Differentiation of adrenal tumors in patients with hepatocellular carcinoma: Adrenal adenoma *versus* metastasis

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ABSTRACT

Objective: To investigate whether computed tomography (CT) attenuation test for differential diagnosis of adrenal nodule is applicable in patients with hepatocellular carcinoma (HCC) which shows similar image characteristics to adrenal adenoma.

Materials and methods: This retrospective study was approved by our institutional review board, and the requirement for informed consent from study patients was waived. Searching picture archiving and communication system, we identified 3678 patients with HCC who underwent upper abdominal unenhanced CT scans between April 2002 and March 2010, and 114 adrenal nodules (39 adenomas and 75 metastases) were included for analysis. Ten nodules were confirmed pathologically while 104 had imaging diagnosis (enlarged or emerged during the study period). Size, CT number, and the internal characteristics of the lesions were recorded.

Results: Mean CT numbers of adrenal adenomas were significantly lower than those of metastases ($P < 0.0001$, *t*-test) on unenhanced CT. Thresholds of 17 and 33 Hounsfield units (HU) provided the following sensitivity, specificity, and accuracy: 46.2%, 100%, and 81.6% at 17 HU, and 94.9%, 89.3%, and 91.2% at 33 HU, respectively. The area under receiver operating characteristic curve for the CT number test was 0.96. Metastases were significantly larger than adrenal adenoma ($P = 0.009$, *t*-test). However, the accuracy of testing using mass size was 64.0% at most. All adenomas and metastases were depicted as homogeneous masses with the exception of two metastases that presented as heterogeneous masses (necrotic or lipomatous).

Conclusion: Adrenal adenomas can be differentiated from HCC metastases using CT number on unenhanced CT.

1. Introduction

Hepatocellular carcinoma (HCC) is the sixth-most prevalent carcinoma globally [1]. Extrahepatic metastasis is reported to occur in 13.5–42% of HCC patients, and the adrenal gland (12%) is the fourth-most common site for metastasis, following the lung (47%), lymph node (45%), and bone (37%) [2].

Adrenal incidentaloma, which is depicted at radiologic examination conducted for indications other than adrenal disease, is not rare. The prevalence of adrenal incidentaloma at computed tomography (CT) is reportedly 0.4–5% [3,4]. If the patient has no history of malignancy, the tumor is most likely an adenoma [3]. Mansmann reported that among patients with adrenal incidentalomas and a history of malignancy, 50–75% have metastasis [5]. As for the primary focus, many kinds of malignant tumors metastasize to the adrenal glands, including lung carcinoma (35%), gastric carcinoma (14%), esophageal carcinoma (12%), and liver/bile duct carcinoma (10%) [6]. In patients with HCC, the choice of treatment depends on whether adrenal incidentaloma is a benign adrenal adenoma or a metastasis; thus, precise diagnosis is very important.

There have been some reports of the differential diagnosis of adrenal incidentalomas [7–12], but to our knowledge none have focused on patients with HCC. Imaging characteristics of adrenal metastasis from HCC may be similar to those of adrenal adenoma. HCC is sometimes depicted as a heterogeneous mass on unenhanced CT with a low-attenuation area that represents fatty change [13], enhancement in the arterial phase, and washout in the delayed phase on dynamic contrast-enhanced CT [14]. These imaging characteristics are similar to those of adrenal adenomas, which have intracytoplasmic fat [7] and show early enhancement [15] and
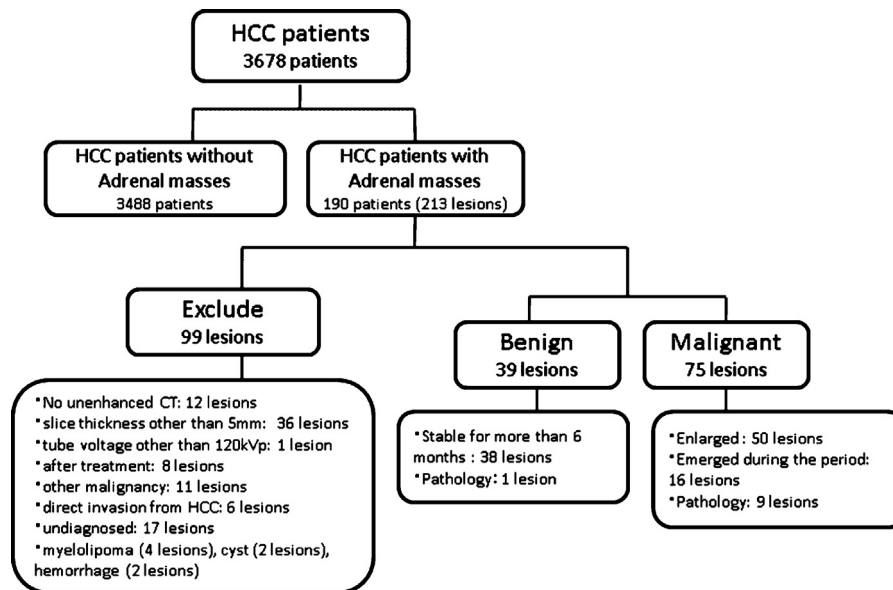
Fig. 1. Flow chart of patient inclusion and exclusion criteria.

washout in the delayed phase [8–11] on contrast-enhanced CT. It is unclear whether adrenal adenomas can be differentiated from adrenal metastases from HCC or not using only unenhanced CT. Studies of the differential diagnoses of adrenal masses in patients with HCC should be performed.

The purpose of our study was to examine whether adrenal adenomas can be accurately differentiated from adrenal metastases in patients with HCC using unenhanced CT.

2. Materials and methods

This retrospective study was approved by our institutional review board, and the requirement for informed consent from study patients was waived.

2.1. Subjects

The study subjects were selected by searching the picture archiving and communication system. All consecutive patients who underwent abdominal CT scans and were diagnosed with HCC in our single tertiary-care center from April, 2002 to March, 2010 were included. Patients who did not have HCC in the liver during this period, but had a past history of HCC, were also included because they had a potential for metastasis from HCC. HCC was defined as a mass showing enhancement in the arterial phase and washout in the delayed phase on dynamic contrast-enhanced CT, according to a previous study [14].

We identified 3678 patients with HCC, and all CT images were reviewed with respect to the presence of an adrenal mass. There were 213 adrenal masses in 190 patients. Exclusion criteria for adrenal lesions were: did not undergo unenhanced CT (12 lesions); underwent CT with a slice thickness other than 5 mm (36 lesions); underwent CT with a tube voltage other than 120 kVp (1 lesion); treated with transarterial embolization, radiofrequency ablation, chemotherapy, and radiation therapy (8 lesions); the presence of other malignancies (11 lesions); direct invasion from HCC in the liver (6 lesions); and no radiological diagnosis by the follow-up criteria described later nor pathological diagnosis (17 lesions). Myelolipoma (4 lesions), cysts (2 lesions), and hemorrhage (2 lesions) were also excluded according to previously reported criteria [8]. Of 213 adrenal nodules, 114 lesions (43 right, 71 left; mean

[SD] patient age 68.5 [8.0] years; 101 males, 13 females) were employed for analysis. A flow chart of the inclusion and exclusion criteria is shown in Fig. 1.

2.2. Referential criteria

Adrenal lesions were diagnosed pathologically or by imaging follow-up criteria. If an adrenal lesion did not increase in size for at least 6 months, it was diagnosed as an adrenal adenoma [9–11,16]. If an adrenal lesion was enlarged [9–11] or emerged during the study period [15], it was diagnosed as a metastasis.

2.3. CT scanning technique

Unenhanced CT images were obtained using multidetector-row CT scanners manufactured by GE Medical Systems, Toshiba, Hitachi, and Philips. Scanning parameters were as follows: slice thickness of 5 mm, slice interval of 5 mm, tube voltage of 120 kVp, and gantry rotation time of 250–1543 ms (mean, 710 ms). A total of 82 lesions were scanned with an automatic exposure control system, and 32 lesions were scanned with fixed milliampere seconds (mAs) (mean, 250 mAs; range, 75–428 mAs).

2.4. Clinical and image analysis

Patient sex and age at the first detection of the adrenal mass were recorded. TNM staging of HCCs was performed for both the benign adrenal adenoma group and the metastasis group according to the seventh edition of the classification of malignant tumors published by the International Union Against Cancer [17]. Lymph node metastasis was defined as 2 cm or larger in its longest diameter, according to a previous report, to avoid lymphadenopathy due to liver cirrhosis [18].

The observation period of the adrenal adenoma and the adrenal metastasis were recorded. The growth rate (changes in size per year) of adrenal metastasis was also recorded.

To analyze the imaging features of adrenal lesions, a commercial viewer (Centricity Radiology RA1000; General Electric Company, Barrington, IL, USA) was used. Adrenal lesions when first detected were recorded in terms of CT number, longest diameter (on transaxial CT images), and internal characteristics