Comparative Study of Images with Pathology: Superparamagnetic Iron Oxide-enhanced Magnetic Resonance Image (MRI) of Splenic VX2 Tumor in Rats

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ABSTRACT

Objective: To establish a rodent model of VX2 tumor of the spleen, to analyze relationship between the change of the signal intensity on superparamagnetic iron oxide enhanced magnetic resonance image (MRI) and pathologic change to evaluate the ability of superparamagnetic iron oxide enhanced MRI for detection of splenic metastases. **Methods:** 8 rodent models of VX2 tumor of spleen were established successfully. The images were obtained before and after administration of superparamagnetic iron oxide. T1-weighted spin-echo (SE) pulse sequence with a repetition time (TR) of 450 msec, and echo time (TE) of 12 msec (TR/TE=450/12) was used. The imaging parameters of T2-weighted SE pulse sequence were as follows: TR/TE=4000/128.   **Results**: On plain MR scanning T1-weighted splenic VX2 tumor showed hypointensity or isointensity which approximated to the SI of splenic parenchyma. Therefore all lesions were not displayed clearly. On superparamagnetic iron oxide enhancement T2WI sequence the SI of splenic parenchyma decreased obviously with percentage of signal intensity loss (PSIL) of 55.04%, But the SI of tumor was not evidently changed with PSIL of 0.87%. Nevertheless the SNR of normal splenic parenchyma around the lesions had obvious difference ($P<0.001$) comparatively. Therefore the contrast between tumor and spleen increased, and tumor displayed more clearly. Moreover the contrast-to-noise (CNR) between VX2 tumor and splenic parenchyma had an evident difference before and after admininstration of superparamagnetic iron oxide ($P<0.001$). **Conclusion:** On superparamagnetic iron oxide enhancement T1WI sequence the contrast of tumor-to-spleen is poor. Therefore it is not sensitive to characterize the lesions in spleen. On superparamagnetic iron oxide enhanced T2WI the contrast degree of lesions increases obviously. Consequently, superparamagnetic iron oxide -enhanced T2WI MRI scanning can improve the rate of detection and characterization for lesions of spleen.

Key words: **Spleen; Tumor; Superparamagnetic iron oxide; Magnetic resonance imaging; Pathology**

The incidence of splenic metastasis is considered an extremely rare event. Computed tomography (CT) and ultrasonography are mostly used screening modalities for the spleen. But CT and MRI have a poor sensitivity for differentiating small nodes of splenic metastasis (<1 cm) from CT and MRI. So we establish a rodent model of VX2 tumor of the spleen to study the relationship between pathologic change of splenic carcinoma and the change of the signal intensity on superparamagnetic iron oxide enhanced MR images, and evaluated the ability of superparamagnetic iron oxide enhanced MR imaging to detect splenic metastases.

MATERIALS AND METHODS

Animals

Establish animal model: twenty SD rats anaesthetized with 3% soluble pentobarbitone were fixed on board, then cut open stomach after

disinfecting the skin. Then the VX2 tumor fragments (size 1–2 mm^3) were implanted into the spleen with a 16-gauge needle under direct vision. The abdominal wall was closed in two continuous layers. Nine to fourteen days after surgery, the rats bearing VX2 tumor were imaged *in vivo*. And five clean SD rats were used as normal control.

Instrument and Contrast Agents

MRI was performed with a 1.5-Tesla whole-body imager (Magnetom vision plus 4, Siemens, Germany) and with a neck coil. All images were analyzed and data were measured on the monitors of a picture archiving and communication system (PACS). Superparamagnetic iron oxide (11.2 mg Fe/ml) was offered by Professor Xu Yi-kai in Imaging Center of Nan Fang Hospital. The gadolinium-diethylene triamine pentaaceticacid (Gd-DTPA, 0.496 g/ml) was produced by Kangcheng Pharmaceutial Company.

MR Sequences and Parameters

The images were obtained before and after administration of superparamagnetic iron oxide. T1-weighted spin-echo (SE) pulse sequence with a repetition time (TR) of 450 msec, and echo time (TE) of 12–15 msec (TR/TE=450/12–15) was used. Field of view was 280×280 mm, and slice thickness was 3–4 mm, and the image matrix was 258×512, and four signals were acquired. The imaging parameters of T2-weighted SE pulse sequence were as follows: TR/TE=4000/128, FOV 280×280 mm, slice thickness was 3–4 mm, and the image matrix was 276×512, and four signals were acquired. All rats were scanned with T1-weighted and T2-weighted sequences in the coronary plane and the axial plane sometimes.

Imaging Analysis

Two MR doctors read MR images. Maximal diameters of lesions were measured. Lesions were determined as hypointensity, isointensity or hyperintensity compared with the adjacent splenic parenchyma on MR images. Signal intensity (SI) over region-of-interest (ROI) draw on lesions and adjacent splenic parenchyma were measured in each image, and ROI were placed at adjacent background outside abdomen and coding direction was the same as the lesions. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of lesions and splenic parenchyma were calculated on all images, as well as percentage of signal intensity

loss (PSIL) after administration of superparamagnetic iron oxide.

Pathologic Examination

After MRI scanning the fresh splenic tissues were immediately chipped into a piece of 1.0 mm^3 and fixed, embedded, sliced up and the slices were observed, and taken photos under a transmission electron microscope. All splenic tissues were fixed in neutral formalin solution and embedded with paraffin and sliced up. These slices were performed with HE and perl's staining. Two pathologists made the pathological diagnosis and two ultrastructure pathologists observed ultrastructure of cells and phagocytes. HE staining was used for qualitative diagnosis. The ultrastructure of splenic cells, and the phagocytes were observed in the different splenic tissues under transmission electron microscope.

Statistical Analysis

Statistical package for social sciences (SPSS 10.0) and the Paired-Sample T Test, Spearman Correlate and Repeated Measures analysis of variance were used. A P value of 0.05 or less was considered to indicate a significant difference.

RESULTS

Establishment of the Splenic VX2 Tumor of Rodent Model

In twenty rats, eight rats (40%) died during surgery. Eight rats (66.7%) were implanted successfully. At autopsy all experimental animals showed a single gray-white and round intrasplenic tumor nodule about 5 mm in size. The VX2 tumor tissues were verified by pathological examination. Specimen of splenic VX2 tumor showed splenic size had no obvious change and a small gray-white nodule (diameter 0.5 cm) in the splenic parenchyma which projected out of the surface of spleen slightly. The lesion in fragment fixed by formalin solution was yellow-white and has no capsule (Fig. 1).

The Signal-time Curve of Spleen after Superparamagnetic Iron Oxide Administration

The MRI signal decreased obviously in five rats after administration of superparamagnetic iron oxide at 60 min, 90 min, 120 min, then kept an