Small Hepatocellular Carcinoma and Dysplastic Nodules in Cirrhotic Livers: Differentiation with Dynamic MR Imaging

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Objective: **To evaluate the usefulness of spin-echo T2 and T1-weighted images and contrast-enhanced dynamic gradient-echo images in differentiating between hepatocellular carcinoma and dysplastic nodules in cirrhotic livers.**

Method: **Thirty-eight patients with liver cirrhosis underwent spin-echo T2 and T1-weighted and contrast-enhanced dynamic gradient-echo imaging. 16 small hepatocellular carcinomas (< 3 cm) in 16 patients and 12 dysplastic nodules (> 1 cm) in 12 patients were included in this study. Spin-echo sequences and dynamic examination were compared for characterisation of liver lesions.**

Results: **On combined SE T2 and T1-weighted images and dynamic MR images, the most common appearances were hyperintensity on T2-weighted images (63%), hyperintensity on T1-weighted images (50%) and hypervascularity (88%) for hepatocellular carcinomas. All of the dysplastic nodules were isointense on T2-weighted images and except one, all dysplastic nodules enhanced similar to the liver parenchyma.**

Conclusion: **In the differential diagnosis of focal lesions in cirrhotic liver, contrast enhancement features are as diagnostic as the signal intensity of the lesions on spin-echo sequences. Hyperintensity on T2-weighted images and hypervascularity on dynamic contrast-enhanced MR imaging are statistically significant features of HCCs developing in cirrhotic livers.**

Key words: *Cirrhosis, MR, liver neoplasms, diagnosis*

Cirrhotic liver disease is characterised by the development of a spectrum of nodules ranging from benign regenerative nodules to overtly malignant hepatocellular carcinoma (HCC). It is critical to detect nodules that contain HCC at an early stage and to differentiate them from other cirrhotic nodules. It has been claimed in prior reports that benign nodules and low-grade dysplastic nodules (CDN) have unique magnetic resonance (MR) signal intensity characteristics that allow them to be reliably distinguished from HCC (1-3). These reports have described HCC as being hypointense on T1-weighted images and hyperintense on T2-weighted images. In recent reports the observation has been made that HCCs may vary in signal intensity on both T1 and T2-weighted images (4-8). Moreover some early HCCs may be isointense on these MR sequences. Because most HCCs have an arterial blood supply greater than that of the surrounding liver and most dysplastic nodules have a portal blood supply, the use of dynamic contrast-enhanced MR imaging may be useful in the differentiation of these lesions in cirrhotic livers (9-10).

In this study, diagnostic ability of the conventional T2 and T1- weighted sequences and multisection dynamic contrast-enhanced MR imaging were compared in the diagnosis of HCCs and dysplastic nodules in patients with cirrhosis and chronic hepatitis.

Material and Method

Between January 1997 and November 1999 thirty eight patients referred to our hospital underwent liver MR imaging for HCC screening. All patients had liver cirrhosis or chronic hepatitis. These patients were suspected to have a neoplasm according to the findings from ultrasound (US), CT or elevated levels of serum alpha-fetoprotein. Of the 38 patients, 26 had HCC and 12 had dysplastic nodules (DNs). In 26 patients there were 49 HCCs. Sixteen small HCCs (< 3 cm) in 16 patients and 12 DNs (> 1 cm) in 12 patients were included in this study. 10 patients with HCCs had other large lesions. The study group consisted of 21 men, and 7 women (age range 41-78 years) with a mean age of 59 years.

Of the 28 patients 15 had histologically proven lesions, while in 13 patients (5 patients with HCC, 8 patients with DNs) diagnosis was reached on the basis of clinical (elevated AFP level) and radiological (US or MR) follow-up. The follow-up periods were 6-18 months.

All MR examinations were performed with a 1.0 T MR imaging unit (Siemens Magnetom). Spin-echo (SE) T1-weighted (TR/TE:500/17) and T2-weighted (TR/TE: 2000/20-80) images, gradient-echo (GRE) breath-hold FLASH 2D (TR/TE: 106/4, flip angle: 65) and dynamic multisection (12 section) axial images were obtained. Slice thickness was 8-10 mm. Acquisition time of breath-hold images was 16 seconds. Dynamic MR examination was performed immediately after rapid hand injection of *gadopentetate dimeglumine* (0.1 mmol/kg) and imaging was then performed at 20, 40, 60, 80, 120 and 300 seconds. From these images, three phase of enhancement were selected: the arterial phase, portal venous phase and delayed phase.

All MR images were interpreted in consensus by two

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reviewers, who had no knowledge of histological findings. Signal intensity of the tumors was analysed on SE images. Lesions were classified as hypointense, isointense or hyperintense relative to liver on unenhanced T1 and T2-weighted images.

For dynamic images, the pattern of enhancement and the hemodynamics were evaluated. Patterns of enhancement were described as diffuse homogeneous, diffuse heterogeneous, peripheral rim and peripheral heterogeneous. Hemodynamics of the tumor were evaluated by determining the lesion-to-liver contrast over time for most typical portions of the tumor. Four distinct patterns were encountered: pattern 1= peak of enhancement is seen within the arterial phase, followed by a decrease during the delayed phase; pattern 2= enhancement increases with time (no peak in arterial phase); pattern 3= slight enhancement; pattern 4= enhancement similar to the liver parenchyma.

Signal intensity and contrast enhancement features of HCCs and DNs were statistically compared (Mc Nemar test).

Results

The mean diameter of HCCs was 2.1 cm (1-3 cm) and of dysplastic nodules was 1.6 cm (1-3 cm). 9 HCCs were equal to or less than 1.5 cm.

Signal intensity (SI) of the lesions on SE T2 and T1-weighted images are shown on Table I.

Table II summarises hemodynamics of the lesions on dynamic contrast-enhanced MR images. Contrast enhancement patterns of the HCCs were as follows: 12 lesions exhibited diffuse homogenous enhancement, 2 lesions exhibited peripheral heterogeneous enhancement, one lesion showed diffuse heterogeneous enhancement and one lesion demonstrated peripheral rim enhancement.

Table III. Comparating features of HCCs and DNs and statistical results

Features	Lesions	p value
Hyperintensity onT2- weighted	HCC- DN	0.0005*
Isointensity on T2-weighted	HCC- DN	0.0078*
Hyperintensity on T1-weighted	HCC- DN	0.2500
Isointensity on T1-weighted	HCC- DN	0.2500
Hypointensity on T1-weighted	HCC- DN	0.1250
Pattern 1 hemodynamic features	HCC- DN	0.0005*
Pattern 4 hemodynamic features	HCC- DN	0.0010*

**Statistically significant*

On combined SE T2 and T1-weighted images and dynamic MR images, the most common appearances were hyperintensity on T2-W images (63%), hyperintensity on T1-W images (50%), pattern 1 hemodynamic appearance (88%) and diffuse homogenous enhancement (75%) for HCCs (Fig.1-2). Except one, all of the dysplastic nodules were iso or hyperintense on T1-weighted images and isointense on T2-weighted images. Of DNs 92% demonstrated pattern 4 hemodynamic appearance (Fig.3).

Table III shows comparative results of HCCs and DNs by means of signal intensity and hemodynamic features. Hyperintensity on T2-weighted images and pattern 1 hemodynamic feature for HCCs and isointensity on T2-weighted images and pattern 4 hemodynamic feature for DNs were found to be statistically distinctive features ($p< 0.05$).

Discussion

The role of MRI is important in the detection, differential diagnosis and follow-up of focal lesions developing in cirrhotic livers. Due to difficulties in

Table I. Signal intensitiy of the lesions on T2- and T1- weighted images

Signal intensity		Number of lesions (%)	
T2- weighted	T1-weighted	HCC (n= 16)	DN (n=12)
Hyperintensity	Hypointensity	4 (25)	-
Hyperintensity	Hyperintensity	6 (37)	-
Isointensity	Hyperintensity	2 (13)	5 (42)
Isointensity	Isointensity	1 (6)	6 (50)
Isointensity	Hypointensity	1 (6)	1 (8)
Hyperintensity	Isointensity	2 (13)	-
Total		16 (100)	12 (100)

Table II. Hemodynamics features of the tumors in dynamic images

Hemodynamic Patterns	Number of lesions (%)	
	HCC (n=16)	DN (n=12)
Pattern 1	14 (88)	-
Pattern 2	-	-
Pattern 3	2 (12)	1(8)
Pattern 4	-	11 (92)

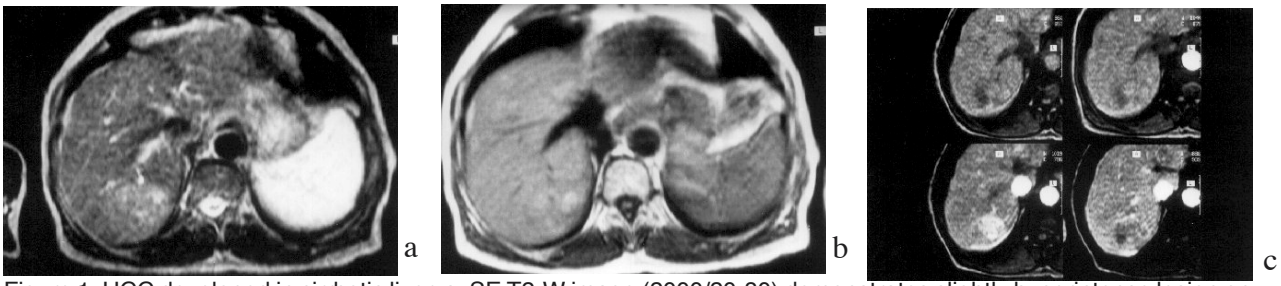

Figure 1. HCC developed in cirrhotic liver. a. SE T2-W image (2000/20-80) demonstrates slightly hyperintense lesion on segment 7. b. On SE T1-W image (500/15) obtained at the same level as a, the lesion shows heterogeneous hyperintensity. c. On dynamic gadolinium-enhanced GRE images (106/4), the lesion shows diffuse homogenous contrast-enhancement during the early portal phase, pattern 1 hemodynamic appearance and late pseudocapsular enhancement.

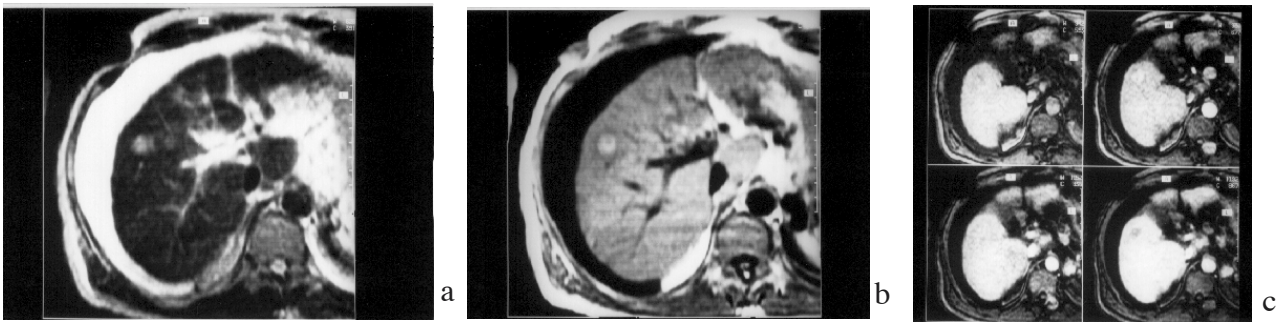

Figure 2. HCC developed in cirrhotic liver. a. SE T2 –W image shows a hyperintense lesion. b. On T1-W image, the lesion is hyperintense and has a hypointense capsule. c. On dynamic gadolinium-enhanced GRE images, the lesion demonstrates diffuse homogenous enhancement during the arterial phase and pattern 1 hemodynamic appearance.

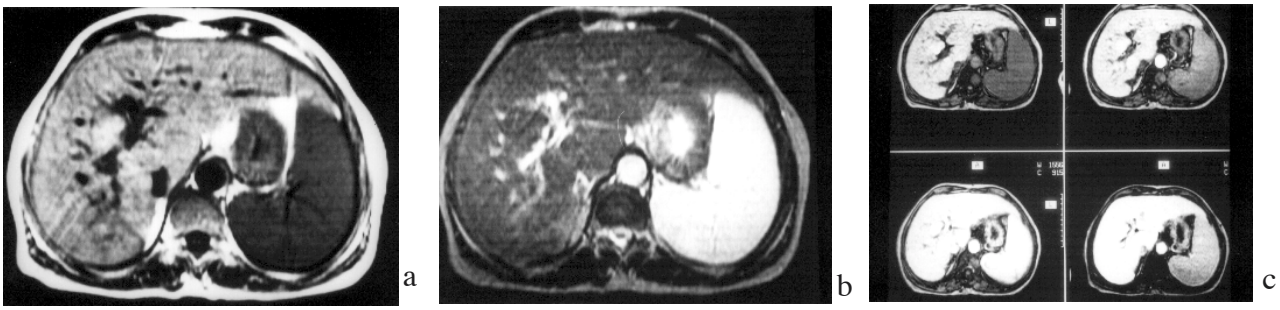

Figure 3. Dysplastic nodule. a. On SE T1-W image, the liver has heterogeneous nodular appearance. A preportal lobulated mass is mildly hyperintense relative to liver. b. The lesion is isointense relative to liver on SE T2-W image. c. On dynamic gadolinium-enhanced GRE images, the lesion has pattern 4 hemodynamic appearance.

histopathological diagnosis of small and well-differentiated HCCs and normal alpha-fetoprotein levels accompanying these lesions, MR imaging findings and vascularization of the lesions are claimed to be useful as a guide to management decisions. Moreover most small HCCs are often detected only with dynamic contrast-enhanced examination (5,6,11-12)

In this study, except one, all of the dysplastic nodules were iso or hyperintense on T1- weighted images (92%) and isointense on T2-weighted images (100%). The hemodynamics of these lesions were not different from normal hepatic vascularity.

Most HCCs were hyperintense on T2-weighted and T1-weighted images. It has been reported that there is a direct relationship with malignant potentials of dysplastic nodules and the hyperintensity on T2-weighted images (1,13). However some early HCCs may be isointense in SE MR sequences (4-7). In our study, 4 HCCs on SE T2-weighted images and 3 HCCs on SE T1-weighted images were isointense. One HCC could be detected only during the arterial phase. Previous studies have shown that small (less than 1.5 cm) HCCs are commonly detected on early contrast-enhanced images and they exhibit diffuse homogeneous enhancement (6,11). In this study 9 HCCs were equal to or less than 1.5 cm. One third of them were isointense on T2- weighted images. While eight demonstrated diffuse homogenous enhancement, one of them showed peripheral rim enhancement. All of them showed pattern 1 hemodynamic appearance.

To our knowledge, there is limited number of reports about dynamic MR imaging findings of dysplastic nodules (14-15). DNs are fed by the portal vein primarily. In a recent study, Hayashi et al. evaluated the histologic grade

of malignancy by evaluation of the blood supply in cirrhotic nodules using CT during arterial portography and CT during hepatic arteriography (10). They reported that intranodular portal supply relative to the surrounding liver parenchyma observed by CT during arterial portography was decreased, whereas the intranodular arterial supply revealed by CT during hepatic arteriography was decreased during the early stages of hepatocarcinogenesis and then increased in accordance with elevation of the grade of malignancy of the nodules. However, these authors have claimed that because those imaging techniques are invasive, the findings revealed in their study should be applied to Doppler sonography, dynamic CT, and dynamic MR imaging. Choi et al. reported that 88% of dysplastic nodules in their study were avascular and 12% of these were slightly vascular (15). Except one, all DNs in our study had pattern 4 hemodynamic appearance. One of the DNs was hypointense on T1-weighted images, isointense on T2-weighted images and hypovascular on dynamic images. In a case report, hypervascular dysplastic nodules have been described in a cirrhotic liver that underwent transplantation (14). In a series of 500 patients with cirrhosis who underwent biphasic helical CT, findings revealed that 2% of arterial phase enhancing masses were not HCCs but rather were benign lesions including transient hepatic attenuation difference, hemangioma, hepatic peliosis, fibrosis, splenic lobule and cryptogenic causes (16).

The drawbacks of this study are the limited number of patients and the absence of histological proof in all patients. In our centre, since arterial chemoembolisation treatment is commonly used in patients with HCCs developing in cirrhotic patients, the number of patients undergoing liver transplantation is limited.

In conclusion, hyperintensity on T2-weighted images and hypervascularity (pattern 1 hemodynamic appearance) on dynamic contrast-enhanced MR imaging are statistically significant features of HCCs developing in cirrhotic livers.

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