Neuroimaging Highlight

Editors: Mark Hudon, Richard Farb

Optic Nerve Enlargement Associated with Globoid Cell Leukodystrophy

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A six-month-old female developed marked irritability, multifocal myoclonic jerks and episodic opisthotonus. Developmental milestones and growth (height and weight) plateaued at three months of age, despite adequate oral intake. Pregnancy, birth and family history were non-contributory. Neurological examination revealed a very irritable baby with poor visual contact and tracking. Head circumference was in the 7th percentile and height and weight were less than the 2nd percentile for age and gender. Funduscopic examination was unremarkable. Appendicular and truncal tone were increased, deep tendon reflexes were difficult to elicit and plantar responses were downgoing. Hands were tightly fisted. There was no significant dysmorphism, skin lesion or organomegaly.

Complete blood count, liver function tests, serum electrolytes, ammonia, lactate, very long chain fatty acids, amino acids and urine organic acids were normal. Cerebrospinal fluid analysis revealed a markedly elevated protein content of 4 g/L with normal glucose, lactate, amino acids, nucleated and red cell count. Electroencephalogram demonstrated relatively normal background rhythms with multifocal independent epileptiform discharges maximal bi-centrally.

Sequential axial images from a non-contrast computed tomography study of the brain (Figure 1), demonstrated moderately severe generalized cerebral atrophy. Abnormal hyperdensities in the thalami (large white arrows) were observed along with patchy hypodensities in the white matter of the centrum semiovale (small white arrows).

On sequential axial FLAIR images of the brain (Figure 2), abnormal T2 hyperintensity was seen within the deep white matter of both hemispheres, sparing the subcortical U-fibres. The abnormal signal extended into the internal capsule, ventral pons and corticospinal tracts to the level of the medulla (small black arrows). Patchy abnormal increased signal was also seen in the dentate nuclei of both cerebellar hemispheres. A striking finding was marked enlargement of the prechiasmatic and intra-orbital segments of the optic nerves bilaterally on para-sagittal T1-weighted images (large white arrows). In conjunction with the clinical history, these imaging findings were suggestive of a progressive leukodystrophy. Krabbe's disease was suspected on the basis of the rarely reported description of optic nerve

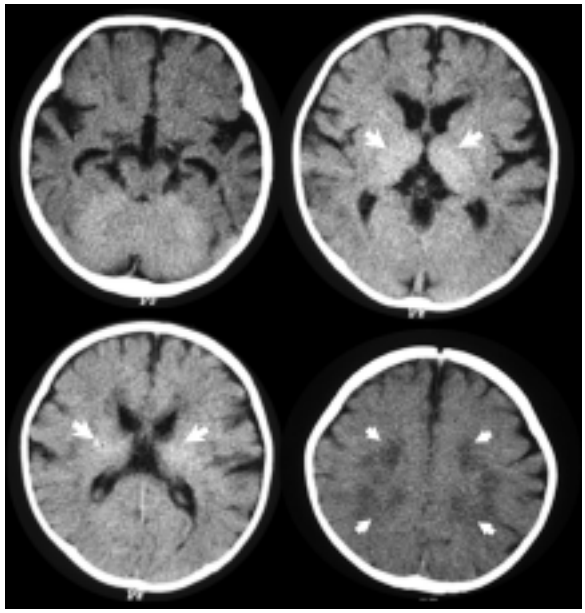

Figure 1: *Sequential axial images from a non-contrast computed tomography study of the brain demonstrated moderately severe generalized cerebral atrophy. Abnormal hyperdensities in the thalami (large white arrows) were also observed along with patchy hypodensities in the white matter of the centrum semiovale (small white arrows).*

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hypertrophy with this disorder.[1-4] The diagnosis was subsequently confirmed by the absence of measurable leukocyte galactocerebrosidase activity.

Globoid cell leukodystrophy or Krabbe's disease is an autosomal recessive lysosomal storage disorder with dysfunctional galactosylceramidase activity resulting in accumulation of galactosylceramide and galactosylsphingosine (psychosine). The major histopathological findings are severe oligodendrocyte loss, leading to profound central demyelination and dysmyelination, and the presence of galactosylceramide-laden macrophages, called globoid cells. Optic nerve hypertrophy results from accumulation of globoid cells within the optic nerves.[1] Unfortunately, no effective therapies exist for this relentlessly progressive disorder which is fatal usually within the first year of life.

Many neurodegenerative disorders can present with white matter changes on imaging including metachromatic leukodystrophy, adrenoleukodystrophy, Alexander's disease, Canavan's disease and Pelizaeus-Merzbacher disease. The white matter changes have a frontal predominance in Alexander's disease and posterior prevalence in adrenoleukodystrophy. Recognition of optic nerve hypertrophy in conjunction with diffuse white matter disease or symmetrical hyperdensities in the thalami, caudate, corona radiata and brainstem on non-contrast computed tomography, should suggest a diagnosis of Krabbe's disease. Optic nerve enlargement and hyperintense white matter lesions can also be commonly seen in patients with neurofibromatosis type 1 (NF-1). In NF-1, however, the white matter changes are patchy and not confluent. In addition, the distinct clinical presentations of NF-1 and Krabbe's should lead to the appropriate diagnosis.

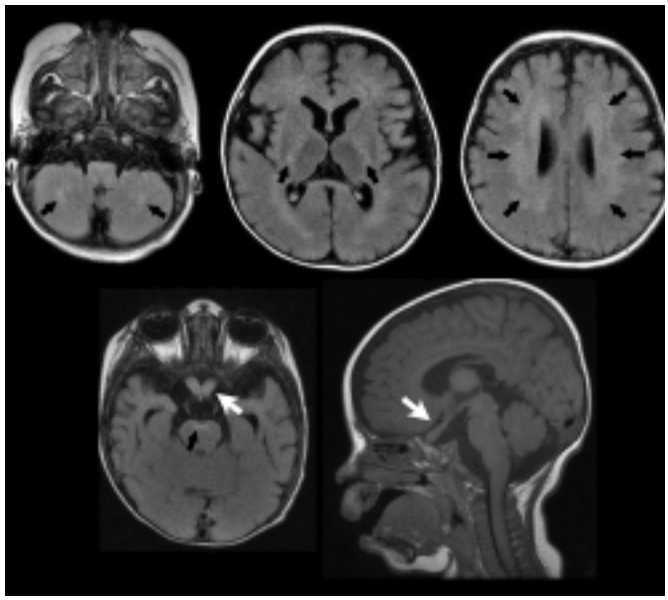

Figure 2: *Sequential axial FLAIR images of the brain demonstrated abnormal T2 hyperintensity within the deep white matter of both hemispheres, sparing the subcortical U-fibres, extending into the internal capsule, ventral pons and corticospinal tracts to the level of the medulla (small black arrows). Patchy abnormal increased signal was also seen in the dentate nuclei of both cerebellar hemispheres. A striking finding was marked enlargement of the prechiasmatic and intra-orbital segments of the optic nerves bilaterally on para-sagittal T1-weighted images (large white arrows).*

References

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