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Encapsulated Hepatocellular Carcinoma: Radiologic Findings and Pathologic Correlation

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Abstract. The encapsulated form of hepatocellular carcinoma (HCC) is a pathologic subtype that has been found to occur with variable frequency in typical HCC in Japanese radiological, surgical, and autopsy series. It is a well-differentiated tumor that tends to grow slowly and noninvasively, and has a better prognosis than other gross forms of HCC.

Among the 73 cases of typical HCC in patients of non-Asian extraction in our files, 11 could be positively identified as encapsulated based on strict pathological criteria. The purpose of this study was to review the radiographic appearance of these encapsulated tumors.

Radiographically, the tumors demonstrated a hyperdense rim in 5 of 9 cases with postinfusion computed tomography scans, an anechoic halo in 4 of 6 cases with ultrasonograms, and an avascular rim on the capillary phase in 5 of the 8 cases with angiograms.

Encapsulated HCC can be found in non-Asian patients, and the radiographic and pathologic findings are similar to the descriptions in the Japanese series.

Key words: Liver neoplasms – Liver neoplasms, diagnosis – Liver neoplasms, computed tomography – Liver neoplasms, ultrasound – Liver neoplasms, angiography.

Hepatocellular carcinoma (HCC) demonstrates great diversity in its gross pathological appearance, pattern of growth, and long-term survival [1, 2]. This great diversity is due in part to the presence of many pathologic subtypes that may have quite different growth rates, and different potentials for local and distant spread. Some subtypes are more amenable to complete surgical excision due to their less invasive nature [2].

Japanese investigators have proposed a classification scheme for HCC that correlates with clinical course and prognosis [3–5]. It is based primarily upon tumor size and number of tumor nodules, growth pattern (expanding vs infiltrating), presence of a fibrous capsule, and degree of cirrhosis in the uninvolved liver parenchyma [3, 4].

The encapsulated type of HCC is characterized as a well-differentiated, slow-growing, noninvasive tumor [3–6]. The frequency of encapsulation in HCC appears to vary from 10.3% in large autopsy series [6] to approximately half of the HCCs in recent radiologic reports; however, not all cases contain pathological proof [7–9]. These studies refer only to a Japanese population where encapsulated HCC is a well-known entity.

Recently, Rummeny et al. [10] described a tumor capsule in 5 of 21 HCCs studied by magnetic resonance imaging (MRI). In this report, however, there is no specific mention of the racial extraction of the patients, and it contains no correlation with sonographic, computed tomography, or angiographic findings.

To our knowledge, there are no reports analyzing the radiographic appearance of encapsulated HCC in the U.S. population of non-Asian origin in a series with pathologic correlation in all cases.

This retrospective study was undertaken to determine if encapsulated HCC can be identified ra-

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diographically in cases in our file by applying the parameters described by Japanese authors.

Materials and Methods

The records of all cases of pathologically proven usual or typical HCC that included two or more imaging studies [computed tomography (CT), ultrasound (US), or angiography] in addition to plain radiographs were retrospectively reviewed. Fibrolamellar, clear cell, and undifferentiated cell types of HCC were excluded from this study group since, in our opinion, they likely represent malignancies distinct from typical HCC. After excluding these cases, the total number of cases was 73.

Phototransparencies of gross specimens and pathologic or surgical reports of these 73 cases were reviewed to determine if a capsule was present. Measurement of the capsule thickness was obtained from the pathological reports and the gross phototransparencies using the scale included in each photo. The presence of a continuous capsule around the tumor and a minimum 3 mm thickness was required for study participation. Eight cases met these criteria. In 12 other cases the presence of a capsule was suspected either from the gross photographs or the radiologic studies, but was not well documented in the pathologic records. In these 12 cases, pathologic slides were reviewed, and in 3 it was clear that a capsule (at least 3 mm thick) was present. In the remaining 9 cases either the periphery of the tumor was not included in the histologic section, or a capsule was not seen at the periphery of the tumor. Thus, in a total of 11 cases we positively identified capsules but did not definitely exclude capsules in all other cases. The incidence of encapsulated HCC in this study, therefore, may be underestimated.

In all 11 cases where a capsule was demonstrated, plain radiographs, contrast enhanced computed tomography (CECT), US, and angiographic images were analyzed to determine the radiographic characteristics of the encapsulated tumors. Demographic and laboratory data were analyzed when available.

Results

Clinical Presentation

The patients studied included 7 men and 4 women ranging in age from 26 to 91 years (mean 63.8). Three patients had hemochromatosis, and the youngest patient had a history of multiple hepatic adenomas and oral contraceptive use for three years prior to the diagnosis of HCC. From the histories obtained in the medical records, no patient was of Asian extraction.

Four patients presented with abdominal pain, which was localized to the right upper quadrant or epigastric region. Two patients presented with anemia and 2 patients presented with weight loss. Clinical presentation in the remaining patients was unknown. α-Fetoprotein was recorded in 4 patients. There was moderate elevation in 3 patients (18, 2156, and 2296 ng/ml) and marked elevation in 1 (8000 ng/ml).

Pathologic Findings

All tumors were typical HCC and well differentiated with trabecular cell patterns. One case was multicentric. In 5 cases tumor size was recorded ranging in size from 21×19 to 5×5 cm (average size 12×9.6 cm). Four cases had normal adjacent liver parenchyma, 2 showed micronodular cirrhosis, 2 showed mixed micro- and macronodular cirrhosis, and 3 had fatty change of the liver.

The fibrous capsule was composed of collagen and reticulum fibers (Fig. 1A and B). Pathologic reports indicated that vascular invasion into the portal vein or one of its branches was present in 3 cases. The tumor extended through the capsule into the adjacent liver parenchyma in 2 cases.

Radiologic Findings

Plain films of the abdomen were available in all cases and in 5 there was mass effect demonstrated by displacement of air-filled bowel loops. Calcification was not seen in any case.

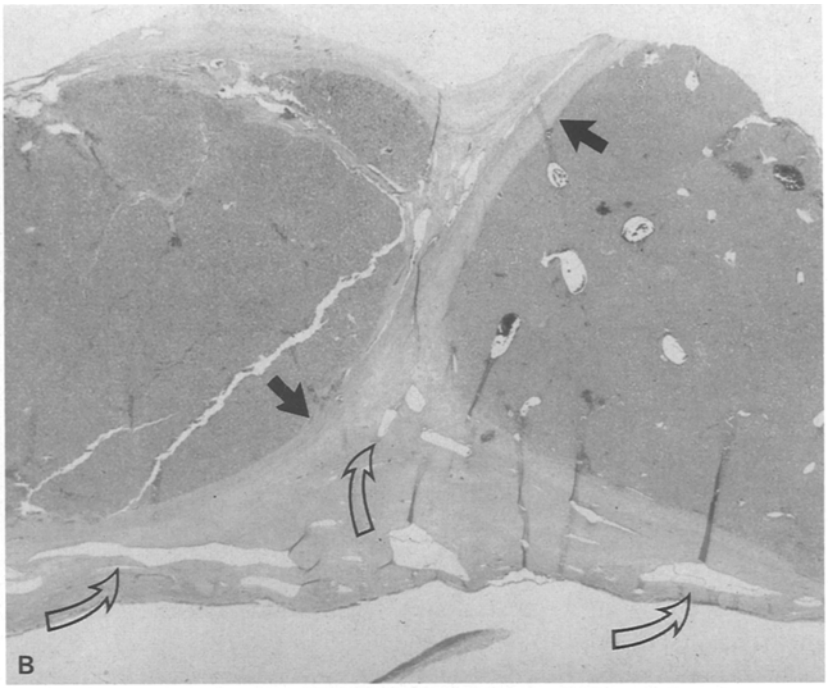
The CECT was available in 9 cases. A hyperdense rim that surrounded the tumor was identified in 5 cases (55%) (Fig. 2A and B). The rim ranged from 3 to 15 mm in thickness and corresponded to the capsule. The tumors were hypodense in relation to normal liver. They were well defined, had smooth margins, and appeared to displace portal branches. No calcifications were detected in any case.

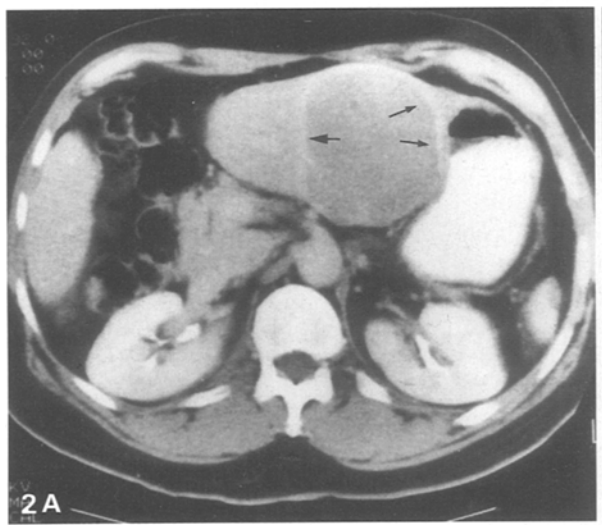
Six patients had ultrasonograms. All lesions were well defined and in 4 cases (67%) an anechoic halo was present at the periphery of the tumor corresponding to the capsule (Fig. 3). The lesions demonstrated a variable pattern of echogenicity, with 2 being hypoechoic, 2 hyperechoic, and 2 mixed echogenicity, compared to surrounding liver.

Selective celiac angiography was performed in 8 patients. In 5 cases (62%) a distinct avascular zone measuring 2–5 mm was seen on late arterial phase films, adjacent to the mass and corresponding to the fibrous capsule (Fig. 4A and B).

Discussion

Hepatocellular carcinoma is the most common form of primary hepatic carcinoma worldwide, and the median survival for all stages combined is approximately four months [2]. Despite this poor overall prognosis, encapsulated HCC has a significantly greater untreated median survival time of 17.3 months [6]. In addition, recent reports suggest





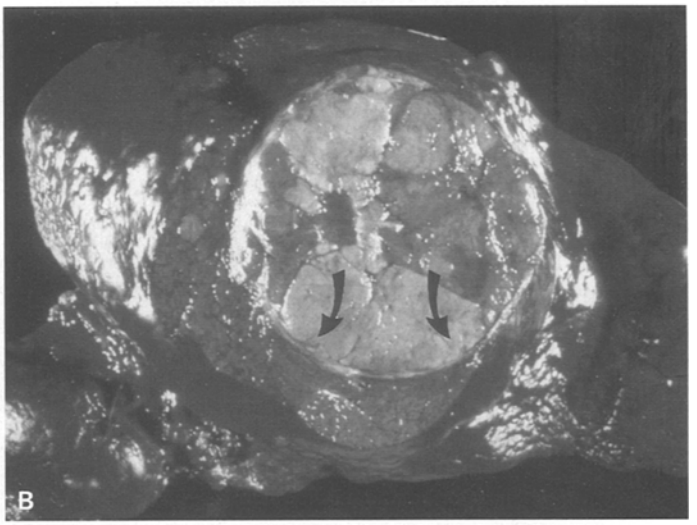


Fig. 1. Encapsulated HCC, gross and microscopic findings. **A** Cut section of liver demonstrates a well-marginated HCC with a central stellate area of hemorrhage. Note the capsule and the band of fibrous tissue surrounding the tumor (*arrows*). **B** Low power field demonstrates the capsule (*solid arrows*) well demarcated from the tumor. Note the vessels (*open arrows*) that run within the capsular surface.

Fig. 2. Encapsulated HCC: CT appearance. **A** Enhanced CT demonstrates a well-defined homogeneous mass in the lateral segment of the left lobe of the liver. Note the thin enhancing rim (*arrows*), corresponding to the capsule. **B** Correlating specimen shows the well-defined margin of this tumor, as well as the capsule (*arrows*).

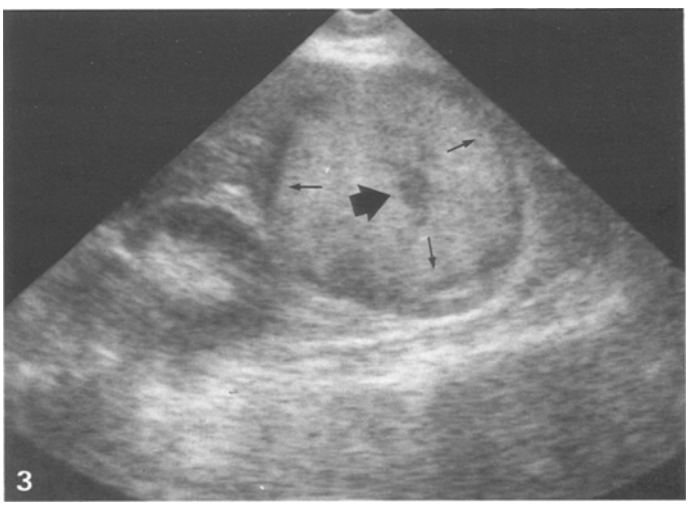


Fig. 3. Encapsulated HCC: sonographic appearance. Ultrasound demonstrates a band of decreased echogenicity (*arrows*) surrounding a pedunculated HCC. Note the central stellate hypoechoic area within the echogenic tumor (*arrowhead*). This correlates with findings of Fig. 1A.

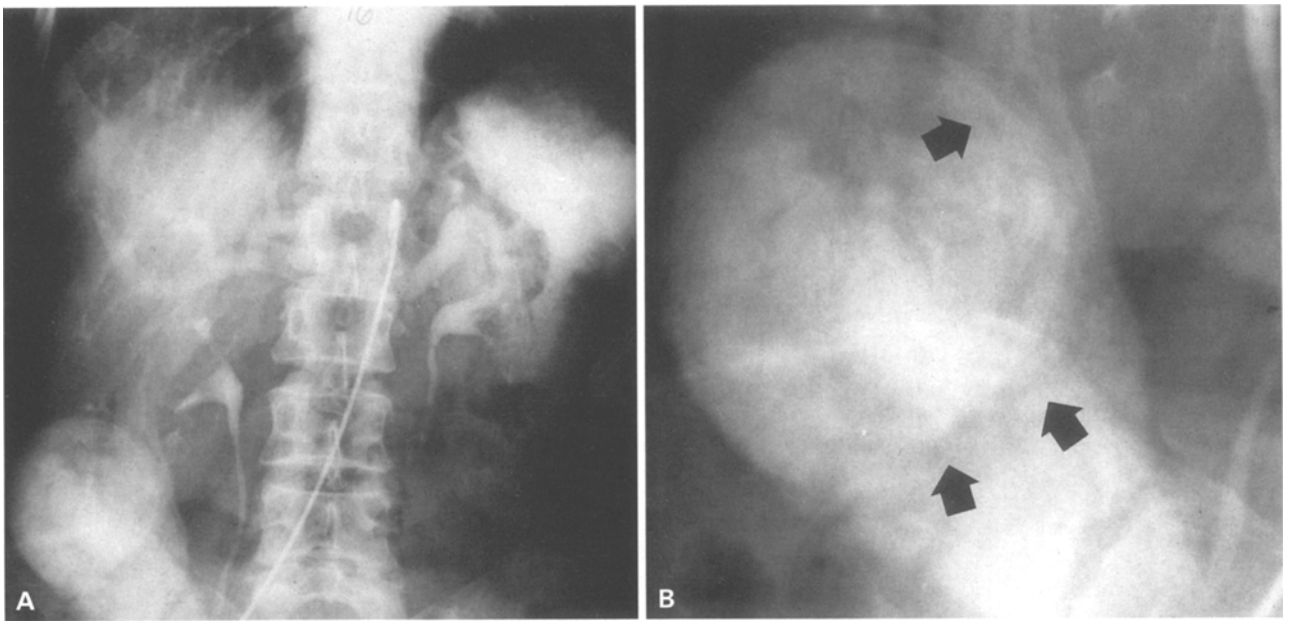


Fig. 4. **A** Selective celiac angiogram shows a hypervascular mass at the inferior aspect of the right lobe of the liver. **B** Close-up view of the mass clearly shows a radiolucent halo (*arrows*).

that hepatic dearterialization of encapsulated HCC with or without combined surgical resection may greatly prolong life expectancy [6, 11]. Therefore, radiologic detection of encapsulated HCC is prognostically of great importance and will influence decisions regarding treatment options.

We were able to identify the encapsulated form of HCC in 15% of our cases. It is possible that some cases of encapsulated HCC were not included since we applied strict criteria (3 mm thickness, continuity around the tumor, and gross/microscopic proof) to approach the parameters defined by Okuda et al. [6]. In his autopsy series of 159 cases of HCC in the Japanese population, this author found 26 cases (10.3%) of encapsulated HCC. Although radiologic series have reported a higher (up to 60%) frequency of encapsulated HCC [7–10] in Japanese patients, we wanted to minimize errors derived from a retrospective review of data and we only included cases with an incontrovertible presence of a capsule.

The male to female ratio of 1.75:1 is indicative of a greater occurrence of encapsulated HCC in women than in HCC overall where the male to female ratio is about 4:1 [1]. There was an association with cirrhosis (54%) and it is interesting that 3 patients with encapsulated HCC had hemochromatosis. This association has not been addressed in other reports [2, 6–10]. The clinical presentations of abdominal pain, anemia, and weight loss are common in all forms of HCC. That the elevation was moderate in 3 of the 4 cases where α-fetoprotein was available may be related to the presence of a capsule.

Portal venous invasion occurred in 3 cases of encapsulated HCC (27%), which is lower than the 42% reported by Okuda [6] and much lower than the 70–90% frequency seen with multinodular and massive types of nonencapsulated HCC [4]. This seems to indicate the lower propensity of this form of HCC to invade adjacent structures, due to the presence of a fibrous capsule.

Fibrous capsules are generally enhancing probably due to the large vascular structures that are frequently found incorporated into the capsule, or due to closely applied normal vessels that are displaced by the mass [12, 13]. This would explain the hyperdense rim seen on CT.

It has been documented that the anechoic halo occasionally observed in both primary and secondary solid liver tumors results from the presence of a fibrous capsule [14, 15] or from peritumoral liver cell compression (pseudocapsule) [15].

The radiolucent avascular zone seen angiographically in the late capillary phase surrounding the mass has been reported to correspond to the fibrous capsule [5, 6, 16]. A feature that is suggestive of a capsule being present is the stretching of large vessels in a smooth spherical manner around the mass. This finding in the arterial phase

of the angiogram should encourage the search for the radiolucent avascular halo on late films.

Our imaging findings of a hyperdense peripheral rim in 5 of 9 cases (55%) with CECT scans of an anechoic halo in 4 of 6 cases (67%) with ultrasonograms, and a distinctive avascular zone in 5 of 8 cases (62%) with selective celiac arteriograms have been well documented by Japanese authors [9, 12, 14, 16].

Although it appears difficult to reconcile that the capsule has enhancement by CT and appears avascular angiographically, this has been explained by the different spatial and contrast resolution of both techniques [16].

The major limitation of our study is that there were no data available pertaining to the survival or the clinical course of these patients with encapsulated HCC.

In conclusion, encapsulated HCC was found in a significant (15%) percentage of our study group of U.S. patients without Asian extraction with typical HCC. This percentage may underestimate the true incidence of encapsulated HCCs in our population due our strict selection process.

The fibrous capsule may be suggested radiographically when a hyperdense peripheral rim is detected on CECT, an anechoic margin or halo is seen in US, or a peripheral avascular zone is seen on capillary selective angiograms. Recently, it has been reported that by MRI the capsule appears as a hypointense rim [10].

The relevance of detecting by imaging a capsule in HCC is that, according to the Japanese literature, there is a better prognosis for this gross subtype of HCC than in nonencapsulated tumors. Encapsulated HCC can be found in non-Asian patients, and the radiographic and pathologic findings are similar to descriptions in the Japanese series.

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