Recent developments in imaging diagnostics for HCC: CT arteriography and CT arterioportography evaluation of vascular changes in premalignant and malignant hepatic nodules

HIROSHI HONDA, TSUYOSHI TAJIMA, KENICHI TAGUCHI, TOSHIRO KUROIWA, KENGO YOSHIMITSU, HIROYUKI IRIE, HITOSHI AIBE, KENJI SHINOZAKI, YOSHIKI ASAYAMA, MITSUO SHIMADA, and KOJI MASUDA

1 Department of Radiology, Faculty of Medicine, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan
2 Second Department of Pathology, Faculty of Medicine, Kyushu University, Fukuoka, Japan
3 Second Department of Surgery, Faculty of Medicine, Kyushu University, Fukuoka, Japan

Abstract: We analyzed the hemodynamic properties and vascular supply changes in relation to the carcinogenesis of hepatocellular carcinoma (HCC), selecting 18 premalignant and malignant nodules less than 3cm diameter (from 14 patients) for our study. The computed tomographic (CT) arteriography and CT arterioportography (CTAP) findings for these nodules were correlated with the histopathologic findings. The ratios of all microscopically counted arteries (normal hepatic and abnormal arteries), normal hepatic arteries, and portal veins in each nodule to those in the surrounding liver were calculated. Well differentiated lesions had low attenuation on CT arteriography and isoattenuation on CTAP. Moderately-to-poorly differentiated lesions had high attenuation on CT arteriography and low attenuation on CTAP. In well differentiated lesions, the ratios of all arteries, normal hepatic arteries, and portal veins were 1.17 ± 0.10, 0.66 ± 0.12, and 0.80 ± 0.10, respectively. In moderately-to-poorly differentiated lesions, the ratios were 2.64 ± 0.23, 0.09 ± 0.03, and 0.07 ± 0.03, respectively. We concluded that blood flow does not parallel the actual number of arteries seen on the histological examination of tumors. In well differentiated lesions, the combination of normal hepatic arterial degeneration and preserved portal veins results in low attenuation on CT arteriography and isoattenuation on CTAP. In advanced HCC, the combination of neoplastic (abnormal) arterial development by angiogenesis and obliteration of portal veins results in high attenuation on CTA and low attenuation on CTAP. These findings are characteristic of early and advanced stage HCC, and may reflect a combination of sequential changes in their hemodynamic states.

Introduction

Hepatic nodular lesions in patients with chronic liver disease include various hepatocytic nodules such as regenerative nodules, large regenerative nodules, adenomatous hyperplasia (AH), atypical AH, early hepatocellular carcinoma (HCC), early advanced HCC, and overt or advanced HCC.1-5 First described by Edmondson,6 AH of the liver is defined as a sizable and discrete parenchymal nodule that occurs after acute or chronic liver injury. AH characteristically contains portal tracts consisting of hepatic arteries, portal veins, and bile ducts.6 In an early study, malignant transformation from AH to overt HCC was clinically confirmed in 9 of 18 nodules which were followed for periods ranging from 6 months to more than 4 years.5 Recent studies have suggested that AH in the cirrhotic liver is a precancerous lesion, because malignant or atypical hepatocellular foci are occasionally found within AH.8-10

Early to overt HCC is histologically classified as well, moderately, or poorly differentiated and undifferentiated HCC, according to the Japanese Liver Cancer Society, or as grade 1 to 4 according to the Edmondson-Steiner (E-S) classification system. Early HCC usually does not substantially alter the existing architecture of surrounding hepatic pseudolobules and frequently contains portal tract structures.1,10 On microscopic examination, cancer cells within these lesions are very well differentiated and correspond to E-S grade 1.12 Early HCC is presumed to be an intermediate step between AH and early advanced HCC in the multistep progression of hepatocellular carcinogenesis.1

Early advanced HCC is a tumor containing advanced HCC within early HCC. Pathologically, it consists of two definite regions: a cancerous nodule of advanced HCC (E-S grade 2 or higher) that is large enough to be detected at gross examination, and a surrounding region of early HCC (E-S grade 1).4,5,13
Recent advances in imaging techniques have made it possible to detect AH, early HCC, and overt HCC in cirrhotic livers. In particular, computed tomographic (CT) arteriography and CT arterioprtography (CTAP) are now considered to be useful diagnostic tools not only for detecting HCC, AH, and other nodular lesions but also for evaluating the vascular supply of these various lesions.

It is well known that HCC contains many arteries and receives its blood supply principally from arterial sources. Furthermore, it is well established that neoplasms (benign and malignant) develop novel blood vessels within themselves (angiogenesis). This neovascularization is invariably seen within HCC. In contrast, AH and early HCC contain portal tracts, and are thought to be supplied by portovenous as well as arterial blood flow.

Pathologically, it is known that in both AH and early HCC, the total number of arteries (normal and abnormal) is equal to or greater than that in the surrounding liver, while the portal veins are much less numerous than in the surrounding liver. However, radiologically, AH and early HCC have been shown to be hypovascular. To the best of our knowledge, few efforts have been made to explain this discrepancy between the histopathologic and radiologic characteristics of these nodules’ vasculature. Recently, we have reported that normal arteries were degenerated or had disappeared in AH and early HCC. These changes may account for the decrease in arterial blood flow seen on CT arteriography.

In this study, we compared the vascular supply of AH, early HCC, and early advanced HCC with overt HCC, using CT arteriography and CTAP. The differing vascular patterns of these lesions were analyzed in relation to the histopathologic quantity and appearances of the arteries and portal veins within them, in the hope of providing a theory to explain the changes in vascular supply for the analysis of carcinogenesis of HCC.

**Subjects, materials, and methods**

At our institution, from November 1996 to October 1997, 57 HCCs, in 39 patients, and 3 AHs, in 3 patients, were resected within 1 week of CT arteriography and CTAP. Of these 60 hepatic nodules, we selected 18 nodules with a diameter of less than 3 cm, from 14 patients, for our study. All 18 lesions were detected preoperatively by ultrasonography, magnetic resonance imaging (MRI), CT, or angiography. Subsequently, all of the lesions were also detected by intraoperative ultrasonography and resected. Results of CT arteriography and CTAP were compared with results of two-phase incremental CT obtained within 1 month often surgery, to confirm that the resected tumors were, in fact, the lesions detected on CT arteriography and CTAP.

Using the E-S criteria, the grade of anaplasia of the HCC cells was assessed by one pathologist (K.T.) as grade 1 to 4 (reflecting increasing degrees of cancer cell anaplasia). Tumor diameter was calculated. The number of arteries (normal hepatic and abnormal arteries) and portal veins per unit area in each nodule, as well as in the surrounding cirrhotic liver, was counted. Ratios of the numbers of all arteries (normal hepatic and abnormal arteries), normal hepatic arteries, and portal veins in each nodule to those in the surrounding cirrhotic liver were then calculated. Hepatic arteries were recognized by their location in the portal triad. Hepatic arteries with thickening of the arterial wall (Fig. 1) and disappearance of the normal structure (blurring) were considered abnormal and were excluded from the normal hepatic artery count. All arteries, including normal hepatic and abnormal arteries and tumor vessels which were newly developed by angiogenesis (Fig. 2), were included in the ratio calculations.

The blood supply of the HCCs and areas of AH was determined in vivo with CT arteriography and CTAP and compared with the histopathologic findings.

CT images were obtained with an X-vigor scanner (Toshiba, Tokyo, Japan). For CTAP, 100ml of Iopamidol contrast medium (Iopamiron 150; Nihon Schering, Osaka, Japan) was administered via a catheter in the superior mesenteric artery at an estimated rate of 2.5 ml/s during sequential helical scanning of the liver. For CT arteriography, 30–50ml of contract medium (Iopamiron 150) was administered via a catheter in the proper hepatic, left, or right hepatic artery at an