Clinical Note

Hepatocellular Carcinoma Exhibiting a Concentric Structure of Different Histologic Grades: Evaluation by Chondroitin Sulfate Iron Colloid-Enhanced MR Imaging

Masayuki Kamba, MD • Yuji Suto, MD • Fumiko Kodama, MD • Yoshio Ohta, MD • Junko Kobayashi, MD
Yutaka Horie, MD • Hironaka Kawasaki, MD

A patient with hepatocellular carcinoma exhibiting a concentric structure of different histologic grades was examined with chondroitin sulfate iron colloid (CSIC)-enhanced MR imaging. After CSIC injection, the advanced component was enhanced in comparison with the surrounding liver, and the well-differentiated component was not enhanced. CSIC-enhanced MR imaging was helpful in evaluating histologic grade on the basis of reticuloendothelial function.

Index terms: Liver neoplasms • MR imaging • Contrast enhancement

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Abbreviations: CSIC=chondroitin sulfate iron colloid, CTAP=computed tomography during arterial portography, HCC=hepatocellular carcinoma, MR=magnetic resonance, MRI=magnetic resonance imaging, TE=echo time, TR=repetition time.

From the Department of Radiology (M.K., Y.S., F.K., Y.O.) and the Second Department of Internal Medicine (J.K., Y.H., H.K.), Faculty of Medicine, Tottori University, 36-1 Nishi-machi, Yonago 683, Japan. Received May 10, 1995; revision requested June 27; revision received November 6; accepted November 7. **Address reprint requests to** M.K.

WE HAVE USED chondroitin sulfate iron colloid (CSIC) (Blutal, Dainippon Pharmaceutical, Osaka, Japan) as a reticuloendothelial contrast agent for magnetic resonance imaging (MRI) (1-4). This agent reduces the signal intensity of liver because of a T2*-shortening effect (1). This effect improves the detection of hepatocellular carcinoma (HCC) (1,3). A significant correlation has been found between the enhancement of tumor-liver contrast after CSIC administration and histologic grade of HCC (4). We report here a comparison between reticuloendothelial function and arterial or portal blood perfusion in a patient with HCC exhibiting a concentric structure of different histologic grades.

• CASE REPORT

A liver tumor was detected on ultrasonography in a 48-year-old man during follow-up of liver cirrhosis because of chronic hepatitis type B. Laboratory tests on admission disclosed increases in aspartate transaminase (44 IU/l), alanine transaminase (61 IU/l), alkaline phosphatase (466 IU/l), and γ-glutamyl transpeptidase (179 IU/l), and a decrease in platelet count (116 × 10^3 /mm^3). Coagulation tests disclosed a prolonged prothrombin time of 64%. The α-fetoprotein level was within normal limits. Ultrasonography revealed a hypoechoic nodule with a central hyperechoic portion.

MR images were obtained with a 1.5 T superconducting unit (Magnetom H15, Siemens-Asahi Medical Technologies, Tokyo, Japan). T1-weighted spin echo MR images—at a repetition time (TR) of 600 msec and an echo time (TE) of 15 msec—revealed a hyperintense nodule with a central isointense component (Fig 1A). T2-weighted images (TR—2,000 msec; TE—90 msec) revealed a peripheral isointense

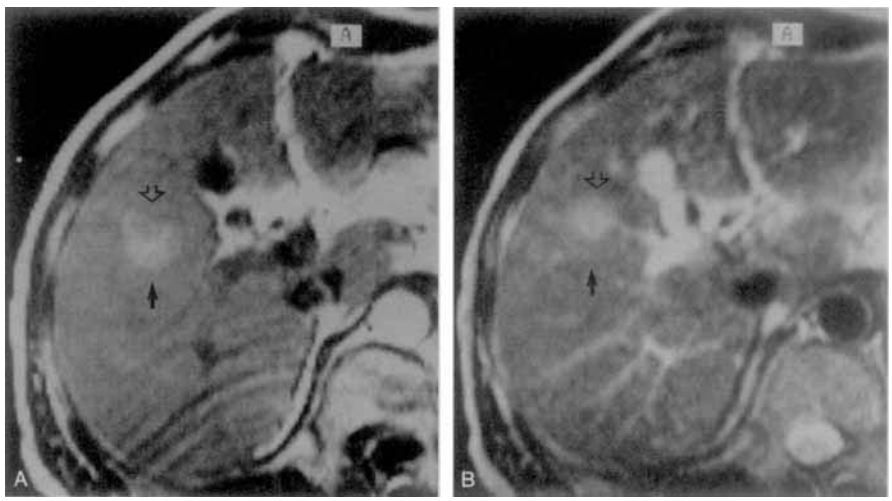

Figure 1. The precontrast T1-weighted image shows a hyperintense nodule (arrow) with a central isointense component (arrowhead) **(A)**. The precontrast T2-weighted image shows a central hyperintense component (arrowhead) within a peripheral isointense area (arrow) **(B)**.

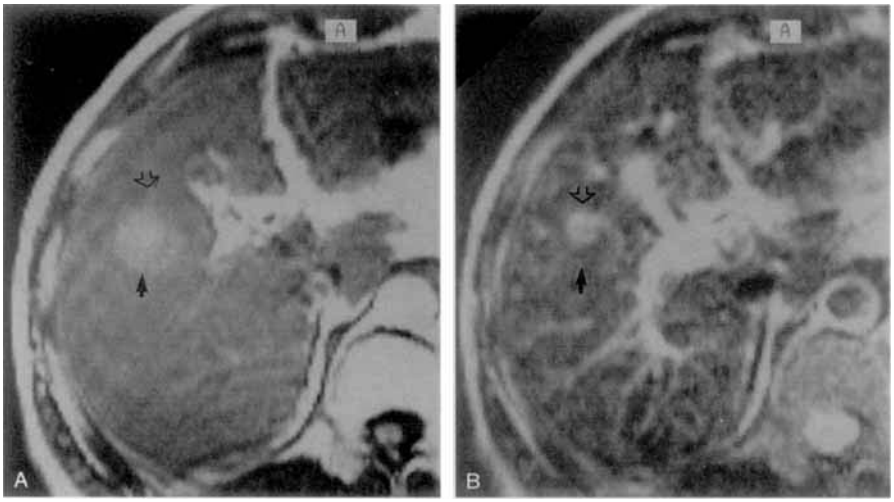

Figure 2. The lesion-liver contrast in the central component is enhanced on both T1- (arrowhead) **(A)** and T2-weighted MR images (arrowhead) **(B)** after CSIC administration. The peripheral component is still isointense on the T2-weighted image (arrow) **(B)**, and it is hyperintense on the T1-weighted image but with reduced lesion-liver contrast (arrow) **(A)**.

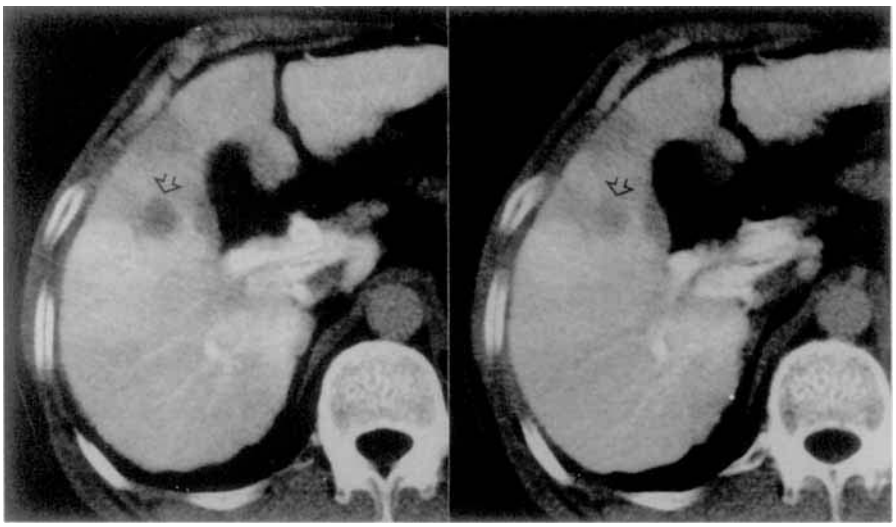

Figure 3. On CTAP, the central component appears as a hypoattenuated area (arrowhead).

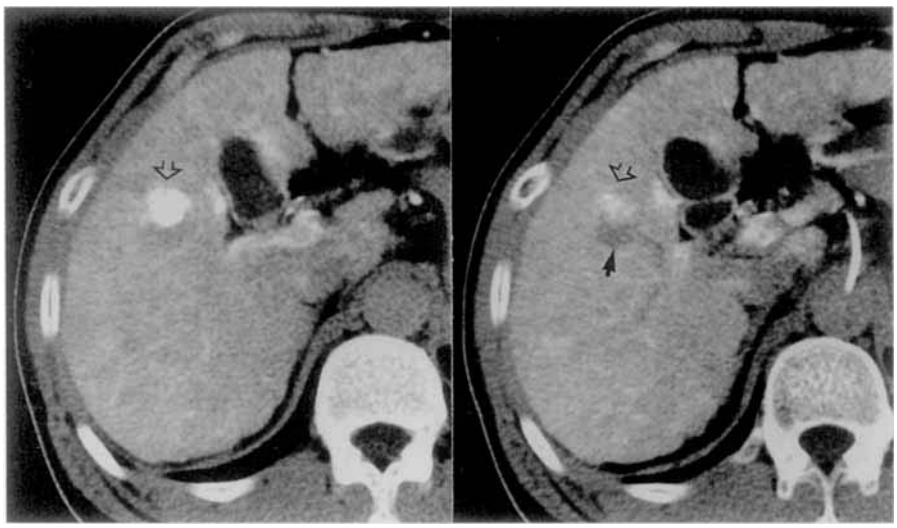

Figure 4. CT arteriography reveals a hyperattenuated component (arrowhead) and a surrounding hypoattenuated area (arrow).

area surrounding a central hyperintense component (Fig 1B). The central component was strongly enhanced and became hyperintense compared with the peripheral component on CSIC-enhanced T1-weighted images. The peripheral component was still hyperintense, but the lesion-liver contrast was reduced (Fig 2A). The central component was also enhanced, but the peripheral component was still isointense on CSIC-enhanced T2-weighted images (Fig 2B). The patient gave informed written consent for participation in the MR study.

Computed tomography during arterial portography (CTAP) revealed a portal perfusion defect corresponding to the central component. The peripheral component was isodense compared with the surrounding liver parenchyma (Fig 3). CT arteriography showed tumor staining and a surrounding hypoattenuated area corresponding to the central and peripheral components of the tumor, respectively (Fig 4). Histological examination of the resected specimen revealed the central component to be moderately differentiated HCC containing small, poorly differentiated foci and the peripheral component to be well-differentiated HCC (Fig 5).

• DISCUSSION

CSIC is a stable iron colloid preparation with a trivalent iron ion. It is a paramagnetic substance, the molecular formula of which is $[(C_{13}H_{19}O_{14}NS)-Fe(OH)_3]_n$, n=150-160. Its mean molecular weight is 75,000, and its particle size is more than 100 nm in water (by ultrafiltration) (5). Its T1 and T2 relaxivities are 0.44 and 2.3 sec^{-1} mM^{-1}, respectively, as measured with a 1.5 T MR spectrometer at 22 °C (5). CSIC is widely used in clinical practice in Japan for the treatment of asiderotic anemia, and its safety has been established.

After intravenous injection, CSIC is taken up by the liver with normal reticuloendothelial cells, and the signal intensity of liver is reduced because of a T2*-shortening effect (1). In liver tumors such as HCC, in which reticuloendothelial function is impaired or absent, the signal intensity of the lesion relative to that of normal liver is increased after the administration of CSIC (1-4). Less differentiated HCC features a more marked increase in tumor-liver contrast because the number of reticuloendothelial cells is lower in less differentiated HCC than in well-differentiated HCC (4).

A correlation between signal intensity on T2-weighted images and the histologic grade of HCC has already been noted (6). Hyperintensity on T1-weighted images is more frequent in well-differentiated HCCs than in classical HCCs (6). The combination of signal intensities on T1- and T2-weighted images is useful in the evaluation of the histologic grade (6). A nodule-in-nodule appearance was present in our case. The lesion featured an isointense area within a hyperintense area on T1-weighted images and a hyperintense area within an isointense area on the T2-weighted images. These features were compatible with the MR appearance of early advanced HCC (7).

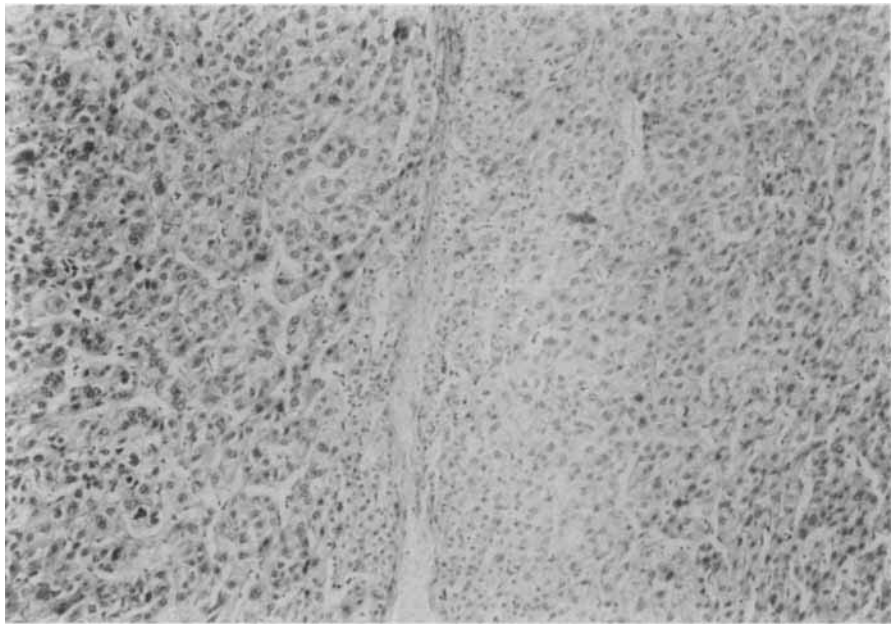

Figure 5. A photomicrograph of the resected specimen shows a well-differentiated HCC (right half) and a moderately differentiated HCC (left half) [Hematoxylin and eosin stain; original magnification ×200].

The changes in tumor-liver contrast before and after CSIC administration correlated well with the histologic grade of each component of the tumor. CSIC accumulated in the peripheral component, well-differentiated HCC, to a greater degree than in the central component, moderately differentiated HCC with small, poorly differentiated foci. The central component of the tumor was clearly enhanced on both T1- and T2-weighted MR images after CSIC administration. Tumor-liver contrast was decreased in the peripheral component on T1-weighted MR images and remained the same on T2-weighted images after CSIC administration.

On the other hand, CTAP and CT arteriography usually are used to evaluate the histologic grade of HCC on the basis of blood supply. A hyperattenuating area within a hypoattenuating area was detected on CT arteriography. CTAP demonstrated the central component as a hypoattenuated area, but the peripheral component was isoattenuated. These findings suggest that a well-differentiated lesion surrounded a less differentiated focus. The CT appearances were also consistent with those of early advanced HCC (7).

CSIC-enhanced MRI was helpful in evaluating the two different components of the tumor before CTAP and CT arteriography. Findings obtained in this case suggest that CSIC has the potential to improve diagnostic accuracy in the differentiation of histologic grade by MRI. Further examination will be necessary to confirm the correlation between reticuloendothelial function and blood supply in HCC.

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