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MRI in acute neuropathic Gaucher's disease

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Abstract We present the cranial MRI findings in a 6-month-old girl with biopsy-proven acute neuropathic Gaucher's disease, which include unilateral cerebral atrophy and dural thickening with contrast enhancement.

Key words Gaucher's disease · Magnetic resonance imaging

Introduction

Gaucher's disease, the most common lysosomal storage disease, results from an inherited defect of acid beta-glucosidase activity [1]. Accumulation of this enzyme's major substrate, glucosylceramide, in cells of monocyte/macrophage lineage leads to hepatosplenomegaly, destructive skeletal disease and bone-marrow compromise [2]. Three major clinical variants of Gaucher disease have been described [3]. Type 1 is characterised by sparing of the central nervous system (CNS) from the primary effects of glycolipid accumulation. Type 3 is termed subacute neuropathic because of the variable onset and progression of CNS disease. Type 2, the acute neuropathic form, usually found in infants, is characterised by progressive CNS deterioration, bulbar involvement and fulminant visceral and pulmonary disease, resulting in death within the first 2 years of life [3–4].

Despite the CNS involvement cerebral MRI in two reported cases of type 2 disease was normal [3, 5]. CT or MRI in 13 patients with type 3 Gaucher disease were normal except for minimal brain atrophy in four cases [6]. We present the unique MRI findings in an infant with bone-marrow biopsy-proven type 2 Gaucher's diseases.

Case report

A 6-month-old girl presented with progressive retrocollis and poor feeding since 4 months of age. She was born at term to non-

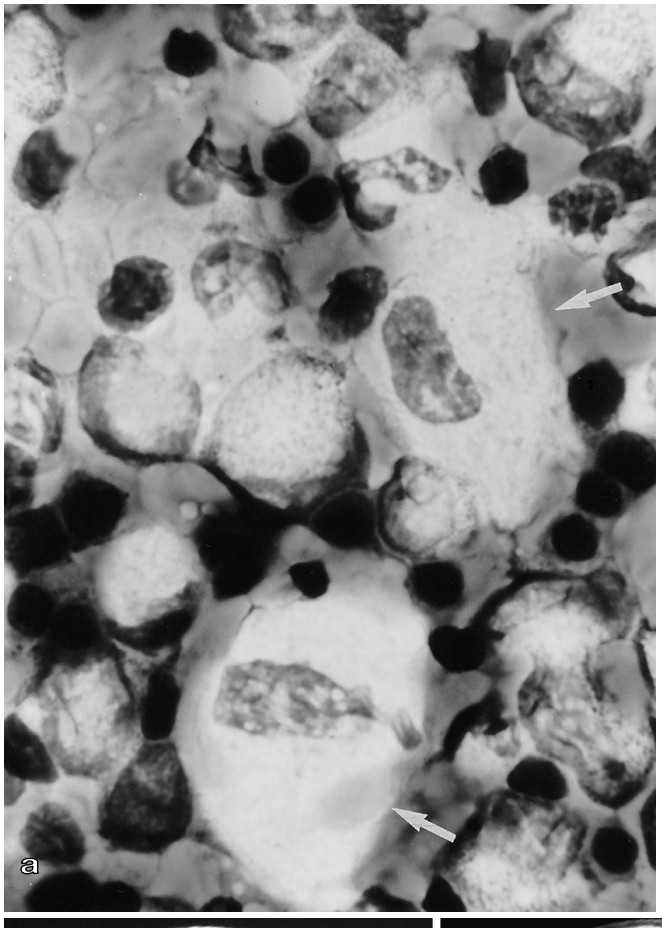
consanguineous parents by spontaneous vaginal delivery and had normal early developmental milestones. However, she developed constant irritability and frequent episodes of breath-holding spells at 4 months. Progressive failure to thrive, hepatosplenomegaly and developmental delay evolved from 4 to 6 months. The liver was 8 cm below the right, and the spleen 6 cm below the left costal margin. Retroflexion of the neck, bulbar paresis, bilateral esotropia and an oculomotor palsy were apparent. Laboratory data showed elevated: SGOT, 136; SGPT, 69; and mild anaemia. Chest radiography showed interstitial infiltration. Bone-marrow aspiration revealed dispersed Gaucher's cells, with the characteristic abundant light-blue cytoplasm with a striped appearance and multiple nuclei; the cells were positive for periodic acid-Schiff and negative for Sudan black staining (Fig. 1 a). Electroencephalography showed sporadic sharp waves over the right central area, and low amplitude left centrotemporal activity.

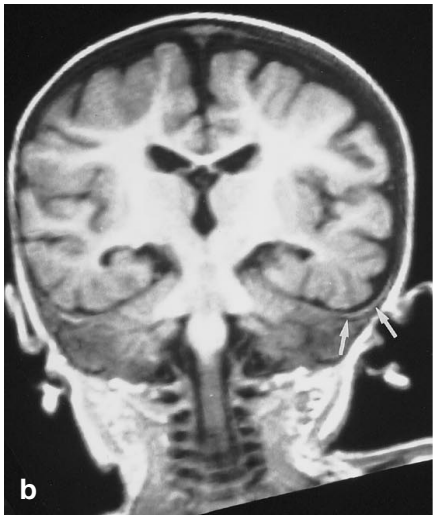
T1-weighted images revealed a large sheet of dural thickening over the left temporoparieto-occipital region and tentorium which enhanced with contrast medium (Fig. 1 b–d). Mild atrophy of the left cerebral hemisphere was seen. Myelination of the cerebral white matter, as shown on T2-weighted images, was normal for age.

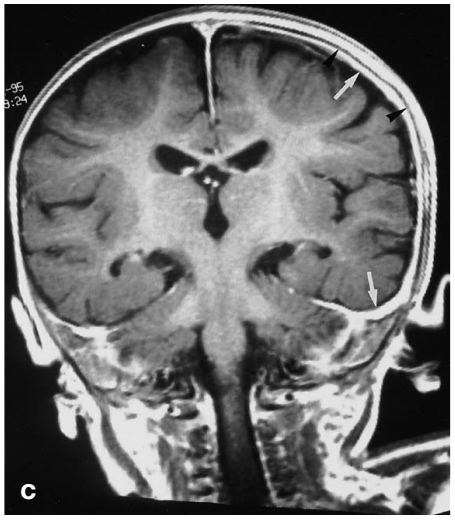
The child developed rapidly progressive spasticity, respiratory difficulties, further hepatosplenomagaly and feeding problems. Follow-up chest radiographs showed progressive infiltrates with a varying bronchiolitic pattern and extensive granular interstitial infiltration with chronic aspiration and presumed infiltration by Gaucher's cells. At 7.5 months the child died of sepsis and respiratory failure.

Discussion

Like the other lysosomal storage diseases, the abnormalities in Gaucher's disease result from an accumulation of undegraded macromolecules (glucosylceramide)







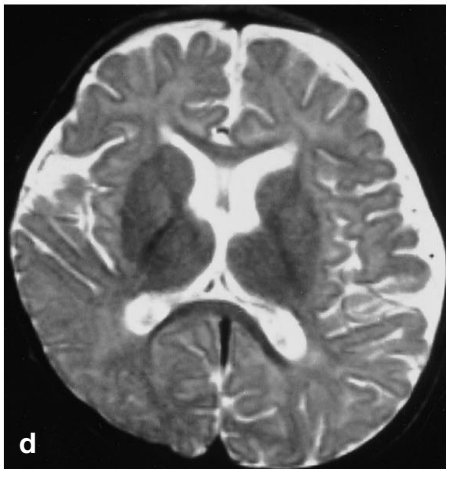


Fig. 1 **a** Bone marrow aspirate shows the typical Gaucher's cells *(white arrows)*. They are characterised by abundant light-blue cytoplasm with a striped appearance and multiple nuclei. (Liu stain, original magnification ×). **b** Coronal T1-weighted image shows a conspicuous subarachnoid space over the left hemisphere and thickening of the left side of the tentorium *(white arrows)*. **c** Extensive dural contrast enhancement *(white arrowheads)* is seen. The left side of the calvarium is thicker than the right *(black arrowheads),* probably due to mild atrophy of the left cerebral hemisphere. **d** A T2-weighted image shows normal white matter myelination for a 6-month old

in the CNS. In contrast to other neurological glycosphingolipid storage diseases, the substrate in Gaucher's disease type 2 and 3 does not accumulate in massively or disrupt normal neuronal architecture [3]. The undegraded circulating glucosylceramide is stored in macrophage of the periadventitial space [7]. Progressive neuronal loss, possibly due to toxic effect of minor metabolites, has been observed [2]. Typical Gaucher's cells are found free in the ganglion and pyramidal cell layers of the cerebral cortex [7]; this may explain the minimal imaging findings in brain parenchyma of neuropathic Gaucher's disease [6].

In our case, MRI revealed unilateral dural thickening with contrast enhancement. Dural thickening has been discribed in a variety of conditions [8–10]. Dural thickening on MRI has been reported in patients with mucopolysaccharidoses in which deposits of mucopolysaccharide have been observed in the dura mater [11]. Similar MRI appearances have been observed in an infant with Pompe's disease, and may be attributable to glycogen deposition [12]. The dural thickening in our case may be related to glucosylceramide infiltration. The predilection for metabolite deposition in the dura mater in these neuropathic lysosomal disease's is unique in lysosomal storage disease.

Our patient showed the clinical course typical of acute neuropathic Gaucher's disease. Dural involvement in type 2 disease on MRI has not been reported previously. Awareness of these neuroimaging features may facilitate early recognition. Enzyme therapy might be initiated earlier, though the effects on type 2 disease are debetable [3].

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