—Originals—

The value of emergency CT studies in spontaneous rupture of hepatocellular carcinoma

Analysis for tumor protrusion and hemorrhagic ascites

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Abstract

CT characteristics of spontaneous rupture of HCC (n=13) were reviewed retrospectively, and the value of emergency CT studies in this disease was evaluated. Especially, tumor protrusion ratio (TPR) and ascitic CT numbers were measured to for comparison with the data for unruptured HCCs and ordinary (e.g. non-hemorrhagic) ascites (n=13). As a result, except for diffuse type HCCs, the TPR was significantly higher than for the unruptured HCCs. Nine cases had intraperitoneal HDAs, and the laterality of the HDAs corresponded with that of the ruptured tumors in 8 cases. Also, the ascitic CT numbers apart from the HDA were still higher than the ordinary ascites. Therefore, a high TPR, HDAs adjacent to the tumor, and elevated ascitic CT numbers are important CT manifestations indicating HCC rupture. Diffuse HCCs, however, require careful clinical evaluation. (J Nippon Med Sch 1997; 64: 532—537)

Key words: hepatocellular carcinoma, spontaneous rupture, computed tomography, tumor protrusion, hemorrhagic ascites

Introduction

Spontaneous rupture causes death in 11.3% of patients with hepatocellular carcinoma (HCC)¹. Several attempts to treat this complication have been described, especially in Asian countries including Japan, where the incidence of HCC is high²⁻¹⁵. Although transarterial embolization is now the treatment of choice for arresting bleeding from tumor vessels⁷⁻¹⁵, the bleeding sites are not clearly defined during the interventional process^{7-11,13-15}. In addition, the problem lies in promptly deciding whether the HCC has ruptured or not, because most patients are admitted after the sudden onset of abdominal catastrophe or shock without localizing signs^{3,6,7}. Computed tomography (CT) can provide important diagnostic clues in such emergency

cases; however, only a few CT studies have dealt with this disease¹⁶⁻¹⁷. The purpose of our study is to delineate comprehensively CT characteristics of spontaneous HCC rupture, with semiquantitative analysis of the degree of tumor protrusion and the grayscale features of hemorrhagic ascites.

Materials and Methods

Thirteen patients with HCC rupture examined by CT between 1990 and 1995 (group A; n=13, M : F = 8 : 5, mean age 65 years) were retrospectively reviewed. None had a history of abdominal trauma. Unfortunately, histological confirmation by operation or autopsy was achieved only in 5 patients, paracentesis was performed in 7 patients, and the diagnosis in the other patients was supplemented by laboratory and physical evaluation (**Table 1**). In

Table 1 Summary of the 13 patients with spontaneous HCC rupture

case No.	Age/Sex	A	B	C	D (day)	Tumor configuration				Ascites			
						Type	Segment*	size (cm)	TPR (%)	HDA	Location	HDA (HU)	non-HDA (HU)
1	69/F	+	—	+	17	nodular	23	3.6	42	—	/	/	24
2	78/F	—	—	—	6	nodular	4	3.2	25	—	/	/	28
3	64/F	+	—	+	4	nodular	3	4.8	32	—	/	/	20
4	68/M	—	—	—	1	nodular	58	5.5	41	+	Rs(Sub)	63	45
5	81/M	+	—	+	1	nodular	7	3.1	35	+	Rt(Sub)	60	33
6	58/M	—	+	+	1	nodular	23	7.5	28	+	Lt(Sub)	64	38
7	72/F	—	—	+	1	nodular	4	4.9	56	+	Rt(Extra)	53	26
8	68/M	—	—	—	1	nodular	23	5.3	32	+	Lt(Extra)	69	40
9	61/M	—	+	+	1	massive	23	16.0	96	+	Lt(Extra)	36	23
10	66/M	—	+	+	2	massive	1	10.5	82	+	Ls(Extra)	53	13
11	60/F	—	+	+	5	massive	12	7.5	26	+	Ls(Extra)	57	41
12	47/M	—	+	+	1	diffuse	5,678	18.0	0	—	/	/	19
13	60/M	—	—	—	1	diffuse	5,678	15.0	0	+	Rt(Extra)	65	37
mean								8.1±5.2	38±27			57±10	30±10

*according to Couinaud's classification¹⁸.
A : Prior therapy for HCC. B : Histological confirmation of HCC. C : Paracentesis. D : Intervals between the onset CT study. HDA : high density area. Ls : lessor sac. Sub : subcapsular. Extra : extracapsular. TPR : tumor protrusion ratio.

Table 2 Summary of the control patients with unruptured HCC and ascites

case No.	Age/Gender	Tumor configuration			CT number of the ascites (HU)
		Type	Size(cm)	TPR (%)	
1	63/ F	nodular	4.2	0	6
2	67/ F	nodular	3.7	1.9	5
3	64/M	nodular	7.6	0	6
4	62/ F	nodular	4.8	23	9
5	67/M	nodular	7.5	59	12
6	61/ F	nodular	4	14	10
7	43/M	nodular	4.1	18	12
8	62/ F	nodular	5	4	12
9	84/M	nodular	6	0	15
10	61/M	nodular	2.1	0	10
11	59/M	nodular	2.1	10	11
12	67/M	nodular	2.9	49	14
13	56/ F	diffuse	13.5	0	15
		mean	5.2±3.0	15±19	11±3

addition, a group of unruptured HCC with non-hemorrhagic ascites was compared for semi-quantitative image analysis (group B; n=13, M : F= 7 : 6, mean 63 years). These cases were sampled randomly from the large data base of patients who underwent CT studies in our department in 1995 (Table 2). Thus, a total of 26 sets of CT images, in two groups, were evaluated.

Each CT scan was made with one of the following commercially available scanners: Xforce, Xvigor

(Toshiba, Tokyo), W 3000 or W 1000 (Hitachi, Tokyo). Among the 13 patients in group A, the interval between the onset and examination was within 48 hours in 9 cases, 3 to 6 days in 3 cases, and more than 7 days in one case. Basically, CT imaging was performed with an x-ray tube voltage of 120 kV and a conventional protocol yielding contiguous 10-mm thick sections of the entire liver a 10-mm intervals. Post-enhanced images were obtained following administration of 100 cc of contrast mate-

Photo. 1 ROI placement to determine TPR and ascitic CT numbers. TPR was calculated as a proportion of the protruding area (cross stripes) to the entire area of HCC mass. Also, the CT numbers of the HDA and non-HDA in hemorrhagic ascites were compared with those of non-hemorrhagic ascites in the other group.

rial.

Initially, the CT images in group A were reviewed by three diagnostic radiologists (M.I., H.K. and T.I.) with a consensus on every finding. Because we focused on the morphological pattern of the tumor and the ascitic density, the following points were observed: 1) type, size (maximum diameter) and location of the tumor, 2) distribution of the ascites, visualization and location of intraperitoneal high density areas (HDAs). We used pre-enhanced images for the observation of the ascites, and both pre- and post-enhanced images for the interpretation of the tumor contour.

Image analysis was applied to both groups based on the region of interest (ROI) measurement (**Photo 1**). First, the tumor protrusion ratio (TPR) was estimated by tracing of the protruding area and the entire area of the tumor. The "protruding area" was defined as the area where the hepatic surface was stretched out beyond its normal boundary by the tumor growth. The estimations were made on the basis of one or the mean of two mid-tumor levels. The TPR was calculated as the proportion of the protruding to the entire area. Second, the density of ascites was evaluated as CT numbers in Hounsfield units (HUs). In group a, HDAs and non-HDAs (which visually are not distinguished from the ordinary ascites) were evaluated independently.

TPR and CT numbers are expressed as means $\pm$ standard deviation, compared statistically by

Welch's unpaired *t*-test and one-way ANOVA respectively. A *p* value of less than 0.05 was considered indicative of a statistically significant difference.

Results

The size of the ruptured HCCs ranged from 3.1 to 18.0 cm (mean 8.1 ± 5.2 cm). Average tumor size was smallest in the nodular type (mean 4.7 ± 1.5 cm) and largest in the diffuse type (16.5 ± 2.1 cm). In 9 cases, the tumors were located entirely in the left lobe (S 1-4). They all lacked normal parenchymal density between the tumor and liver capsule. The tumors tended to protrude extrahepatically, except 2 diffuse HCC cases. All patients displayed abnormal fluid adjacent to the liver that varied in amount and distribution. Nine cases exhibited focal HDAs associated with this fluid, including 3 cases in which HDA was located under the hepatic capsule alone. The tumors which were entirely located on the right (Cases 5, 7 and 13) and the left (Cases 6, 8 and 9) side of the body yielded the HDAs on the same side of the abdomen. The caudate lobe tumors (Cases 10, 11) yielded the HDAs in the lesser sac. Therefore, the laterality of the HDAs corresponded with that of the ruptured tumors including the caudate lobe tumors. Subcapsular HDAs were associated with relatively small lesions (mean 5.4 ± 2.2 cm) among the present cases.

Fig. 1 and **2** shows scatter plots of the TPRs and ascitic CT numbers of the two groups. The TPR was $38 \pm 27\%$ in group A and $11 \pm 18\%$ in group B. The standard deviation was rather large in both groups, nevertheless the TPR in group A was significantly larger than in group B ($p < 0.01$, *t*-test). The 2 diffuse type HCCs in group A were determined as 0% TPR. The TPR of 5 cases in group B was also 0% because the tumor was completely surrounded by normal hepatic parenchyma. There was a sub-statistical difference between the TPR in the groups when these 0% TPR case were excluded ($p = 0.05$, *t*-test). Regarding the ascitic CT numbers, the HDAs and non-HDAs in group A yielded values of 57 ± 10 and 30 ± 10 HU, respectively. The ascites in group B yielded an average CT numbers of 11 ± 3 HU. These CT numbers showed a significant

Fig. 1 Scatter plot of the TPR in group A and group B. Excluding 6 cases with 0% TPR, mean TPRs between the two groups were significantly different ($p < 0.05$).

Fig. 2 Scatter plot of the ascitic CT numbers in HDA and non-HDA in group A and in group B. It is noteworthy that mean CT numbers in non-HDAs (30 ± 10 HU) were significantly higher than those in non-hemorrhagic ascites (11 ± 3 HU, $p < 0.01$).

HDAs were higher than in group B ($p < 0.05$).

Discussion

This study enabled us to identify three important CT manifestations of HCC rupture based on the tumor configuration and the ascites. First, the TPR, an index of the degree of tumor protrusion, was associated with the presence of HCC rupture. Second, intraperitoneal HDAs were a reliable marker for the presence and location of recent bleeding. Third, measurement of ascitic CT numbers was helpful in confirming a bleeding event, even in cases lacking a HDA.

Before discussing the significances of these CT characteristics, we have to mention some limitations of the study. The essential limitation is a selection bias due to the retrospective nature of the study in which the diagnosis for rupture or nonrupture was not completely performed on a pathological basis. Thus, some ruptured HCCs may have been missed because they did not show up clinically or radiographically. Also, the control cases might not represent morphological features of unruptured HCCs adequately, because most of them were of a relatively small nodular type. This study showed an interesting radiographical aspect of HCC rupture which has been carefully observed; however, prospective experimental design and analysis well be required in future.

So far, several intrinsic and extrinsic factors that promote HCC rupture have been described^{2,5,17}. According to Chearanai et al⁵, HCC rupture usually occurs secondary to hemorrhage and/or necrosis within the tumor. Probably, coagulopathy and portal hypertension due to the background cirrhosis upsets blood flow balance within the tumor, which increases the intratumor pressure. Therefore, HCCs of peripheral origin expand toward the intraperitoneal free space that renders them susceptible even to subtle external stress such as respiratory movements or minimal trauma⁵. Here we consider that TPR would represent these pathological conditions of the peripheral HCCs under which tumor continuity is interrupted. This index is considered equivalent to the length of protruded tumor margins which was the most reliable factor for prediction of HCC rupture by Kanematsu et al¹⁷. Especially from

difference ($p < 0.01$, ANOVA). Also, the CT numbers of the non-HDA which did not associate with

Photo. 2 Case 2, 69 y.o. Female. A 3.6-cm-diameter nodular HCC (white arrow) was located in the lateral segment of the left lobe. The relatively narrow space in this area seems to be responsible for the tumor protrusion.

Photo. 3 Case 14 47 y.o. Male. An 18.0-cm-diameter ill-defined HCC (white asterisk) was confirmed at autopsy. No intraperitoneal HDA was demonstrated on the CT images, despite the fact that paracentesis revealed obvious contamination by blood.

our study, tumor location seems to be crucial, because 70% of ruptured tumors were located in the left lobe and relatively small ones showed high TPR values in the left lobe (**Photo 2**).

On the contrary, diffuse type HCCs, spreading invasively into the neighboring parenchyma without pseudocapsular formation, did not alter the hepatic contour dramatically. Their distributions, estimated from the post-enhanced images, seemed extremely large. In addition, one case did not exhibit an intraperitoneal HDA despite the fact that paracentesis showed vivid contamination by blood (**Photo 3**). According to Chearanai et al⁵, HCC of this type tends to bleed as a result of multifocal oozing. Generally speaking, an intraperitoneal HDA

Photo. 4a, b Case 13, 60 y.o female. (a) CT demonstrating a 7.5-cm-diameter nodular HCC in the caudate lobe (white arrow). (b) HDA was seen anterior to the pancreatic tail (white arrow), suggesting a lesser sac deposit.

reflects a focal accumulation of fresh clots within the ascites, probably related to the amount of bleeding in a short interval. Oozing might be insufficient for overt HDA formation. Therefore, it should be borne in mind that CT assesment of diffuse type HCCs is sometimes difficult.

Except for these diffuse type HCCs, the greatest advantage of CT in identifying HCC rupture is direct visualization of hemorrhagic ascites because of the superb contrast resolution it provides¹⁶. In our study, 89% HDAs were closely matched to the laterality of each lesion. For example, 2 lesions located in the caudate lobe (S1) yielded HDAs anterior to the pancreatic tail, suggesting lesser sac deposits (**Photo 4a, b**). Accordingly, HDAs demonstrated by CT studies should be useful not only in demonstrating recent bleeding, but in localizing the site of rupture. Interventional papers have documented that the extravasation of contrast material was proved in less than 24% of ruptured HCC cases, and concluded that it is difficult to

verity the bleeding site from a ruptured mass angiographically^{7-11,13-15}. These reports enhance the value of preinterventional CT studies in HCC rupture. However, it seems important they be evaluated soon after onset, because 80% of cases lacking a HDA were primarily due to their having been studied more than 2 days after the onset.

Finally, we focused on the CT numbers of non-HDAs that we had regarded as ordinary ascites at first. In fact, the CT numbers of the non-HDAs were significantly higher than ordinary ascites because of blood contamination. It was also noteworthy that 3 patients who lacked HDAs still showed increased ascitic density. Of course, we have to consider the errors in calculating CT numbers within or between the systems. Also, we did not evaluate the correlation between ascitic blood content and CT numbers, and this should be attempted in a follow-up study. Nevertheless, our results indicated that calculation of ascitic CT numbers would help clinical judgment as to whether the case is hemorrhagic or not, and this should be helpful where paracentesis can not be performed.

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