An 85-year-old Case with Hashimoto’s Encephalopathy, Showing Spontaneous Complete Remission

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Abstract

We report an 85-year-old man with Hashimoto’s encephalopathy (HE) who showed spontaneous complete remission. The autoantibody against the amino (NH₂) terminal region of α-enolase was positive in our patient. Neuropsychological manifestations, such as personality change and progressive cognitive impairment, gradually improved over approximately 6 weeks after onset of disease without corticosteroid treatment in parallel with a decrease in the anti-thyroglobulin antibody in the cerebrospinal fluid. HE should be considered as a possible diagnosis even in elderly patients with neuropsychiatric symptoms, particularly when a previous history of thyroid disease is present.

Key words: Hashimoto’s encephalopathy, anti-thyroglobulin antibody, anti-α-enolase antibody, thyroid disease, spontaneous remission

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Introduction

Hashimoto’s encephalopathy (HE) is a neurological disorder of unknown etiology associated with thyroid autoimmunity. This disease occurs preferentially at age 40 to 50, and shows subacute-onset neuropsychological symptoms such as confusion and cognitive impairment (1, 2). The effectiveness of corticosteroid is an important clue in the diagnosis of HE (1, 2). In this report we describe an elderly patient with HE who showed spontaneous complete remission without corticosteroid treatment. HE may be a possible diagnosis also in elderly patients with neuropsychological symptoms, particularly when neuroradiological examinations, such as magnetic resonance imaging (MRI), demonstrate no abnormal findings suggestive of other central nervous system (CNS) diseases, including cerebrovascular disorders (CVD) and Creutzfeldt-Jakob disease (CJD).

Case Report

An 85-year-old man with no previous psychiatric history abruptly developed personality change and cognitive impairment with no apparent precipitating causes while being treated for chronic thyroiditis with L-thyroxine at a dose of 125 μg/day. There was no fever or headache. He gradually became unable to continue his work as a farmer during the next two weeks because of progressive worsening of cognitive impairment with two sudden-onset attacks of right hemiplegia or speech disturbance persisting for approximately 10 min. On admission to our hospital one month after onset of disease, physical examination showed no abnormal findings in either the chest or the abdomen. He was in a confusional state with poor concentration, postural fine tremor and myoclonus with no paresis in the extremities predominantly on the right side, and no signs of meningeal irritation. On the revised Hasegawa’s dementia scale (HDS-R) he scored 13/30 (normal level higher than 20/30). No involvement was seen in either cranial nerves or sensation. All deep tendon reflexes were normal with negative Babinski’s sign on both sides. There were no abnormal findings in routine laboratory data, including urinalysis, hematology, blood chemistry and thyroid function (free T3 2.53 pg/ml, normal 2.3-4.0 pg/ml; free T4 1.38 ng/dl, normal 1.0-2.0 ng/dl), except for a mildly elevated level of thyroid-stimulating hormone (TSH, 10.86 μU/ml, normal 0.2-4.0 μU/ml). The anti-

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thyroid peroxidase antibody was within normal limits (1.8 IU/ml, normal value less than 10.0 IU/ml), but anti-thyroglobulin antibody (TGAb) was markedly elevated (29,043 IU/ml, normal value less than 10.0 IU/ml). The autoantibody against the amino (NH$_2$) terminal region of $\alpha$-enolase (NAE) could be detected in serum (Fig. 1), and the anti-nuclear antibody was negative. Cerebrospinal fluid (CSF) showed normocytosis and increased levels of total protein (88 mg/dl, normal 10-40) and TGAb (579.0 IU/ml) with negative cytology and bacterial culture. The IgG index in CSF was within normal limits. No abnormal findings were detected either on radiological examinations, such as MRI (Fig. 2) and single photon emission computed tomography (SPECT) of the brain, or on the electroencephalogram (EEG). Magnetic resonance angiography demonstrated no significant stenosis in any branch of the main cerebral arteries.

After admission to our hospital, both cognitive impairment and involuntary movement gradually improved without any treatment other than successive administration of L-thyroxine, and disappeared with normalization of HDS-R in approximately 2 weeks (Fig. 3). TSH showed no obvious alterations and TGAb in serum increased after admission, while TGAb in CSF clearly decreased in conjunction with the disappearance of neuropsychological symptoms. The patient completely recovered with no neurological sequelae, and was discharged from our hospital 3 weeks after admission. He has been in good neurological condition without any relapse of neuropsychological symptoms for 1 year to date.

### Discussion

The present patient showed cognitive impairment and personality change of abrupt onset, and these psychiatric symptoms gradually worsened with the appearance of involuntary movement within 1 month after onset of disease. Subacute meningoencephalitis was excluded as a possible diagnosis because of the lack of clinical findings suggestive of CNS inflammation, such as fever and pleocytosis in CSF. Elderly-onset generalized myoclonus is often a characteristic feature of CJD, but other evidence of this disease, including a cortical high-intensity signal on MRI and periodic synchronous discharge on EEG, was absent. Routine laboratory data showed no abnormal findings typical of other disorders causing neuropsychological symptoms, and our patient was finally diagnosed as having HE on the basis of a high concentration of TGAb in serum and a characteristic history of stroke-like episodes (1, 2). Several recent reports have suggested that the serum autoantibody against NAE is a useful diagnostic marker of HE (3-5), and in our patient also this antibody was positive. HE has been reported to sometimes show generalized myoclonus similar to that of CJD as seen in our patient (6-8). Our patient showed no obvious abnormalities on either EEG or SPECT on admission, but these
Figure 3. Clinical course of the patient. Neuropsychiatric symptoms improved without corticosteroid treatment in parallel with an increase on the revised Hasegawa’s dementia scale (HDS-R) and a decrease in the anti-thyroglobulin antibody (TGAb) in the cerebrospinal fluid (CSF), and completely recovered within approximately 6 weeks after onset of disease. Change in clinical symptoms is subjectively demonstrated on the basis of neurological examinations.

results might be due to his having already entered the recovery phase of HE at examination.

There are 3 notable characteristics in our patient. First, he developed HE at age 85, which was a remarkably late onset for this disease. HE usually occurs in the forties, and only 2 cases have been reported as developing over the age of 80 (6, 9). Neuropsychiatric symptoms such as confusion and cognitive impairment are easily caused by other disorders, including CVD and metabolic diseases, in elderly people. HE might be important in the differential diagnosis of neuropsychiatric manifestations even in elderly patients. Second, HE in our patient showed spontaneous complete remission within approximately 6 weeks after onset. The therapeutic efficacy of corticosteroid has been emphasized as one of the most characteristic features of HE, and steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) has been proposed as another name for this disease (9-11). Nevertheless, a recent report has demonstrated that some patients with HE can recover without any treatment as seen in our patient, and others do not respond to corticosteroid (2). Since HE shows a broader spectrum than previously thought with respect to the clinical course and responsiveness to corticosteroid, some patients with this disease might be overlooked or misdiagnosed as having a different neurological disorder, particularly when elderly.

Third, TGAb in CSF was well correlated with the disease activity of HE in our patient. The precise pathogenetic mechanisms of HE remain unclear, but anti-thyroid autoantibodies in CSF, including TGAb, are considered to play an important role in manifesting CNS symptoms because these antibodies are undetectable in patients with autoimmune thyroiditis or other neurological disorders (12, 13). Our patient showed an elevated level of TGAb in CSF on admission, and a quick decrease in conjunction with improvement of CNS symptoms. These clinical findings support the above-mentioned hypothesis concerning the pathogenetic mechanisms of HE but also suggest that TGAb in CSF may be helpful as a clinical marker indicating disease activity. TGAb in CSF was still elevated even on disappearance of neuropsychological symptoms, but this result might be due to a discrepancy in time between normalization of laboratory data and clinical improvement. As the IgG index was normal throughout the clinical course in our patient, part of the TGAb produced in large quantity outside the CNS might have successfully traversed the blood-brain barrier (BBB). Considering that our patient showed a higher serum level of TGAb after clinical improvement than before, a transient increase in the permeability of BBB probably caused easy migration of this antibody from the peripheral blood to the brain, leading to the development of neuropsychological symptoms of HE.

In conclusion, HE can occur even in elderly people over 80 years. When elderly patients with neuropsychiatric symptoms show no abnormal findings on either MRI or EEG suggestive of other neurological disorders, HE should be considered as a possible diagnosis, particularly in people with a previous history of thyroid disease. Corticosteroid is of course the first line treatment for HE, but some patients can spontaneously recover without any treatment in parallel with a decrease in TGAb in CSF.

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References


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