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• BRIEF REPORTS •

Diagnosis and treatment of hepatic angiomyolipoma in 26 cases

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Abstract

AIM: To summarize the experience of the diagnosis and treatment of hepatic angiomyolipoma (HAML).

METHODS: The clinical, imaging and pathological features, and treatment strategies of 26 patients with HAML treated at the authors' institute between October 1998 and January 2003 were retrospectively analyzed. All the patients received liver resection and were followed up till the study. Immunohistochemical assays were performed with a panel of antibodies.

RESULTS: There was an obvious female predominance (21:5), and most of the patients (18/26) had no symptoms. Heterogeneous high echo was found in ultrasonography and punctiform or filiform vascular distribution pattern was found in color Doppler-sonography in most of the lesions (21/26). All of the 5 lesions further enhanced with Levovist showed early and prolonged enhancement. At contrast-enhanced spiral CT, the soft-tissue components of 24 lesions were markedly enhanced in the arterial phase and 18 lesions remained enhanced in the portal venous phase. MRI was performed in 9 patients, and showed hypointensity or hyperintensity on T1-weighted images and heterogeneous hyperintensity on T2-weighted images. Histopathologically, all lesions were composed of adipose tissues, smooth muscle and blood vessels with different proportions. Most lesions showed positive immunohistochemical staining for HMB45 (26/26), A103 (24/26) and SMA (24/26). All of the 26 patients showed a benign course with no sign of recurrence.

CONCLUSION: Preoperative radiological diagnosis of HAML is possible. The demonstration of intratumoral fat and central vessels is helpful in the diagnosis. HMB45, A103 and SMA are promising markers for pathologic diagnosis of HAML, and surgical resection is effective for the treatment of HAML.

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INTRODUCTION

Hepatic angiomyolipoma (HAML) is a rare benign mesenchymal neoplasm of the liver. Since its first description by Ishak in 1976[1], not more than 200 cases have been reported in the English literatures[2-7]. However, with recent progress in imaging diagnostic techniques, the reported cases of HAML are increasing in number, and the significance of accurate diagnosis is becoming more important clinically. The purpose of this study was to investigate the clinical, imaging and pathological features of HAML and to summarize our experience in the diagnosis and treatment of this disease.

MATERIALS AND METHODS

Patients and clinical data

Twenty-six patients with HAML were surgically treated in Liver Cancer Institute of Fudan University from October 1998 to January 2003. There was a marked female predominance (21/26) and the mean age was 44.3 with a range of 31 to 64 years. Most of the patients (18/26) had no symptoms and were detected incidentally by medical check-up. Seven of 26 patients had symptoms caused by tumor oppression and one patient had slight fever as a chief complaint. The average tumor size at detection was 6.1 cm ranging from 1.5 to 15 cm. None of them was found complicated with a diagnosis of tuberous sclerosis and renal AML. Concomitant hepatic hemangioma was found in one patient. None of them had the history of hepatitis virus infection. Serum alpha-fetoprotein (AFP) levels were all within normal limits.

Imaging examinations

All of the patients underwent ultrasonography, color Doppler-sonography and computer tomography (CT) examinations. Nine patients also received magnetic resonance imaging (MRI) examination.

Treatment and follow-up

Limited partial liver resections were performed in 19 patients, left lateral lobectomy in 4, left hemihepatectomy in 2, and right hemihepatectomy in 1. All the patients have been followed up till the study.

Pathological and immunochemical assays

Routine histopathological examination with hematoxylin and eosin staining was performed. Immunohistochemical studies were performed by the EnVision™ method using a panel of antibodies (HMB45, A103, smoothmuscle actin, S100, Vimentin and CK8) in all of the tumor tissues.

RESULTS

Imaging features

Most lesions (21/26) showed heterogeneous high echo in ultrasonography, and punctiform or filiform vascular distribution pattern in color Doppler-sonography. Five lesions were further enhanced with Levovist, and all of them were found to have early and prolonged enhancement.

In contrast-enhanced spiral CT examination, the soft-tissue components of 24 lesions were markedly enhanced in the arterial phase, and 18 lesions remained enhanced in the portal venous phase.

MRI was performed in 9 patients, hypointensity or hyperintensity was found on T1-weighted images and heterogeneous hyperintensity on T2-weighted images.

Histopathological and immunochemical characteristics

The tumors were well circumscribed but no obvious capsule could be found. The non-tumorous liver parenchyma was normal, and no cirrhosis was found. All tumors were composed of adipose tissues, smooth muscle and blood vessels in different proportions. In immunohistochemical studies, most tumors were positive for HMB45 (26/26), A103 (24/26), SMA (24/26), S100 (20/26) and Vimentin (16/26), but negative for CK8 (22/26).

Treatment and prognosis

All of the 26 patients received hepatectomy. Six patients were followed-up for more than one year and finally decided to receive operation because of the enlargement of the lesions. All the patients have been followed up since their surgical resection. No recurrence was found in any patient during the follow-up period.

DISCUSSION

Angiomyolipoma, which occurs relatively frequent in kidney, is a rare benign mesenchymal neoplasm of the liver. The tumor size of HAML at the first diagnosis is variable, ranging from 0.1 cm to ⩾36 cm. Clinically, most of the patients have no symptoms and are detected incidentally by medical check-ups. Patients with large tumors usually have some symptoms caused by tumor compression. The diagnosis of HAML before operation mainly depends on imaging examination.

According to our experience, typical performance of HAML is a smoothly contoured heterogeneous high echo lesion, with a well-defined border separating it from adjacent normal hepatic tissues by ultrasonography and punctiform or filiform vascular distribution pattern by color Doppler-sonography. In further enhanced imaging with Levovist, the tumor showed early and prolonged enhancement. The lesions appeared as hypodense, and adipose dense could be found in pre-contrast CT scans. In the arterial phase, the soft-tissue components of the lesions were markedly enhanced and central vessels could be found. In the portal venous phase, the lesions remained in enhancement[8]. As reported, the adipose fraction of HAML varied from 5 % to 90 %, so adipose signals could be found on MRI in most lesions. Sakamoto *et al*.[9] described MRI studies showing extensive enhancement on gadolinium-enhanced images. In addition, fat could be seen with great sensitivity on T1-weighted images as high-signal intensity. However, HAML showed various patterns of imaging features, because the relative proportions of vessels, muscle and fat varied widely from tumor to tumor. So, although diagnosis may be suggested by imaging methods, histological confirmation remains mandatory.

Histopathologically, in our study, most tumors were well-circumscribed, but not encapsulated. The lesions were composed of adipose tissue, smooth muscle and blood vessels in different proportions. The tissue components in the tumor were highly variable from case to case, and even between different areas of the same mass. According to the line of differentiation and predominance of tissue components, Tsui *et al*.[6] subcategorized the tumors into mixed, lipomatous (⩾ 70 % fat), myomatous (⩽ 10 % fat), and angiomatous types. We found that the mixed type was the most common category which comprised sheets of epithelioid muscle cells admixed with islands of adipocytes, abnormal vessels, and frequently, hematopoietic cells. Some authors advocated to diagnose HAML by fine-needle aspiration (FNA)[10], for the presence of adipocytes was a clue to the diagnosis. However, adipose tissue might be a minute fraction of HAML, in which FNA diagnosis may be difficult. So we think that immunohistochemical examination may be the only authoritative method to diagnose HAML. According to our results, all the 26 tumors were positive for HMB45, the staining was intense, granular, and concentrated in tumor cell perinuclear cytoplasm. For A103, 24 tumors showed strongly and diffusely granular cytoplasmic staining in the majority of myoid cells, the staining in the other two was only focal. Smooth muscle actin (SMA) staining was weak to moderate in epithelioid cells and strong in spindle cells in 24 tumors. So HMB45, A103 and SMA are promising markers in pathologic diagnosis of HAML.

Exclusion of hepatocellular carcinoma (HCC) is the most important issue in the diagnosis of HAML, because both kinds of the lesions show similar imaging characteristics, including rich blood flow detected in Doppler-sonography, early enhancement in CT contrast scan, etc. Most of the patients with HAML had no histories of hepatitis virus infection or negative for hepatitis marker, and had no liver cirrhosis, and AFP level was normal, which might be helpful in the differential diagnosis. In CT contrast scan, there are also differences in the peak time and duration of enhancement between HAML and HCC. Ahmadi *et al*.[11] reported that HAML showed early and prolonged enhancement (>4 min) with delayed peak enhancement at 40-80 seconds, as opposed to HCC which had peak enhancement at 10 seconds and absent or minimally delayed enhancement. Further more, differentiation from HCC with fatty metamorphosis can also be made based on the angiomyolipomas prolonged tumor enhancement (>6 min) relative to HCC. Fat suppression MRI was also reported to be successful in distinguishing HAML from HCC[12].

HAML is a benign lesion and often grows slowly without any clinical symptom, so conservative treatment with close follow-up is recommended after diagnosis. For the rarity of the cases most of which are diagnosed by pathology after operation, there has been no report about culture doubling time or growth velocity of HAML yet. In this series, one patient was followed up for five years before operation, the tumor increased from 4 cm to 10 cm in size. Another one was followed up for thirteen years before operation, the size of tumor increased from 1.5 cm to 5 cm.

Spontaneous rupture, later recurrence and vascular invasion of HAML have been reported[13-15]. So surgery may be recommended for patients with symptoms, for patients in whom diagnostic imaging can not exclude malignancy, and for patients in whom the tumor enlarges obviously in short time or shows extrahepatic growth and has a risk of spontaneous rupture. All our cases received hepatectomy and have been followed up till the study for a period between 1 month and 52 months, no mortality and serious morbidity were found in these patients. Follow-up information of the 26 cases showed a benign course with no signs of recurrences. So surgical resection is safe and effective for the treatment of HAML.

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