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Assessment of the liver and spleen in children with Gaucher's disease type I with diffusion-weighted MR imaging

Ahmed Abdel Khalek Abdel Razek [a,*], Ahmed Abdalla [b], Tarik Barakat [b], Heba El-Taher [b], Khadiga Ali [c]

[a] Department of Diagnostic Radiology, Mansoura Faculty of Medicine, Mansoura, Egypt
[b] Gastroenterology and Hepatology Unit of Mansoura Children Hospital, Mansoura Faculty of Medicine, Mansoura, Egypt
[c] Department of Pathology, Mansoura Faculty of Medicine, Mansoura, Egypt

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ABSTRACT

Purpose: To assess hepatic and splenic apparent diffusion coefficient (ADC) in children with Gaucher's disease type I with diffusion-weighted MR imaging and to correlate hepatic and splenic ADC with parameters of disease severity.

Subjects and methods: Prospective study was conducted upon 25 children (11 treated and 14 untreated) with Gaucher's disease and 12 age and sex matched control children. They underwent diffusion-weighted MR imaging of abdomen. Hepatic and splenic ADC and volume were calculated.

Results: There was statistically difference in hepatic and splenic apparent diffusion coefficient ($P = 0.001$) between patients and controls. The cutoff ADC of liver and spleen used to differentiate patients from controls were 0.47 and 0.39×10^{-3} mm^2 with area and curve of 0.947 and 0.886 respectively. There was significant difference in hepatic and splenic ADC between untreated and treated patients ($P = 0.003$ and 0.001). Hepatic ADC correlated with splenic volume ($r = -0.721$), hepatic volume ($r = -0.555$) and chitotriosidase ($r = -0.413$). Splenic ADC correlated with splenic volume ($r = -0.652$), hepatic volume ($r = -0.544$) and chitotriosidase ($r = -0.355$).

Conclusion: Hepatic and splenic ADC can detect hepatic and splenic infiltration in Gaucher's disease and correlated with some parameters of disease severity.

1. Introduction

Gaucher's disease is a metabolic disorder caused by an autosomal inherited deficiency of the lysosomal enzyme glucocerebrosidase and characterized by the accumulation of macrophages in the liver, spleen and bone marrow [1–3]. There are three forms of Gaucher's disease are recognized. Type 1 is the mild-to-moderately severe and most commonly seen in the United States and Europe. There is accumulation of Gaucher's cells in the liver and spleen and bone marrow. Patients typically presented with hepato-splenomegaly, and the patients often have a long life. Type 2 is the infantile form, with severe neurological findings and rapid fatal course. Type 3 is much less common than type 1 [2–4]. Early detection of splenic and hepatic infiltration in patients with Gaucher's disease type I is important to start treatment with enzyme replacement therapy [4–6]. Different imaging techniques used to assess visceral involvement in patients with Gaucher's disease but they have some limitations [7]. Ultrasound is a simple technique, but it is operator dependent, computed tomography associated with radiation exposure and contrast medium injection and routine MR imaging cannot evaluate diffuse infiltration of the liver and spleen [7–10].

Diffusion is the random Brownian motion of the molecules, and MR imaging can detect signal changes caused by positional changes of molecules at this microscopic scale. Diffusion-weighted MR imaging provides image contrast that based on the diffusivity of water molecules within the tissues. The diffusivity and apparent diffusion coefficient of the water molecules is substantially altered by cellularity of the lesions [11–12]. Diffusion-weighted MR imaging used for assessment of diffuse and focal liver lesions in the children [13–17]. Also, this technique used for detection of bone marrow infiltration and central nervous system affection in children with Gaucher's disease [18–19].

The aim of this work is to assess apparent diffusion coefficient of the liver and spleen in children with Gaucher's disease type I with diffusion-weighted MR imaging and to correlate apparent diffusion coefficient of the liver and spleen with parameters of the disease severity.

2. Material and method

2.1. Patients

An institutional board approval of this study was obtained and informed consent was taken from parents of all patients and

* Corresponding author at: Department of Diagnostic Radiology, Mansoura Faculty of Medicine, Mansoura 13551, Egypt.
E-mail address: arazek@mans.edu.eg (A.A.K.A. Razek).

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controls. This concurrent cohort prospective study included 27 consecutive patients with Gaucher's disease type I and 12 age and sex matched controls. The inclusion criteria were children with Gaucher's disease proved with low glucocerebrosidase activity in leukocytes. We excluded two patients from study due to motion artifact at MR images. The final patients included in this work were 25 patients (19 boys and 6 girls, age range from 2 to 16 years; mean age 7 years). The age and sex matched children underwent MR imaging for reasons other than abdominal abnormalities were chosen as controls. The final diagnosis of Gaucher's disease was confirmed by laboratory investigation in the form of measurement of glucocerebrosidase activity in leukocytes and genotyping. Eleven patients were under treatment with intravenous enzyme replacement therapy (ERT) with glucocerebrosidase (Cerezyme—Ceredase, Genzyme Biotherapeutics, Naarden, Netherlands) at dose of 60 U/Kg every 2 weeks.

2.2. MR imaging technique

All patients and controls underwent MR examination of the abdomen. Patients were kept fasting for 4–6 h prior to the study. Sedation was achieved using oral chloral hydrate (70–80 mg/kg body weight given 30 min before MR examination) in 10 patients and 15 older patients were scanned without sedation. This study was conducted on T1.5 T MR unit (Ingenia, Philips Best, Netherlands) using bipolar diffusion encoding gradient. The 16-channel anterior phased array torso surface coil (dStream Torso coil) with posterior body coil embedded in the table (dStream Total Spine coil) was applied. Routine axial T1-weighted images (TR/TE = 500/20 ms) and T2-weighted images (TR/TE = 6000/80 ms) were obtained. Diffusion-weighted MR imaging were done using a single shot echo-planar imaging. The parameters used were b value: 0, 500, 1000 s/mm2, TR/TE = 4200/38 ms, scan time was 1 min. The apparent diffusion coefficient map was reconstructed automatically.

2.3. Imaging analysis

Image analysis was performed by one radiologist expert in MR imaging since 25 years (AA). Quantitative analysis of diffusivity of hepatic and splenic parenchyma was performed. A circular region of interest (3–4 cm^2) was placed on the apparent diffusion coefficient map at hepatic and splenic parenchyma, on three consecutive slices away from the biliary and vascular structures (Fig. 1). The apparent diffusion coefficient of the liver and spleen was automatically calculated in $\times 10^{-3}$ mm^2/s. The mean of these 3 values of the liver and spleen represent the final apparent diffusion coefficient of the liver and spleen that used for statistical analysis. The length of the liver and spleen was measured from the most superior margin to the most inferior margins of the organ, the width was measured as maximum distance from most medial to most lateral aspect of the organ and thickness was the distance from post anterior part to posterior part of the organ. The volume of the liver and spleen was calculated using this formula: volume of a prolate ellipsoid ($0.524 \times W \times T \times L$, in which W = maximum width, T = thickness and L = length) [20].

2.4. Laboratory assessment

Chitotriosidase activity was assayed by incubation of 5 μl of plasma in EDTA blood with 100 μl of 4-methyumbelliferyl chitotrioside with normal serum activity of chitotriosidase is 4–76 nmol/ml/h.

2.5. Statistical analysis

The statistical analysis of data was done by using SPSS program statistical package for social science version 20. First, mean and standard deviation of apparent diffusion coefficient of the liver and spleen and volume were calculated. Then, *t*-test was done to show if there was significant difference in the apparent diffusion coefficient and volume of the liver and spleen between patients and controls as well as between untreated and treated patients. The *P* value of less than 0.05 was considered to represent significant. A receiver operating characteristic (ROC) curve was done to evaluate the diagnostic capability of apparent diffusion coefficient for differentiating patients from controls. The area under the curve (AUC), sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Pearson's correlation test was used to correlate apparent diffusion coefficient of the liver and spleen with hepatic and splenic volume and chitotriosidase activity. The correlation coefficient *r* and *P* value were calculated.

3. Results

The mean apparent diffusion coefficient of the liver and spleen in Gaucher's disease were 1.30 ± 0.1 and $81 \pm 0.07 \times 10^{-3}$ mm^2/s and of control were 1.49 ± 0.06 and $0.99 \pm 0.08 \times 10^{-3}$ mm^2/s respectively. There was statistically significant difference in apparent diffusion coefficient of the liver and spleen between patients and controls ($P = 0.001$ respectively) (Table 1). Selection of 1.38×10^{-3} mm^2/s as threshold of apparent diffusion coefficient of the liver for differentiating Gaucher's disease from controls revealed accuracy of 89.2%, sensitivity of 84%, specificity of 100% and the area under the curve of 0.96. When apparent diffusion coefficient of the spleen of 0.93×10^{-3} mm^2/s was used as a threshold value for differentiating Gaucher's disease from controls, revealed accuracy of 89.2%, sensitivity of 92%, specificity of 83.3% and the area under the curve of 0.935 (Fig. 2).

The mean apparent diffusion coefficient of the liver and spleen in untreated patients were 1.25 ± 0.09, $0.79 \pm 0.06 \times 10^{-3}$ mm^2 and in treated patients were 1.37 ± 0.06, $0.85 \pm 0.07 \times 10^{-3}$ mm^2 respectively. There was statistically significant difference in

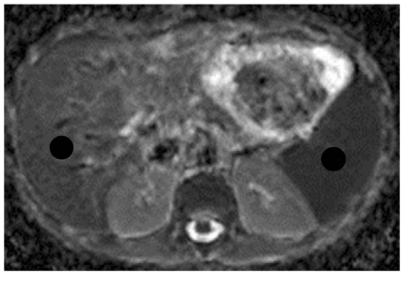

Fig. 1. Localization of regions of interest: the ADC map shows localization of the regions of interest of the liver and spleen in child with Gaucher's disease.

Table 1
The mean, SD, minimum and maximum splenic and hepatic ADC and volume in patients and controls.

	Gaucher's disease (n = 25)	Controls (n = 12)	*P* value
Splenic ADC (10^{-3} mm^2/s)	0.81 ± 0.07 (0.71–0.98)	0.99 ± 0.08 (0.87–1.15)	0.001
Hepatic ADC (10^{-3} mm^2/s)	1.30 ± 0.10 (1.09–1.47)	1.49 ± 0.06 (1.41–1.61)	0.001
Splenic volume (cm^3)	387.3 ± 150.2 (145–666)	154.0 ± 17.2 (130–178)	0.001
Hepatic volume (cm^3)	671 ± 132.7 (488–955)	487.2 ± 50.7 (390–554)	0.001

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