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CASE REPORT

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# Gaucher's disease, type I (adult type), with massive involvement of the kidneys and lungs

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**Abstract** A 33-year-old Japanese male, first diagnosed as having Gaucher's disease at the age of 3 years, died of renal and pulmonary failure. Autopsy findings disclosed the proliferation of Gaucher's cells in the liver, bone marrow, lymph nodes, kidneys and lungs. Electron-microscopical findings suggested that the Gaucher's cells observed in the renal glomeruli might be derived from circulating macrophages.

**Key words** Gaucher's disease (adult type)
Renal involvement

## Introduction

In the adult type of Gaucher's disease, Gaucher's cells with accumulated glucocerebroside are rarely observed in the viscera except for the reticuloendothelial tissue. Only a few cases with renal and/or pulmonary involvement have been reported. In the present paper, we report an autopsy case of the adult type of Gaucher's disease with an unusual involvement of the kidney and lung.

## Case report

The patient was a 33-year-old Japanese male. His parents were cousins, as were his mother's parents. His elder brother also had Gaucher's disease. At 3 years of the age, splenomegaly was discovered and a bone marrow aspirate revealed a proliferation of Gaucher's cells. After splenectomy for progressive hypersplenism at 5 years of age, an Erlenmeyer's flask deformity occurred.

In November 1987, he was admitted to the Rehabilitation Iizaka Spa Hospital because of dyspnoea and generalized oedema. On examination there were massive ascites, hepatomegaly and oedema. Laboratory data showed mild anaemia (RBC 348× $10^4$/mm$^3$), hypoproteineamia (4.5 g/dl), proteinuria (50 mg/dl) and an elevated blood urea nitrogen (40 mg/dl) and creatinine (0.8 mg/dl). Serum acid phosphatase was 31.2 kU/dl and preliminary assay of fibroblastic β-glucosidase showed a 4.5% level relating to a normal adult.

Despite peritoneal dislysis, he gradually deteriorated and died of renal failure 4 months after admission. An autopsy was performed 18 h after death.

### Pathological observations

#### Gross description

The emaciated patient, weighing 31.7 kg, had a protuberant abdomen because of the enlarged liver and 1500 ml of ascites. The liver was greatly enlarged (5515 g) and had an abnormal whitish-tan colour on gross appearance (Fig. 1). The kidneys were slightly enlarged (left 162 g; right 142 g), pale and yellowish in the cortices. The lungs were voluminous, heavy (left 480 g; right 519 g) and firm. A whitish thickening of the alveolar walls was observed. Swollen cervical, pulmonary hilar, retroperitoneal and inguinal lymph nodes appeared homogeneously whitish-yellow on cut sections. The bone marrow of the vertebrate, sternum and femur was very soft and pink. Cortical bone appeared thin and eroded.

#### Microscopic findings

Gaucher's cells, round and polygonal, had small pyknotic nuclei and abundant pale cytoplasm resembling "wrinkled tissue paper". Multinuclear giant cells with phagocytic capacity were occasionally observed. Cytohistochemistry of frozen sections revealed that Gaucher's cells were positive for acid-phosphatase, naphthyl acetate esterase, and α-naphthyl butylate esterase. In the liver, sinusoidal spaces were filled with Gaucher's cells and hepatic cell cords were atrophic and distorted (Fig. 2). The alveolar walls were thickened by a marked infiltration of Gaucher's cells. In the kidneys, Gaucher's cells were seen in mesangium of entire glomeruli (Fig. 3), and they obliterated capillaris accompanying destruction of basement membrane. Many Gaucher's cells were also found in lymph nodes, bone marrow digestive tracts and adrenal glands.

Electron microscopy revealed Gaucher's cells with varying amounts of specific tubular structures in the cytoplasm, in glomerular mesangial regions. The nuclei of Gaucher's cells had more dispersed chromatin than those of the mesangial cells. Focal intracapillary macrophages containing small tubular structures in cytoplasm showed a prolongation of their cytoplasmic process to mesangial matrix (Fig. 4).

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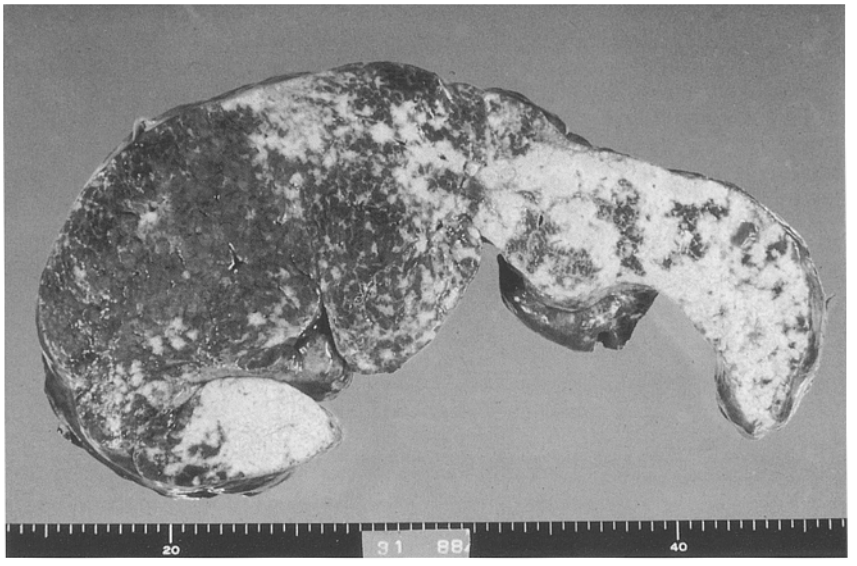


**Fig. 1** Firm, yellowish-tan areas with necrosis were prominent in the enlarged liver

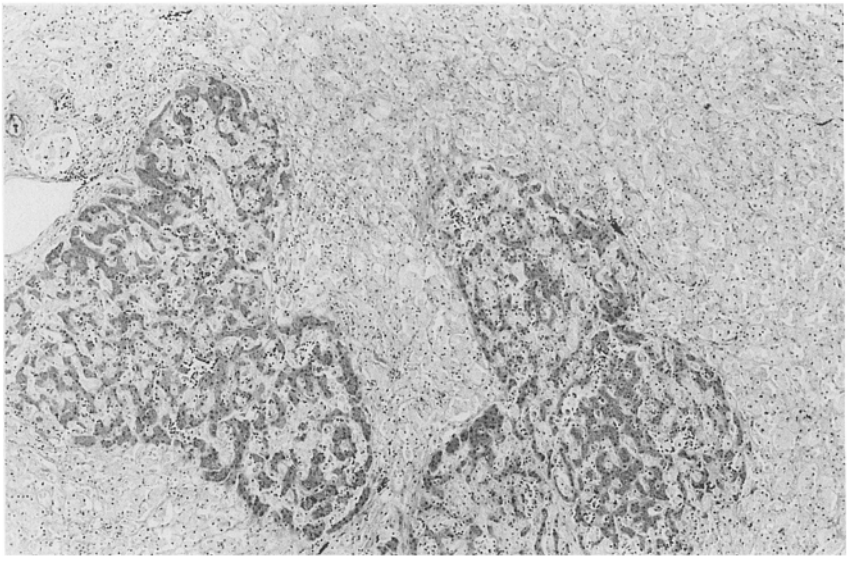

**Fig. 2** Masses of Gaucher's cells were present between hepatic lobules and invaded the sinusoids; hepatic parenchyma is subsequently atrophic and degenerated. H&Estain, ×52

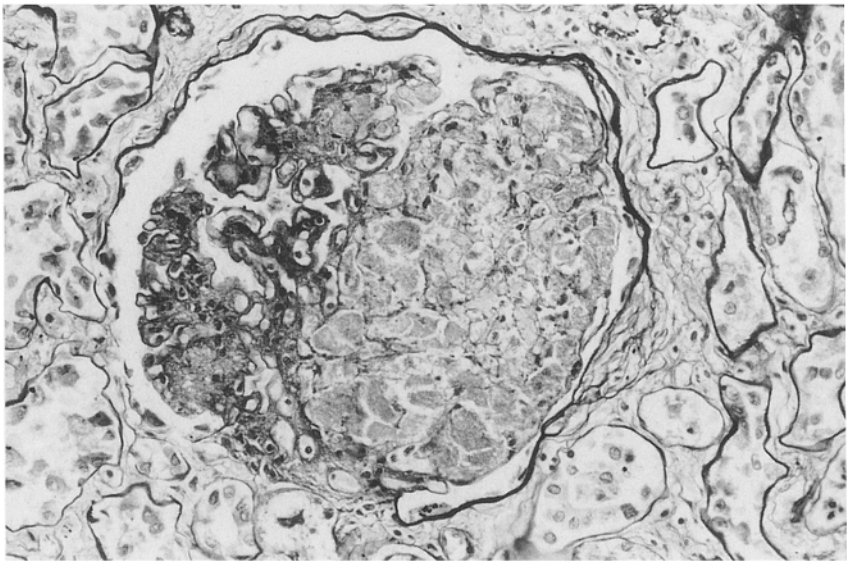

**Fig. 3** Clusters of Gaucher's cells obliterated capillary lumina of glomerular lobule in part (*right*). Periodic acid-Schiff stain, ×264

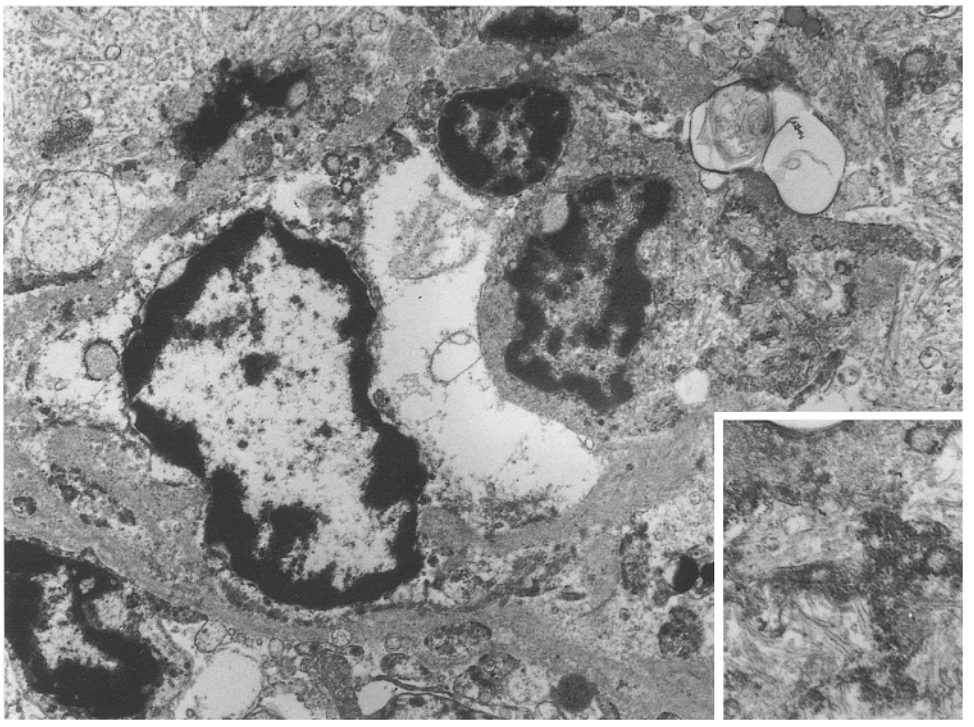

**Fig. 4** Gaucher-like cell with dense nuclear chromatin and small tubular structures in cytoplasm were observed in glomerular capillary. Gaucher-like cell contacts to mesangial areas by cytoplasmic process. ×9000. *Inset*: The characteristic tubular structures in cytoplasm of Gaucher-like cell. ×25000

**Table 1** Five cases of Gaucher's disease with severe renal involvement (*n.d.* not described)

| Source | Age/sex/race | Renal involvement | Splenectomy | Pulmonary involvement | Bone involvement | Liver involvement | Serum acid phosphatase (kU) |
|---|---|---|---|---|---|---|---|
| DeBritto et al. [4] | 30/F/Black | Glomeruli | +(8 years)[a] | + | +(E)[b] | + | 22.5 |
| Chander et al. [3] | 21/F/Black | Glomeruli, interstitium | +(4 years)[a] | + | n.d. | + | n.d. |
| Smith et al. [13] | 51/F/Black | Glomeruli, interstitium | +(8 years)[a] | + | +(E)[b] | + | n.d. |
| Sigel et al. [12] | 25/F/Ashkenazi | Glomeruli | +(22 years)[a] | + | +(E)[b] | + | n.d. |
| Present case | 33/M/Oriental | Glomeruli | +(28 years)[a] | + | +(E)[b] | + | 31.2 |

[a] Time between splenectomy and renal involvement
[b] Erlenmeyer's deformity

## Discussion

Gaucher's disease is known as a lysosomal borne disease in which the activity of lysosomal β-glucosidase is genetically deficient [2]. The deficiency of this enzyme leads to systemic accumulation of glucocerebroside in reticulo-endothelial cells. Based on clinical observations, there are three types of Gaucher's disease: type I (adult type), type II (infant type), and type III (juvenile type) [5]. Type I Gaucher's disease is characterized by sparing of the central nervous system. It usually shows slow progression accompanied hypersplenism and pathological bone fracture. Primary involvement of organs by Gaucher's cells in type I Gaucher's disease occurs in the spleen, liver, bone marrow, lymph nodes [11] and rarely in parenchymal organs, such as lung and kidney [10, 13]. It is unusual that to find massive infiltration of Gaucher's cells leads to organ dysfunction directly [12].

Pulmonary involvement of Gaucher's disease has been described in several cases [6, 14]. The present case showed a diffuse infiltration of Gaucher's cells in the alveolar septum and perivascular area. Type I Gaucher's disease is usually slowly progressive, but some cases with pulmonary involvement have a poor prognosis and die rapidly of respiratory dysfunction [1].

Renal involvement in Gaucher's disease has been reported in nine cases. However, five cases showed only focal involvement of the kidney, observed incidentally at autopsy. The other four cases revealed severe glomerular involvement [3, 4, 12, 13]. Table 1 shows the pathological findings of these four cases and the present case. Splenectomy was performed in all five cases, and in four of them it was performed between 4 and 22 years prior to renal involvement. The present case also had a splenectomy 28 years prior to death and the period from onset to splenectomy was longer than that in the other four cases. After splenectomy, hepatic and bone involvement by Gaucher's disease tended to be more extensive [8] but renal involvement did not. The relation between splenectomy and renal involvement in these cases is not clear.

Many authors consider the origin of Gaucher's cells in glomeruli to be due to a proliferation of mesangial and

endothelial cells, since circulating Gaucher's cells are rare [15]. However, typical mesangial and endothelial cells with inclusion bodies [7] were not detected in the present case, by electron microscopy. Gaucher-like cells observed in the capillaries of the glomeruli had dispersed chromatin similar to macrophages. These cells showed cytoplasmic prolongation to the mesangial matrix, suggesting that some renal Gaucher's cells might be derived from circulating macrophages. A report of mesangial cells derived from macrophages may support our observation [9].

We experienced a rare case of type I Gaucher's disease with massive infiltration of Gaucher's cells in multiple organs. Type I Gaucher's disease is slowly progressive and the cause of death is usually infection or haemorrhage induced by marrow involvement and subsequent pancytopenia. Death caused by organ dysfunction from massive Gaucher's cells involvement is rare.

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