Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor of low- to intermediate-grade malignancy that occurs in the liver and other organs. Its etiology is unknown. We report a 57-year-old female with incidental finding of abnormal liver function by blood biochemistry studies. Multiphasic helical CT imaging revealed multifocal hypovascular nodules predominantly at the periphery of both hepatic lobes with concentric filling of contrast medium and delayed enhancement.

Key words: Computed tomography; Epithelioid hemangioendothelioma; Liver

Epithelioid hemangioendothelioma (EHE) was first described by Weiss and Enzinger in 1982 [1]. It is a rare vascular tumor of low- to intermediate-grade malignancy, with clinical course between that of a benign hemangioma and a malignant angiosarcoma [2, 3]. Etiology remains unknown. This tumor generally occurs in adults, with a female predominance. It arises in soft tissue, liver, lung, bone, and spleen [4]. The clinical manifestations of hepatic EHE are usually nonspecific. Some patients may be asymptomatic [2]. Complete surgical excision is recommended for resectable lesions. Orthotopic liver transplantation remains the only treatment option in selected patients with extensive liver involvement or with rapidly progressive hepatic failure [2].

Pathologic diagnosis may be difficult and misdiagnosis is not uncommon [2]. Therefore, radiologists should be acquainted with the imaging features of this entity to help make correct diagnosis. Here we present a case of hepatic EHE, and describe the multiphasic helical CT imaging features.

CASE REPORT

The patient, a 57-year-old female, came to our hospital for treatment of urinary tract infection. Blood biochemistry revealed mild elevation of aminotransferases (SGOT and SGPT). Subsequent abdominal sonography demonstrated multiple hypoechoic nodules in the liver. Multiphasic helical CT scanning was performed for further evaluation. After initiation of contrast medium injection (100ml) at 2.0 to 3.5ml/s, the helical acquisition started at 23 seconds for the arterial phase, at 60 seconds for the portal venous phase, and at 4 minutes for the delayed phase. Multiple ovoid and round nodular lesions, ranging from 1 to 2cm in diameter, were found at both lobes of the liver (Fig. 1). No calcification was seen. Most of the lesions were located at the periphery of the liver parenchyma, without causing retraction of the liver capsule. These lesions were isodense to the surrounding liver parenchyma, which demonstrated mild fatty infiltra-
tion. No obvious enhancement was detected in these lesions during the arterial phase. Rim enhancement was depicted at the portal venous phase. At the delayed phase, homogeneous enhancement of these lesions was shown. Metastasis of unknown origin was the first impression. The levels of the serum carcinoembryonic antigen and alfa fetoprotein were within normal limits. Chest radiography, breast sonography, panendoscopy, and colonoscopy were done, but all showed negative findings. Liver biopsy was recommended, but the patient refused.

Eight months later, a follow-up CT scan demonstrated stable hepatic lesions. The patient agreed to undergo a percutaneous liver biopsy under sonographic guidance. Pathologic examination showed a few individual or rarely tiny groups of atypical spindle to mildly plump short fusiform (mildly “epithelioid”) cells with one or two to multiple hyperchromatic nuclei and small amount of cytoplasm scattered among the hepatic cords, which were unremarkable (Fig. 2a). The atypical cells showed positive stain for vimentin, factor VIII-related antigen, and CD34. The diagnosis was peripheral portion of hepatic epithelioid hemangioendothelioma. A repeat needle biopsy was performed in another hospital two months later, and revealed the scarred pattern of hepatic EHE, which was characterized by dense fibrous stroma containing sparse oval plump tumor cells and large intracellular vacuoles (lumina) (Fig. 2b).

Figure 1. Multiphasic helical CT scan reveals multiple nodules at both lobes of the liver. Shown here are three nodules of the same slice at different phases of acquisition. a. Before enhancement, the nodules are isodense to surrounding liver parenchyma, which shows mild fatty infiltration. b. No obvious enhancement of the tumors is observed at the arterial phase. c. Rim enhancement (arrow head) is found in three peripheral nodular lesions (arrow) during the portal venous phase. d. At the delayed phase, homogeneous enhancement (arrow) is demonstrated in these nodules. Neither liver capsular retraction nor calcification is shown.
EHE is a rare vascular tumor of low- to intermediate-grade malignancy that occurs in soft tissue, liver, lung, bone, and spleen. Etiology is unknown. Most of the patients with hepatic EHE are adult female with highest tumor incidence in the age 30-40 years range [2]. The clinical manifestations are nonspecific, such as right upper quadrant pain or weight loss. Some patients may present with liver failure, Budd-Chiari syndrome, or portal hypertension; other patients may be asymptomatic. The clinical course and prognosis of the hepatic EHE are variable and unpredictable, with a 5-year survival rate of 43% [2].

Histopathologically, the tumors are comprised of dendritic and epithelioid cells that often contained vacuoles representing intracellular lumina. The stroma is fibrous, with myxohyaline areas. The tumors grow in an infiltrative pattern with infiltration of epithelioid cells in the preexisting sinusoids, terminal hepatic venules, and portal vein branches. Invasion of hepatic and portal veins is characteristic, which may cause formation of intravenous polypoid or glomeruloid projections comprised of epithelioid cells and even venous occlusion. As the tumor nodules infiltrate and destroy hepatic parenchyma, they are associated with progressive fibrosis, which becomes sufficiently dense and sclerotic to cut off the circulation to the neoplastic cells. Immunohistochemically, all tumors are positive for at least one endothelial marker (factor VIII-related antigen, CD34, and CD31), and this is the key to diagnosis [2].

At imaging studies, two different types of hepatic EHE have been described, nodular and diffuse [5-9]. The nodular type is considered an early manifestation of the disease. In this stage, multifocal nodules varying in size from a few millimeters to several centimeters are observed. These lesions tend to be located in the periphery of the liver, and may cause retraction of the liver capsule due to a fibrotic reaction [6]. Calcification may be seen [2, 10]. These solid tumors characteristically have a dense fibrotic, hypovascular central area and a peripheral hyperemic rim [7]. Therefore, a rim enhancement is usually observed on the contrast-enhanced CT scan and MR imaging. The lesions increase in size and coalesce to result in diffuse type of the disease. In this stage, the tumor infiltrates the surrounding liver parenchyma, invading the hepatic and portal veins and obliterating them, with resultant decreased perfusion of the tumor areas and increased blood flow to the non-involved areas [8]. Budd-Chiari syndrome, portal hypertension, secondary splenomegaly, ascites, and compensatory enlargement of the non-involved liver parenchyma may occur [6, 9].

In our patient, multiple peripheral small nodules corresponded to the early nodular stage of the disease. No apparent tumor enlargement was found during 8 months of follow-up, indicating low malignant potential of this tumor. After administration of
contrast medium, gradual centripetal enhancement reflected hypovascularity and fibrous stroma within the tumor. As mentioned above, EHEs contain variable amount of fibrous stroma, one main histologic feature, which is responsible for prolonged and delayed contrast enhancement on CT images [11]. Although many reports described enhancement of a peripheral hyperemic zone surrounding a hypovascular central zone in their small series of EHE cases, they did not correlate enhancement pattern with lesion size. Smaller EHE lesions may have a more homogeneous fibrous myxoid stroma, which may account for uniform enhancement at the delayed phase [7, 11]. Capsular retraction was not observed, which is seen in fewer than 25% of patients [10]. This feature is suggestive of, but not specific for, diagnosis of EHE.

Multifocal hepatic neoplasms are not uncommon in our daily practice, and most are caused by hemangioma, metastasis, and hepatocellular carcinoma. Multiphasic helical CT scan depicts hypovascular and fibrous nature of this tumor, and may aid in narrowing the spectrum of differential diagnosis to EHE, metastasis, and multifocal cholangiocarcinoma (also containing abundant fibrous tissue). Final diagnosis depends on pathologic study of the lesion.

In conclusion, we present a case of hepatic EHE in which multiphasic helical CT scan was helpful in suggesting the diagnosis. Signs revealed by CT scan are multifocal hypovascular nodules, peripheral location, concentric filling of contrast medium, and delayed enhancement due to fibrous stroma.

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**REFERENCE**

肝臟的上皮狀血管內皮瘤：電腦斷層之影像表現

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上皮狀血管內皮瘤是一種罕見的低至中度惡性血管腫瘤，可發現於肝臟及其他器官。發生原因仍不明。我們報告一名57歲女性於血液檢查中意外發現肝功能異常。多相螺旋式電腦斷層掃瞄發覺有多顆低血管性小結節主要分布於左右兩葉肝臟的周邊，並呈現出向心的顯影劑填充及延遲顯影。

關鍵詞：電腦斷層；上皮狀血管內皮瘤；肝臟