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S Choi and D R Enzmann

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Infantile Krabbe Disease: Complementary CT and MR Findings

Samuel Choi and Dieter R. Enzmann

Summary: This case report of the infantile form of Krabbe disease in a 2½-month-old boy illustrates the complementary findings that may be seen on CT and MR scans. The key finding on the CT scan was increased density in a bilateral symmetrical distribution involving the thalami with extension into the centrum semiovale. The MR scan, on the other hand, more clearly showed demyelination in the brain stem and cerebellum. In cases in which this involvement is minimal or absent, the MR scan may fail to detect an abnormality, and a CT scan will, therefore, still be necessary to detect characteristic abnormalities.

Index terms: Krabbe disease; Demyelinating disease; Degenerative brain disease; Brain, white matter disease; Brain, magnetic resonance; Brain, computed tomography; Pediatric neuroradiology

Krabbe disease, globoid cell leukodystrophy, is caused by a deficiency of galactocerebroside-β-galactosidase (1). Computed tomographic (CT) findings in Krabbe disease described as normal in the early stage show abnormal low density of periventricular white matter on CT in the intermediate stage (2). Several studies have noted that before and in conjunction with this white matter involvement, there is symmetric increased attenuation of the brain stem, cerebellum, thalami, caudate nuclei, posterior limb of the internal capsule, and corona radiata (3–5). Magnetic resonance (MR) images have shown findings consistent with prolonged T1- and T2-weighted relaxation times in the white matter (6, 7). We present an infant with the infantile type of Krabbe disease who exhibited characteristic intermediate-stage CT findings with different and complementary MR findings.

Clinical Findings

A 2½-month-old Hispanic boy was admitted for myoclonic movements, failure to thrive, and vomiting. Toxoplasmosis, rubella, cytomegalovirus, herpes, and syphilis screening were negative except for a positive herpes titer. Tests for phenylketonuria, galactosemia, and hypothyroidism were also negative. Electroencephalography results were normal. Cerebrospinal fluid was remarkable for a protein of 374 with a glucose of 49. Lactate dehydrogenase was 151. Leukocyte enzyme assays yielded galactocerebroside-β-galactosidase activity of 0.04, which is less than 1% of the normal range (1.7 to 6.1), β-galactosidase 157.5 (normal), β-mannosidase 181.8 (normal), β-hexosaminidase 474.1 (normal), and acetyheuraninic acid 25.3 (normal).

CT findings at 2½ months demonstrated symmetric areas of increased density in the thalami, subthalami, and corona radiata (Fig 1). Low density was noted bilaterally in the cerebellar corpus medullaris, medial and lateral to the dentate nuclei (Fig 1). Axial, coronal, and sagittal MR images were obtained with a 1.5-T imager. Axial T2-weighted images showed high signal intensity in the white matter surrounding the dentate nucleus, corresponding to the low-density CT findings (Fig 2). Increased signal was also noted in the brain stem extending from the dorsal medulla to the pons and inferior cerebellar peduncles bilaterally. This was less evident on CT. The areas of increased density in the basal ganglia region on CT were of low signal on the T2-weighted images. A relatively normal pattern of myelination was seen on the T1-weighted scans except for the low-signal cerebellar white matter findings (Fig 2).

Discussion

Because of the deficiency in galactocerebroside-β-galactosidase activity, there is abnormal accumulation of galactocerebroside and its deacylated derivative, psychosine, to toxic levels that kill oligodendroglial cells. Multinucleated globoid cells, macrophages of mesodermal origin, accumulate in the white matter and are associated with extensive demyelination and marked astrogliosis (1, 2, 8). As expected, these histologic changes are seen as low density on CT. The symmetric areas of increased density located in deep gray and white matter on CT scans, which appear characteristic for infantile Krabbe disease, have not been explained histologically.

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Both authors: Department of Radiology, Stanford University Medical Center, S072, Stanford, CA 94305-5105. Address reprint requests to Dieter R. Enzmann, MD.

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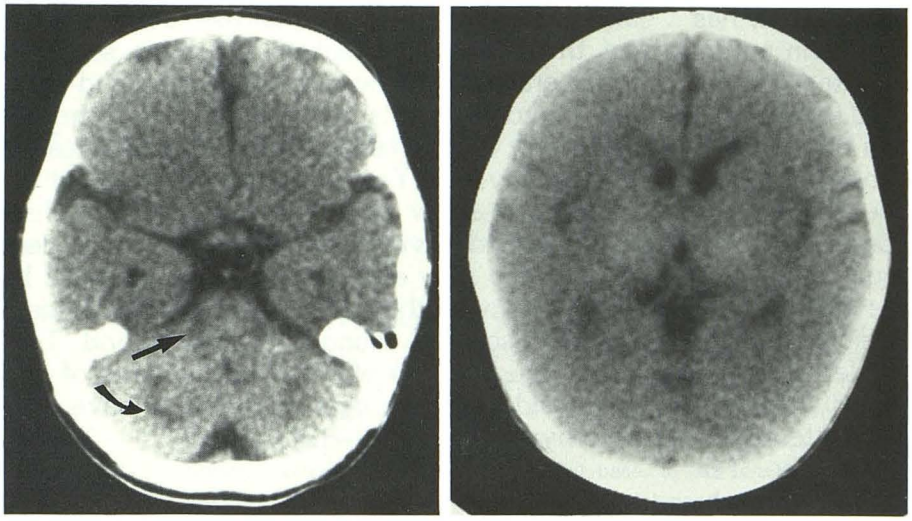


Fig. 1. Noncontrast CT scan in a 2½-month-old boy with Krabbe disease.

A, Note the cuneiform areas of low density (*curved arrow*) in the cerebellar white matter lateral to the dentate nuclei. Symmetric, peripheral areas of low density are also noted in the pons (*straight arrow*).

B, At the level of the basal ganglia, diffuse high density is noted in the thalami, globus pallidi, and posterior limbs of the internal capsule.

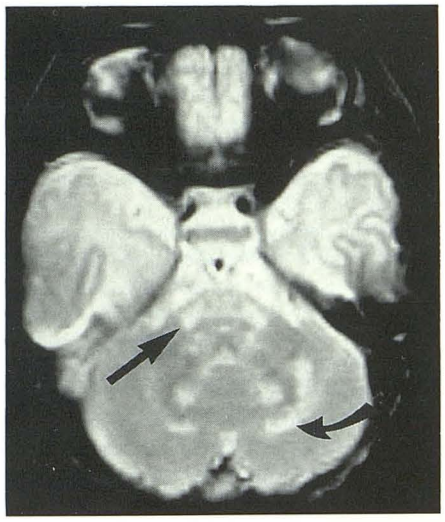


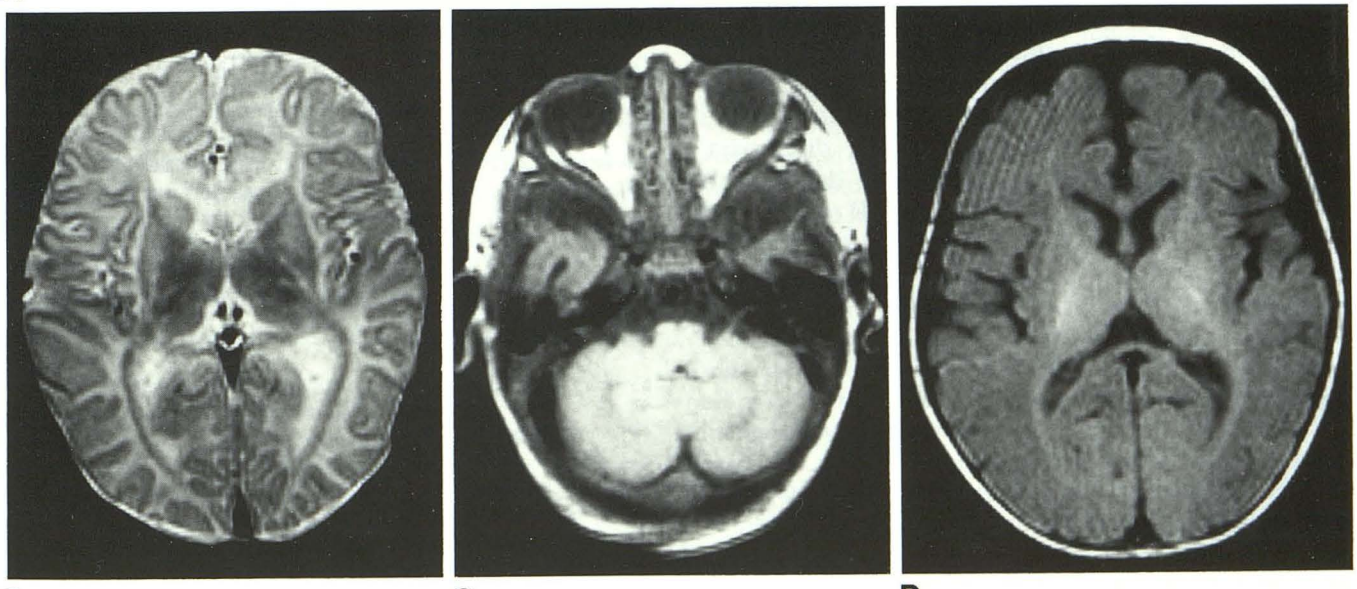
Fig. 2. Axial T2-weighted scans (2500/80) (repetition time/echo time) (*A* and *B*) and T1-weighted (800/20) scans (*C* and *D*) of the cerebellum (*A* and *C*) and basal ganglia (*B* and *D*).

A, Abnormal high signal intensity was noted bilaterally and symmetrically in the white matter medial and lateral (*curved arrow*) to the dentate nuclei, in pontine white matter tracks (*straight arrow*), and in the inferior cerebellar peduncles. The pontine and corpus medullaris abnormalities correspond to the low-density CT findings.

B, At the level of the thalamus the predominant finding was lower signal intensity than expected in the thalami, globus pallidi, and posterior limbs of the internal capsule bilaterally.

C, The white matter lateral to the dentate nuclei is of lower signal intensity than normal.

D, The pattern of myelination and signal intensity of the internal capsule and thalamus, however, appears within normal limits.



MR evaluation of infant brain maturation has shown myelination changes that occur in an orderly manner on T1- and T2-weighted images (8). T1-weighted images are expected to be useful in evaluation of normal myelination of the brain in the first 6 to 8 months. This corresponds to the time of onset of infantile Krabbe disease, and thus changes in myelination may be seen on T1- and T2-weighted images (8). In our patient abnormal cerebellar myelination was detected as abnormal low signal on the T1-weighted scan. The T1-weighted scan, however, underestimated the degree of abnormality in the brain stem and cerebellum compared with the T2-weighted scan. In the brain stem and cerebellum, the T2-weighted scan can be useful even in this early age group, because significant myelination has already occurred in these areas. Cerebellar white matter, one of the earliest sites of myelination, can be expected to show abnormalities of demyelination in early onset Krabbe disease on the T2-weighted images, although this has not been previously reported. How common this is cannot be determined from this case report. Pathologic studies of Krabbe disease have demonstrated cerebellar involvement with decrease of galactosylceramide, gliosis, demyelination, and loss of Purkinje and granule cells (9). Infiltration of globoid cells, epithelioid cells, and marked fibrillary astrogliosis would increase tissue water content, which would be reflected as increased signal on T2-weighted images (10).

Because MR will often be the first imaging modality ordered for an infant with developmental delay, the spectrum of MR abnormalities in Krabbe disease need to be defined. The hallmark MR finding is demyelination and in the infantile form may be best detected in myelinated areas of the brain stem and cerebellum. These findings may be the key to the MR diagnosis, because the characteristic increased density on CT does not appear to have a clear MR correlation with routine imaging. The diffuse low density in the thalami can be subtle but does serve as corroborative evidence. If brain stem and cerebellar involvement is minimal or absent, the MR scan may fail to detect any significant early abnormality. A CT scan, therefore, may still be indicated to show the complementary and characteristic findings of symmetrical, increased density of deep gray and white matter. It should be noted that two other rare childhood neurodegenerative disorders, Sandhoff disease and Tay-Sachs disease (two of the three variants of G_{M2} gangliosidosis) have been reported to have thalamic hyperdensity (11–12).

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