Incidental case of Alexander disease in a patient admitted for Pyelonephritis

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Introduction:

Alexander's disease is a very rare fatal leukodystrophy, which usually becomes clinically evident in the infantile period, although neonatal, juvenile and even adult variants are recognized.

Pathophysiology involves mutations in the gene for glial fibrillary acidic protein (GFAP) that maps to chromosome 17q21. It is inherited in an autosomal dominant manner; however, most cases arise *de novo* as the result of sporadic mutations. Most common type is the infantile form that usually begins during the first 2 years of life. The juvenile form of Alexander disease has an onset between the ages of 2 and 13 years. The disease can affect both males and females equally.

Case Presentation: A Twelve years old boy recently immigrated from Pakistan, admitted for pyelonephritis had a large head size of 58cm (above 95th centile). On further questioning mother described delayed neck holding, sitting and walking, fine motor, social and language skills. Patient is a fourth child of related parents without any family history of early death of 3 close relatives due to a kidney disease. On examination patient had coarse facial features, poor eye contact and bilateral palpable kidneys. Neurometabolic investigations of serum were unremarkable. CT head consistent with frontal lobe leukodystrophy while MRI showed: Symmetrical T2/flair periventricular centrum semi ovale, hyper intensities most pronounced in bi frontal region and involving the subcortical U fibers. Periventricular cystic leukomalacia Representing alexander's disease. Genetic testing is pending.

Diagnosis: presence of four of the five following criteria establishes an MRI-based diagnosis of Alexander disease: a) Extensive cerebral white matter abnormalities with a frontal preponderance. b) Periventricular rim of decreased signal intensity on T_2-weighted images and elevated signal intensity on T_1-weighted images. c) Abnormalities of the basal ganglia and thalami that may include one or both of the following: Swelling and increased signal intensity on T_2-weighted images or Atrophy and increased/decreased signal intensity on T_2-weighted images d) Brain stem abnormalities, particularly involving the medulla and midbrain. e) Contrast enhancement of one or more of the following: ventricular lining, periventricular rim, frontal white matter, optic chiasm, fornix, basal ganglia, thalamus, dentate nucleus, and brain stem.

Conclusion:

Alexander disease is progressive, often fatal and debilitating disease for patient and families. Making correct diagnosis is essential. Clinical, MRI Findings and Genetic testing for GFAP peptide sequencing mutation can confirm the diagnosis. Treatment of Alexander disease remains supportive. A multidisciplinary and comprehensive approach can improve function and quality of life for affected individuals. Supportive management such as: Anti seizure medications, baclofen and benzodiazepines for hypertonia and spasticity.

References: Messing A, Brenner M. GFAP at 50. ASN Neuro 2020; 12:1759091420949680.
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