—Original—

Clinical Usefulness of Computed Tomography Arteriography and Computed Tomography during Arterial Portography for the Diagnosis of Early and Early Advanced Hepatocellular Carcinoma

Taro Ichikawa and Tatsuo Kumazaki

Department of Radiology, Tama Nagayama Hospital, Nippon Medical School

Abstract

1) Objective: We examined the clinical usefulness of two techniques of Angio Computed tomography (CT), namely, CT arteriography (CTA) and CT during arterial portography (CTAP), for the diagnosis of early hepatocellular carcinoma (HCC) and early advanced HCC.

2) Materials and Methods: The subjects were six patients with a total of seven lesions: three had one early HCC lesion each, and three had four early advanced HCC lesions between them. There were five men and one woman, aged 61～73 years (mean: 65 years). A catheter was inserted into each inguinal artery according to Seldinger's method, and the results of CTA and CTAP were compared with those of conventional CT.

3) Results: Visualization of tumor borders, arterial blood feeding areas, and portal blood flow areas gave results equal to or better than those of conventional CT.

4) Conclusions: A combination of CTA and CTAP is useful for the diagnosis of early HCC and early advanced HCC. (J Nippon Med Sch 2000; 67: 105—109)

Key words: early HCC, early advanced HCC, CT arteriography, CT during arterial portography

Introduction

Recently, a new model for the development of hepatocellular carcinoma (HCC) has been proposed. It is known as the multi-step progression theory[1,2]. With advances in diagnostic imaging technology, many small liver tumors are being resected. It has been found that some of these tumors contain a Glisson's sheath but no fibrous capsule on their borders, and that others contain malignant foci[3,4].

In the present study, we investigated the clinical usefulness of combining two techniques of Angio-CT, CT arteriography (CTA) and CT during arterial portography (CTAP), on the same day for the diagnosis of early HCC and early advanced HCC. These tumors are considered to be a part of the process of development of classic hepatocellular carcinoma. In the present article, the term advanced HCC is used to indicate classic HCC.

Materials and Methods

Six patients with a total of seven lesions participated in the study, so that there were three cases of early HCC with three lesions and three cases of early

Corresponding to Taro Ichikawa, Department of Radiology, Tama Nagayama Hospital, Nippon Medical School, 1-7-1, Nagayama, Tama City, Tokyo, 206-8512, Japan

Journal Website (http://www.nms.ac.jp/jnms/)

Table 1 Summary of patients

No.	Ys.	Sex	Location	Size (mm × mm)	Type	AFP (ng/m*l*)	HBsAg	HCV
1	64	M	S5	13 × 10	early HCC	21.1	(−)	(+)
2	73	F	S2	8 × 10	early HCC	15.7	(−)	(+)
3	61	M	S5	13 × 13	early HCC	33.6	(−)	(+)
4	61	M	S6—7 S5—8	42 × 32 32 × 20	early advanced HCC	24.9	(−)	(+)
5	66	M	S6	24 × 26	early advanced HCC	15.3	(−)	(+)
6	67	M	S8	36 × 32	early advanced HCC	65.4	(−)	(+)

advanced HCC with four lesions, in which both CTA and CTAP were performed on the same day (**Table 1**).

The patients comprised five men and one woman, aged 61～73 years, with a mean of 65 years. There were two lesions in case 4.

The CT equipment used in this study was an Xforce (Toshiba, Tokyo). Conventional CT was obtained by intravenously injecting 100 m*l* of contrast medium at a speed of 2 m*l*/sec with an automatic injector, and images were acquired as early as 35 seconds after the injection. For one case, unenhanced CT alone was performed.

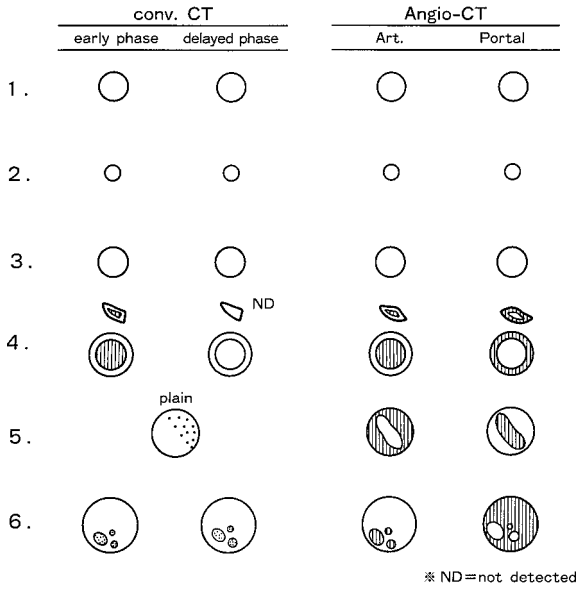
Angio-CT was performed by inserting one catheter into each inguinal artery according to Seldinger's method, and both CTA and CTAP images were acquired. For CTA, we inserted a catheter into the common hepatic artery, the proper hepatic artery, or the left gastric artery, depending on the case, and then injected 30 m*l* to 60 m*l* of a 1/4 to 1/5 dilution of contrast medium (ioxaglic acid 320 mgI/m*l*) at a speed of 2 to 4 m*l* per second, and obtained images as early as two seconds after the injection.

For CTAP, after inserting a catheter into the superior mesenteric artery, we injected 60 m*l* to 70 m*l* of a 1/3 dilution of contrast medium at a speed of 3 m*l* per second, and then acquired images from about 25 seconds after the injection.

We compared the images acquired from conventional CT and Angio-CT and examined the following three items:

1) Clarity of visualization of the tumor borders,
2) Visualization of the area supplied by arterial blood,
3) Visualization of the area supplied by portal blood.

Table 2 Tumor enhancement pattern



Results

With Angio-CT, the visualization of the three items was equal to or better than that using conventional CT. **Table 2** shows a schema of the CT image for each case. The hatched line indicates an enhanced area, and the dotted area, a lower attenuation than in the surrounding area.

There was no significant difference in tumor borders between the conventional CT and the Angio-CT images in cases 1 , 2 and 3. Additionally, the Angio-CT revealed that there was less of both arterial blood flow and portal blood flow in tumor in cases 1, 2 and 3 than in livers without tumors.

In one of the lesions in case 4, there was almost no difference in the Angio-CT visualization of arterial

Fig. 1 Case 1. CTA

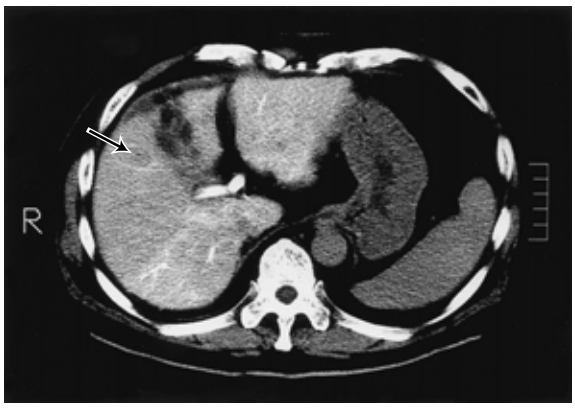


Fig. 2 Case 1. CTAP

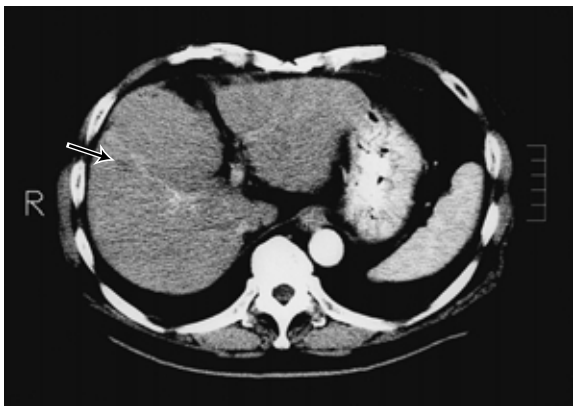


Fig. 3 Case 1. An early conventional CT image

Fig. 4 Case 4. An early conventional CT image

Fig. 5 Case 4. A CT image delayed by seven minutes

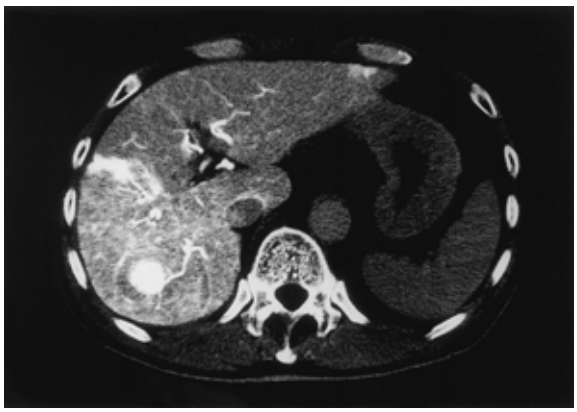


Fig. 6 Case 4. CTA

blood from that depicted by conventional CT. But in the rest of the lesions in cases 4, 5 and 6, Angio-CT offered clearer visualization of tumor borders, areas fed by arterial blood, and those receiving portal blood flow in all instances.

Case presentation

The first case was seen in a 64-year-old man in whom early HCC was diagnosed. **Fig. 1** presents the CTA image, and **Fig. 2**, the CTAP image. **Fig. 3** is an early conventional CT image. The tumor (arrow), 1.3×

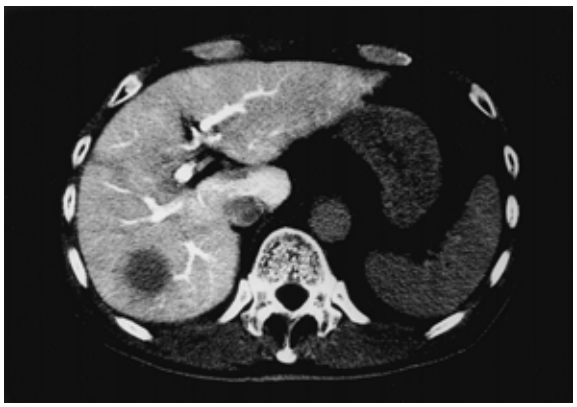


Fig. 7 Case 4. CTAP

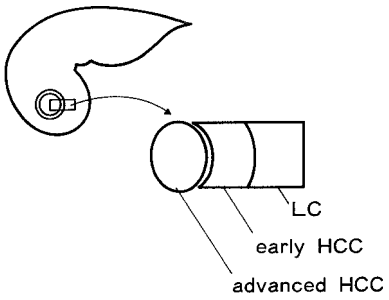


Fig. 8 Case 4. Schematic image of the larger lesion

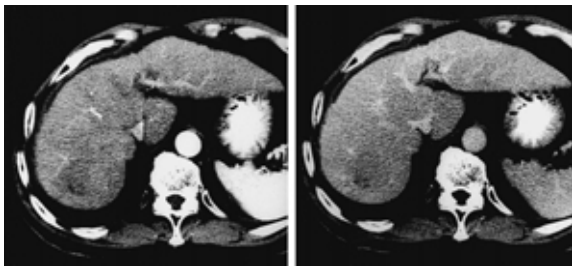


Fig. 9 Case 6. An early conventional CT image (left side) and a CT image taken seven minutes later (right side)

1.0 cm in dimensions, was found at S 5 from the hypoattenuation revealed by both CT techniques. Early HCC was diagnosed from an open biopsy.

The next patient was a 61-year-old man diagnosed as having early advanced HCC. **Fig. 4** is an early conventional CT image and **Fig. 5**, a delayed CT image taken seven minutes later. Two lesions can be identified, one of 4.2× 3.2 cm on the border between S 6 and 7, and the other of 3.2 x 2.0 cm on the border between S 5 and 8. In the early CT, the images of both tumors show strong enhancement in their central regions, but not in the surrounding areas. Delayed CT revealed the larger lesion as a low density area, but the smaller

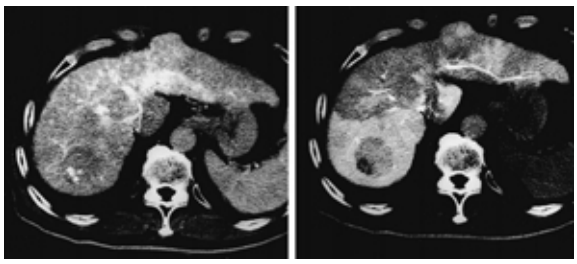


Fig. 10 Case 6. CTA (left side) and CTAP (right side)

lesion was not identifiable. **Fig. 6** shows a CTA image with strong enhancement in the central tumor area. **Fig. 7** shows CTAP, where the central part was not enhanced, and a slightly enhanced effect was identified in the surrounding area. There is a distinctly visualized presence of portal blood flow in this area.

Right lobectomy was performed in this case. **Fig. 8** shows a schematic image of the larger lesion.

The next case, diagnosed as early advanced HCC, was encountered in a 67-year-old man. **Fig. 9** shows an early conventional CT image and a CT made after an interval of seven minutes. The images in **Fig. 10** are Angio-CT, with a CTA image on the left and a CTAP image on the right. In a conventional CT image, it is difficult to identify the enhanced area, since the tumor is shown as a low density area with indistinct borders in both early and delayed images. The advanced HCC portion, which has an abundant arterial blood flow and shows no portal blood flow region, can be clearly identified in Angio-CT, and its blood flow distribution is plainly visible. Also, Angio-CT images indicate that a portal blood flow was present in part of the early HCC but not in advanced HCC. Furthermore, the tumor borders are more easily recognized.

Discussion

Identification of the distribution of both the hepatic arterial blood flow and the portal blood flow is important evidence in the diagnosis of early HCC and early advanced HCC.

Classic HCC is fed by arterial blood only and derives no nourishment from portal blood[5,6]. On the other hand, no hyperarterialization was recognized in early HCC, and some portal blood is thought to remain inside the tumor. In addition, it is believed that

foci fed by the same blood flow as the classic HCC are present inside early advanced HCC[7,8].

Generally, however, only conventional CT is used for the diagnosis of hepatocellular carcinoma. But even with contrast enhanced CT, not to mention unenhanced CT, it is difficult to diagnose early HCC and early advanced HCC[9]. This is because the diagnosis of these tumors relies on the conditions of arterial and portal blood flow.

Angio-CT is a method for diagnosing liver tumors that has become popular in the last ten years. To detect intrahepatic metastatic tumors before surgery, it is mainly CTAP that is used[5].

We made use of the Angio-CT technique, which offers detailed visualization of the involvement of arterial blood and portal blood in feeding a tumor; and we obtained both CTA and CTAP images on the same day for the purposes of analysis.

Since both were performed on the same day, both right and left inguinal regions of each patient had to punctured, which was somewhat burdensome for the patients. However, no complications were observed. Furthermore, no particular problem with blood coagulation arose after the examination. It will in future be possible to reduce the patient's burden by using an IVR-CT system, which combines a CT system with a fluoroscope.

Compared with a liver without tumors, the early HCC had restricted blood flow through both the hepatic artery and the portal vein systems. However, on the basis of the multi-step progression theory of HCC, various blood flow conditions can be predicted. Further investigations with more patients are required[9].

The employment of both CTA and CTAP for the diagnosis of early advanced HCC is a significant stride forward that is necessary for the visualization of the foci of advanced HCC and for its diagnosis. Furthermore, we found multiple advanced HCC foci in the early HCC of case 6. HCC is considered to originate multi-centrically inside the liver. It is interesting, moreover, to note that the images obtained in this study also indicate that the malignancy has progressed multi-centrically inside the tumor. This case may link the HCC's multi-step progression theory with multi-centric origin.

Acknowledgments: The authors express appreciation to Prof. Masahiko Onda and Takashi Tajiri MD, and their staff, of the 1 st Department of Surgery. We are also grateful to the staff of the CT and Angiography Division of the Department of Radiology.

References

1. Kanai T, Hirohashi S, Upton MP, Noguchi M, Kishi K, Makuuchi M,Yamasaki S, Hasegawa H, Takayasu K, Moriyama N: Pathology of small hepatocellular carcinoma. A proposal for a new gross classification. Cancer 1987; 60; 810－819.
2. Kenmochi K, Sugihara S, Kojiro M: Relationship of histologic grade of hepatocellular carcinoma (HCC) to tumor size, and demonstration of tumor cells of multiple different grades in single small HCC. Liver 1987; 7: 18–26.
3. Takayama T, Makuuchi M, Hirohashi S, Sakamoto M, Okazaki N, Takayasu K, Kosuge T, Motoo Y, Yamasaki S, Hasegawa H: Malignant transformation of adenomatous hyperplasia to hepatocellular carcinoma. Lancet 1990 ; 336 : 1150–1153.
4. Winter TC 3rd, Takayasu K, Muramatsu Y, Furukawa H, Wakao F, Koga H, Sakamoto M, Hirohashi S, Freeny PC: Early advanced hepatocellular carcinoma: Evaluation of CT and MR appearance with pathologic correlation. Radiology 1994; 192: 379–387.
5. Matsui O, Kadoya M, Suzuki M, Inoue K, Itoh H, Ida M, Takashima T: Dynamic sequential computed tomography during arterial portography in the detection of hepatic neoplasms. Radiology 1983; 146: 721–727.
6. Prando A, Wallace S, Bernardino ME, Lindell MM Jr: Computed tomographic arteriography of the liver. Radiology 1979; 130: 697–689.
7. Takayasu K, Moriyama N, Muramatsu Y, Makuuchi M, Hasegawa H, Okazaki N, Hirohashi S: The diagnosis of small hepatocellular carcinomas: Efficacy of various imaging procedures in 100 patients. AJR 1990; 155: 49–54.
8. Fujii K, Takayasu K, Ohkubo T, Muramatsu Y, Mizuguchi Y, Yamasaki S: Imaging of large early and early advanced hepatocellular carcinoma of more than 5 cm in diameter: Report of two cases. Hepato-Gastroenterology 1998; 45: 1085–1092.
9. Takayasu K, Furukawa H, Wakao F, Muramatsu Y, Abe H, Terauchi T, Winter TC 3 rd, Sakamoto M, Hirohashi S: CT diagnosis of early hepatocellular carcinoma: Sensitivity, findings, and CT-pathologic correlation. AJR 1995; 164: 885–890.

(Received, December 6, 1999)
(Accepted, December 24, 1999)