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Sonographic Characteristics of Small Hepatocellular Carcinoma

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Abstract. Fifty-four lesions of small hepatocellular carcinoma under 5 cm in diameter detected by real-time sonography were reviewed to characterize the sonographic feature. Twenty-nine lesions were smaller than 3 cm in diameter and 25 were between 3 and 5 cm in diameter. Sonographic characteristics of hepatocellular carcinoma were peripheral hypoechoic halo (52%), lateral shadow (26%), posterior acoustic enhancement (44%), and mosaic pattern (24%) of the mass. Small tumors less than 3 cm in diameter showed a hypoechoic pattern in half of the cases, whereas most of the tumors between 3 and 5 cm in diameter showed a hyperechoic or mixed pattern. Posterior acoustic enhancement was commonly seen in small tumors less than 3 cm in diameter, while a mosaic pattern was commonly seen in large tumors between 3 and 5 cm in diameter. These results suggest that sonography might be useful for the characterization of small hepatocellular carcinoma.

Key words: Liver, neoplasms – Hepatocellular carcinoma, diagnosis, ultrasound.

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in the world, particularly in Southeast Asia and in Subsaharan Africa [1]. The prognosis is extremely poor because of the difficulty in early detection and its frequent association with cirrhosis. Recent advances in body imaging techniques such as scintigraphy, sonography, computed tomography (CT), and angiography make it possible to detect small HCCs, and asymptomatic HCC is more frequently recognized now than in the past [2–5]. Among the imaging techniques, sonography is a procedure of choice for mass screening of small HCCs [5–7].

Recently, screening and regular follow-up in high-risk populations of HCCs with sonography have been used for early detection of this cancer [8–10] because surgical resection is the most effective treatment when the tumor is small. However, with the popular use of real-time sonography, many small hepatic tumors that mimic HCCs on sonography have been increasingly found. Therefore, differentiation from each other is important.

While the role of real-time sonography in detecting HCC is well established [8–10], only a few papers [6, 11, 12] have dealt with the characteristics of this tumor. No comprehensive study for the sonographic characteristics of small HCCs has been undertaken in a large series of patients.

This study attempts to identify the sonographic characteristics of small HCCs and describes the differential diagnosis of small HCCs from other small hepatic tumors.

Materials and Methods

During a two-year period, 54 small HCCs occurring in 44 patients were studied by real-time sonography. A small HCC was defined as one in which the largest dimension was less than 5 cm. The series included 39 male patients and 5 female patients, 30–72 years of age (mean age, 54 years). The diagnosis of HCC was confirmed by surgery in 24 patients, elevated serum alpha-fetoprotein (AFP) levels and/or characteristic angiographic findings, and CT after intra-arterial injection of iodized poppy seed oil (Lipiodol; Andre-Gelbe Laboratories, France) in 20 patients.

Clinical and laboratory data were reviewed in all patients. Most of the patients had chronic liver disease. Hepatitis B surface antigen (HBsAg) was positive in 33 patients (75%) and Hepatitis B surface antibody (HBsAb) was positive in 7 patients. Liver cirrhosis was found in 39 patients (89%). Thirteen patients had normal serum AFP level (<20 ng/ml) and 10 had

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an AFP level of 20–400 ng/ml. In 21 patients, serum AFP levels were above 400 ng/ml.

Sonographic examinations were performed on real-time scanners using Aloka SSD 280, Toshiba SAL 35A, and Diasonics SPA 1000. Depending on patient size, 3.5- or 5.0-MHz transducers were used. Scans were generally performed across the entire upper abdomen in both transverse and sagittal planes.

The sonographic findings in these patients were analyzed for (a) size, location, and number of the tumor; (b) echogenicity of the tumor, which is classified as hyperechoic, isoechoic, hypoechoic, or mixed on the basis of the difference in echogenicity between the lesion and the surrounding liver parenchyma; (c) presence of peripheral halo, which is a thin hypoechoic rim around the tumor; (d) presence of lateral shadow, which is an acoustic shadow behind both edges of the tumor; (e) presence of posterior acoustic enhancement, which represents a zonal increase in echogenicity behind the tumor; and (f) presence of mosaic pattern, which is a configuration composed of small areas of the same or different echogenicities within the tumor.

Results

Of the 44 patients with small HCCs, 38 patients had 1 tumor, 3 patients had 2 tumors, 2 patients had 3 tumors, and 1 patient had 4 tumors. The diameters of the tumors were as follows: less than 20 mm (12), 21–30 mm (17), and 31–50 mm (25). The tumor was located in the anterior segment of the right hepatic lobe in 20 cases, the posterior segment of the right hepatic lobe in 28 cases, the medial segment of the left hepatic lobe in 2 cases, and the lateral segment of the left hepatic lobe in 4 cases.

Sonographic findings of small HCCs are summarized in Tables 1 and 2. With respect to echogenicity of the tumor, 14 of 29 cases (48%) with HCCs less than 3 cm in diameter showed a hypoechoic pattern (Fig. 1A), whereas 4 of 25 cases (16%) with HCCs more than 3 cm in diameter showed a hypoechoic pattern. Eighty percent of HCCs larger than 3 cm in diameter showed a hyperechoic or mixed pattern (Fig. 1B and C).

Peripheral halo (Fig. 2A) was seen in 28 of 54 cases (52%). There was no significant differences of frequency of this halo related to size of the tumor. This peripheral halo corresponded to the fibrous capsule of tumor in the resected specimens (Fig. 2B). Lateral shadow was seen in 14 of 54 cases (26%). No tumor less than 2 cm in diameter demonstrated this shadow, whereas 9 of 25 cases (36%) with HCCs more than 3 cm in diameter showed this shadow (Fig. 3). Posterior acoustic enhancement (Fig. 4) occurred in 24 of 54 cases (44%) of HCCs and was more frequently observed in tumors smaller than 3 cm in diameter. Mosaic pattern was seen in 13 of 54 cases (24%). Only one tumor smaller than 3 cm in diameter showed this pattern, whereas 12 of 25 cases (48%) of HCCs larger than 3 cm in diameter showed this pattern (Fig. 5A). Pathologically, this pattern corresponded to multiple, aggregated, small nodules in the tumor (Fig. 5B).

Table 1. Echogenicity of the small HCC

Tumor size (mm)	Echogenicity				Total
	Hyperechoic	Hypoechoic	Isoechoic	Mixed	
≤20	6	6	0	0	12
≤30	7	8	1	1	17
≤50	14	4	1	6	25
Total	27	18	2	7	54

Table 2. Sonographic characteristics of small HCC

Tumor size (mm)	Peripheral halo (%)	Lateral shadow (%)	Posterior acoustic enhancement (%)	Mosaic pattern (%)
≤20 ($n=12$)	6 (50)	0 (0)	6 (50)	0 (0)
≤30 ($n=17$)	8 (47)	5 (29)	9 (53)	1 (6)
≤50 ($n=25$)	14 (56)	9 (36)	9 (36)	12 (48)
Total ($n=54$)	28 (52)	14 (26)	24 (44)	13 (24)

Discussion

Depending upon the capability of imaging modalities to detect small asymptomatic HCCs, the definition of small HCCs has been changed. In 1977, Okuda et al. [13] used the term of "minute" HCC, which was defined as a solitary tumor smaller than 4.5 cm or a few tumor nodules smaller than 3.5 cm in diameter. In 1982, Chen et al. [14] described the term of "small" HCC to denote a tumor smaller than 3.0 cm in diameter. The current criteria set by the Japan Liver Cancer Study Group for designating small HCC call for a single tumor less than 2 cm in diameter, reflecting the recent progress in the diagnosis [15]. However, other investigators [2, 4, 5, 10] defined "small" HCC as a tumor less than 5 cm in diameter. We believe that until now, definition of small HCC is not based on the pathophysiologic criteria of the tumor, but is based on the capability of detection of the tumor. We define "small" HCC as a tumor less than 5 cm in diameter, because detection of a small HCC less than 2 cm is still difficult and the majority of the focal tumors that could be candidates for surgical resec-

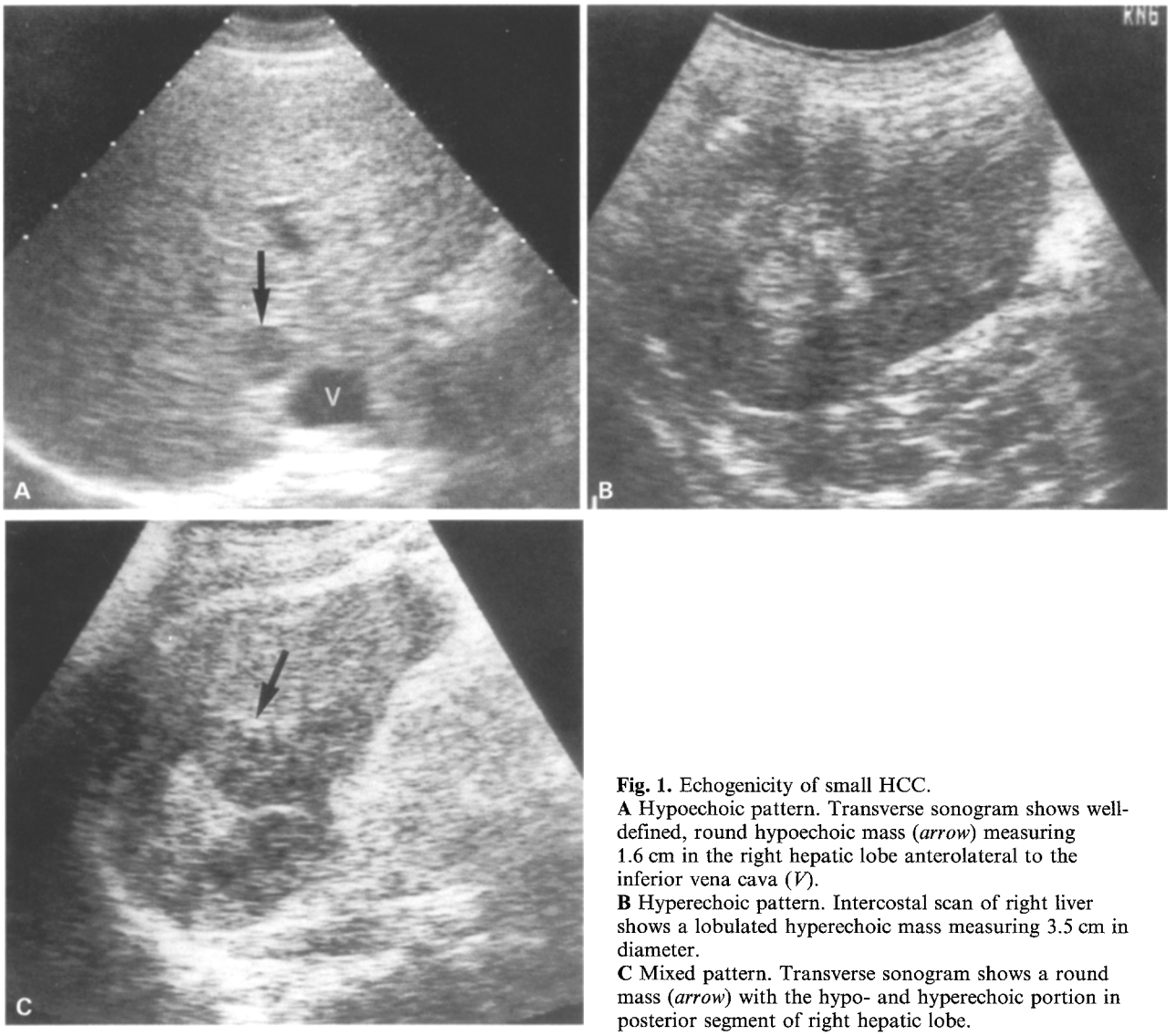

Fig. 1. Echogenicity of small HCC.
A Hypoechoic pattern. Transverse sonogram shows well-defined, round hypoechoic mass (*arrow*) measuring 1.6 cm in the right hepatic lobe anterolateral to the inferior vena cava (*V*).
B Hyperechoic pattern. Intercostal scan of right liver shows a lobulated hyperechoic mass measuring 3.5 cm in diameter.
C Mixed pattern. Transverse sonogram shows a round mass (*arrow*) with the hypo- and hyperechoic portion in posterior segment of right hepatic lobe.

tion are larger than 2 cm in diameter. Therefore, evaluation of sonographic findings of the tumors less than 5 cm including smaller tumors less than 2 cm in diameter is more practical in clinical application.

HCCs frequently appear in relation to chronic liver disease and the HBsAg carrier state [16–18]; however, there was no relationship between the severity of the background liver changes and the incidence of HCCs [5]. Therefore, periodic follow-up of high-risk patients by imaging techniques or other methods is essential for the early detection of HCCs.

There are several useful methods for detecting HCCs. Serum AFP assay can be used, but recent studies performed on patients with small HCCs demonstrate that AFP assay is not very useful in the detection of HCCs since the positive detection rate is low [9, 10, 18]. Angiography, although invasive, often provides the information that other modalities do not give such as identification of feeding vessels of the tumor, vascular invasion, and growth pattern of the tumor. However, recent studies indicate that angiography is not the best procedure for detection of small HCCs [5, 10]. Computed tomography after intra-arterial injection of iodized poppy seed oil (Lipiodol) has been known as the best method to detect the small HCC [19, 20], but we cannot use this method as a screening procedure of HCC. The high sensitivity of real-time sonography for detection of small HCCs has been established [5–7, 10]. As real-time sonography is simple, noninvasive, and sensitive, it may be the procedure of choice for early detection of HCCs, especially in high-risk patients.

The echo pattern of small HCCs has been re-

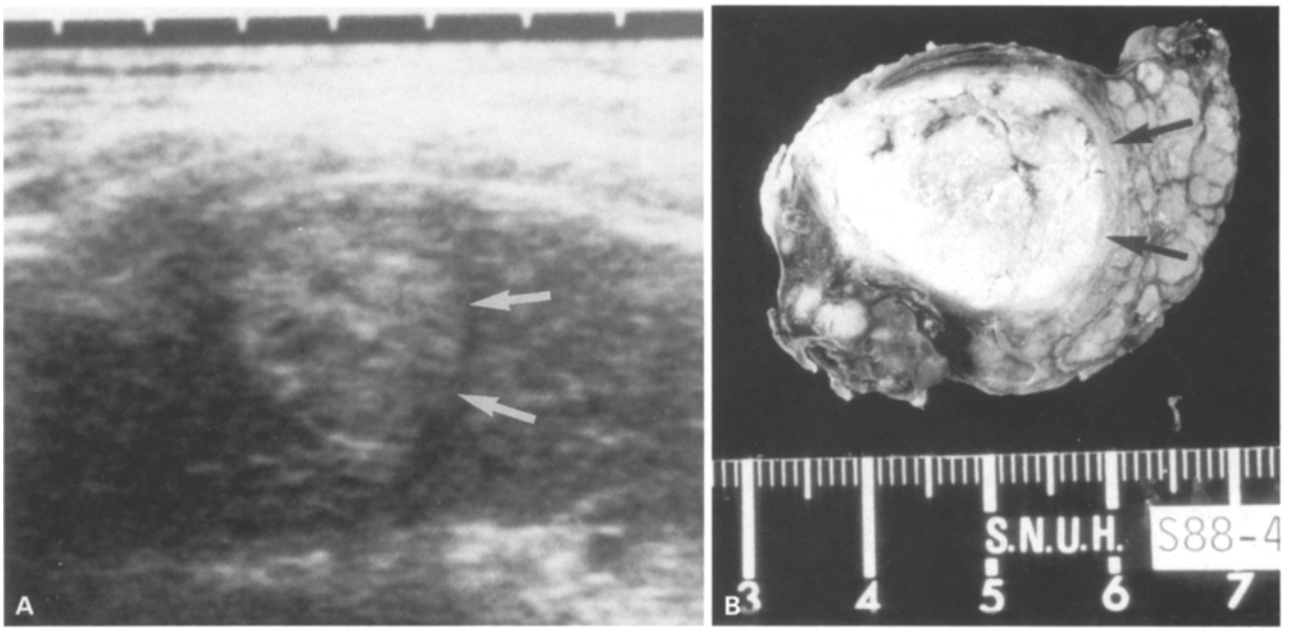

Fig. 2. Peripheral halo of HCC. **A** Intercostal scan of right liver shows well-defined hyperechoic mass with thin, sharply defined, hypoechoic peripheral halo (*arrows*). **B** Resected specimen of the tumor shows a well-defined mass. Surrounding fibrous capsule (*arrows*) is also seen.

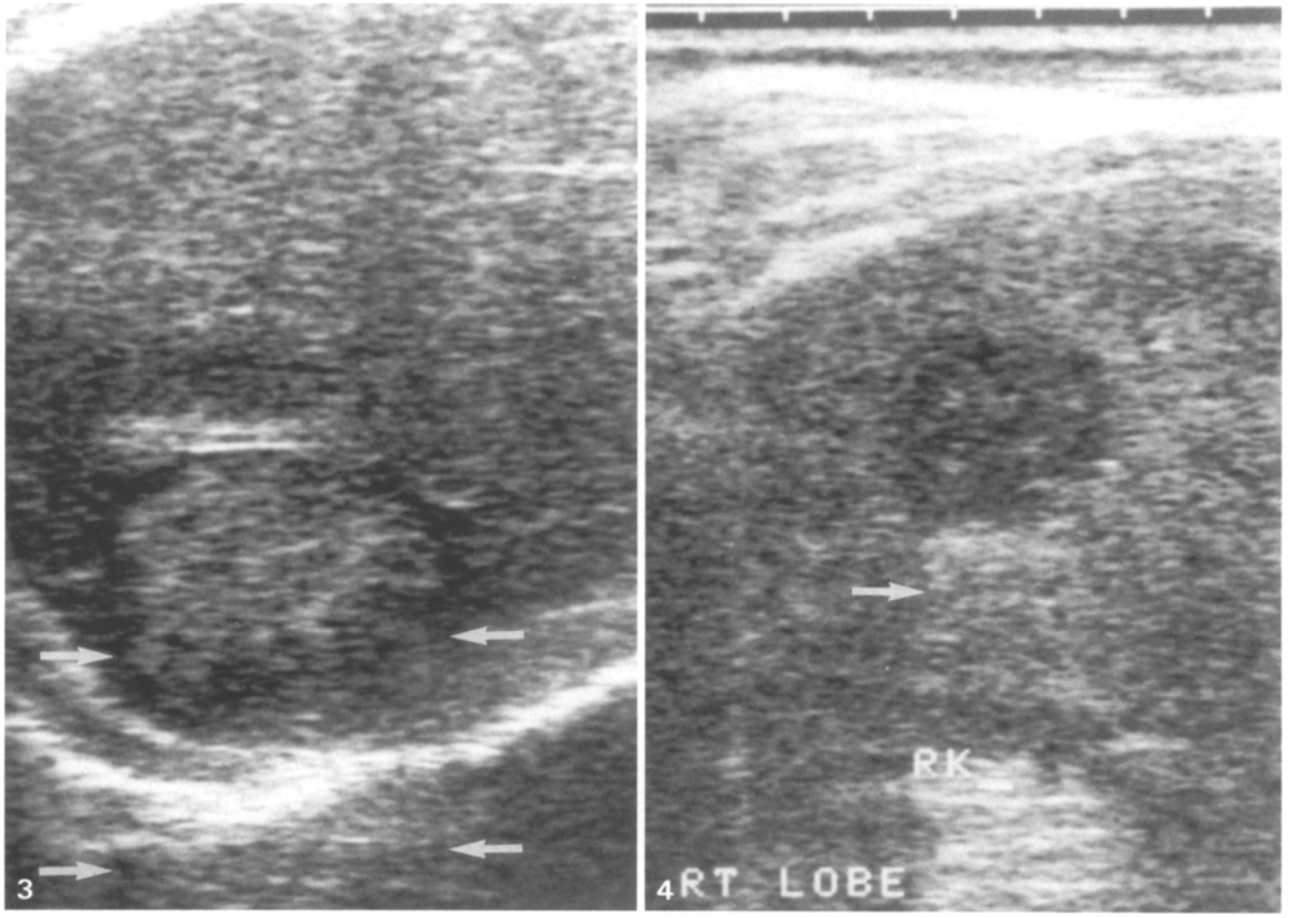

Fig. 3. Transverse sonogram of the right liver shows a well-defined isoechoic mass with peripheral halo. Lateral shadow (*arrows*) can be noted.

Fig. 4. Transverse sonogram of the right liver shows a well-defined hypoechoic mass measuring 2.5 cm in diameter, with posterior acoustic enhancement (*arrow*). (*RK*, right kidney.)

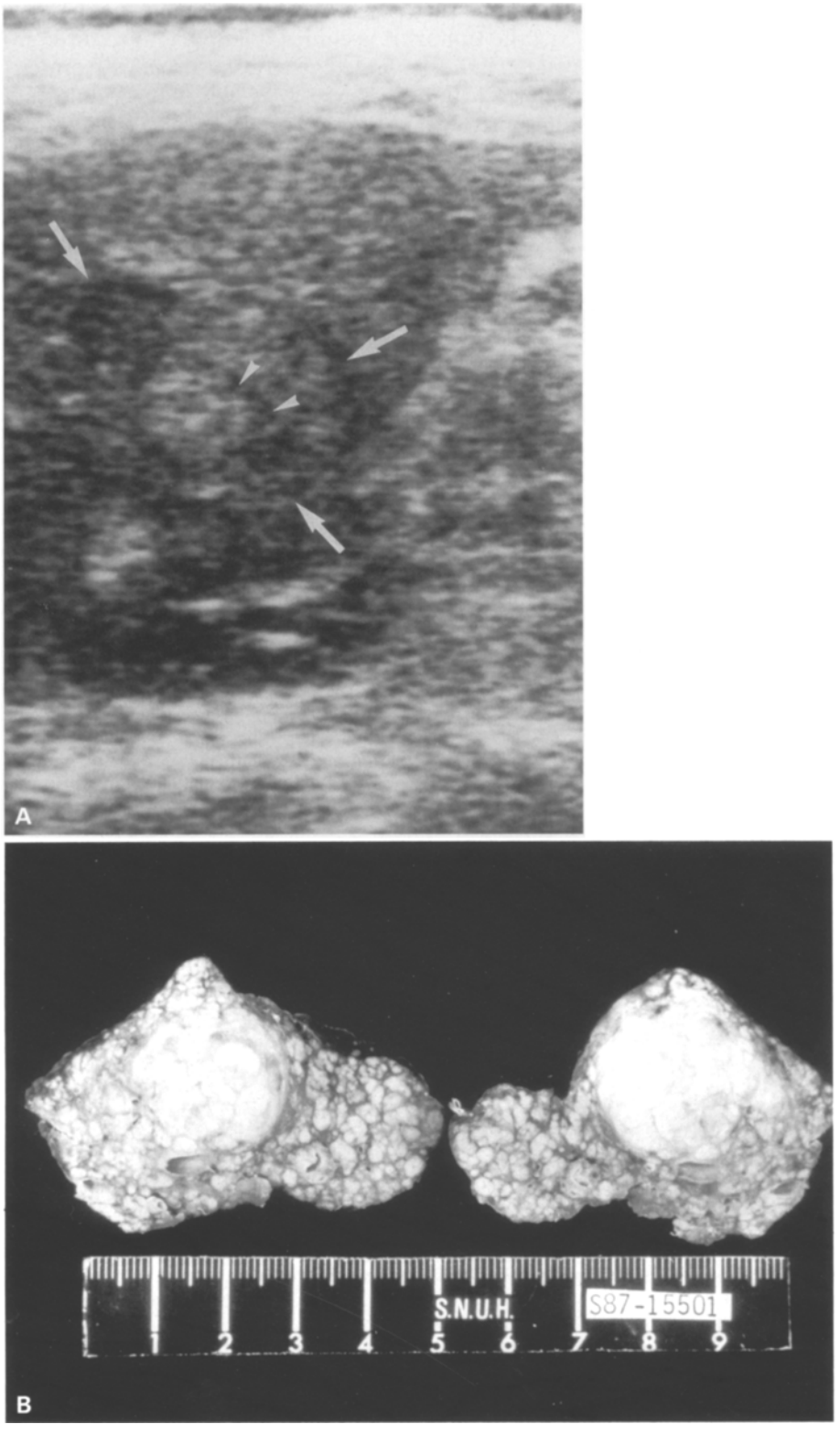

Fig. 5. Mosaic pattern of HCC. **A** Intercostal scan of the right liver shows lobulated mass with mixed echo pattern (*arrows*). Thin hypoechoic internal septa (*arrowheads*) can also be seen in the tumor. **B** Resected specimen of the tumor shows a well-defined mass with relatively irregular margin. Note thin partitions that separate the tumor into several irregularly shaped nodules.

ported previously [6, 11]. However, there are few reports describing detailed sonographic characteristics in a large series of patients. Most of the small HCCs have been reported as hypoechoic, in contrast to advanced HCCs, which are mostly hyperechoic [6, 11, 21]. Our data support these observations. Pathologically, in cases of hypoechoic HCCs, solid tumor tissue without necrosis was observed in resected specimens. Recent studies, including ours, claimed that sonographic findings were correlated with microscopic findings in HCCs [11, 22]. A pure cell mass was believed to have a low-echo, presumably because of the lack of any structure within the tumor to serve as a reflective source for echoes, whereas nonliquefactive necrosis, hemorrhage, fatty change, interstitial fibrosis, and sinusoidal dilatation were believed to produce high echogenicity.

In our series, a thin, peripheral, hypoechoic halo was more often observed than that in the previous reports [6, 22]. This halo, which corresponded to a fibrous capsule in resected specimens, is one of the characteristic findings of small HCCs [23]. Lateral shadow was frequently seen in the tumor with peripheral halo in our series and this finding may be related to the fibrous capsule of the tumor. Posterior acoustic enhancement of the tumor was more often seen in smaller HCCs. Sonographically, posterior acoustic enhancement represents good transmission of ultrasonic waves through the tumor; however, it is yet unclear what kinds of histologic changes produce the posterior enhancement. Mosaic pattern is a configuration of confluent small nodules separated by thin septa within the tumor. This pattern represents the characteristic growth pattern of the HCC. No case of HCCs less than 2 cm in diameter showed mosaic pattern, while large HCCs more than 3 cm in diameter showed mosaic pattern in 12 of 25 cases (48%). The incidence of mosaic pattern in our series is lower than that of Yoshida's series [12], in which 42 of 64 cases (65.6%) showed this pattern, because this pattern is more often seen in large HCCs.

Differential diagnosis of small HCCs includes cavernous hemangioma, metastatic tumor, and regenerating nodules in liver cirrhosis. Most small hemangiomas universally appear as a strongly echogenic mass without a peripheral halo [24, 25]. In metastatic tumors, sonographic characteristics of HCC such as mosaic pattern, posterior enhancement, and lateral shadow were rarely observed [12]. Peripheral hypoechoic halo of metastatic tumor, the so-called bull's-eye-like pattern, which is a hyperechoic central portion with relatively thick hypoechoic rim, is also helpful in diagnosing the metastatic tumor. It is clinically important to differentiate cirrhosis with regenerating nodules from cirrhosis with HCC. Most regenerating nodules are innumerable and range from 0.5 to 1.5 cm in diameter. The numerous closely spaced nodules and their thin connective tissue borders produce a cobblestone appearance and are recognized by thin, slightly more echogenic borders, which correspond pathologically to fibrous and fatty connective tissue surrounding and separating the nodules [26].

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