Pediatric Neurology 99 (2019) 92–93

Contents lists available at ScienceDirect

Pediatric Neurology

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

Visual Diagnosis

Progressive Cognitive Decline and Gait Instability in a Four-Year-Old Boy

Kabelo Thusang, MD *, Suad Khalil, MD

Department of Neurology and Ophthalmology, Michigan State University, East Lansing, Michigan

ARTICLE INFO

Article history:
Received 27 February 2019
Accepted 22 March 2019
Available online 29 March 2019

Keywords:
Pediatric
Leukodystrophy
MRI
Adrenal insufficiency
Krabbe disease

This four-year-old boy presented with a one-year history of progressive cognitive regression, visual impairment, left-sided weakness, and gait instability. Neurological examination was significant for decreased visual acuity, weakness of his left extremities, diffuse spasticity that was more pronounced in the left extremities, and a spastic gait. Magnetic resonance imaging revealed prominent T2-hyperintense signal abnormality in the splenium of the corpus callosum and the peritrigonal deep white matter along the occipital horns (Fig A and B) along with subtle enhancement along the left parietal leading edge in the subcortical deep white matter. Laboratory evaluation showed decreased cortisol level, normal serum amino acids, urine organic acids, ammonia, liver function tests, and acyl carnitine. He began taking fludrocortisone with marked improvement. In view of the neuroimaging and adrenal insufficiency, the patient was thought to have X-linked adrenoleukodystrophy. However, very-long-chain fatty acid levels were normal. A leukodystrophy panel revealed a *GALC* mutation.

Discussion

The *GALC* gene encodes galactosyl ceramide beta-galactosidase, and deficiency of this enzyme causes Krabbe disease, an autosomal recessive sphingolipidosis. The incidence of Krabbe disease has been estimated to be 1:100 000; however, newborn screening identified 1:6000 individuals with reduced enzyme activity of unclear significance.[1] Different mechanisms have been suggested to explain how *GALC* mutations cause nervous system pathology, including inflammatory and direct toxicity from psychosine.[2] Beyond the nervous system, the manifestations of Krabbe disease have not been fully elucidated. One patient with Krabbe disease showed extremely rare hepatic macrophages at autopsy.[3] We describe the first patient with Krabbe disease and adrenal insufficiency. In individuals with X-linked adrenoleukodystrophy, the adrenal glands show lamellae and lamellar lipid profiles, with very-long-chain fatty acid esterified to cholesterol, in adrenocortical cells.[4] Perhaps substrates of galactosyl ceramide beta-galactosidase induce similar changes in the adrenal cells. In the future autopsy of adrenal glands may clarify this.

Author contributions: Kabelo Thusang: Acquisition of data, analysis and interpretation, and critical revision of manuscript for intellectual content. Suad Khalil: Data analysis and interpretation and critical revision of manuscript for intellectual content.

Conflict of interest and source of funding statement: The authors report no financial disclosure and have no conflict of interest to disclose. No funding or sponsorship was obtained for producing this manuscript.

* Communications should be addressed to: Thusang; Department of Neurology and Ophthalmology; Michigan State University; 788 Service Road, B-401 Clinical Center; East Lansing, MI 48824.

E-mail address: kabelo.thusang@msu.edu (K. Thusang).

https://doi.org/10.1016/j.pediatrneurol.2019.03.022
0887-8994/

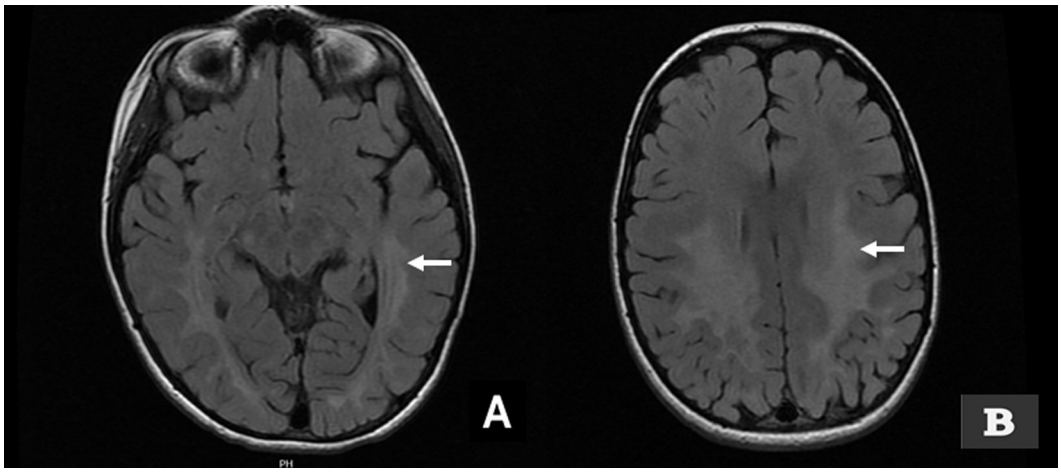

FIGURE. Magnetic resonance imaging of the brain, axial images. (A and B) (Fluid-attenuated inversion recovery) T2-hyperintense signal in the splenium of the corpus callosum and the peritrigonal deep white matter along the occipital horns of the lateral ventricles, extending into the temporal lobes and corona radiata bilaterally (white arrows). Post-gadolinum T1-weighted image showing subtle enhancement along the left parietal leading edge in the subcortical deep white matter (not shown).

References

1. Turgeon CT, Orsini JJ, Sanders KA, et al. Measurement of psychosine in dried blood spots–a possible improvement to newborn screening programs for Krabbe disease. J Inherit Metab Dis. 2015;38:923.
2. Hawkins-Salsbury JA, Shea L, Jiang X, et al. Mechanism-based combination treatment dramatically increases therapeutic efficacy in murine globoid cell leukodystrophy. J Neurosci. 2015;35:6495–6505.
3. Del Bigio MR. Autopsy neuropathology findings in a child with chronic infantile krabbe leukoencephalopathy. Pediatr Neurol. 2018;82:51–52.
4. Powers JM, Moser HW, Moser AB, Schaumburg HH. Fetal adrenoleukodystrophy: the significance of pathologic lesions in adrenal gland and testis. Hum Pathol. 1982;13:1013–1019.