Images in Neurology

Severe Hippocampal Atrophy in a Patient With Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy

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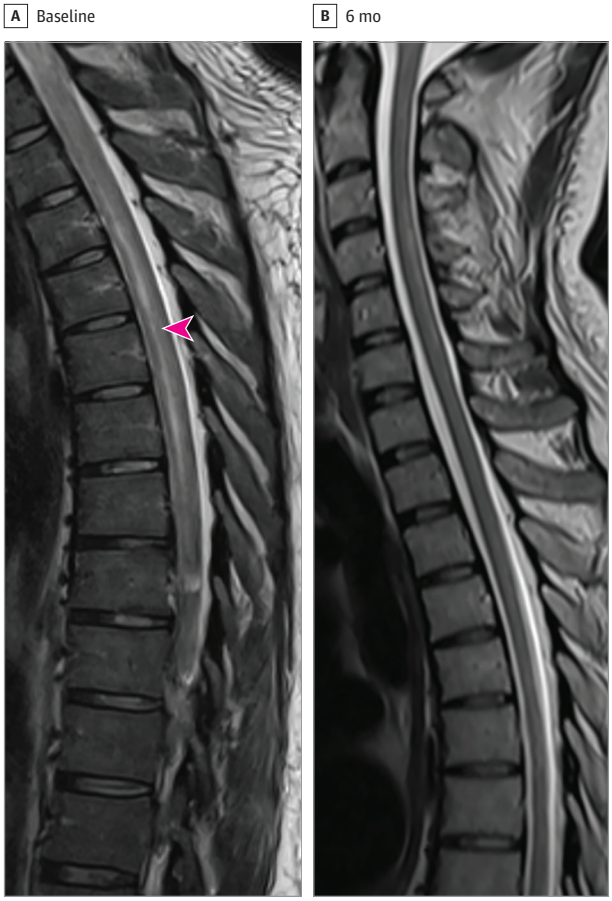
A 33-year-old man with autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy presented with headache, fever, quadriparesis, and reduced visual acuity in the left eye to the emergency department. Magnetic resonance imaging (MRI) showed longitudinally extensive spinal cord hyperintensities and a normal cerebral scan (**Figure 1**A and **Figure 2**A). Cerebrospinal fluid (CSF) analysis revealed an elevated lymphocytic cell count (154 cell/µL). CSF polymerase chain reaction test results for herpes simplex virus 1 and 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, John Cunningham virus, HIV, and varicella-zoster virus IgG/IgM were negative. The patient was diagnosed with noninfectious meningoencephalomyelitis and received high-dose intravenous methylprednisone.

Figure 1. Spinal Cord Magnetic Resonance Imaging

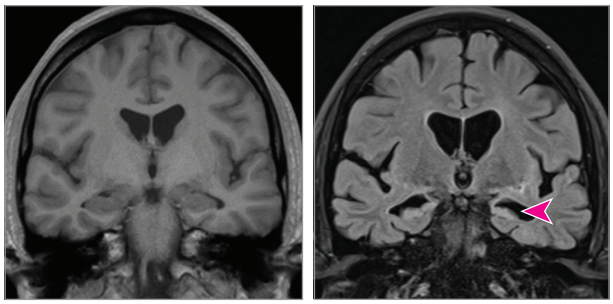


A, Baseline sagittal spinal cord T2-weighted sequences showed longitudinally extensive spinal cord lesion (arrowhead). B, At 6-month follow-up, the spinal cord T2-weighted magnetic resonance imaging showed that the lesion was markedly improved.

Six-month follow-up at our center showed persistent quadriparesis and new-onset cognitive deficits (concentration, attention). MRI showed regressing multisegmental nonenhancing spinal cord lesions (Figure 1B) but new bilateral cerebellar peduncle, periaqueductal lesions, mild to moderate global, and severe bilateral hippocampal volume loss (Figure 2B). CSF analysis showed persistent pleocytosis (10 cells/µL) and CSF-specific oligoclonal bands. A large panel of neuronal autoantibodies including *N*-methyl-D-aspartate receptor, leucine-rich glioma-inactivated 1, GABA-B receptor, aquaporin-4, MOG, and others and onconeural antibodies were negative in CSF and serum. Further workup revealed IgG GFAP autoantibodies in CSF (1:32) on immunofluorescent assay and cell-based assay, confirming the diagnosis of autoimmune GFAP astrocytopathy (serum cell-based assay positive, immunofluorescent assay negative). Positron emission tomography–computed tomography showed no malignant neoplasms. The patient started taking methotrexate, 15 mg, and continued oral prednisone, 10 mg. He remained clinically stable on regular follow-up visits.

On 18-month follow-up, the patient had persistent severe paraparesis with sphincter dysfunction and severe visual impairment in the left eye. Neuropsychological assessment revealed impaired verbal and visuospatial memory function and reduced information processing speed. Cerebral MRI showed persistent bilateral hippocampal atrophy. Quantitative volumetric MRI analysis using FreeSurfer version 6.0 confirmed significantly reduced hippocampal volumes (43.5% reduction; 2262.5 mm^3 vs mean [SD] of 4000.9 [235.0] mm^3; $P < .001$) compared with age- and sex-matched (1:15) healthy

Figure 2. Cerebral Magnetic Resonance Imaging



A, Baseline cerebral magnetic resonance imaging without global or regional atrophy (T1-weighted sequence). B, At 6-month follow-up, severe hippocampal atrophy (arrowhead) with mild to moderate global atrophy (fluid-attenuated inversion recovery) as well as bilateral cerebellar peduncle were observed. Cerebral magnetic resonance imaging at 18- and 30-month follow-up was stable showing persistent T2-hyperintense lesions in the cerebellar peduncles as well as moderate global and severe bilateral hippocampal atrophy. Compared with the previous scans, no new signs of inflammatory lesions or other changes were observed.

controls measured at the same MRI scanner. Furthermore, volumetric analyses confirmed whole-brain volume loss (−9.5%) and revealed additional regional brain volume loss in thalamus (−20.7%), basal ganglia (−12.9% to −24.5%), and cerebellum (−11.2%). GFAP antibodies were positive in CSF (1:8) on immunofluorescent assay and cell-based assay but negative in serum. Cerebral MRI remained unchanged 30 months after onset.

Autoimmune GFAP astrocytopathy is a rare inflammatory central nervous system disorder typically presenting with meningoencephalomyelitis.[1] MRI frequently shows linear periventricular radial gadolinium enhancement,[2] but a broad spectrum of other brain and spinal cord MRI lesions has been reported, including T2-weighted/fluid-attenuated inversion recovery lesions in the periventricular region, the brainstem, cerebellum, thalamus, and basal ganglia.[3]

We identified severe hippocampal atrophy together with global and subcortical regional brain atrophy and longitudinally extensive spinal cord lesions in a patient with persistent cognitive impairment following autoimmune GFAP astrocytopathy. No affected brain regions showed T2/fluid-attenuated inversion recovery hyperintense lesions on previous MRI scans. This case highlights substantial hippocampal involvement in GFAP astrocytopathy and potential structural central nervous system damage with subsequent atrophy even in normal-appearing brain regions.

ARTICLE INFORMATION

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