PostScript

LETTERS

Hashimoto's encephalopathy presenting with progressive cerebellar ataxia

Hashimoto's encephalopathy is an autoimmune encephalopathy that came to be regarded as a new clinical entity distinct from myxo-oedema encephalopathy, associated with Hashimoto's thyroiditis.[1 2]

Hashimoto's encephalopathy has a wide clinical spectrum with various neuropsychiatric features. The detection of antithyroid antibodies in patient sera is helpful but not sufficient for the diagnosis of Hashimoto's encephalopathy because of the high prevalence of antibodies in the normal population.

Recently, we reported serum autoantibodies against the amino (NH_2) terminal region of α enolase (NAE) as a useful diagnostic marker of Hashimoto's encephalopathy.[3]

We describe here a patient with Hashimoto's encephalopathy, who presented with progressive cerebellar ataxia with mild abnormality on electroencephalography (EEG) and showed marked improvement after steroid administration. The patient was diagnosed as having Hashimoto's encephalopathy owing to the presence of the anti-NAE antibodies as well as antithyroid antibodies in the serum.

A 41-year-old woman, who had a normal dietary history, became aware of a slight unsteadiness while walking and mild dysarthria in December 2003. She had no familial history of neurological disorders or episodes of seizures. The symptoms gradually worsened, and she was admitted to the University of Fukui hospital in September 2004 because she could not stand or walk without support.

Neurological examinations showed severe gait ataxia, slurred speech and dysmetria on finger-to-nose and heel-to-knee manoeuvres. Cognitive functions and intellectual performance were normal. Ocular movement was full and smooth and without nystagmus. Deep tendon reflexes were normal and without any pathological reflex. No apparent paresis abnormal sensations including deep sensations, extrapyramidal signs or autonomic dysfunctions were found.

Magnetic resonance imaging of the brain did not detect any atrophy of the cerebellum or any abnormal signal. EEG showed diffuse slow-wave activities (7–8 Hz) without any epileptic discharge. Analysis of the cerebrospinal fluid did not show any pleocytosis or increases in protein (15 mg/dl) and immunoglobulin (Ig)G (1.2 mg/dl) levels. Peripheral blood cell counts, electrolytes, liver and kidney functions, and levels of lactate, ammonia, vitamins B_1, B_{12} and E were all normal. Serological markers specific for collagen diseases such as antinuclear, anti-DNA, anti-Sm, anti-RNP, anti-SSA, anti-SSB, anti-glutamic acid decarboxylase (GAD) antibodies, c-antineutrophil cytoplasmic antibodies and myeloperoxidase-antineutrophil cytoplasmic antibodies were either negative or in the normal range. Titters of antibodies against Herpes simplex, Varicella-zoster, Epstein-Barrvirus, cytomegalovirus and echo viruses were not raised in the serum or in the cerebrospinal fluid. Anti-Hu, anti-Yo and anti-Ri antibodies were also negative. Tumour markers such as carcinoembryonic antigen, cancer antigen (CA)19-9 and CA125 were normal. Investigation for malignancy did not detect any sign of malignant disease. Gene analyses did not detect any mutation for hereditary spinocerebellar ataxia (SCA1, SCA6, Machado–Joseph disease and dentate-rubro-pallido-luysian atrophy) or mitochondrial diseases (MELAS and MERRF).

Investigation for thyroid showed euthyroidism (thyroid-stimulating hormone (TSH), 1.7 μU/ml; normal, 0.4–4.0 μU/ml, free T_3, 3.4 pg/ml; normal, 2.4–4.3 pg/ml, free T_4, 0.9 ng/dl; normal, 0.9–1.8 ng/dl) and raised levels of antithyroid peroxidase (50.0 U/ml; normal, 0–0.3 U/ml) and antithyroglobulin antibodies (4.9 U/ml; normal, 0–0.3 U/ml). Anti-NAE antibodies in the serum—a diagnostic marker of Hashimoto's encephalopathy—were strongly positive before steroid treatment, then changed to a weak signal on an immunoblot, after treatment, determined using its recombinant protein expressed in human cultured cells, as described previously (fig 1).[3] The ethics committee of the University of Fukui approved this research. Written permission was obtained from the patient.

After intravenous administration of high-dose methylprednisolone (1 g/day) for 3 days, followed by oral administration of prednisolone (30 mg/day), the ataxia improved markedly, and the patient was able to walk unaided 3 weeks after the start of the treatment. The ataxia almost disappeared after continuous treatment for 3 months. Severity of ataxia was evaluated by the size of the estimated area when the patient stood on a stabilimeter. Estimated areas became markedly smaller on the stabilimeter after steroid treatment: pre-treatment area, $13.9 \times 8.4 = 116.76$ cm^2, post-treatment area, $4.8 \times 3.4 = 16.32$ cm^2. Slow-wave activities on EEG partially improved after the treatment.

Pure cerebellar ataxia can be caused by various reagents (alcohol or drugs), or may accompany vitamin deficiencies, viral infections, collagen diseases, autoimmune conditions (anti-GAD antibodies), spinocerebellar degenerations, neoplasm or mitochondrial diseases with or without cerebellar atrophy. Although anti-GAD antibodies were detected in the sera from patients with ataxia and type 1 diabetes,[4] the antibodies were not detected in our patient. Other possible causes of ataxia were excluded by the clinical history, and laboratory and radiological findings in the present case. Although hypothyroidism is another well-known cause of ataxia, she had normal thyroid functions.

Patients with Hashimoto's encephalopathy present with a variety of neuropsychiatric symptoms or signs such as hypertonia, tremors, myoclonus, choreoathetosis, seizures, dementia, psychiatric symptoms and strokes.[1 2] Ataxia is also reported in some patients with Hashimoto's encephalopathy.[2 5] Compared with these reported cases of Hashimoto's encephalopathy with ataxia, the clinical findings in our patient are unique: (1) absence of neurological findings other than ataxia except for mild EEG abnormality and (2) the insidious onset and slow progression of ataxia. Other reported cases of ataxia showed acute or subacute progressions accompanied by other neurological symptoms or signs.[2 5] Selim and Drachman[5] reported six patients with cerebellar ataxia associated with

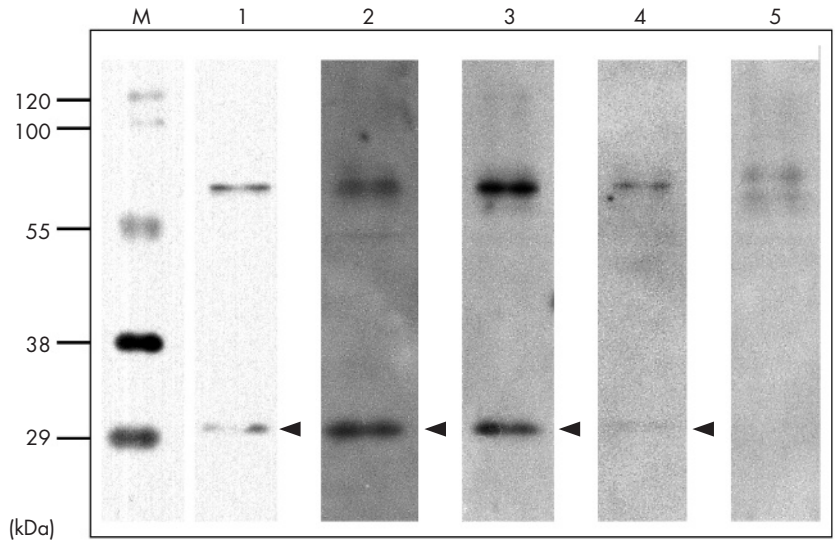

Figure 1 Immunoblot of a recombinant amino (NH_2) terminal region of α enolase (NAE) with sera from an ataxic patient with Hashimoto's encephalopathy. M, molecular weight marker; lane 1, recombinant NAE protein; lane 2, serum from a positive control (patient with Hashimoto's encephalopathy, lanes 3, serum from the present case before steroid treatment; lane 4, serum from the present case after steroid treatment; lane 5, serum from a normal control. Arrowheads indicate the position of NAE. Sera were diluted 300-fold. A strong signal against the NAE was detected in serum from the present case, and became weaker after steroid administration.

Hashimoto's thyroiditis, in most of whom cerebellar atrophy was shown on magnetic resonance imaging. One of their reported cases was treated by intravenous immunoglobulin IgG, and ataxia partially improved.[5] Although responsiveness to intravenous immunoglobulin suggested autoimmune mechanisms in the pathogenesis of ataxia in this patient, it remains uncertain whether or not ataxia and cerebellar atrophy were aetiologically associated with Hashimoto's thyroiditis. By contrast, our patient with progressive ataxia had a positive serological diagnostic marker, anti-NAE antibodies and showed an excellent response to steroid treatment, leading to a diagnosis of Hashimoto's encephalopathy.

In conclusion, this report suggests that a diagnosis of Hashimoto's encephalopathy is warranted in patients with progressive pure ataxia and anti-NAE antibodies are a useful serological marker of diagnosis. Moreover, Hashimoto's encephalopathy should be included in a differential diagnosis of a treatable ataxia.

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Third-nerve palsy heralding dissecting aneurysm of posterior cerebral artery: digital subtraction angiography and magnetic resonance appearance

Dissections of intracranial arteries are rare and occur most commonly in the vertebrobasilar system.[1] Isolated dissecting aneurysms of the posterior cerebral artery (PCA) are very uncommon. We report a case of subarachnoid haemorrhage (SAH) heralded by a 3-month history of diplopia due to dissection of the right PCA documented with digital subtraction angiography (DSA), magnetic resonance imaging (MRI) and angiography (MRA). The patient was treated conservatively, with a good outcome.

Case report

A 58-year-old male farm worker was found unconscious in the countryside and admitted to hospital. His medical history was unremarkable except for treated arterial hypertension and diplopia for 3 months. On admission, he had a Glasgow Coma Scale (GCS) score of 14 and a complete right third-nerve palsy. Vision and corneal reflexes were normal. A computed tomography scan showed diffuse SAH and intraventricular haemorrhage with hydrocephalus (fig 1A). Soon after arrival, he became less responsive and underwent temporary external ventricular drainage. DSA disclosed a fusiform dilatation of the P1–P2 segment of the right PCA with a focal ''blister'', suggesting a dissecting aneurysm (fig 1B).

Twenty days later, his GCS score was 15. MRI showed an area of hyperintensity in fluid-attenuated inversion recovery images in the right portion of the ambiens cistern and isohyperintensity in T1-weighted images and in axial source images of 3D time-of-flight MRA consistent with intramural haematoma in the subacute phase (fig 1C, D). The haematoma surrounded the P1–P2 segment of the PCA. We found no evidence of ischaemic brain lesions. The patient was transferred to a rehabilitation centre.

Four months later, the patient returned to his normal activities. Neurological examination showed partial third-nerve palsy with ptosis, impaired adduction and a right mydriatic pupil with no reaction to light. A follow-up DSA showed a reduction of the right PCA fusiform dilatation, with disappearance of the focal blister (fig 1E). MRI and MRA showed a decrease in size of the intramural haematoma (fig 1F).

Discussion

We found a description of 26 cases with isolated PCA dissection in the English literature. The clinical presentation is usually with ischaemic symptoms in the PCA territory (17 patients) whereas SAH was described in 9 patients.[1–3]

Our case has some peculiarities, which include the clinical presentation, the findings on diagnostic imaging and the clinical evolution.

In patients with PCA dissection, third-nerve palsy was reported in one, which was related to ischaemic lesion in the mid-brain.[1] In our patient, diplopia appeared 3 months before admission and was probably due to progressive enlargement of intramural haematoma with compression of the third-nerve trunk before rupture in the subarachnoid space.

The aetiology of PCA dissection and more generally of intracranial dissections remains obscure, although it has been associated with trauma and sport-related activities, cervical manipulations, arteritis, atherosclerosis, fibromuscular dysplasia, surgery, delivery,

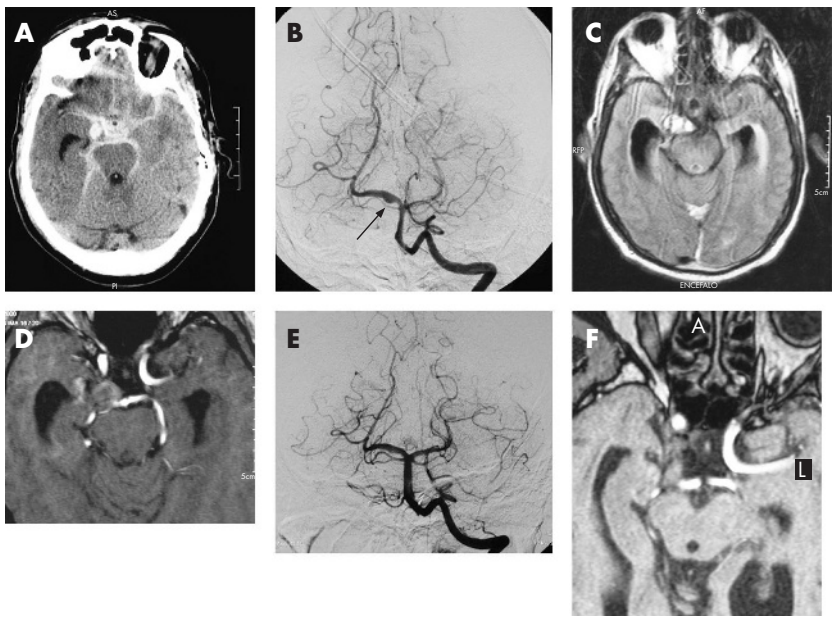

Figure 1 Computed tomography scan at admission showing extensive subarachnoid haemorrhage (SAH) (A). Digital subtraction angiography (DSA; anteroposterior projection) showing a fusiform ectasia of the P1–P2 segment of the right posterior cerebral artery (PCA) with a focal ''blister'' (arrow) (B). Twenty days later, axial fluid-attenuated inversion recovery magnetic resonance (FLAIR MR) image (C) and axial T1-weighted source image of three-dimensional time-of-flight magnetic resonance angiography (3D TOF MRA) (D) show an area of abnormal signal intensity in the right portion of the ambiens cistern surrounding the P1–P2 segment of the right PCA, consistent with intramural haematoma in the subacute phase. DSA (E) and source image of 3D TOF MRA (F) 4 months after SAH showing a near normalisation of the right PCA calibre without focal blister (E) and a decrease in the size of the intramural haematoma (F).