Hashimoto’s encephalopathy with gait disturbance caused by sensory ganglionopathy: A case report and review of the literature

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ABSTRACT

Hashimoto’s encephalopathy (HE) is a steroid-responsive encephalopathy characterized by several neurological symptoms. HE mainly involves the central nervous system; the peripheral nervous system is rarely involved. We treated a previously healthy elderly man showing mild cognitive decline and subacute progressive gait disturbance due to severe sensory deficits, including sensation of touch and deep sensation with elevated anti-NH2 terminal of α-enolase and anti-thyroid antibodies. His sensory disturbance symptoms improved after steroid therapy, suggesting that the neuropathy was related to HE. His disease was characteristic of HE in that his sensory deficits responded well and rapidly to steroid therapy. A nerve conduction study showed reduced sensory nerve action potentials in all limbs, indicating that his neuropathy was not “axonopathy”, but “sensory ganglionopathy”, which can occur concurrently with autoimmune disorders. Dysautonomia may be the responsible pathomechanism because of the vulnerability of the blood–nerve barrier at the ganglia. Although the pathophysiology of HE has not been clearly elucidated, autoimmune inflammation has been reported in a number of autopsy cases, indicating that sensory ganglionopathy can develop with HE. Therefore, HE should be recognized as one type of “treatable neuropathy”.

1. Introduction

Hashimoto’s encephalopathy (HE) is a rare steroid-responsive encephalopathy involving elevated anti-thyroid antibodies, and about half of all patients with HE are normal thyroid function [1]. Due to central nervous system (CNS) involvement, patients with HE usually show different neuropsychiatric symptoms. The peripheral nervous system is rarely affected [2–7]. Here, we report a case involving an 85-year-old male patient with HE who presented with gait disturbance due to sensory ataxia. Our case suggests that inflammation or antibody reactions, which have been reported as pathophysiology in HE, can cause “sensory ganglionopathy”.

2. Case description

An 85-year-old male patient without a notable medical history presented with a 2-month history of progressive gait disturbance. He had severe frostbite on his toes and showed mild cognitive impairment, with particular disturbance of his frontal lobe function. He had no nystagmus, dysarthria, weakness, or limb ataxia; however, he could not walk without support. Deep tendon reflex showed hyperreflexia at the patella and hyporeflexia at the Achilles. Sensory functions, particularly deep sensory functions, were impaired in all limbs, but were dominant in the lower limbs, and Romberg’s sign was positive. He also showed orthostatic hypotension without compensation of an elevated pulse. A blood test showed elevated anti-NH2 terminal of α-enolase (NAE) and anti-thyroid antibodies with normal thyroid function, whereas diabetes mellitus, vitamin deficiency, infectious diseases, collagen diseases, and malignant tumor markers were all negative. Onconeuronal antibodies, including anti-amphiphysin, CV2, PNMA2, Ri, Yo, Hu, recoverin, SOX1, titin, GAD65, and Tr, were negative, whereas anti-GM1 IgG antibody with phospholipidic acid was weakly positive. Cerebrospinal fluid (CSF) was normal. Brain magnetic resonance (MR) imaging showed mild diffuse atrophy, and spinal MR imaging showed a herniated disc at the L4/5 level without nerve root compression. 123I-Iodoamphetamine single photon emission computed tomography demonstrated a marked reduction in blood flow in the bilateral rear cingulate gyrus, and electroencephalography demonstrated that his basic rhythm was within normal limits. A nerve conduction study (NCS) revealed reduced sensory nerve action potentials (SNAPs) in the ulnar and radial nerves (ulnar 2.4 μV, radial 0.7 μV), SNAPs below the detection limit in the median and sural nerves, and slightly decreased compound muscle action potentials (CMAPs) in the peroneal nerves. Taken together, these results suggested that sensory ataxia was responsible for his gait disturbance and that HE may be the cause. Anti-GM1 IgG antibody usually causes motor-dominant axonopathy, such as acute motor axonal neuropathy in Guillain–Barré syndrome, or multifocal motor neuropathy. We consider that the positive antibody in this case may have been caused by impaired autoimmunity, which is one of the pathomechanisms of HE. Therefore, we started intravenous methylprednisolone followed by oral prednisolone, which markedly improved his gait, allowing him to be able to walk without support at 1 week after treatment. During his outpatient care, he could walk faster and more stably following the amelioration of his sensory disturbance and a reduction in the titer of anti-thyroid antibodies; however, another NCS revealed no significant changes.

3. Discussion

The symptoms of HE, including seizures or disturbance of consciousness during acute onset and progressive dementia, psychosis, or...
involuntary movement during subacute or chronic onset, are generally related to the CNS [2]. Cerebellar ataxia is also a common neurological syndrome in HE [1]. However, this case showed remarkable sensory-dominant neuropathy as opposed to cerebellar signs or a decline in cerebellar blood flow, suggesting sensory ataxia.

A few cases with peripheral neuropathy accompanied by HE have been reported (Table 1). Those cases developed a variety of symptoms during the subacute course. An NCS demonstrated demyelinating peripheral neuropathy with multiple conduction blocks and decreased conduction velocity in some patients [3-5], and a reduction in SNAPs or CMAPs in others, including the present case [6-8]. Cao and colleagues [6] reported a case involving a 54-year-old female patient with progressive gait disturbance for 3 months without weakness and a decline in SNAPs based on an NCS. She also showed hallucinations, cognitive decline, and hyperreflexia, suggesting the involvement of both the CNS and peripheral nervous system. Vincenzo [6] reported a case involving a young female patient with sensory disturbance, including the pain and touch sensations at not only the distal, but also the proximal limbs; these previous cases were similar to the present case. Importantly, in almost all cases, regardless of the type of “neuropathy”, steroid therapy improved the symptoms within 1 month. The present case also rapidly improved after immunotherapy, suggesting that the nerves were disturbed functionally as opposed to physically.

Recently, the concept of “sensory ganglionopathy” has been established. Sensory ganglionopathy is defined as sensory disturbance caused by affected sensory ganglia with preserved muscle strength, and is non-nerve-length-dependent, resulting in effects in both the distal and proximal limbs or trunk [9]. Symptom onset commonly occurs in the distal limbs in polyneuropathies. In that condition, large nerve fibers, including those that detect vibrations or proprioception, are also damaged over a period of days or weeks. A previous report [10] revealed enhancement of dorsal root ganglia in MR imaging, which was not established. Sensory ganglionopathy is defined as sensory disturbance caused by affected sensory ganglia with preserved muscle strength, and is non-nerve-length-dependent, resulting in effects in both the distal and proximal limbs; these previous cases were similar to the present case. Importantly, in almost all cases, regardless of the type of “neuropathy”, steroid therapy improved the symptoms within 1 month. The present case also rapidly improved after immunotherapy, suggesting that the nerves were disturbed functionally as opposed to physically.

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In summary, peripheral neuropathy is rare in HE, but may be underestimated. Although the pathomechanism also remains poorly understood and further study is necessary, HE should be considered a “treatable neuropathy” using immunotherapy.

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**Table 1**

Characteristics and clinical courses of cases with Hashimoto’s encephalopathy showing neuropathy.

| Ref. | Age/sex | PNS symptoms | CNS symptoms | Clinical course | Anti-thyroid Ab | NCS | Treatment and clinical prognosis |
|------|---------|---------------|--------------|----------------|----------------|-----|---------------------------------|
| [2]  | 35M     | Distal dominant mild weakness (L/E) | Deterioration of execution function | 2 m | Titer of AMA: 6400 U/ml | Reduced MCV/NCV with CB | IVMP improved within 1 w |
| [3]  | 26M     | Distal dominant dysaesthesia and mild weakness | (-) | 1 m | anti-TPO: 2009 U/ml; anti-TG: 1983 U/ml | Reduced MCV with TD | IVlg, IVMP improved within 1 m |
| [4]  | 27F     | Distal dominant weakness (sensory loss (all modalities)) | (-) | 2 m | anti-TPO: 600 IU/ml; anti-TG: 546 IU/ml | Reduced MCV with prolonged DL | IVMP improved slowly |
| [5]  | 54M     | Postural tremor | Speech difficulty | 3 m | Titer of AMA: 6,600,000 | Reduced SNAP | Oral PSL improved slowly |
| [6]  | 13F     | Ataxic gait (cerebellar sign (−)) | Visual hallucinations (sensory) | 2 d | Anti-TPO: 886 IU/ml; anti-TG: 2121 IU/ml | Reduced SNAP | IVlg improved within 2 w |
| [7]  | 16F     | Hand Tremor | Agitation | 4 m | Anti-TPO: 1010 IU/ml | Reduced CMAP and SNAP (CMAP< SNAP) | IVMP, PP No improvement |
| Our case | 85M | Sensory deficiency (pain (−) deep sensory) | Deterioration of executive function | 2 m | Anti-TPO: 140 IU/ml | Reduced CMAP and SNAP (CMAP< SNAP) | IVMP, oral PSL improved within 1 w |

M: male; F: female; PNS, peripheral nervous system; CNS, central nervous system; L/E, lower extremity; m, month; w, week; Ab, antibody; AMA, AMAN; antinuclear antibody (normal <9 IU/ml), TPO, anti-thyroid peroxidase antibodies (normal <28 IU/ml), TG, anti-thyroglobulin antibodies (normal <16 IU/ml), SNAP, sensory nerve action potential, CMAP, compound muscle action potential, CB, conduction block; TD, temporal dispersion; DE, distal latencies, IVMP, intravenous methylprednisolone, PSL, prednisolone, PP, plasmapheresis, NA, not available.
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Ethical publication statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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