MRI and CT in Krabbe’s disease: case report

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Abstract. A case of infantile Krabbe’s disease was first recognised as areas of relatively increased density on CT in the thalamus lateral geniculate body and dentate nucleus. These sites were subsequently shown on MRI to have a paramagnetic effect, being characterised by short T2 and T1. Subsequent examinations showed development of atrophy and high signal in white matter.

Key words: Krabbe’s disease – Globoid cell leukodystrophy – CT – MRI

Globoid cell leukodystrophy (GLD), described by Krabbe in 1916 [1], is a rare disease caused by a congenital deficiency of a lysosomal enzyme (beta-galactocerebrosidase) normally present in white and grey matter and involved in metabolism of galactosylcerebroside-beta-galactosidase, hydrolyzing the galactose moiety from the galactocerebroside. A genetic disorder, it has an autosomal recessive transmission with an incidence of 1 in 100 000–200 000 live births.

The enzyme deficiency causes an accumulation of beta-galactosylerceramide and of a metabolic substrate (psycosine) of the failing enzyme. Psycosine may be responsible for the neuropathological pattern of early loss of oligodendrocytes, demyelination and globoid cell infiltration, but the mechanism is unknown [2]. While the disorder is present at birth, symptoms may occur later; three types are described: early infantile, late infantile and juvenile [3], the age of onset of the first two being 1–6 months [4], and 1–3 years [3, 5]. The juvenile form is genetically distinct with a more benign course and often no peripheral neuropathy or high cerebrospinal fluid (CSF) protein [6]. Farrel and Swedberg [7] suggested that allelic mutations of the galactocerebrosidase gene could be responsible for the different clinical types.

Hagberg [8] divided the clinical course of the “classic” early infantile type into three stages. Stage I is characterised by irritability, unmotivated crying, hypertonia and recurrent fever; psychomotor development soon stops and then regresses. Within two to four months of the onset, most patients reach Stage II, which is characterised by opisthotonus, hypertonic flexion of limbs, exaggerated tendon reflexes and minor tonic or clonic seizures. Visual failure and optic atrophy begin to appear. At this time the CSF protein level is elevated. Stage III is the “burnt out stage”: the infants are decerebrate and blind and have no contact with their surroundings. Death occurs in about a year. There is evidence of parallel progression of pathological, CT and MRI findings. We report the clinical, neurophysiological, CT and MRI course in a patient with an infantile onset at 6 months of age.

Case report

A boy born at term, after an uncomplicated pregnancy, began to show developmental delay at 6 months of age. At 9 months, after a fever of unknown origin, he worsened, developing hyperirritability and transient hypertonia. At 11 months he showed irritability, alternating with varying unresponsiveness, mild dysphagia, spastic limbs and abnormal eye movements; head size was normal. CT at 11 months of age demonstrated mild dilatation of the ventricles, cisterns and sulci with normally appearing white matter. Bilaterally symmetrical lesions of moderately increased density were present in the posterior limb of the internal capsule, posterior thalamus and lateral geniculate body (Fig. 1). The brainstem appeared mottled, with areas of mixed and isointense increased density. MRI showed on proton density (PD) and T2-weighted (T2) images symmetrical areas of increased signal within the periventricular white matter and centrum semiovale mainly in the posterior frontal and parieto-occipital regions. By 15 months of age, hypertonicity and dysphagia increased, muscle stretch reflexes decreased and visual response was poor. At 18 months, MRI demonstrated more widespread high signal in the white matter of the centrum semiovale, periventricular region and the posterior limb of the internal capsule on both PD and T2 images (Fig. 2). The medulla and pons appeared mottled with scattered areas of increased signal on T2 images. The ventricles and extracerebral spaces were enlarged. At 19 months, extensor spasms and loss of social skills were evident and CT showed slightly high density in the thalamocapsular areas.

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and dentate nuclei, with more peripheral low density; the periven-
tricular white matter and centrum semiiovale was of diffusely low
density (Fig. 3), as were the optic radiations. Atrophic enlargement
of ventricles and extracerebral CSF spaces was more evident than
on the first CT study.

At 21 months, the child became unresponsive, decorticate, with
a very poor visual response and required nasogastric feeding. A
third MRI showed more marked enlargement of CSF spaces and
an increase in the abnormal signal intensities in areas such as the
and centrum semiiovale periventricular white matter, the optic ra-
diations and the splenium of the corpus callosum. The cerebellar
white matter also had areas of abnormal high signal on T2 images.
Within the brainstem high signal lesions involved the corticospinal
tracts, periaqueductal grey matter, and the floor of the 4th ventricle
(Fig. 4). The abnormal areas gave low signal on both T1-weighted
spin-echo (SE) and inversion recovery (IR) images. The thalamus,
adjacent corona radiata and dentate nucleus were slightly dense on
CT and had a short T1 and slightly shortened T2 (Fig. 4). On T2 images, the dentate nuclei showed a target appearance, with high
signal in the center, surrounding low signal and then high signal in
the adjacent white matter (Fig. 4).

The CSF proteins remained normal. The EEG was abnormally
slow, as were nerve conduction velocities. The brainstem auditory
evoked potentials (BAEPs) had shown prolonged interpeak latencies,
increasing during the course of the disease, that indicated mid-
brain involvement. Flash visual evoked potentials (FVEP) wors-
ened with progression of the disease, with disappearance of the
first early components and delay in the remaining ones. Galactosyl-
ceramidase activity of the leukocytes was 0.22 mmol/mg/hr (normal
2.5 ± 0.9), and that of fibroblasts 0.9 (normal 2.16 ± 0.6).

Discussion

Loonen et al. [2] proposed the clinical classification of
GLD into an early infantile, late infantile (early child-
hood) and late childhood or juvenile forms, with an ex-
tension of the spectrum to a debated fourth group comprised by patients with adolescent or adult onset who
had galactosylceramide deficiency.

The typical infantile form is the most frequent and se-
vere. Seizures are not uncommon in the late stages of the
disease and micro- or macrocephaly may be seen [4, 6].
The pathological changes are progressive. In the first
stage, the grey matter is microscopically normal, while
in the white matter, around small vessels, there are glo-
boid cells with large cytoplasm that contain galactocere-
brosidase. The parietal white matter is more involved
than the subcortical U fibres, centrum semiiovale and cer-
ebellum. Phylogenetically newer areas are more severely
affected than the older fornix, hippocampus, mamillo-
thalamic tracts and white matter of the basal ganglia.
In the spinal cord, the corticospinal tracts are more
severely involved than the dorsal columns. The lack of
myelin is associated with a specific astrocytic gliosis that
has little inflammation. The grey matter is affected later
and to a lesser extent. The neurons of pons, dentate nu-
cleus and thalamus are more involved than those of the
cortex. In the final stage there is a predominant gliosis
with few globoid cells and severe loss of myelin and
axons.

The clinical classification into three groups is deter-
mined not only by the age of onset, presentation and
and course of the disease, but also by other findings. The early
and late infantile groups are characterised by the pre-

cence of increased CSF protein and delayed nerve con-
duction. The late infantile form shows delayed nerve con-
duction that lasts throughout the illness to death,
which occurs in 1–3 years. In the juvenile group, the
course is more protracted, with normal or increased
CSF protein and little or no peripheral neuropathy [3, 6].

Our case had an onset at 6 months and clinical fea-
tures compatible with the early or late infantile forms.
The minor peripheral neuropathy is compatible with the
late infantile and juvenile forms, but CSF protein is
usually normal in the latter. We followed the neuroradi-
ological course from a mildly affected child aged 11 months to a severely affected one of 21 months.

CT showed progressive, diffuse enlargement of CSF
spaces with symmetrical slightly increased density in
the posterior thalamus, portion of corona radiata, pos-
terior limb of internal capsule, dentate nucleus and lateral
geniculate body, which appeared early in the course of
the disease and was most evident on the first examina-
tion. On MRI areas appeared to have an accumulation
of paramagnetic substances. Low density in the white
matter, indicating lack of myelin and tissue reaction,

was manifest later. Optic pathway involvement was
shown by high density in the lateral geniculate bodies
and low density in the optic radiations. The early MRI

Fig. 1. Non-contrast CT at
11 months of age.

a symmetrical dense lesions
(arrow) in the posterior thalamus.

b Lower section shows symmetrical
dense areas in the lateral geniculate
bodies (arrows)

Fig. 2. MRI at 18 months of age.

High signal abnormalities in the
white matter on T2 images (TR/TE
2000/100)