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CT and MR Imaging of Canavan Disease

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Canavan (Van Bogaert-Bertrand) disease is a rare dysmyelinating disorder of the CNS that presents in the first year of life with spasticity, blindness, and megalencephaly [1, 2]. The origin of this disease has not been definitely established, but it may relate to a deficiency in aspartoacyclase, an enzyme in the myelin synthesis pathway [3]. Without brain biopsy, it may be quite difficult to distinguish clinically from a similar disorder, Alexander disease, although a serum marker may be forthcoming [3-5]. CT in Canavan disease usually reveals diffuse, symmetrically decreased attenuation within the subcortical white matter without lobar predominance or areas of abnormal contrast enhancement [1, 6, 7]. Late cerebral atrophy has also been described [8].

We report here the MR findings (with CT correlation) in two siblings with Canavan disease and offer a review of the literature.

Case Reports

Two siblings with Canavan disease were studied on a Technicare 1.5-T superconducting MR magnet. T1- and T2-weighted spin-echo sequences, 700/32, 2000/40, and 2000/100 (TR/TE), were used in both patients. Images were obtained in the axial plane with supplemental coronal and sagittal images. Noncontrast CT scans were also obtained.

Case 1

J. C. is the male product of a consanguineous marriage who presented with megalencephaly, mild spasticity, and psychomotor retardation at 10 months of age. The birth history was unremarkable. At the time of presentation, all urine, serum, and CSF parameters were normal. Evoked potentials were abnormal, but nonspecific. A cranial CT scan at that time showed diffuse, symmetrically decreased attenuation within the centrum semiovale and the corona radiata. A diagnosis of Canavan disease was clinically suspected and confirmed by brain biopsy. A follow-up MR scan was obtained at 42 months of age (Fig. 1). This showed marked prolongation of T1 and T2 relaxation times throughout the centrum semiovale, corona radiata, and cerebellum (not shown).

Case 2

S. C., the sister of J. C., presented at 4 months of age with a similar history. Again, all chemical indices were normal. Evoked potentials were grossly abnormal. Cranial CT (Fig. 2A) revealed changes consistent with Canavan disease. Follow-up MR scans at 24 months of age (Figs. 2B and 2C) confirmed the earlier findings and demonstrated progressive ventriculomegaly. A brain biopsy was not pursued owing to the strong clinical and imaging evidence of Canavan disease. Both siblings are currently alive.

Discussion

Canavan disease, or spongy degeneration of the CNS, usually presents in early infancy with hypotonia, followed by spasticity, cortical blindness, and megalencephaly [1, 2]. This is a rapidly progressive illness with a mean survival time of 3 years, although protracted cases do occur [9, 10]. It may be inherited as an autosomal recessive trait, and it frequently appears in groups with high rates of consanguinity. Originally described in Polish Jews, it has since been reported in a broad range of ethnic and racial groups [1, 2].

Differentiating Canavan disease from other dysmyelinating disorders is usually not difficult clinically, except in the case of Alexander disease, which may present with similar clinical findings, most notably megalencephaly [4-6]. The standard metabolic screens as well as the CSF examination are unrevealing in both disorders [2, 4]. Evoked potentials are usually abnormal, but nonspecific [11]. Thus, definitive diagnosis usually requires brain biopsy or autopsy [5].

The origin of Canavan disease is unknown. No consistent metabolic abnormality has been reported [1, 2, 12]. The most compelling data to date points to a deficiency of aspartoacyclase activity (an enzyme in the myelin synthesis pathway) leading to an abnormal accumulation of *N*-acetylaspartic acid in the urine and serum of affected patients [3]. Although this observation awaits independent confirmation, it could prove useful as both a diagnostic and a prenatal marker for the disease [3].

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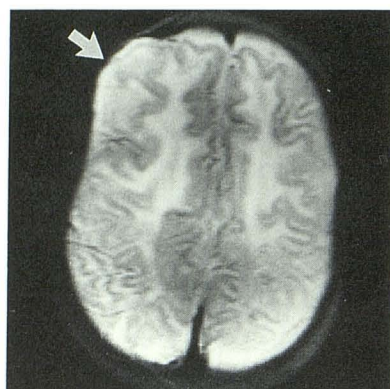


Fig. 1.—Case 1: T2-weighted (2000/100) MR image at age 3½ years shows diffuse T2 prolongation within subcortical white matter tracts. Site of prior biopsy is indicated by arrow.

Canavan disease is characterized pathologically by extensive vacuolization of cortical gray matter and, to a much greater extent, subcortical white matter tracts throughout the cerebrum with abnormal proliferation of type II astrocytes [1, 2, 13, 14]. Electron microscopy demonstrates increased water content within the glial tissue as well as dysmyelination [13, 14]. Similar changes may occur in the brainstem and cerebellum, particularly in the Purkinje and granular cell layers [14]. As is characteristic of the dysmyelinating disorders, no inflammatory reaction is observed [2, 13, 14]. Severe cortical atrophy and ventriculomegaly are noted late in the course of the disease [8].

The CT and MR findings in our cases explicitly reflected the known pathologic abnormalities in Canavan disease. Symmetric, diffusely decreased attenuation within the subcortical white matter tracts without areas of abnormal contrast enhancement was observed by CT [1, 6, 7]. These changes were best appreciated in the centrum semiovale and the corona radiata. The MR images, as expected, revealed

marked prolongation of both the T1 and T2 relaxation times in the same regions, as well as within the cerebellum. Although internal capsule sparing and brainstem lesions have been described in the CT literature, they were not present in our cases by either imaging method [1, 6, 7].

The CT and MR findings in Canavan disease are similar to those reported in other dysmyelinating disorders and are thus nonspecific [15]. However, from a clinical standpoint (as noted earlier), the principal differential diagnostic concern is often Alexander disease [4–6]. From a pathologic standpoint, however, Alexander disease tends to affect the brain in a focal manner, usually involving the frontal lobes earlier and to a greater extent than the rest of the cerebrum [16]. Such a frontal lobe predominance has been observed on CT scans [4, 6]. Also, the MR findings in two cases of Alexander disease, while not showing preferential frontal lobe changes, have confirmed the relative focality (cerebellar, occipital) of early Alexander disease [15]. Thus, in the absence of biopsy, the distribution of white matter abnormality may help differentiate these two similar disorders. In addition, contrast enhancement on CT within the frontal periventricular regions, basal ganglia, and thalami has been reported in Alexander disease but not in Canavan disease [4, 6]. This has obvious implications for Gd-enhanced MR imaging.

A potential source of diagnostic error has to do with the normal MR appearance of the neonatal and infant brain, which, as Barkovich et al. [17] point out, is quite different from that of the adult and may, in certain instances, mimic the appearance of a dysmyelinating disorder. These images must therefore be interpreted with careful attention to the clinical scenario in order to avoid a misdiagnosis. Follow-up imaging to document persistence of the white matter findings and to exclude simply a delay in brain maturation may then prove useful.

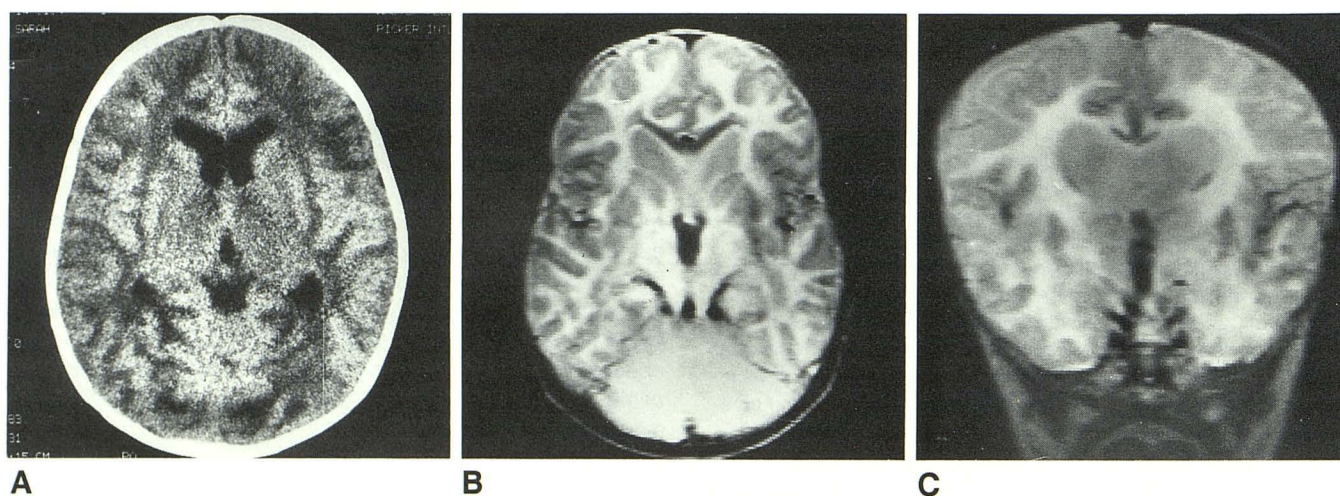


Fig. 2.—Case 2.

A, Cranial noncontrast CT scan at age 4 months shows diffuse hypodensity within the white matter with mild ventriculomegaly.

B, T2-weighted (2000/100) MR image at age 2 years shows T2 prolongation within subcortical white matter tracts. Signal intensity is paradoxically low within the genu of the corpus callosum, suggesting that it is pathologically unaffected (J. Barkovich, personal communication). Apparent lack of structure within the cerebellum is artifactual.

C, T2-weighted (2000/100) MR image in coronal projection emphasizes marked abnormality within the white matter. CSF pulsation artifact is noted within third ventricle and basilar cisterns (B and C).

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