Hemidystonia Associated with Alexander Disease

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Case Presentation

- Alexander disease is an autosomal dominant progressive leukodystrophy caused by mutation in the glial fibrillary acidic protein (*GFAP*) gene
- Three clinical variants: infantile, juvenile and adult onset

Background

- 35-year-old woman with progressive difficulty walking and using her left hand since age 14
- Progressive vision loss and ophthalmoparesis since age 8
- Examination: macrocephaly, absent ocular pursuits, left arm and leg dystonia, spastic ataxic gait
- Progressive vision loss was attributed to retinitis pigmentosa (RP) (Fig. 1)
- Initial MRI: right frontal lobe mass, porencephalic cyst
- Mass and cyst were resected at age 9, with a rendered diagnosis of pilocytic astrocytoma (PA), WHO grade I
- Serial surveillance MR imaging showed variable enhancement in the left middle cerebellar peduncle, hypothalamus and thalamus (Fig. 2, Image A)
- Diagnosis was changed to Alexander disease (AD) after re-examination of pathology, which showed profuse Rosenthal fibers and Rosenthal fiber-like granular inclusions in astrocytic cell bodies, characteristic of AD and not a feature of PA (Fig. 3)

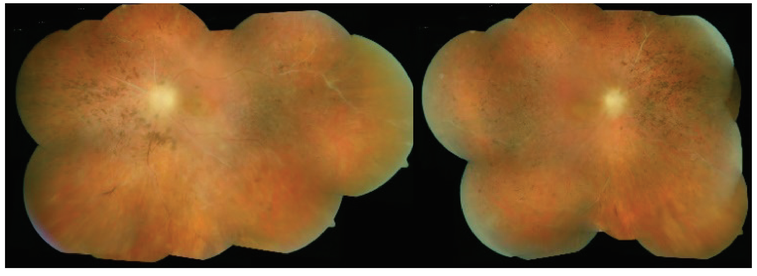

Figure 1. Right and left eyes show atrophic gliosis from optic disc edema, retinal atrophy and secondary pigmentary degeneration. Retinal vasculature shows glial sheathing and peripheral vaso-obliteration.

Imaging Findings

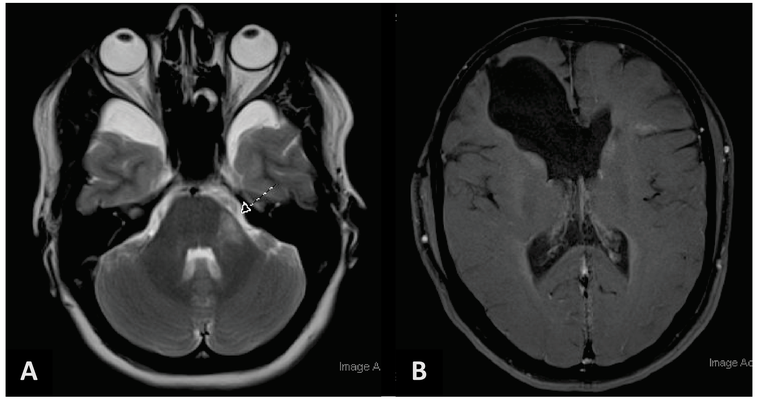

Figure 2. A: Left middle cerebellar peduncle lesion (arrow); B: Porencephaly, post-resection of right frontal mass

Movement Disorder

- Ataxia and palatal myoclonus are the two most frequent movement disorders in patients with AD (typically late onset)
- Ataxia is present in about 46% of juvenile AD, and in 82% of adult onset AD
- Palatal myoclonus is present in about 34% of adult onset AD, 2% of juvenile AD, and almost never seen in infantile variant
- "Extrapyramidal symptoms," "rigidity," "spasticity" and "unsteady gait" have been previously described, but this is the first case of AD associated with dystonia
- Although left hemidystonia in our patient is probably due to the right frontal porencephalic cyst, cystic degeneration and basal ganglia lesions are frequently found in patients with AD

Pathology

- In addition to AD, Rosenthal fiber formation can be seen in pilocytic astrocytoma, ganglioglioma and pleomorphic xanthoastrocytoma
- Cytologically atypical astrocytes, a recognized feature of AD, could contribute to misdiagnosis as brain tumor
- This diagnostic pitfall can be avoided by awareness of one distinctive histologic feature of AD - the presence of Rosenthal fiber-like eosinophilic cytoplasmic inclusions in astrocyte cell bodies, which is not typically seen in other mimicking conditions

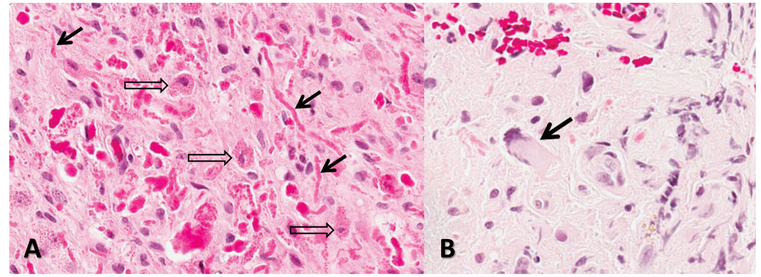

Figure 3. A: Prominent Rosenthal fiber formation (solid arrows); Rosenthal fiber-like eosinophilic cytoplasmic inclusions in astrocyte cell bodies (A, open arrows); B: Astrocytes with markedly atypical nuclei (B, solid arrow) are also a characteristic morphologic feature of AD

Selected References

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