Optic nerve enlargement in infantile form of Krabbe disease

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Abstract

Krabbe disease (KD) is an autosomal recessive lysosomal storage disorder caused by dysfunctional galactosylceramidase activity. Infantile form is the most common subtype, occurring at about 6-month of age. We present a rare case of infantile KD with magnetic resonance imaging showing white matter, thalamic and basal ganglia lesions rarely associated with an enlargement of the optic nerves bilaterally.

Introduction

Krabbe disease (KD) is an autosomal recessive lysosomal storage disorder with an estimated incidence of 1 in 100,000-200,000 live births caused by dysfunctional galactosylceramidase activity resulting in accumulation of galactosylceramide and galactosylsphingosine.[1,2] Infantile form is the most common subtype, occurring at about 6-month of age, usually presenting with neurodegenerative symptoms, progressive spastic quadriparesis, tonic spasms, extreme irritability, inconsolable crying, secondary blindness and progressive optic atrophy.[3] Typical neuroimaging findings of KD include signal abnormalities in the cerebral and cerebellar white matter and thalami.[4] Great heterogeneity may occur with radiological examinations of patients with KD varying from normal brain magnetic resonance imaging (MRI),[1] with spinal cord enlargement[4] and optic nerve enlargement.[5] We present on a case of infantile KD with MRI showing white matter, thalamic and basal ganglia lesions associated with an enlargement of the optic nerves bilaterally.[5]

Case Report

A 11-month-old caucasian male patient was referred to pediatric neurology consult for progressive loss of developmental milestones, associated with incosolable crying, generalized hypertonicity and movement disorders. The patient was born to non-consanguineous parents with an uneventful pregnancy and delivery at term. On familial history, the patient had a brother with similar neurological condition who died at seven months of age due to respiratory insufficiency. Perinatal history was not relevant until the age of four month old when he started to present a progressive loss of his developmental milestones associated with movement disorders characterized by dystonia, choreoathetosis, and opisthotonos.

Neurological examination revealed a very irritable baby with poor visual contact. He presented macrocrania with head circumference above 95th centile and unremarkable fundoscopic examination. The patient presented hypertonicity of the four limbs, hyperrefexia and bilateral extensor plantar refex. On neuroimaging examination, computed tomography (CT) revealed difuse cerebral atrophy associated with bilateral thalamic involvement. MRI revealed reduction of brain volume and abnormal hyperintensity within the deep white matter of both hemispheres (Figure 1) associated with marked enlargement of the prechiasmatic segment of the optic nerves bilaterally (Figure 2). Blood, cerebrospinal fluid (CSF) and urine investigations were normal, including complete blood count, blood and CSF biochemistry panels, thyroid function tests, adrenal function tests, vitamin B12 levels, homocystein, vitamin E, ammonia, creatine-kinase, blood and urinary amino acids, organic acids, very long-chain fatty acids, and blood and CSF lactate. Serum β-galactocerebrosidase level was 3.2 nmol/17h/MG prot (reference value: 14-53) confirming the diagnosis of KD.

Discussion

With the widespread use of CT and MRI, several articles have reported imaging findings in the brains of patients with KD.[6,7] Typically, on CT images, early in the disease, high density is seen bilaterally in the thalami, caudate nuclei, corona radiate, and cerebellar dentate nuclei. As the disease progresses, diffuse white matter atrophy ensues.[6] On MRI there is T1 and T2 shortening in caudate nuclei, thalami, corona radiata, and dentate nuclei of the cerebellum is seen as well as in the cerebral and cerebellar white matter.[8] In our patient, the typical neuroimaging feature was associated with marked enlargement of the prechiasmatic segment of the optic nerves. Optic nerve enlargement (ONE) is considered unusual in KD. One of the five cases originally reported by Krabbe had solid, hard and thickened optic nerves at autopsy.[9] Although there have been multiple

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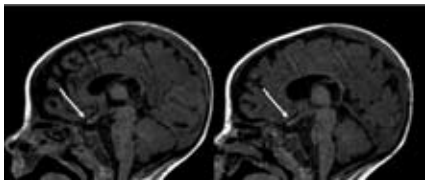

Figure 1. Magnetic resonance image T2 images demonstrated reduction of brain volume and abnormal hyperintensity within the deep white matter of both hemispheres, sparing the subcortical U-fibers, extending into the internal capsule and corticospinal tracts to the level of the medulla (arrows). Patchy abnormal increased signal was also seen in the dental nuclei of both cerebellar hemispheres.

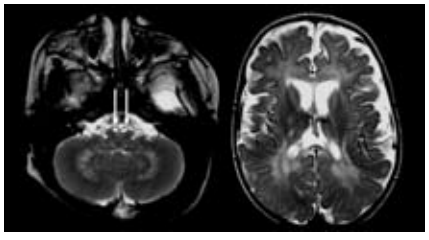

Figure 2. Marked enlargement of the prechiasmatic segment of the optic nerves.

descriptions of imaging characteristics of Krabbe disease, there are relatively few reports that describe enlargement of the optic nerves.[4-6] It is unclear as to why the optic nerves enlarge while the remainder of the brain undergoes significant atrophy. According to Garcia *et al.*[5] and to Harcourt *et al.*[10] ONE in KD could represent an initial phase, an early neuroimaging correlate of this condition, prior to subsequent atrophy.[11] Ieshima *et al.*[7] and Jones *et al.*,[3] in previously reported cases of ONE in KD state that this enlargement is due to the accumulation of numerous globoid cells suggesting that neuronal tissue outside the brain may react differently, with enlargement rather than atrophy in response to the presence of cerebroside in Krabbe disease.[3,7] Several disorders should be included in the differential diagnosis of KD: optic nerve glioma with dural ectasia, frequently in type 1 neurofbromatosis; nerve sheath meningioma; granulomatous or histiocytic infltration of optic nerves, leukemia, orbit pseudotumor, juvenile xanthogranuloma, post viral optic neuritis; optic nerve medulloepithelioma; and retinoblastoma with optic nerve compromise.[3,5]

Distinct clinical presentations and adequate laboratory investigation with measurement of serum β-galactocerebrosidase performed in our patient lead to appropriate diagnosis. Although uncommonly found in KD, ONE is not found in other types of leukodystrophies that present similarities in clinical and imaging findings such as metachromatic leukodystrophy, adenoleukodystrophy, Alexander's disease, canavan's disease and Pelizaeus-Merzbacher disease.[2,5] The addition of sequences tailored to the optic pathway may increase the sensitivity of identifying optic nerve abnormalities and may be of value in inherited metabolic disorders, particularly KD.[8,11,12] As a conclusion, recognition of ONE in conjunction with diffuse white matter disease or symmetrical involvement in the thalami, caudate, corona radiata and brainstem should suggest a diagnosis of KD.

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