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Letter to the Editor

Abnormal evoked potentials in autoimmune glial fibrillary acidic protein astrocytopathy

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ABSTRACT

Autoimmune GFAP astrocytopathy is a new clinical entity and only a limited number of cases have been reported. Here we report the results of multimodal central conduction studies performed in a case of this disorder.

A 72-year-old woman developed gradual cognitive decline and gait disturbance. A neurological examination revealed moderate amnesia, papilloedema, and pyramidal tract impairment of the bilateral lower limbs. The diagnosis of autoimmune GFAP astrocytopathy was made based on the typical MRI findings of periventricular radial linear gadolinium enhancement in the brain and longitudinally extensive lesions in the spinal cord, and anti-GFAP antibody detected in the cerebrospinal fluid. Somatosensory evoked potentials and transcranial magnetic stimulation studies revealed prolongation of conduction times. Visual evoked potentials showed an unusual W-shaped pattern. To our knowledge, this is the first neurophysiological demonstration of prolonged central conduction times in the autoimmune GFAP astrocytopathy. Further investigations are needed to establish the clinical value the neurophysiological examinations in this disorder.

Dear Editor

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is a new disease entity that was first described in humans by Fang et al. in 2016 [1]. Various clinical features have been reported, including encephalopathy, seizures, and optic disc edema. Longitudinally extensive spinal-cord lesions and linear perivascular radial enhancement are characteristic radiological findings of autoimmune GFAP astrocytopathy. The neurological and radiological spectrum is unified by the detection of the specific anti-GFAP antibody in cerebrospinal fluid (CSF) [2]. While there is insufficient pathological evidence, it has been speculated that activation of lymphocytes and microglia causes extensive inflammation around microvessels [3,4]. However, neurophysiological studies of autoimmune GFAP astrocytopathy are largely missing.

Here we report abnormal findings in the following multimodal evoked potentials in a case of autoimmune GFAP astrocytopathy: sensory evoked potentials (SEPs), motor evoked potentials (MEPs), and visual evoked potentials (VEPs).

1. Case report

A 72-year-old woman had experienced gradual cognitive decline and gait disturbance during the 6-month period before being admitted to our hospital. On examination, she had moderate amnesia with confabulation. Papilloedema was present. She had mild leg weakness and her deep tendon reflexes were generally exaggerated with positive Babinski's sign. Her sensations were normal, but she had bilateral postural hand tremor and urinary incontinence. The blood test results were not remarkable. The CSF showed mild pleocytosis (32/μl), elevated protein (93 mg/dl), and positive oligoclonal bands. CSF myelin basic protein was negative, and the IgG index was normal (0.73). Brain magnetic resonance imaging (MRI) demonstrated T2 elongation of the white matter in the occipital region, with T1-weighted gadolinium (Gd) enhanced images showing prominent linear perivascular radial enhancement (Fig. 1A, B, C, D). Spinal-cord T2-weighted MRI revealed a longitudinally extensive T2 hyperintense lesion between segments C2 and L5. The central canal of this lesion was enhanced with Gd. In addition, there were patchy multiple Gd-enhanced lesions in the dorsal spinal cord at segments C2 and C3 (Fig. 1E, F). Positron-emission tomography with ^{18}F-fluorodeoxyglucose and ^{11}C-methionine indicated no pathological uptake.

The conduction times of SEPs were prolonged for tibial-nerve stimulation at 22.8 ms (N21 to P38; normal limit, 19.3 ms) and normal for median-nerve stimulation at 4.45 ms (N13 to N20; normal limit, 4.70 ms). The central motor conduction time measured by using transcranial magnetic stimulation was normal for the upper extremity at 6.95 ms (the motor cortex to C8 nerve root; normal limit, 7.7 ms), but prolonged for the lower extremity at 19.5 ms (the motor cortex to L5 nerve root; normal limit, 17.0 ms) (Fig. 2A) [5]. VEPs showed an unusual W-shaped pattern (Fig. 2B) [6]. Serum autoantibodies to aquaporin 4, myelin oligodendrocyte glycoprotein, and *N*-methyl-D-aspartate receptor were negative, but anti-GFAP antibody was positive in the CSF, leading to the diagnosis of autoimmune GFAP astrocytopathy. Treatments with intravenous and oral corticosteroids improved the clinical symptoms, particularly the cognitive impairments and gait disturbance. However, the central conduction times remained to be delayed one month after the start of oral steroid.

2. Discussion

We have reported the clinical and electrophysiological features of a patient with subacute encephalomyelitis, whom we diagnosed with autoimmune GFAP astrocytopathy. The radiological hallmark of linear perivascular radial Gd enhancement and the presence of the specific anti-GFAP antibody in CSF strongly support its diagnosis.

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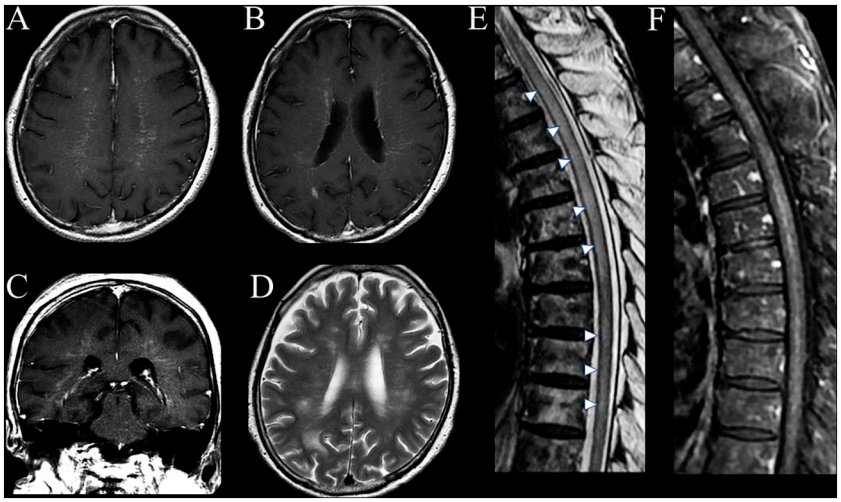

Fig. 1. MRI of the brain (A–D) and spinal cord (E, F), Gd-enhanced T1-weighted images revealed perivascular radial enhancement (A, B, C). T2-weighted images showed hyperintense lesions in the periventricular white matter (D). Spinal-cord MRI showed longitudinally extensive lesions on T2-weighted images (E, arrow heads) and Gd enhancement along the central canal (F).

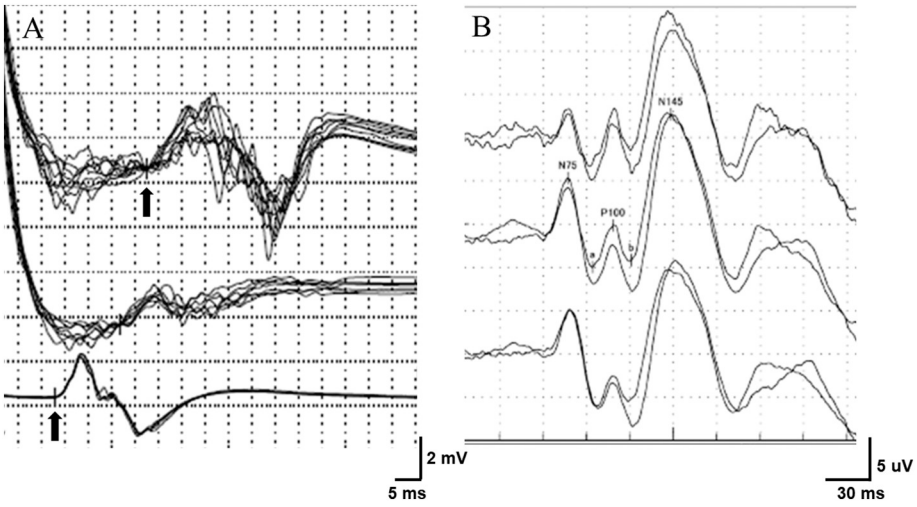

Fig. 2. Waveforms of motor evoked potentials from tibialis anterior muscles (A) and visual evoked potentials (B). Motor evoked potentials recorded from the anterior tibialis muscles are shown for stimulations at the motor cortex (top), C8 nerve root (middle), and L5 nerve root (bottom) (A). Central motor conduction time calculated as the difference between the latencies of cortical and L5 nerve root stimulations (arrows) was abnormally prolonged. Visual evoked potentials showed an unusual triphasic form in a bifid or W-shaped pattern (B).

To our knowledge, this is the first neurophysiological demonstration of central conduction delay in autoimmune GFAP astrocytopathy. Central conduction in both motor and sensory pathways was delayed for the lower limbs, suggesting the involvement of the pyramidal tract and dorsal column–medial lemniscus pathways.

The involvement of the visual pathway was suggested by the abnormal W-shaped pattern of the VEPs. W-shaped VEPs are significantly associated with MS and regarded to be equivalent to a P100 delay [6]. It is notable that our patient had papilloedema without cranial hypertension, which is one of the characteristic clinical features of autoimmune GFAP astrocytopathy [2]. However, w-shaped VEPs might not be explained by papilloedema, and the abnormal VEPs instead suggest the involvement of the visual pathway, such as retrobulbar optic neuritis.

Previous pathological studies have revealed inflammatory infiltrates in perivascular regions in autoimmune GFAP astrocytopathy [3]. Neurofilament light chain in CSF, a marker of axonal damage and neuronal death, is known to be elevated in patients with amyotrophic lateral sclerosis, relapsing-remitting multiple sclerosis, and autoimmune GFAP astrocytopathy. Central conduction delay is also not specific to the disease processes, and it remains controversial whether the immune reactions cause demyelination or axonal loss. Further investigations of autoimmune GFAP astrocytopathy are needed, particularly of its pathological and neurophysiological aspects.

Consent form

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Declaration of Competing Interest [7]

None.

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Ryo Tokimura[a,*], Nozomu Matsuda[a], Shunsuke Kobayashi[a], Akio Kimura[b], Kazuaki Kanai[a]
[a] *Department of Neurology, Fukushima Medical University, 1 Hikarigaoka, Fukushima, Fukushima 960-1295, Japan*
[b] *Department of Neurology and Geriatrics, Gifu University Graduate School of Medicine, 1-1 Yanagido, Gifu 501-1194, Japan*
E-mail address: ryotok@fmu.ac.jp (R. Tokimura).

* Corresponding author.