Pediatric Neurology 93 (2019) 61–62

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Visual Diagnosis

Progressive Head Enlargement in a Child With Motor Delay

Indar Kumar Sharawat, DM, Renu Suthar, DM *

Pediatric Neurology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ARTICLE INFO

Article history:
Received 1 September 2018
Accepted 22 September 2018
Available online 25 September 2018

Keywords:
Alexander disease
Leukodystrophy
Macrocephaly
Magnetic resonance imaging
Epilepsy

This three and a half-year-old boy presented with progressively increasing head size. He had mild motor delay but his cognitive and language abilities were age appropriate. He had a seizure at age two years. There was no family history of a neurological disorder. He was born to nonconsanguineous parents and the perinatal period was unremarkable. On examination, he had macrocephaly (head circumference: 55 cm, greater than 3 *z*score WHO growth chart), and rest of the neurological examination was normal. Magnetic resonance imaging of the brain was suggestive of frontal-predominant white matter changes (Fig). Next generation sequencing revealed a pathogenic heterozygous missense variation in exon 4 of the glial fibrillary acidic protein (GFAP) gene (c.715C > T), confirming the diagnosis of Alexander disease (AD).

Inherited genetic-metabolic disorders presenting with macrocephaly include AD, Canavan's disease, Tay-Sachs disease, glutaric aciduria type-1, and megalencephalic leukoencephalopathy with subcortical cysts. MRI is diagnostic in AD, and characteristically shows frontal predominant extensive white matter changes, a thin rim of periventricular T1 hyperintense and T2 hypointense signal changes, abnormal signal changes in basal ganglia, thalamus and brainstem, and selective contrast enhancement.[1] AD is an extremely rare, progressive, autosomal dominant inherited leukodystrophy.[2]The pathological hallmark of AD is Rosenthal fibers, characteristically present in subependymal, perivascular, and

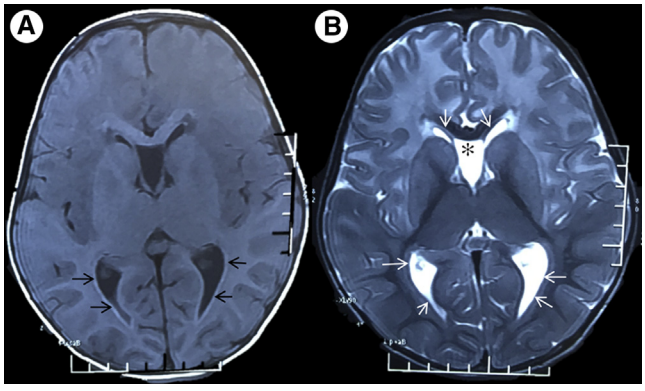

FIGURE. Axial T1-weighted MRI sequence (A) shows a thin rim of periventricular hyperintense signal changes (black arrows). Axial T2-weighted (B) sequence shows extensive symmetrical bilateral involvement of the frontal white matter and subcortical U fibers with relative sparing of parieto-occipital white matter, thin irregular periventricular rim of low signal intensity (white arrows), and cavum septum pellucidum (asterix). Both caudate nuclei and the putamena showed hyperintense signal changes and the caudate heads were mildly enlarged (B). Post-gadolinium axial images showed ependymal enhancement (not shown). The color version of this figure is available in the online edition.

Conflict of interest and source of funding statement: The authors declare no conflict of interest or financial disclosures concerning the materials or methods used in this study or the findings specified in this article.

* Corresponding author.
E-mail address: drrenusuthar@gmail.com (R. Suthar).

https://doi.org/10.1016/j.pediatrneurol.2018.09.009

subpial region. Classically three variants have been described: infantile, juvenile, and adult-onset AD. Infantile onset AD is the most common and severe form, with onset before two years of age. It is characterized by progressive macrocephaly, developmental delay or regression, seizures, pyramidal signs, and hydrocephalus. Seizures are present in a significant proportion of the patients and can include generalized tonic-clonic, tonic, focal, and rarely epileptic spasms.[3] Treatment is supportive and most of the children with infantile AD die before 10 years of age.[4]

References

1. Messing A. Alexander disease. Handbook of Clinical Neurology. Elsevier; 2018, 693–700. Available at: https://linkinghub.elsevier.com/retrieve/pii/B9780444640765000442. Accessed August 26, 2018.
2. Johnson AB, Brenner M. Alexander's disease: clinical, pathologic, and genetic features. J Child Neurol. 2003;18:625–632.
3. Lee JM, Kim AS, Lee SJ, et al. A case of infantile Alexander disease accompanied by infantile spasms diagnosed by DNA analysis. J Korean Med Sci. 2006;21:954.
4. Messing A, Brenner M, Feany MB, Nedergaard M, Goldman JE. Alexander disease. J Neurosci. 2012;32:5017–5023.