Multiple Space-Occupying Lesions of the Spleen in a Case of Gaucher's Disease

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A 50-year-old female patient was admitted because of an enormously enlarged spleen and thrombocytopenia. Ultrasonography and magnetic resonance imaging revealed multiple space-occupying lesions in the spleen. She was diagnosed as having Gaucher's disease based on the low level of beta-glucosidase activity in leukocytes and Gaucher's cells present in bone marrow aspirate. Severe hypersplenism necessitated splenectomy. Pathological studies of the excised spleen, including ultrastructural examinations, demonstrated that multiple space-occupying lesions in the spleen were composed of typical Gaucher cells.

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Key words: ultrasonography, MRI, Gaucher cells, microtubules

Introduction

Gaucher's disease is a rare lysosomal storage disease caused by a deficiency of glucocerebrosidase, which results in the accumulation of beta-glucocerebroside in the reticuloendothelial tissues. Gaucher's disease is characterized by bone lesions and splenomegaly, sometimes associated with hypersplenism (1). Although the radiographical manifestation of the spleen in Gaucher's disease has recently been reported, there are very few reports focusing on the histopathological corroboration concerning multiple splenic space occupying lesions which were revealed by ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) (2-6). In Japan, there has been no radiological or pathological descriptions of multiple lesions of the spleen in Gaucher's disease to the best of our knowledge. Here we describe the radiographical and pathological findings of multiple lesions in the spleen of one patient with Gaucher's disease.

Case Report

A 50-year-old female suffered from fatigue for 2 weeks before admission. She had had abdominal swelling and hemorrhagic diathesis from the age of 20. On physical examination, an enlarged spleen was palpable and purpura were noted on the arms and legs. No abnormal signs were noted on neurological examination. Laboratory examination revealed that her platelet count was reduced to 36,000/mm³. Her serum acid phosphatase was 6.4 U (normal value, 1-4 U), angiotensin-converting enzyme 41.6 IU/l (normal value, 8.3-21.4 IU/l) and beta-glucosidase activity in leukocytes 1.3 nmol/mg protein/h (10-30% of control activity). Other laboratory data were within normal limits. A bone marrow aspirate showed a hypercellular marrow accompanied by numerous histiocytes or reticuloendothelial cells with macrophage-like appearance. These cells showed the characteristic features of Gaucher cells; the typical fibrillar nature of the cytoplasm (Fig. 1). The diagnosis of Gaucher's disease (adult type) was confirmed. Ultrasonography revealed an markedly enlarged spleen containing multiple hypoechoic lesions of various sizes (Fig. 2). CT demonstrated multiple low density lesions, which were positively enhanced after intravenous bolus contrast injection. Both T1- and T2-weighted images on MRI also revealed multiple space-occupying lesions with low-signal intensity (Fig. 3). Furthermore, MRI study disclosed that some of the relatively larger lesions contained high-signal inner zones.

Splenectomy was performed because of severe hyper-
spleenism. Macroscopically, the excised spleen (27 × 10 × 5 cm) was occupied by multiple grayish-white nodules up to 3 × 2 cm in diameter with a total weight 1,135 g (Fig. 4). Microscopically, Gaucher cells were diffusely observed within the multiple nodules and within the splenic parenchyma as well (Fig. 5). These multiple nodules corresponded to multiple space occupying lesions revealed by ultrasonography, CT and MRI. Fibrotic changes of various degrees were observed in the inner zones of the relatively large nodules.

For electron microscopical examination, small pieces of formalin-fixed tissue were immersed in a fixative containing 3% glutaraldehyde and 1% paraormaldehyde buffered with 0.1 M phosphate buffer, pH 7.4, post-fixed with 2% osmium tetroxide, dehydrated by graded changes of ethanol, and then embedded in Epon 812. Ultrathin sections were cut and stained with uranyl acetate and lead citrate and then examined with a JEM-100B electron microscope. At the ultrastructural level, multiple nodules were composed of numerous round
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Discussion

Gaucher’s disease is a rare autosomal recessive disorder characterized by an abnormally low activity of beta-glucosidase, resulting in the accumulation of glucocerebroside in the reticuloendothelial cells throughout the body (1). There are three clinical types of Gaucher’s disease, which differ in course and in extent of neurologic involvement. The adult type is known as chronic non-neuronopathic Gaucher’s disease, while the infantile type is the acute neuronopathic form. The juvenile type is intermediate in severity and is the subacute neuronopathic form (8). The present case was diagnosed as Gaucher’s disease (adult type) on the basis of the following: 1) presence of Gaucher cells, 2) low activity of beta-glucosidase, 3) chronic and nonneuropathic form with splenomegaly.

The major clinical symptom in adult type Gaucher’s disease is splenomegaly, which is sometimes accompanied by hypersplenism. Several radiographical features of the spleen in Gaucher’s disease have recently been reported with or without histopathological corroboration. Hill et al. reported sonographic appearance of the spleen in Gaucher’s disease, demonstrating multiple space occupying lesions in the spleen in 16 of 47 patients with splenomegaly (4). Most patients had well-defined hypoechoic lesions that corresponded pathologically to focal homogeneous clusters of Gaucher cells as in this case. The use of MRI has recently brought a new

Fig. 5. Gaucher cells in the excised spleen. The characteristic fibrillar appearance in the cytoplasm (arrows), similar to bone marrow Gaucher cells, is seen.

cells containing one or two round nuclei, abundant cytoplasm and well-developed Golgi apparatus. The most striking feature of these cells at the ultrastructural level was the presence of numerous tubular structures in the cytoplasm (Fig. 6). These findings further confirmed the diagnosis of Gaucher’s disease (7). After splenic resection, the platelet count returned to normal in the first 16 days.

Fig. 6. a) Low power electron micrograph of Gaucher cells in the spleen. The cytoplasm is packed with typical tubular structures. b) Higher magnification reveals that these microtubules have straight or branched structures.
radiographical insight concerning the splenic lesions of Gaucher’s disease. In the present case, more precise features of the splenic lesions were obtained by MRI study. An earlier report on the MRI findings in the spleen revealed multiple splenic lesions with thin low-signal intensity margins, giving a “target-like appearance.” The study, however, could not obtain detailed histopathological findings because the Gaucher-affected spleen was not operated on (5, 6). In our case, however, it was clearly demonstrated that the heterogenous nodules were relatively large in size and their “target-like appearance” was the result of the presence of fibrosis within the inner zones of the lesions.

In the present case, the presence of multiple splenic space occupying lesions was demonstrated by ultrasonography, CT, MRI and histopathological studies, including electron microscopic examinations. Thus, we hope to add new information regarding the nature of the splenic lesions in Gaucher’s disease.

References