Histologic characteristics of small hepatocellular carcinomas showing atypical enhancement patterns on 4-phase multidetector CT examination

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ABSTRACT

Histologic characteristics of small hepatocellular carcinomas showing atypical enhancement patterns on 4-phase multidetector CT examination

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OBJECTIVE: The purpose of this study is to retrospectively define which histologic characteristics of small hepatocellular carcinomas (HCCs) are related to atypical dynamic enhancement on multi-detector computed tomography (MDCT) imaging.

MATERIALS AND METHODS: Seventy-three patients with 83 HCCs (3cm or less in diameter) were included in this study. All patients underwent 4-phase MDCT imaging and subsequent surgery withineight weeks. Two independent radiologists blinded to the histologic findings retrospectively categorized the HCCs as either typical (showing increased enhancement on arterial phase

images followed by washout in late phase images) or atypical lesions demonstrating any other enhancement pattern. From the original pathologic reports, various histologic characteristics including gross morphology, nuclear histologic grades, presence of capsule formation, and capsule infiltration if a capsule is present were compared between the two groups.

RESULTS: Atypical enhancement pattern was seen in 30 (36.2%) of the 83 HCCs. The mean size of atypical HCCs (1.71 ± 0.764) was significantly smaller than that of typical HCCs (2.31 ± 0.598, $p<0.001$). Atypical HCCs were frequently found to be vaguely nodular in gross morphology (n=13, 43.3%) and to have grade I nuclear grades (n=17, 56.7%). Capsule formation was significantly more common in typical HCCs ($p<0.001$). Capsular infiltration was also more common in typical HCCs ($p=0.001$).

CONCLUSION: HCCs showing atypical dynamic enhancement on MDCT imaging are usually smaller than typical HCCs, mostly of the vaguely nodular type in gross morphology, well-differentiated in nuclear grades, and lack capsule formation or capsular infiltration.

Key words : hepatocellular carcinoma, multi-detector computed tomography, enhancement pattern, histology

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I. INTRODUCTION

The main workflow for the diagnosis of hepatocellular carcinoma (HCC) has changed dramatically over the past few decades from invasive procedures such as angiography or biopsy to noninvasive ones such as either dynamic contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) [1]. The most recent guidelines issued by the American Association for the Study of Liver Diseases (AASLD) state that if a lesion seen in patients with a risk of HCC is more than 1cm in diameter and shows the typical enhancement patterns on dynamic CT or MRI; which is arterial

hypervascularity and venous or delayed phase washout, can be treated under the diagnosis of HCC [2]. If the appearance is not typical for HCC, a second imaging study (either CT or MRI) or biopsy is necessary [2].

Of the two modalities, multi-detector CT (MDCT) is more widely used technique to diagnose HCCs, although gadolinium-enhanced dynamic MRI may be superior to MDCT [3,4]. CT is more widespread and takes shorter examination time. The typical appearance of HCC on dynamic CT or MRI is increased enhancement on the arterial phase (arterial hypervascularity) followed by decreased enhancement (washout) of the tumor in the portal venous or delayed phases [5]. However, some HCCs, especially less than 2–3 cm in diameter [6,7], and well-differentiated ones lacking typical hemodynamic changes can make diagnosing HCC a challenge [8]. However, histologic differences are not well known between the HCCs showing typical and atypical dynamic imaging features. The purpose of this study was to retrospectively compare the histologic characteristics of HCCs with typical and atypical dynamic enhancement patterns on preoperative MDCT imaging in small HCCs of 3 cm or less in diameter.

II. MATERIALS AND METHODS

1. Patients

Our institutional review board approved this retrospective study and waived the informed consent requirement. Surgical resection pathology records from June 2007 to February 2010 were reviewed to identify the cases of patients with a pathologic diagnosis of HCC. Among these patients, the study sample was selected on the basis of the following inclusion criteria: pathologic diagnoses of HCC 3 cm or smaller in diameter, available preoperative 4-phase MDCT scans obtained according to the standard protocol for dynamic liver

CT, interval between pathologic diagnosis and CT of no longer than 8 weeks, and no history of previous adjuvant treatment, such as transcatheter arterial chemoembolization, percutaneous ethanol injection, or radiofrequency ablation. All the patients underwent surgery were non-cirrhotic or have cirrhosis but still have well preserved liver functions. In our institution, atypically enhancing but suspicious lesions for HCC were closely followed up or treated with surgical resection because of the malignant potential for development to HCC through multistep progression of hepatocarcinogenesis[9].

A total of 83 HCCs in 73 consecutive patients were included in the study. Among the 73 patients, 64 patients had one HCC each, eight had two HCCs, and one had three HCCs. Among the 83 HCCs, 12 HCCs were 1cm or less in diameter. Three of these 12 HCCs were newly appeared with typical enhancement during the surveillance. Remaing 9 HCCs showed atypical enhancement, but were resected together in the surgery for another typical HCCs found in the preoperative MDCT.

2. Pathologic analysis

In all cases, pathologic reports including gross and histological analyses were reviewed. Tumor size, gross morphology, tumor necrosis or hemorrhage/peliosis, tumor grade, histology type, cell type, fatty change, capsule formation (capsule infiltration if a capsule was present), portal vein invasion, bile duct invasion and microvascular invasion were reviewed. Tumor size grade was classified into three groups: group 1 was 1 cm or less in diameter, group 2 was between 1 and 2 cm in diameter, and group 3 was between 2 and 3 cm in diameter. The tumor grade of the HCCs was classified as grade I(well differentiated), grade II(moderately differentiated) and grade III (poorly differentiated), or IV, according to the nuclear grading scheme by Edmondson

and Steiner [10]. If the histologic grade of tumor consisted of more than two grades, the major component of the grade was recorded for the analysis. Gross morphology was stratified into vaguely nodular, expanding, nodular and perinodular extending, multinodular confluent or infiltrative type. Histologic types were trabecular, pseudoglandular, scirrhous, compact and lymphoid. Cell types were hepatic, clear or giant. Fibrous capsule formation was recorded as either present (whether complete or partial) or absent.

3. CT Techniques

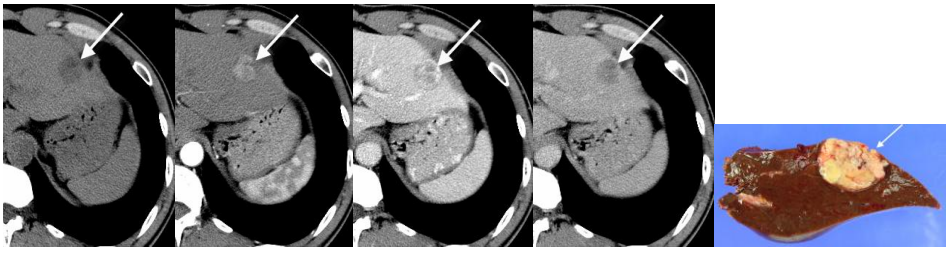
All CT scans were performed with multidetector scanners (Somatom Sensation 16 or Sensation 64; Siemens Medical Solutions, Forchheim, Germany). All patients received a 2 mL/kg dose (total volume <150 mL) of nonionic contrast material (Iopromid [Ultravist]; Bayer Schering, Berlin, Germany, or iohexol [Omnipaque 300]; Nycomed Amersham, GE Healthcare, Milwaukee, Wis, NJ) intravenously with a power injector (EnVisionCT; Medrad, Pittsburgh, Pa) with a 30-second fixed injection duration. A precontrast scan was obtained before administration of contrast media. Using a bolus tracking technique, arterial phase imaging was started after an 18-second delay from the time of 100 Hounsfield units of aortic enhancement. A 30-second scan delay after arterial phase imaging was used for portal venous phase imaging. Equilibrium phase imaging was also obtained 150 seconds after the end of portal venous phase imaging. The scanning parameters were as follows: collimation, 16 rows×0.75mm or 64 rows×0.6mm; gantry rotation speed, 0.5 seconds; section thickness, 3 mm; image reconstruction increment, 1 mm; 120kV; and effective tube current-time charge, 200-250mA.

4. Image analysis

The attenuation of HCC was classified as hyperattenuated, isoattenuated, and hypoattenuated, as compared with the surrounding liver

parenchyma on the unenhanced phase, arterial phase, portal venous phase, and equilibrium phase images. Increased arterial enhancement was considered when the tumor showed hyperattenuation compared to the surrounding liver parenchyma during the arterial phase or the attenuation of tumor seen on unenhanced images. On the portal venous phase and equilibrium phase images, each lesion was subjectively evaluated for the presence of washout. Subjective tumor washout was defined as present if the tumor hyper- or isoattenuating to the liver on an arterial phase image subsequently appeared to be hypoattenuated as compared to the surrounding liver parenchyma on the portal venous or equilibrium phase images. Two independent radiologists blinded to the histologic findings retrospectively stratified the HCCs into either typical or atypical HCCs. Disagreements in interpretation were resolved by consensus. Typical HCC was defined as a lesion that showed increased arterial enhancement on arterial phase images followed by washout in late phase images (Figure 1). Atypical HCC was defined as a lesion that did not show typical enhancement pattern (Figure 2). After classification as typical and atypical HCC, gross and histologic characteristics of the HCCs were compared between the two groups.

Figure 1. A 43-year-old man with underlying B-viral hepatitis.
(A) Precontrast, (B) hepatic arterial, (C) portal venous, (D) equilibrium phase images from triphasic MDCT scan. A hypoattenuating lesion is seen on the precontrast phase image (A). The lesion shows increased arterial enhancement on the arterial phase image (B) and washout of contrast enhancement on the portal venous(C) and equilibrium phase image (D).
(E) Gross specimen of the lesion. Histologic examination demonstrated a poorly differentiated (nuclear grade III) hepatocellular carcinoma of expanding type gross morphology with partial capsule formation and infiltration.

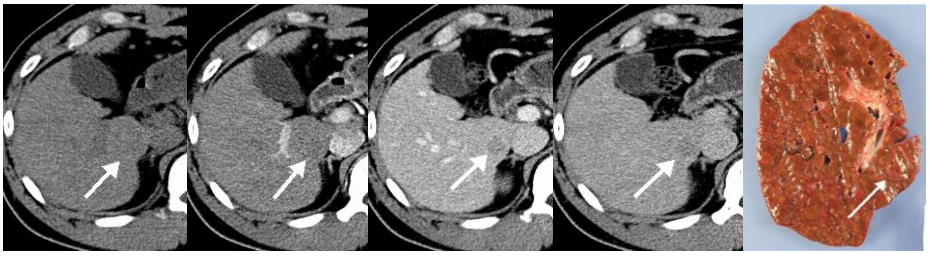


(A) (B) (C) (D) (E)

Figure 2. A 49-year-old man with B-viral liver cirrhosis

(A)Precontrast, (B) hepatic arterial, (C) portal venous, (D) equilibrium phase images from triphasic MDCT scan. On the precontrast (A) and arterial phase(B), the lesion shows isoattenuation as compared to the surrounding parenchyma. On the portal venous (C) and equilibrium phase (D), the lesion shows hypoattenuation as compared to the surrounding parenchyma.

(E) Gross specimen of the lesion. Histologic examination showed a well differentiated (nuclear grade I) hepatocellular carcinoma of vaguely nodular type in gross morphology without capsule formation.



(A) (B) (C) (D) (E)

5. Statistical Analysis

An independent t-test was used to compare age and mean difference in tumor size between the two groups. A chi-square test was used to compare sex differences between two groups. The chi-square test or Fisher's exact test was used to compare categorical data according to the expected frequency in each cell of the tables. P values of less than 0.05 were considered statistically

significant. All statistical analyses were done using statistical software (SPSS, version 17.0.1, SPSS, Chicago, Ill).

Results

A total of 83 HCCs (2.09 ± 0.71 cm in diameter, 0.4cm to 3.0cm in range) in 73 patients (54.7 ± 10.5 years old, 60 men and 13 women) were included in this study. 69 (94%) out of 73 patients had liver cirrhosis. Most of patients had cirrhosis caused by hepatitis B virus infection (n=60; 82.2%), and the rest had cirrhosis caused by hepatitis C virus infection (n=6; 8.2%) or alcohol (n=3; 4.1%).

Fifty–three (63.8%) HCCs were classified as typical and 30 (36.2%) as atypical HCCs. (Table 1). Sixteen of 30 atypical HCCs show delayed phase washout without arterial enhancement and 9 of 30 atypical HCCs show arterial enhancement only without delayed phase washout. Five of 30 atypical HCCs show neither arterial enhancement nor delayed phase washout.

The mean size of the atypical HCCs (1.7 ± 0.7) was significantly smaller than that of the typical HCCs (2.3 ± 0.6, $p<0.001$). According to the criteria of 2cm in diameter, 40(48.2%) HCCs were 2cm or less than 2cm in diameter and 43(51.8%) HCCs were between 2cm and 3cm in diameter. Among 40 HCCs 2cm or less than 2cm in diameter, 19(47.5%) HCCs were typical HCC and 21(52.5%) HCCs were atypical HCCs. But among 43 HCCs between 2cm and 3cm in diameter, 34(79.1%) HCCs were typical HCC and 9(20.9%) HCCs were atypical HCCs. Sex and age were not significantly different between the typical and atypical HCCs.

Gross morphology of the vaguely nodular type was significantly more common in atypical HCCs ($p<0.001$), but the expanding type was significantly more common in typical HCCs ($p=0.001$). As for Edmondson-Steiner nuclear histologic grades, well-differentiated (Grade I) HCCs were more common in

atypical HCC (p<0.001), but moderate (grade II) or poorly differentiated (grade III) HCCs were significantly more common in typical HCCs (p<0.001). Capsule formation was significantly more common in typical HCCs (p<0.001). Capsular infiltration was more common in typical HCCs (p=0.001).

Other pathologic characteristics including tumor necrosis, hemorrhage/peliosis, histologic types, cell types, fatty change, portal vein invasion, bile duct invasion and microvascular invasion showed no significant differences between the atypical and typical HCCs.

Table 1. Histologic and clinical characteristics of atypical and typical HCC

	Atypical (n=30)	Typical (n=53)	p-value
N=83 Mean age = 54.72 ± 10.557 / M : F = 69 : 14			
Sex (Male/Female)	25 / 5	44 / 9	0.971
Age	53.20 ± 10.162	55.58 ± 10.773	0.295
Size Grade			
Mean	1.71 ± 0.764	2.31 ± 0.598	<0.001
1cm or less	9 (30.0%)	3 (5.7%)	0.001
<1cm – 2cm	12 (40.0%)	16 (30.2%)	
<2cm – 3cm	9 (30.0%)	34 (64.2%)	
Gross Type			
Expanding	5 (16.7%)	28 (52.8%)	0.001
Multinodular confluent	9 (30.0%)	19 (35.8%)	0.636

Nodular/perinodal extension	1 (3.3%)	5 (9.4%)	0.411
Vagulely nodular	13 (43.3%)	1 (1.9%)	<0.001
Infiltrative	2 (6.7%)	0 (0.0%)	0.128
Tumor necrosis (Available n = 82)			
No	25 (86.2%)	40 (75.5%)	0.252
Yes	4 (13.8%)	13 (24.5%)	
Hemorrhage/peliosis (Available n = 82)			
No	27 (93.1%)	38 (71.7%)	0.022
Yes	2 (6.9%)	15 (28.3%)	
Grade(major)			
1.0	17 (56.7%)	6 (11.3%)	<0.001
2.0	10 (33.3%)	40 (75.4%)	
3.0	3 (10.0%)	7 (13.3%)	
Grade(worst)			
1.0	16 (53.3%)	1 (1.8 %)	<0.001
2.0	8 (26.7%)	26 (49.1%)	
3.0	6 (20.0%)	26 (49.1%)	
Histology Type			
Trabecular	30 (100.0%)	53 (100.0%)	
Pseudoglandular	8 (26.7%)	18 (34.0%)	0.624
Scirrhous	1 (3.3%)	3 (5.7%)	1.000
Compact	3 (10.0%)	7 (13.2%)	0.741
Lymphoid	0	4 (7.5%)	0.291

Cell type			
Hepatic	29 (96.7%)	53 (100.0%)	0.361
Clear	11 (36.7%)	20 (37.7%)	1.000
Giant	1 (3.3%)	4 (7.5%)	0.649
Fatty change (Available n = 82)			
No	14 (48.3%)	32 (60.4%)	0.291
Yes	15 (51.7%)	21 (39.6%)	
Capsule formation (Available n = 82)			
No	19 (65.5%)	8 (15.1%)	<0.001
Yes	10 (34.5%)	45 (84.9%)	
Capsule infiltration (Available n = 82)			
No	22 (75.9%)	19 (35.8%)	0.001
Yes	7 (24.1%)	34 (64.2%)	
Portal vein invasion(Available n = 78)			
No	24 (96.0%)	52 (98.1%)	0.541
Yes	1 (4.0%)	1 (1.9%)	
Bile duct invasion (Available n = 78)			
No	24 (96.0%)	51 (96.2%)	1.000
Yes	1 (4.0%)	2 (3.8%)	
Microvascular invasion (Available n = 78)			
No	17 (68.0%)	29 (54.7%)	0.266
Yes	8 (32.0%)	24 (45.3%)	

IV. DISCUSSION

Our results showed that various histologic characteristics of HCCs are related to atypical dynamic enhancement patterns on contrast-enhanced dynamic CT.

In our study, 63.8% (50/83) of HCCs showed the typical enhancement pattern of HCC of increased enhancement on arterial phase and washout on portal venous or delayed phase images [11]. This typical enhancement pattern is consistent with hepatocarcinogenesis, which causes vascular changes toward a predominantly hepatic arterial supply with a lack of portal venous supply [12-14]. However, the predominant enhancement patterns of HCC during the arterial and portal venous phases differed significantly according to tumor size and cellular differentiation of the tumor. In our study, the mean size of HCCs showing typical enhancement pattern was larger than that of HCCs with atypical enhancement pattern ($p<0.001$). And there was a significantly higher proportion of typical HCCs among HCCs between 2cm and 3cm in diameter ($p=0.0057$). These results are similar to those of previous studies [15-17]. Also, in our study, well-differentiated HCCs were more common among atypical HCCs ($p<0.001$), while moderate and poorly differentiated HCCs were significantly more common among typical HCCs ($p<0.001$). A previous study that evaluated the relationship of the vascularization of small HCC and the cellular differentiation has shown that abnormal arterial supply within a nodule increases as the grade of malignancy increases, while the normal hepatic arterial and portal venous supply to the nodule gradually decreases [18]. Another studies reported that well differentiated and small HCCs more often show various atypical CT enhancement features [19,20].

Early HCCs showed the typical dynamic enhancement pattern less often than more advanced lesions in our study. Thirteen (43.3%) atypical lesions were vaguely nodular in gross morphology, and 17 (56.7%) atypical lesions were well-differentiated in tumor grade. These characteristics are

compatible with early HCC, defined as well-differentiated lesions that are usually less than 2 cm in diameter, vaguely nodular in gross morphology, not showing capsule formation, and usually hypovascular [21].

Fibrous capsule that is known to be frequently observed around a tumor during the growth of HCC was more frequently seen in typical HCCs in our study. And our study also showed moderate and poorly differentiated HCCs were significantly more common among typical HCCs ($p<0.001$). The capsule is formed by host mesenchymal cells not by HCC cells. And the capsule formation may result from interaction between tumor and host liver and interfere the growth and invasion of HCC[22]. This is supported by the clinical evidence that the prognosis of patients with a HCC having capsule is better than for those without [23-26] Therefore progressed HCC with typical enhancement pattern in spite of its small size more often forms capsule than indolent early HCC with atypical enhancement pattern in our study.

There are limitations to our study. First, our study is retrospective and we included surgically confirmed HCC to compare the dynamic imaging patterns with histologic characteristics. Therefore, small HCC that were diagnosed based on the presence of a typical dynamic pattern and subsequently treated with locoregional treatment were not included. This might have increased the proportion of atypical lesions in our study. Second, the definitions we used for increased arterial enhancement and presence of washout may differ from those used by other investigators. We determined the presence of increased arterial enhancement by comparing with precontrast images; some investigators may determine the presence of increased arterial enhancement on the arterial phase images alone. However, we believe that increased arterial enhancement can be correctly assessed by referring to precontrast images because some lesions showing hypoattenuation on precontrast images may show isoattenuation on arterial phase images even though they have increased arterial vascularity within the lesions. We considered washout to be present when a

lesion showed hypointensity relative to the surrounding liver on late phase images. Some radiologists could argue that washout may not be present when a lesion does not show increased arterial enhancement. However, we thought that such comparison would cause greater interobserver variability. Third, atypical HCCs are consisted of diverse subgroups according to the presence of the arterial enhancement or delayed phase washout. But we considered atypical HCCs as lesions that did not show typical enhancement pattern and did not divided into subgroups in the analysis process. Further studies are needed to define the characteristics of diverse subgroups of atypical HCCs. Lastly, we did not analyze how many hypovascular lesions transform to hypervascular lesions. A recent study revealed that hypoattenuating hepatic nodular lesions in chronic liver disease depicted on dynamic CT have high malignant potential [27]. There are chances that atypically enhancing HCCs progressed to typically enhancing HCCs according to the hepatocarcinogenesis, but we analyzed only the preoperative CT scan of just before the surgery, not serial CT scans.

V. CONCLUSION

We conclude that various histologic characteristics of HCC are associated with atypical dynamic enhancement on contrast-enhanced dynamic CT images. HCCs with atypical enhancement patterns tend to be smaller than HCCs with typical enhancement pattern and are vaguely nodular type in gross morphology and well-differentiated in histologic grades. Capsule formation and capsular infiltration are significantly more common in typical HCCs. Awareness of atypical enhancement patterns in small HCC and their histologic implications may guide patient management.

REFERENCES

1. Choi BI, Lee JM. Advancement in HCC imaging: diagnosis, staging and treatment efficacy assessments: imaging diagnosis and staging of hepatocellular carcinoma. J Hepatobiliary Pancreat Sci 2010;17:369-73.
2. Bruix J, Sherman M. Management of hepatocellular carcinoma: An update. Hepatology 2011;53:1020-2.
3. Colli A, Fraquelli M, Casazza G, Massironi S, Colucci A, Conte D, et al. Accuracy of ultrasonography, spiral CT, magnetic resonance, and alpha-fetoprotein in diagnosing hepatocellular carcinoma: a systematic review. Am J Gastroenterol 2006;101:513-23.
4. Willatt JM, Hussain HK, Adusumilli S, Marrero JA. MR Imaging of hepatocellular carcinoma in the cirrhotic liver: challenges and controversies. Radiology 2008;247:311-30.
5. Marrero JA, Hussain HK, Nghiem HV, Umar R, Fontana RJ, Lok AS. Improving the prediction of hepatocellular carcinoma in cirrhotic patients with an arterially-enhancing liver mass. Liver Transpl 2005;11:281-9.
6. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. Int J Cancer 2001;94:153-6.
7. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med 1996;334:693-9.
8. Bolondi L, Gaiani S, Celli N, Golfieri R, Grigioni WF, Leoni S, et al. Characterization of small nodules in cirrhosis by assessment of vascularity: the problem of hypovascular hepatocellular carcinoma. Hepatology 2005;42:27-34.
9. Takayama T, Makuuchi M, Hirohashi S, Sakamoto M, Okazaki N, Takayasu K, et al. Malignant transformation of adenomatous hyperplasia to hepatocellular carcinoma. Lancet 1990;336:1150-3.

10. Edmondson HA, Steiner PE. Primary carcinoma of the liver: a study of 100 cases among 48,900 necropsies. Cancer 1954;7:462-503.
11. Forner A, Vilana R, Ayuso C, Bianchi L, Sole M, Ayuso JR, et al. Diagnosis of hepatic nodules 20 mm or smaller in cirrhosis: Prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. Hepatology 2008;47:97-104.
12. Hwang SH, Yu JS, Kim KW, Kim JH, Chung JJ. Small hypervascular enhancing lesions on arterial phase images of multiphase dynamic computed tomography in cirrhotic liver: fate and implications. J Comput Assist Tomogr 2008;32:39-45.
13. Lee J, Lee WJ, Lim HK, Lim JH, Choi N, Park MH, et al. Early hepatocellular carcinoma: three-phase helical CT features of 16 patients. Korean J Radiol 2008;9:325-32.
14. Shimizu A, Ito K, Koike S, Fujita T, Shimizu K, Matsunaga N. Cirrhosis or chronic hepatitis: evaluation of small (<or=2-cm) early-enhancing hepatic lesions with serial contrast-enhanced dynamic MR imaging. Radiology 2003;226:550-5.
15. Hytiroglou P, Park YN, Krinsky G, Theise ND. Hepatic precancerous lesions and small hepatocellular carcinoma. Gastroenterol Clin North Am 2007;36:867-87, vii.
16. Monzawa S, Ichikawa T, Nakajima H, Kitanaka Y, Omata K, Araki T. Dynamic CT for detecting small hepatocellular carcinoma: usefulness of delayed phase imaging. AJR Am J Roentgenol 2007;188:147-53.
17. Monzawa S, Omata K, Shimazu N, Yagawa A, Hosoda K, Araki T. Well-differentiated hepatocellular carcinoma: findings of US, CT, and MR imaging. Abdom Imaging 1999;24:392-7.
18. Nakashima Y, Nakashima O, Hsia CC, Kojiro M, Tabor E. Vascularization of small hepatocellular carcinomas: correlation with differentiation. Liver 1999;19:12-8.

19. Yoon SH, Lee JM, So YH, Hong SH, Kim SJ, Han JK, et al. Multiphasic MDCT enhancement pattern of hepatocellular carcinoma smaller than 3 cm in diameter: tumor size and cellular differentiation. AJR Am J Roentgenol 2009;193:W482-9.
20. Kim SH, Lee WJ, Lim HK, Park CK. SPIO-enhanced MRI findings of well-differentiated hepatocellular carcinomas: correlation with MDCT findings. Korean J Radiol 2009;10:112-20.
21. Pathologic diagnosis of early hepatocellular carcinoma: a report of the international consensus group for hepatocellular neoplasia. Hepatology 2009;49:658-64.
22. Ishizaki M, Ashida K, Higashi T, Nakatsukasa H, Kaneyoshi T, Fujiwara K, et al. The formation of capsule and septum in human hepatocellular carcinoma. Virchows Arch 2001;438:574-80.
23. Okuda K, Musha H, Nakajima Y, Kubo Y, Shimokawa Y, Nagasaki Y, et al. Clinicopathologic features of encapsulated hepatocellular carcinoma: a study of 26 cases. Cancer 1977;40:1240-5.
24. Nagao T, Inoue S, Goto S, Mizuta T, Omori Y, Kawano N, et al. Hepatic resection for hepatocellular carcinoma. Clinical features and long-term prognosis. Ann Surg 1987;205:33-40.
25. Lai EC, Ng IO, Ng MM, Lok AS, Tam PC, Fan ST, et al. Long-term results of resection for large hepatocellular carcinoma: a multivariate analysis of clinicopathological features. Hepatology 1990;11:815-8.
26. Ng IO, Lai EC, Ng MM, Fan ST. Tumor encapsulation in hepatocellular carcinoma. A pathologic study of 189 cases. Cancer 1992;70:45-9.
27. Takayasu K, Muramatsu Y, Mizuguchi Y, Okusaka T, Shimada K, Takayama T, et al. CT Evaluation of the progression of hypoattenuating nodular lesions in virus-related chronic liver disease. AJR Am J Roentgenol 2006;187:454-63.

ABSTRACT(IN KOREAN)

MDCT에서 비전형적 조영증강양상을 보이는 소간세포암의 조직학적 특성

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김 인 중

목적: MDCT상 비전형적인 조영 증강 양상을 보이는 소간세포암의 조직학적 특성을 후향적으로 분석한다.

대상 및 방법: 2007년 6월부터 2010년 2월까지 본원에서 간암 수술을 시행한 환자 중에서 총 73명 환자의 83개의 소간세포암(직경이 3cm 이하)이 연구에 포함되었다. 모든 환자들은 4-phase MDCT를 시행한 후 8주 이내에 수술을 진행하였다. 두 명의 영상의학과 의사가 간암의 전형적인 조영 증강 양상(동맥기 조영 증강과 지연기의 조영 감소)을 보이는지에 따라 병변을 전형적 또는 비전형적 조영 증강 군으로 나누었다. 수술 후 병리 보고서를 통하여 육안적 분류, 조직학적 분화도, 피막 형성 유무, 피막이 있을 경우 피막 침습 유무 등에 대하여 두 군을

비교 분석하였다.

결과: 총 83개의 소간세포암중에서 30개(36.2%)의 병변이 비전형적 조영 증강을 보였다. 비전형적 조영 증강군의 평균 크기(1.71±0.764)가 전형적인 조영 증강군의 평균크기(2.31±0.598)에 비하여 작았다(p<0.001). 비전형적 조영 증강을 보인 소간세포암의 경우에 육안적 분류상 경계불명료 결절형이 더 많았으며(13개, 43.3%), 조직학적 분화도는 등급 I 이 많이 관찰되었다(17개, 56.7%). 피막 형성은 전형적 조영 증강을 보인 소간세포암의 경우에 더 흔하게 관찰되었다(p<0.001). 피막 침습도 또한 전형적 조영 증강을 보인 소간세포암의 경우에 더 흔하게 관찰되었다(p=0.001).

결론: MDCT에서 비전형적 조영 증강을 보이는 소간세포암은 전형적 조영 증강을 보이는 소간세포암에 비하여 크기가 작고, 육안적 분류상 경계불명료 결절형이 더 많았으며, 조직학적 분화도상 고분화도를 보였고 피막 형성이나 피막 침습이 적었다.

핵심되는 말 : 간세포암, MDCT, 조영증강 양상, 조직학