prednisolone therapy were effective. The anti-thyroglobulin (TG) antibody titers decreased by one-fifth, and anti-thyroid peroxidase (TPO) antibody titers decreased by half. After tapering of the steroid and rehabilitation, the patient was discharged home.

Discussion

In this patient, rapid progression of disturbance of consciousness with fever developed after 1 year with a fluctuating state. We found no significant change on brain MRI or SPECT before and after therapy. On laboratory examinations, the high titers of anti-TG antibody and anti-NAE antibody were characteristic features. For the diagnosis of Hashimoto's encephalopathy, we used the Shaw PJ et al. (1991) criteria, which include psychosis, anti-thyroid antibody positiv-

ity, and effectiveness of steroid therapy. Perschen-Rosin R et al. added findings from cerebrospinal fluid, EEG and brain MRI to these criteria (1999). However these criteria are not adequate for Japanese patients in terms of the disease specificity of anti-thyroid antibody. Yoneda et al. discovered the diagnostic significance of anti-NAE antibody and reported its high prevalence in Hashimoto's encephalopathy (Fujii et al., 2005 ; Yoneda et al., 2007). Recently, Yoneda proposed new criteria, which include positivity for anti-NAE antibody (2013).

In a study of 80 patients with Hashimoto's encephalopathy, Yoneda reported various clinical phenotypes such as the acute encephalopathy form (58%), chronic psychiatric form (17%), and other particular clinical forms, including progressive cerebellar ataxia (16%), limbic encephalitis, and the Creutzfeldt-Jakob disease-like form. Neurological findings include disturbance of consciousness (66%), mental disturbance (53%), dementia (38%), involuntary movement (31%), convulsion (29%), and cerebellar ataxia (28%) (Yoneda, 2013a). The clinical manifestations of Hashimoto's encephalopathy are wide-ranging, and steroid therapy is highly effective (Yoneda, 2012 ; Ota et al., 2009). As mentioned above, we should consider Hashimoto's encephalopathy as a treatable form of dementia.

In the present case, the disease transitioned from chronic to acute after symptoms began to fluctuate. Although steroid non-responsive cases have been reported (Mijajlovic et al., 2010), steroid-treated Hashimoto's encephalopathy generally has a good prognosis. In our case, the preserved cerebral blood flow and absence of irreversible changes in the brain as observed on MRI may have contributed to the good prognosis. Hashimoto's encephalopathy is a disorder that involves immune pathogenic mechanisms, but the roles of anti-thyroid antibodies and anti-NAE antibodies have not been fully elucidated (Schiess et al., 2008).

This case suggests that we should evaluate anti-thyroid antibodies when the cause of neurological disturbances and disturbance of consciousness is unidentified, because Hashimoto's encephalopathy has various patterns of onset.

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