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Cauda equina syndrome due to an intra-dural sacral cyst in type-1 Gaucher disease

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Abstract The authors report a rare case of type-1 Gaucher disease with neurological and haematological involvement. The first onset was epilepsy, the diagnosis of GD1 was then confirmed and the patient experienced parkinsonism. The biological analysis revealed monoclonal gammopathy and factor-II mutation. The patient's condition worsened due to cauda equina syndrome. Magnetic resonance imaging and surgery revealed an intra-theal sacral cyst which, to our knowledge, has not been reported previously; therefore, when confronted with the fractures commonly observed in GD1, other unusual causes of spinal cord and root compression should not be overlooked.

Keywords Type-1 Gaucher disease · Epilepsy · Parkinsonism · Cauda equina syndrome · Monoclonal gammopathy · Factor-II mutation

Introduction

Gaucher disease (GD) is an autosomal-recessive disorder caused by a deficiency of glucocerebrosidase [1, 2] owing to mutations in the β glucocerebrosidase gene 1q21 [6].

The most frequent type of GD (more than 99% of cases) is type 1 (GD1). Its clinical manifestations include anaemia, thrombocytopaenia, hepato-splenomegaly and skeletal lesions [1, 2, 3, 4]. Absence of neurological involvement is a defining feature [1, 2], although occasional cases of GD1 with neurological signs have been reported [7, 8, 13, 16, 17].

We report a patient with GD1 and lumbo-sacral cauda equina syndrome due to an intra-theal sacral cyst.

Case report

History and examination

Ten years previously, a 65-year-old man was diagnosed as having type-1 GD. The diagnosis was confirmed biologically (see Table 1). The patient genotype is N 307 S / 1263 del 55. The first symptom was epilepsy, and he then successively experienced parkinsonism, hip and rib fractures, splenectomy, and in the 5 months prior to admission lower back pain.

One month before admission, he developed confusion, episodic visual hallucinations, hyperthermia, and intractable back pain over the sacral region, the posterior surfaces of his thighs and leg weakness without sphincter incontinence. The neurological examination revealed severe dyskinesia, sacral hyperaesthesia and inability to stand up. Deep tendon reflexes in the lower extremities were absent.

Table 1 Biological assay of glucosidase activity

White-cell B glucosidase activity	0.29 μ Kat/kg proteins	Reference range 1.97	SD 0.54
4 MU-B-galactosidase	73 μ kat/kg proteins	Reference range 62	SD 19
Leukocyte sphingomyelinase	0.40 μ kat/kg proteins	Reference range 0.67	SD 0.25
Glucosylceramidase	0.18 μ kat/kg proteins	Reference range 2.40	SD 0.60
Chitotriosidase activity ^a	1047 nkat/	Reference range <40	–

^aChitotriosidase activity was evaluated according to [21]

Fig. 1 **a, b** Immuno-electrophoresis analysis demonstrating monoclonal gammopathy IgG kappa in the patient's serum which **c** was also found in the urine. **d** Immuno-electrophoresis of the lumbar puncture and **e** pre-operative cyst fluid showed the same immunological aspect as the patient's serum

Fig. 2 Detection of the pro-thrombin G20210A with a transition in the 3'untranslated region of the pro-thrombin gene [using polymerase chain reaction (PCR)-mediated site directed mutagenesis creating a Taq I endonuclease cleavage site in the PCR product]

Biological analysis revealed IgG kappa monoclonal gammopathy (Fig. 1a,b), which was also found in the urinary immuno-electrophoresis (Fig. 1c).

He also has a factor-II heterozygote mutation (Fig. 2) with no thrombocytopaenia or any other coagulation anomalies.

A lumbar puncture revealed a yellow fluid with 42 g of protein with no cells, and the immuno-electrophoresis analysis was similar to that of the plasma (Fig. 1d).

Spinal MRI revealed an intra-dural sacral cyst, which was mostly individualised on T2 (Fig. 3). Cranial MRI was normal.

Operation

Decompressive lumbo-sacral laminectomy was performed, involving widening of the thecal sac which was compressed along with the sacral roots due to a narrowing of the sacral canal. Epidural tissue infiltration was observed. Per-operative puncture of the dural sac revealed the same yellowish fluid. On opening, the thecal sac released yellow fluid, and a brown thin membrane was dissected partially from the inner face of the dura, but the cyst limits could not be accurately identified.

The cyst liquid and the liquid from the lumbar puncture both showed the same immuno-electrophoresis profile as the patient's plasma (Fig. 1e).

The postoperative course was uneventful with improvement in the patient's gait but moderate pain that still requires analgesic drugs. At 2-year follow-up, the patient remains well.

Fig. 3 **a** Spinal MRI on T1 reveals the sacral S2–S3 fracture narrowing the spinal canal and the isointense intra dural cyst. **b** After gadolinium infusion, the sacrum appears heterogeneous with a hyperintense epidural infiltration. **c** On T2 the cyst is markedly hyperintense, and the sacrum appears isointense

Fig. 4 **a** Gaucher cells invaded the sacrum, muscles and fat epidural tissue (hematoxylin and eosin stain, $\times 100$). **b** At high magnification, the cytoplasm of the Gaucher cells has a crumpled silk appearance (hematoxylin and eosin stain, $\times 400$). The Gaucher cells have a characteristic crinkled-tissue-paper cytoplasm. The cells are 20–100 μm in diameter and usually have one eccentric nucleus (hematoxylin and eosin stain, $\times 1000$; *right inset*). **c** and **d** stained with periodic acid–Schiff. **d** Membrane cyst with a few Gaucher cells (hematoxylin and eosin stain, $\times 20$; *black arrow*). *Inset* shows the detail of the Gaucher cell (hematoxylin and eosin stain, $\times 40$; *white arrow*) stained with CD 68 streptavidin biotin immuno-staining

Histopathology

The Gaucher cells have invaded the surrounding tissue (Fig. 4a–c). The membrane cyst contains scarce cells with a crinkled tissue-paper appearance (Fig. 4d), which correspond to Gaucher cells.

Discussion

Expression of skeletal involvement in GD1 ranges from asymptomatic to symptomatic disease, which can be se-

vere, and cause considerable pain and disability. Skeletal involvements were observed in 70–100% of patients with GD1 [4], and the long bones were typically affected. Spinal deformities and vertebral collapses were described in both adults and children [10, 12, 14], and may lead to gibbus, and kyphotic deformity with occasional neurological compromise [7, 14, 15, 19].

The most reported spinal involvement is vertebral collapse which has also been described as Kümmel disease [9]. The dorso-lumbar junction is preferentially involved

[12, 14], but the lumbo-sacral spine is not spared [8]. Neurological deterioration occurs progressively and belatedly. The usual mechanisms of root and cord compression are a narrowing of the spinal canal by the collapsed body and/or spinal epidural deposits of Gaucher cells due to extrusion of the abnormal marrow [7, 10, 15]. In our patient, the cauda equina syndrome is due to the combined effect of the cyst and sacral fracture; therefore, when common fractures are observed in GD1, other possible causes of neurological deterioration, such as spontaneous haematomyelia [8], or intra-dural cyst, should not be overlooked.

Although Gaucher cells were observed in the meninges, and in the adventitia of small and medium-sized vessels as perivascular aggregates [5, 17, 18, 20], we are not aware of any case with an intra-dural cyst containing a fluid showing the same electrophoresis profile as the patient's serum. This electrophoresis similarity does not favour intra-thecal secretion. It may be the result of lysis of a sub-

dural haemorrhage favoured by the bleeding tendency despite normalisation of the platelet count after spleen removal [11].

Primary involvement of the central nervous system (CNS) in GD1 is unusual, and the association of epilepsy and parkinsonism has rarely been described [13, 17, 18, 20].

Conclusion

The clinical picture reported herein reminds us not to overlook other unusual causes of spinal cord or root compression when confronted with the related common fractures observed in GD1.

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