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Teaching Neuro*Images*: Late-onset Alexander disease

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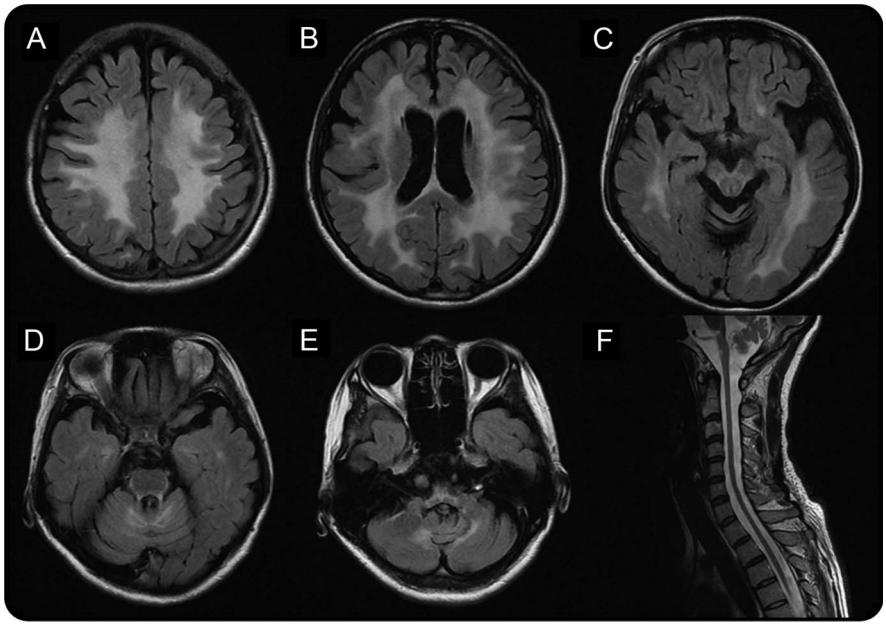
Figure 1 Brain and spine MRI



Fluid-attenuated inversion recovery images show diffuse hyperintensities involving periventricular and subcortical white matter (A–C). Pial signal changes around pons (D) and medulla (E) as well as diffuse atrophies of spinal cord (F) are diagnostic clues.

A 38-year-old woman presented with an 8-year history of progressive dysarthria, gait disturbance, and hyperreflexia. MRI revealed leukodystrophy involving brainstem with pial signal changes and spinal cord atrophy (figure 1). Brain biopsy showed Rosenthal fibers (figure 2). She had a de novo mutation of the glial fibrillary acidic protein (GFAP) gene (c.799G>C causing p.Ala267Pro).

Alexander disease is caused by gain-of-function mutation of the GFAP gene. GFAP is an intermediate filament, and mutations result in astrocytic accumulation of eosinophilic inclusions known as Rosenthal fibers.[1] Late-onset patients show brainstem features (ataxia, dysphagia, dysphonia, and palatal myoclonus) with hindbrain-predominant leukodystrophy and spinal cord atrophy.[1,2]

AUTHOR CONTRIBUTIONS

Drs. Keon-Joo Lee and Jangsup Moon: drafting the manuscript. Drs. Keon-Joo Lee, Jangsup Moon, and Soon-Tae Lee: study concept, design, and chart review. Dr. Soon-Tae Lee: critical revision of the manuscript and funding support.

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DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

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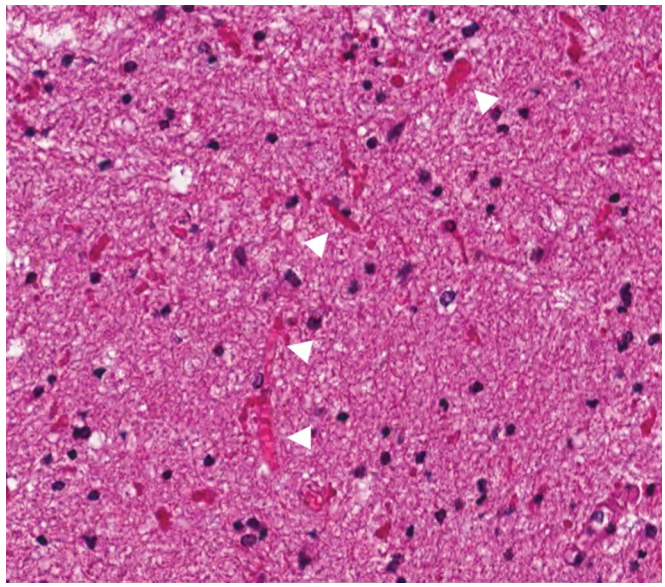
Figure 2 Rosenthal fibers



Hematoxylin & eosin staining of the white matter biopsy showed typical morphology of Rosenthal fibers (arrowheads). Rosenthal fibers are beaded, elongated, or corkscrew-shaped intracytoplasmic inclusions that represent accumulation of intermediate filament. Rosenthal fibers are seen in neoplasms (such as pilocytic astrocytomas), Alexander disease, and reactive tissues with gliosis.

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