

Case Report

A Comparison of Ultrasonography, Computerised Tomography, and Conventional MRI Findings for Splenic Nodules Associated with Type 1 Gaucher's Disease with Diffusion-Weighted MRI Findings

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Abstract

A 26-year-old female patient with Type 1 Gaucher's disease (GD) was admitted to our clinic with complaints of stomachache and signs of anemia. The patient underwent ultrasonography (US), computerised tomography (CT), and magnetic resonance imaging (MRI) scan. Imaging studies revealed massive hepatosplenomegaly, choledocolithiasis, and six nodules in the spleen with a mean size of 14 mm. The nodules appeared hyperechoic, hypoechoic, and of mixed echogenicity on the US and hypodense on the CT. While the nodules were observed to be iso-hypointense in T1-weighted (T1WI) images, they appeared to be hyperintense in the T2-weighted (T2WI) images. There were no diffusion restrictions in these nodules that appeared on the diffusion-weighted magnetic resonance imaging (DWI). A nodule located at the lower pole was observed to be hypointense in the T2WI images. The nodule located at the lower pole, which appeared hypointense in T2WI series, had restricted diffusion upon DWI.

In this study, we aimed to present the properties of splenic GD nodules using US, CT, and conventional MRI, together with DWI. This case report is the first to apply US, CT, and conventional MRI, together with DWI, to the splenic nodules associated with Gaucher's disease.

Keywords: diffusion magnetic resonance imaging, lysosomal storage diseases, multidetector computed tomography

Introduction

Gaucher's disease (GD) is a lysosomal storage disease that is inherited in an autosomal recessive fashion. Glucocerebroside deposits accumulate in the macrophages of the reticuloendothelial system as a result of glucocerebrosidase enzyme deficiency. Eventually, enlarged macrophages with deposited glycolipids, called Gaucher cells,

develop, mostly in the bone marrow, spleen, and liver. Three clinical subtypes of GD have been defined. Type 1 does not have central nervous system (CNS) involvement and is the most frequent type (also known as the non-neuropathic type). These patients present with progressive anemia, thrombocytopenia, hepatosplenomegaly, skeletal deformities, and sometimes pulmonary and renal disorders. Type 2 is called the acute neuronopathic type and is characterised by severe CNS involvement.

It progresses rapidly and typically results in premature death. Type 3 is the subacute neuronopathic type and presents with CNS involvement. Compared to type 2, type 3 is less severe and less progressive.

Clinical manifestations of GD are seen as a result of the accumulation of Gaucher cells in the reticuloendothelial system of the spleen and liver, and this condition presents with various clinical signs. This especially applies for type 1, in which some patients might remain asymptomatic for life (1).

Splenic nodules are common in GD and seen in 30% of patients. The differential diagnosis of malignant splenic masses, such as lymphoma and leukemia, should be considered first when evaluating patients with GD who have splenic nodules (2). Ultrasonography (US), computerised tomography (CT), and magnetic resonance imaging (MRI) are used for the detection, differential diagnosis, and follow-up of these nodules (1). For the observation of clinical response to the recently developed enzyme replacement treatment, MRI has become the most efficient imaging technique due to the applicability of advanced imaging techniques such as high-resolution multi-planar imaging capacity and diffusion-weighted MRI (DWI) (3). We aimed to present the properties of the splenic nodules in a 26-year-old patient with GD using US, CT, and conventional MRI, along with DWI.

Case

A 26-year-old female patient with type 1 GD was admitted to our clinic with complaints of stomachache and anemia. The patient underwent whole-abdominal US, followed by upper abdominal CT and MRI scan. The US scan was performed with a digital sonography scanner (Aplio 500, Toshiba Medical Systems Corporation, Otawara, Japan) and a convex 3.5–5 MHz multifrequency transducer. The CT scan was performed with an eight-channel multidetector computerized tomography (MDCT) (GE Healthcare, Milwaukee, WI, USA). Axial consecutive sections of 5 mm slice thickness were obtained via abdominal MDCT with 5 mm collimation at 120 kVp and automatic tube modulation at 120–220 mA.

The MRI was performed with 1.5 Tesla (T) (General Electric Signa EXCITE 14.0 Waukesha, WI). Conventional MRI sections included T1-weighted images (T1WI) and T2-weighted images (T2WI) series. T1WI series were obtained

in phase (time repetition [TR]/ time echo [TE], 200/4.2) and out of phase (200/2.004). T2WI series were obtained with FIESTA (4.022, 1.76), single shot fast-spin echo (SSFSE) (491, 85.44), and fatsat SSFSE (462, 86.5) in 7 mm thick axial sections. DWI images were obtained in the axial plane with a diffusion-weighted echo planar imaging (DW-EPI) sequence using $b = 0$, $b = 500$, and $b = 1000$ as parameters without breath holding. The DWI parameters used were as follows: TR: 3000 ms; TE: 90.4 ms; field of view (FOV): 400 mm; number of excitations: 3; matrix size: 128x128; section thickness: 7 mm; number of sections: 19, intersection gap: 1.5 mm.

Imaging studies revealed massive hepatosplenomegaly (craniocaudal size of liver 206 mm, craniocaudal size of spleen 174 mm) and a calculus in the lumen of the gallbladder (measuring 5 mm) and six nodules in the parenchyma of the spleen with a mean size of 14 mm.

Table 1 shows the radiologic findings for the nodules. Three nodules located [group 1] at the middle and lower pole were iso-hyperechoic, while two nodule [group 2] located at the middle and lower pole appeared to be of mixed echogenicity (peripheral hyperechogenicity and central hypoechogenicity) upon the US scan (Figure 1). One of the nodules [group 3] located at the lower pole was observed to be a nodular hypoechoic structure.

Group 1 nodules were seen as hypodense on unenhanced and enhanced CT, isointense on T1WI, and hyperintense on T2WI MRI. There were no diffusion restrictions in these nodules on DWI.

Group 2 nodules were observed to be hypodense on unenhanced CT, and they showed a ring enhancement on enhanced CT. They were seen as isointense on T1WI and hyperintense on T2WI MRI. There were no diffusion restrictions in these nodules on DWI.

The Group 3 nodule was hypodense on unenhanced and enhanced CT, iso-hypointense on T1WI, and hypointense on T2WI MRI. There was a diffusion restriction in this nodule on DWI, and the nodule had decreased apparent diffusion coefficient (ADC) values, proving significant diffusion restriction as compared to the spleen parenchyma. The mean ADC value measured in the spleen parenchyma was $839 \times 10^{-6} \text{ mm}^2/\text{s}$, while it was $299 \times 10^{-6} \text{ mm}^2/\text{s}$ at the nodule (Figure 2 and Figure 3).

Table 1. The radiologic findings of the Gaucher's splenic nodules

Group	US	CT unenhanced	CT enhanced	T1WI	T2WI	DWI
1 (n=3)	iso-hyperechoic	hypodense	hypodense	isointense	hyperintense	no diffusion restriction
2 (n=2)	mix echogenicity	hypodense	a ring enhancement	isointense	hyperintense	no diffusion restriction
3 (n=1)	hypoechoic	hypodense	hypodense	iso-hypointense	hypointense	diffusion restriction



Figure 1. Splenic nodule with hypoechoic center and hyperechoic peripheral zone forming a target sign appearance observed upon the ultrasonographic evaluation of a 26-year-old woman with type-1 Gaucher's disease

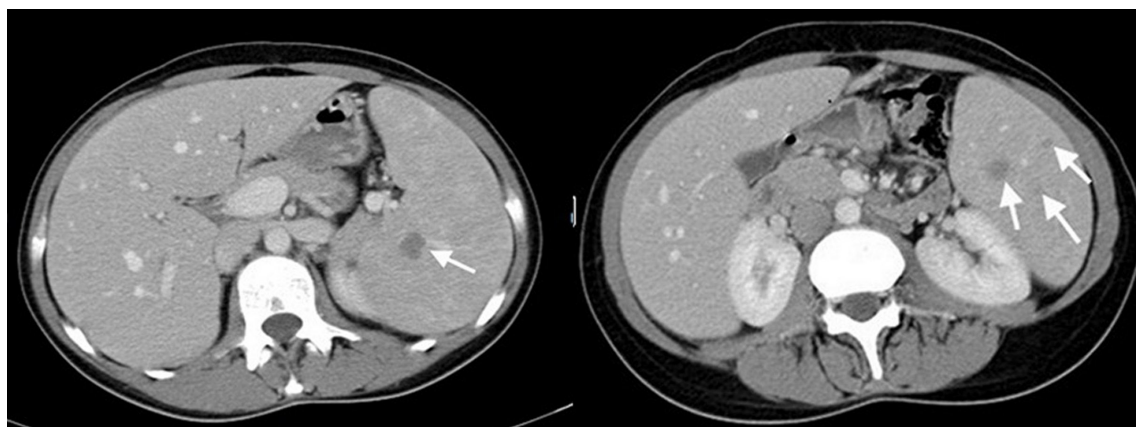


Figure 2. Contrast-enhanced abdominal CT scan of a 26-year-old woman with type-1 Gaucher's disease. Some of the nodules were observed in a peripheral hyperdense and central hypodense fashion (a ring enhancement) (2a), while most of them appeared to have a hypodense structure upon contrast-enhanced CT (2b)

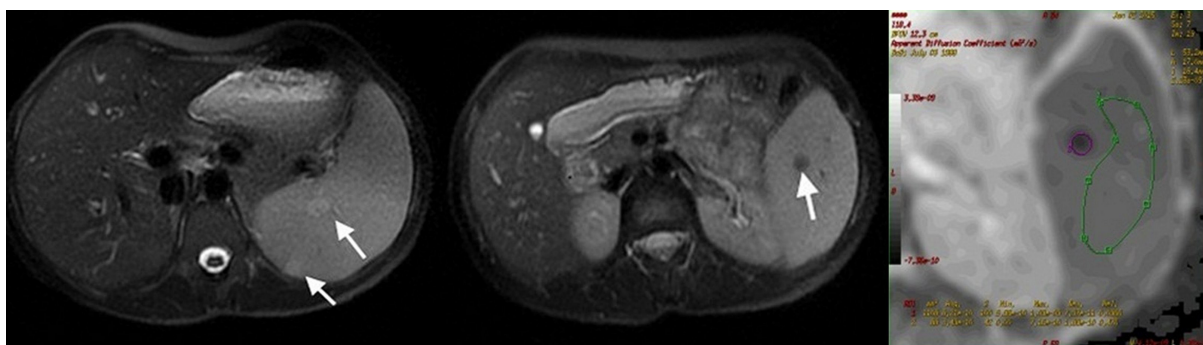


Figure 3. T2W MRI (a, b) and ADC map (c) of a 26-year-old woman with type-1 Gaucher's disease. While most of the nodules were observed at a hyperintense signal intensity (3a), the nodule at the lower splenic pole was observed to be hypointense (3b) during a fat suppressing T2W SSFSE sequence. The nodule at the lower pole of the spleen has significantly lower signal intensity and a lower ADC value as compared to the splenic parenchyma at the ADC map (3c)

Discussion

Various imaging studies have been performed regarding the detection and characterisation of structural changes observed in the abdominal organs of patients with GD. Hill et al. evaluated the upper abdominal organs of 48 US patients with Gaucher's disease and reported multiple lesions located in the spleens of 16 of 48 patients (33%). Seven of the 16 patients who had multiple lesions in the spleen underwent partial or total splenectomy. Four of these seven patients had hypoechoic lesions with well-defined borders, and two patients had hyperechoic lesions with well-defined borders (4).

Aspestrand et al. reported a patient who had focal changes in the spleen; these changes were detected using various diagnostics methods. This patient had splenomegaly, accompanied by multiple hypoechoic lesions with a hyperechoic rim upon US scan, focal changes with a target sign appearance upon CT, and lesions with low attenuation and less contrast than the spleen parenchyma following the use of intravenous contrast medium (IVCM) (5). Our patient also has hypoechoic nodules at the lower pole [Group 3], and they were hypodense on unenhanced and enhanced CT. Our patient had other nodules that were different from those in the above study: iso-hyperechoic nodules [Group 1] and mixed echogenic nodules [Group 2]. Group 1 nodules were hypodense on both unenhanced and enhanced CT scan, and Group 2 nodules were hypodense on unenhanced CT and showed a ring enhancement on enhanced CT scan.

The nodules can appear as round masses with well-defined borders upon MRI. Hill et al. evaluated the abdominal MR imaging findings for 46 Gaucher's patients. In their study, splenic nodules appeared to be T1WI isointense-T2WI hypointense or T1WI and T2WI hyperintense. In addition, some nodules had a mixed target-sign-shaped signal intensity with a T2WI hypointense center and a hyperintense rim (6). In our patient, the hyperechoic nodules [Group 1] are isointense on T1WI and hyperintense on T2WI, and the hypoechoic nodule [Group 3] is iso-hypointense on T1WI and hypointense on T2WI.

Conventional MRI is an effective method of diagnosing GD. Furthermore, the addition of DWI to conventional MRI provides very useful information during diagnosis. DWI is a non-invasive technique that allows the quantitative measurement of the diffusion activity of water molecules in the tissues. While the diffusion restriction is increased in tissues with high signal intensity, it is decreased in tissues with lower signal intensity because the extracellular space is larger or the cellular membrane integrity is damaged. When the areas with higher cellular properties and restricted diffusion are compared to areas with lower cellular properties, they have lower ADC values, and these areas are observed with a lower signal intensity (7). The ADC values of the central nervous system and bone marrow in GD have been reported in the literature. Abdel Razek et al. conducted a study in which they compared 20 infants with GD with a control group of 20 infants with matching age and sex properties and found significant differences between the two groups in terms of the ADC values of the vertebral bone marrow

(8). The ADC values of brain parenchyma in GD were measured in a study. This study found that ADC values obtained from seven regions of the brain were significantly lower in the patient group than in the control group (9). Also, a significant difference between ADC values in the frontal and temporal gray matter were detected in a homozygous and heterozygous group in this study (9).

In a study in which the DWI-MRI characteristics of the spleen were compared between cirrhotic patients and a control group, the ADC values of the splenic parenchyma were found to be $0.87 \pm 0.04 \times 10^{-3} \text{ mm}^2/\text{s}$ in the control group and $1.34 \pm 0.05 \times 10^{-3} \text{ mm}^2/\text{s}$ in the cirrhotic group (10). The first DWI study focused on the intra-abdominal organs of patients with GD and was conducted by Kalaycı et al. The ADC values at the nodules of the spleen were found to be $215\text{--}770 \times 10^{-6} \text{ mm}^2/\text{s}$ and $1157 \times 10^{-6} \text{ mm}^2/\text{s}$ in normal splenic parenchyma (11). We obtained the DWI-MRI of splenic nodules. In our patient, Group (1) and (2) nodules revealed no restrictions on DWI. The ADC value of Group 1 and Group 2 is $820\text{--}862 \times 10^{-6} \text{ mm}^2/\text{s}$. This was close to the mean ADC value ($839 \times 10^{-6} \text{ mm}^2/\text{s}$) for splenic parenchyma. However, there is restricted diffusion in the Group (3) nodule, which has an ADC value of ($299 \times 10^{-6} \text{ mm}^2/\text{s}$.) This was much lower than the mean ADC value of splenic parenchyma. These values suggested significantly lower ADC values in the nodule in concordance with the report of Kalaycı et al.

Hill et al. evaluated upper abdominal organs with US, and the authors suggested that hypoechoic lesions were pathologically focal homogenous accumulations of Gaucher cells, which replaced normal spleen cells. They also suggested that hyperechoic lesions were composed of Gaucher cells, fibrosis, and infarct areas (4). Hill et al. (6) also analysed the MRI properties of 46 patients with GD and compared the histopathologic examination results of the patients with the MRIs of the patients. This study suggests that microscopically, the red nodules contained collections of Gaucher cells and dilated sinusoids filled with blood, whereas the white nodules were composed predominantly of Gaucher cells alone. Hill et al. believe that the high-intensity lesions seen on T2-weighted images of the spleen are red nodules grossly and dilated sinusoids microscopically based on the known tendency of a hemangioma to appear bright on T2-weighted images. In the other case, the lesions in the spleen that showed decreased

signal intensity on T2-weighted images appeared to represent the pale nodules grossly and sheets of Gaucher cells microscopically. Using these literature references, we concluded that the Group 3 nodule, which had lower ADC values because of restricted diffusion, may be associated with Gaucher cell accumulation. We also concluded that Group 1 and Group 2 nodules, which had no restricted diffusion, may be associated with dilated sinusoids and/or fibrosis.

Splenic nodules are common in GD and observed in 30% of patients (2). The size of the nodules varies between 5 mm and 60 mm (6). The mean size of the nodules was 14 mm in our case. Abnormal signal intensity in the liver can be observed in 20% of patients with GD. High signal intensity in T2WI images is consistent with inflammation, fibrosis, and/or ischemia or relative ischemia regions caused by the infiltration of hepatic sinusoids by Gaucher cells (6). Our patient only had hepatomegaly of the liver, and no areas with abnormal signals were detected.

Gaucher's disease has a tendency to produce gallbladder stones. Taddei et al. investigated the frequency of gallbladder stones in 417 patients with type 1 Gaucher's and detected stones in 32% of patients. Also, they reported the prevalence of gallbladder stones in these patients to be five times higher than in the normal population (12). Our patient also had a 5 mm calculus inside the gallbladder, which was detected in all imaging studies.

Conclusion

Splenic nodules are frequently observed in GD, and malignant splenic nodules, such as lymphoma and leukemia, should be considered first during differential diagnosis. The US, CT, and MRI can be used in the diagnosis of splenic nodules. The addition of DWI imaging to these methods allows us to have more information about the structural and functional characteristics of the nodule. This is the first study that provides the US, CT, MRI, and DWI characteristics of splenic nodules. In order to better understand the efficacy of the DWI technique when evaluating the abdominal organs of patients with GD, studies with higher numbers of cases are required.

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Conflict of Interest

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Analysis and interpretation of the data: FA
Drafting of the article: EA
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