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Newly Diagnosed Amyotrophic Lateral Sclerosis in a Patient with Multiple-System Atrophy

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Dear Editor,

Multiple-system atrophy (MSA) is a rapidly progressive neurodegenerative disorder due to alpha-synucleinopathy that presents with extrapyramidal, cerebellar, autonomic, or pyramidal symptoms.[1] Amyotrophic lateral sclerosis (ALS) is a motor neuron disease with clinical hallmarks of upper motor neuron (UMN) and lower motor neuron (LMN) signs.[2] There have been very few reports of the coexistence of MSA and ALS.[3] Here we report a case of newly diagnosed ALS in a patient with MSA.

A 68-year-old woman who had been diagnosed with MSA visited the emergency room due to dyspnea. She had been diagnosed 2 years previously with MSA based on her clinical history of 4 years of progressing symptoms of gait and limb ataxia, autonomic dysfunction, mild bradykinesia, and hoarse voice. Urinary dysfunction was checked using a postvoiding residual urine test, which showed 100 mL of residual urine in her bladder. The tilt test induced an orthostatic decrease of >60 mm Hg in the systolic blood pressure. No obvious muscle atrophy or pathologic reflex was observed. The patient had no specific past medical history except for lumbar spinal stenosis, and no family history of neurodegenerative disease. Brain MRI performed at the time of the MSA diagnosis revealed prominent atrophy bilaterally in the putamen, cerebellum, and pons. Also, brain ^{18}F-fluorodeoxyglucose positron emission tomography showed decreased glucose metabolism bilaterally in the cerebellum and pons.

The patient was diagnosed with probable MSA of cerebellar and parkinsonian type and observed for her clinical symptoms and course.[4] She had been in a bedridden state for 1 year and had developed dysphagia a few months previously. The findings suggestive of stridor in her history were not clear. Her mental status was alert on admission. There was Medical Research Council (MRC) grade 3 weakness in her left arm and both legs, MRC grade 2 weakness in her right arm, and muscle atrophy in all four extremities. Intrinsic muscle atrophy was seen in both the first dorsal interosseous and both tibialis anterior muscles. Tongue atrophy was also observed. Truncal weakness prevented her from maintaining an erect posture. The deep tendon reflex was absent on the right knee and slightly increased on the left knee and both arms, despite the presence of muscle weakness. The plantar reflexes were extensor bilaterally, the glabellar reflexes were present, and abdominal skin reflexes were absent. A sensory examination revealed no deficit, and no stridor was observed.

On the second hospital day her dyspnea aggravated, and arterial blood gas analysis revealed severe CO_2 retention (pH 7.32, pCO_2=73.3 mm Hg, pO_2=63.5 mm Hg, and O_2 saturation=90.6%), which was corrected by mechanical ventilation. Eventually a tracheostomy was performed to install a portable ventilator. A brain MRI diffusion scan was done due to her asymmetric weakness, which did not reveal acute infarction or hemorrhage. However, bilateral atrophy of the putamen, cerebellum, and brain stem was observed in the fluid attenuated inversion recovery images (Fig. 1). A nerve conduction study revealed reduced compound muscle action potential amplitudes. Electromyography (EMG) revealed spontaneous denervation po-

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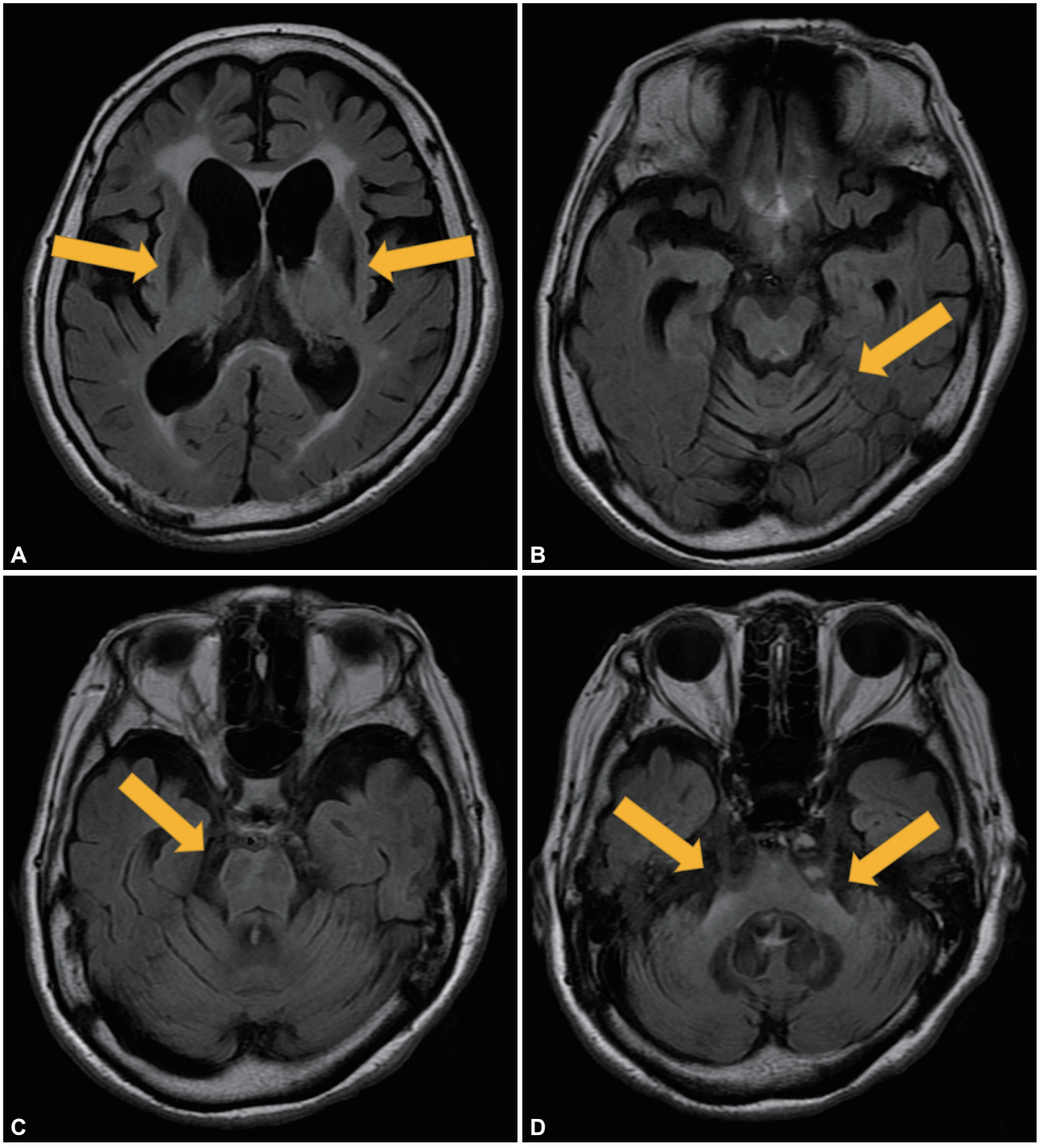

Fig. 1. Brain MRI findings (arrows). Axial fluid attenuated inversion recovery T2 weighted image showing bilateral putaminal atrophy (A), prominent cerebellar folia (B), a cruciform hyperintensity (hot-cross-bun sign) in the pons (C), and hyperintensity in the middle cerebellar peduncle (D).

tential (fibrillations and positive sharp waves) and enlarged motor-unit potentials in the cervical, thoracic, and lumbosacral regions. The patient met the revised El Escorial diagnostic criteria for clinically definite ALS with UMN and LMN signs in the bulbar, cervical, and lumbosacral regions.

Very few cases of concurrently diagnosed MSA and ALS have been reported.[3] To the best of our knowledge, this case is the first report of sporadic MSA and ALS detected in the same patient. The pathophysiology underlying this coexistence remains unclear. Based on previous studies of the pathology of the MSA and ALS, mitochondrial dysfunction might explain the coexistence of these two diseases.[2,5] It is possible that the loss of an-

terior horn cells in an MSA patient results in amyotrophy,[6,7] but this is not sufficient to explain the EMG findings in our patient. Obtaining a clearer explanation of the cause requires more case reviews and experimental studies. We suggest that MSA patients with LMN or UMN involvement should be thoroughly examined for other neurodegenerative disease such as ALS in order to make an accurate diagnosis and prognosis prediction.

Author Contributions

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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