**MR Imaging of Carcinosarcoma of the Liver using Gd-EOB-DTPA**

Tsuyoshi Yasutake,1*, Shigeru Kiryu,2 Hiroyuki Akai,1 Takeyuki Watadani,1 Masaaki Akahane,1 Nobuo Tomizawa,1 Wataru Gono,1 Masako Ikemura,3 Masamichi Takahashi,4 Yujiro Matsuoka,4 and Kuni Ohtomo1

1Department of Radiology, Graduate School of Medicine, University of Tokyo
7–3–1 Hongou, Bunkyo-ku, Tokyo 113–8655, Japan
2Department of Radiology, Institute of Medical Science, University of Tokyo
3Department of Pathology, Graduate School of Medicine, University of Tokyo
4Department of Radiology, Tokyo Metropolitan Bokutoh Hospital

(Received February 13, 2013; Accepted October 30, 2013; published online April 28, 2014)

We present a case of a 69-year-old man with primary hepatic carcinosarcoma who underwent computed tomography that revealed a hypervascular hepatic tumor with local dense calcification. Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging revealed hyperintense lesions in the hepatobiliary phase that indicated hepatocellular carcinoma with bile production. The patient underwent right lobectomy, and the presence of a sarcoma component within the tumor on histopathology confirmed liver carcinosarcoma that included hepatocellular carcinoma. In cases with atypical images that resemble this case, the hyperintensity of a lesion in the hepatobiliary phase aids differential diagnosis.

**Keywords:** carcinosarcoma, Gd-EOB-DTPA, liver, magnetic resonance imaging

**Introduction**

The World Health Organization (WHO) describes primary hepatic carcinosarcomas as carcinomas that have undergone sarcoma-like differentiation.1 Diagnosis of a tumor as carcinosarcoma of the liver requires the presence of both hepatocellular carcinoma and a sarcoma component. Carcinosarcoma is quite different from sarcomatoid hepatocellular carcinoma, a type of hepatocellular carcinoma that contains spindle-shaped cells and shows no osteogenesis. Primary hepatic carcinosarcomas are very rare, difficult to diagnose clinically, and usually aggressive with a poor prognosis.2 Therefore, it is clinically beneficial to narrow the differential diagnosis of carcinosarcoma of the liver by accumulating findings of carcinosarcoma. The differential diagnosis with carcinosarcoma often includes hepatocellular carcinoma (including sarcomatoid hepatocellular carcinoma), cholangiocellular carcinoma, and sarcoma, but at this time, diagnosis largely depends on histopathological diagnosis. On gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance (MR) imaging in the hepatobiliary phase, hepatocellular carcinomas usually reveal hypointense lesions but can reveal hyperintense lesions.3

We present a case of primary hepatic carcinosarcoma in which enhancement in the hepatobiliary phase on preoperative Gd-EOB-DTPA-enhanced MR imaging suggested the tumor contained hepatocellular carcinoma as a carcinomatous component.

**Case Report**

A 69-year-old man was referred to our hospital for discomfort in his right hypochondriac region. He had no history of chronic hepatitis. Serum alpha-fetoprotein was 38.4 ng/mL, and concentration of protein induced by vitamin K absence (PIVKA-II) was 94 mAU/mL. Computed tomography (CT) of the abdomen showed a huge multilocular mass in the right lobe of the liver that was invading and expanding above the diaphragm. Plain CT showed local dense calcification and faint calcifications in...
the peripheral zone of the tumor (Fig. 1A). Especially, attenuation of the dense calcification of the center of the tumor was near bone. On contrast-enhanced CT, the tumor was well enhanced in the early phase (Fig. 1B) and demonstrated low density in the late phase (Fig. 1C). CT findings suggested a primary hypervascular hepatic tumor, such as a hepatocellular carcinoma. On the other hand, calcifications suggested other pathological tumor types, such as carcinosarcoma or extraskeletal osteosarcoma.

Gd-EOB-DTPA-enhanced MR imaging using liver acquisition with volume acceleration (LAVA) was conducted on a 3-tesla MR imaging system (Signa Excite; GE Medical Systems, Milwaukee, WI, USA). The hepatobiliary phase was obtained 20 min after injection of Gd-EOB-DTPA. On pre-contrast T1-weighted MR imaging (repetition time [TR]/echo time [TE], 3.3/1.6 ms; matrix, 320 × 140; slice thickness, 5 mm; slice spacing, 2.5 mm), the tumor revealed a heterogeneous hypointense lesion (Fig. 2A). Gd-EOB-DTPA-enhanced dynamic study demonstrated tumor enhancement in the early phase (Fig. 2B). Some parts of the tumor were characteristically enhanced in the hepatobiliary phase (20 min after injection), indicating uptake of Gd-EOB-DTPA. Other parts of the tumor were not enhanced. T2-weighted image reveals a heterogeneous hyperintense lesion. Most of the hyperintense lesion expresses extensive hemorrhage. Chemical shift subtraction image reveals hyperintense lesions (arrows) in the tumor that indicate fatty change. Coronal image reveals extension of the tumor into the thoracic cavity (arrow). The tumor compressed the adjacent lung, causing atelectasis (*).

**Fig. 1.** Computed tomography (CT) images. A. Plain CT reveals local dense calcification (arrow) and faint calcifications (arrowheads) in the tumor. B. Contrast-enhanced CT reveals a well enhanced lesion (arrows) in the early phase. C. The lesion (arrows) reveals an area of low density in the late phase.

**Fig. 2.** Magnetic resonance (MR) imaging. A. Pre-contrast T1-weighted image reveals the tumor as a heterogeneous hypointense lesion in the right hepatic lobe. Most of the internal part expresses extensive hemorrhage. B. Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced dynamic study reveals early enhancements (arrows) in the tumor. C. Enhancement of some parts of the tumor (arrow) is clearly seen in the hepatobiliary phase (20 min after injection), indicating uptake of Gd-EOB-DTPA. Other parts of the tumor were not enhanced. D. T2-weighted image reveals a heterogeneous hyperintense lesion. Most of the hyperintense lesion expresses extensive hemorrhage. E. Chemical shift subtraction image reveals hyperintense lesions (arrows) in the tumor that indicate fatty change. F. Coronal image reveals extension of the tumor into the thoracic cavity (arrow). The tumor compressed the adjacent lung, causing atelectasis (*).
cal shift MR imaging using dual-echo sequences (TR/TE, 120/2.1 ms for opposed phase and 120/4.4 ms for in phase) was also performed, and opposed-phase chemical shift MR images were subsequently subtracted from in-phase images. The subtracted images (matrix, 256 × 192; slice thickness, 6 mm; slice spacing, 7.8 mm) revealed fatty change in the tumor (Fig. 2E). The uptake of EOB and presence of fatty change ruled out diagnosis of such tumors as hepatoblastoma. The tumor extended into the thoracic cavity and compressed the lung (Fig. 2F).

The patient underwent right lobectomy with combined resection of the diaphragm, and histopathology confirmed carcinosarcoma of the liver. The patient was discharged from the hospital 18 days after surgery.

The resected tumor (Fig. 3A) measured 20 × 19 × 13 cm. Tumor cells near the diaphragm were necrotic and accompanied by hemorrhage. Necrosis was severe in the center of the tumor, and some cavities were observed. In the caudal part, the tumor was multinodular, yellowish, and encapsulated, and septae had formed. Some portions of the tumor’s periphery were hard because of calcifications.

Histopathologically, the tumor was diagnosed as carcinosarcoma comprising a mixture of hepatocellular carcinoma and a osteosarcoma component. In the area of hepatocellular carcinoma, atypical hepatocytes with nuclear swelling and anisokaryosis were trabecularly proliferative and formed glandular cavities. Necrosis and hemorrhage were extensive and corresponded with CT and MR imaging findings. Bile acids were also observed. The lesion appeared to be moderately differentiated hepatocellular carcinoma with bile production (Fig. 3B). The hepatocellular carcinoma revealed fatty change (Fig. 3C). Conversely, in the osteosarcoma component, cancellous bone and cartilage formation were relatively conspicuous, and spindle-shaped cells were present at low density and replaced fibrosis and osteogenesis (Fig. 3D). Because sarcomatoid hepatocellular carcinoma never shows osteogenesis, it was clear the tumor in this case was carcino-
sarcoma. The osteosarcoma component that contained bone corresponded exactly with the area of very high attenuation on plain CT. The hepatocellular carcinoma and osteosarcoma component had transitional sites (Fig. 3E). Moreover, the results of immunohistochemical staining fit the interpretation of each component and supported the diagnosis. The osteosarcoma component expressed vimentin (Fig. 3F). AE1/AE3 and hepatocytes were not expressed in the osteosarcoma component but were expressed in the area of hepatocellular carcinoma (Fig. 3G, H).

Discussion

Hepatic carcinosarcomas are carcinomas that have undergone sarcoma-like differentiation. Primary hepatic carcinosarcomas are very rare. Yamamoto and associates reported one case and reviewed 20 cases that met the histological definition of hepatic carcinosarcoma according to WHO criteria. Their patients included 15 men and 6 women with a mean age of 60 years. Mean patient survival of 8.7 months indicated the poor prognosis of hepatic carcinosarcomas. In many cases, the sarcomatous component of hepatic carcinosarcoma comprises osteosarcomatous or chondrosarcomatous elements. The carcinomatous component can be hepatocellular carcinoma, cholangiocellular carcinoma, or a combination of both. The present case showed both an osteosarcoma component and hepatocellular carcinoma. A transitional zone between carcinoma and sarcoma is observed in many cases of carcinosarcoma.

In our case, calculations on plain CT were considered to correspond to osteosarcomatous elements of the tumor. Murakami and colleagues observed macroscopic calcification in untreated hepatocellular carcinoma rarely, in only 1.9 to 3.3% of cases. Although hepatic tumors reveal a wide spectrum of calcification, dense calcification on CT is rare and may be a specific finding of hepatic carcinosarcoma.

Some radiologists report that hepatocellular carcinoma with sarcomatous change did not enhance in the early phase on CT. In our case, the carcinosarcoma revealed an area of hypointensity on contrast-enhanced CT and enhancement of a part of the tumor in the early phase. These findings were not definitive but, in addition to dense calcification, may aid diagnosis of hepatic carcinoma on CT.

In addition to the CT findings, enhancement of some parts of the tumor in the hepatobiliary phase on Gd-EOB-DTPA-enhanced MR imaging also supported the presence of elements of hepatocellular carcinoma. From these radiological findings, hepatocellular carcinoma is suspected initially, and carcinosarcoma, though a very rare tumor, is also suspected. Hepatocellular carcinomas usually do not take up Gd-EOB-DTPA and appear as hypointense lesions in the hepatobiliary phase, as do other tumors without normal hepatocyte function. However, some hepatocellular carcinomas can show hyperintense lesions in the hepatobiliary phase, as in the present case. The mechanism of the uptake of Gd-EOB-DTPA is currently being researched. At this time, uptake of Gd-EOB-DTPA in the hepatobiliary phase is considered to be related to the expression of a few types of transporters, such as OATP1B3. Therefore, the presumption was well considered that the hyperintense lesion in the hepatobiliary phase on preoperative Gd-EOB-DTPA-enhanced MR imaging suggested that the tumor contained a hepatocellular carcinoma component. Moreover, fatty change in the tumor on the chemical shift subtraction image ensured the possibility of hepatocellular carcinoma because it is well known that hepatocellular carcinomas often reveal fatty change.

We believe this is the first case in the English literature in which uptake of Gd-EOB-DTPA in the hepatobiliary phase on preoperative Gd-EOB-DTPA-enhanced MR imaging suggested the presence of hepatocellular carcinoma in a primary hepatic carcinosarcoma.

References

1. Miettinen M, Fletcher CD, Kindblom LG, Zimmerman A, Tsui WM. Mesenchymal tumours of the liver. In: Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. Lyon: IARC, 2010; 249.
2. Yamamoto Y, Ojima H, Shimada K, et al. Long-term recurrence-free survival in a patient with primary hepatic carcinosarcoma: case report with a literature review. Jpn J Clin Oncol 2010; 40:166–173.
3. Lee SA, Lee CH, Jung WY, et al. Paradoxical high signal intensity of hepatocellular carcinoma in the hepatobiliary phase of Gd-EOB-DTPA enhanced MRI: initial experience. Magn Reson Imaging 2011; 29:83–90.
4. Endo K, Terajima H, Imai Y, et al. A case of hepatic carcinosarcoma with bile duct tumor thrombi. Jpn J Gastroenterol Surg 2008; 41:99–104.
5. Murakami T, Morioka D, Takakura H, Miura Y, Togo S. Small hepatocellular carcinoma with ring calcification: a case report and literature review. World J Gastroenterol 2013; 19:129–132.
6. Stoupis C, Taylor HM, Paley MR, et al. The rocky liver: radiologic-pathologic correlation of calcified
hepatic masses. Radiographics 1998; 18:675–685.
7. Yu RS, Chen Y, Jiang B, Wang LH, Xu XF. Primary hepatic sarcomas: CT findings. Eur Radiol 2008; 18: 2196–2205.
8. Shu RY, Ye M, Yu WY. A case of primary liver carcinosarcoma: CT findings. Chin J Cancer 2010; 29:346–348.
9. Honda H, Hayashi T, Yoshida K, et al. Hepatocellular carcinoma with sarcomatous change: characteristic findings of two-phased incremental CT. Abdom Imaging 1996; 21:37–40.
10. Said Y, Trabelsi S, Kourda N, et al. Hepatocellular carcinoma with sarcomatous change. Tunis Med 2010; 88:957–960.
11. Reimer P, Rummeny EJ, Shamsi K, et al. Phase II clinical evaluation of Gd-EOB-DTPA: dose, safety aspects, and pulse sequence. Radiology 1996; 199: 177–183.
12. Saito K, Kotake F, Ito N, et al. Gd-EOB-DTPA enhanced MRI for hepatocellular carcinoma: quantitative evaluation of tumor enhancement in hepatobiliary phase. Magn Reson Med Sci 2005; 4:1–9.
13. Narita M, Hatano E, Arizono S, et al. Expression of OATP1B3 determines uptake of Gd-EOB-DTPA in hepatocellular carcinoma. J Gastroenterol 2009; 44: 793–798.
14. Kitao A, Zen Y, Matsui O, et al. Hepatocellular carcinoma: signal intensity at gadoxetic acid-enhanced MR imaging–correlation with molecular transporters and histopathologic features. Radiology 2010; 256: 817–826.