

Case Report

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Resectable single hepatic epithelioid hemangioendothelioma in the left lobe of the liver: a case report

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Abstract: Hepatic epithelioid hemangioendothelioma (HEHE) is an extremely rare malignancy of vascular origin. When most patients with HEHE are diagnosed, they have a diffuse nodular phenotype, which is usually unresectable. A single nodular phenotype is found in only a small proportion (13%) of patients, and most are reported to be located in the right lobe of the liver. Although the prognosis of HEHE is considered more favorable than that of other hepatic malignant tumors, the 5-year survival rate is reported to be 64% after treatment. Herein, we present an unusual case of resectable HEHE of a single nodular type in the left lobe of the liver. The patient survived 15 years without recurrence after the multimodal treatment of radical resection and postoperative chemotherapy with thalidomide. The aim of the present study is to emphasize that multimodal treatment of radical resection followed by chemotherapy with thalidomide may achieve a relatively good survival outcome in patients with resectable HEHE of a single nodular type.

Keywords: Hepatic epithelioid hemangioendothelioma; Single nodular; Early surgery; Chemotherapy.

1 Introduction

Derived from endothelial cells, hepatic epithelioid hemangioendothelioma (HEHE) is an extremely rare vascular tumor with unpredictable malignant potential [1, 2]. The clinical features and treatment options of HEHE remain unclear. On the basis of imaging features, HEHE can be divided into two forms: single nodular and diffuse nodular [3, 4]. Most patients diagnosed with HEHE have a diffuse nodular type involving both lobes of the liver, which is usually unresectable. The single nodular type is found in only a minor proportion (13%) of patients, and most single tumors are reported to be situated in the right lobe of the liver [5]. Without timely treatment, the single nodular type of HEHE can easily progress to the diffuse nodular type [6], which is considered an advanced tumor stage. The prognosis of HEHE is considered more favorable than that of other hepatic malignant tumors. It is reported that patients with HEHE have a 5-year survival rate of 64% after treatment [7].

Herein, we present an unusual case of resectable HEHE of the single nodular type in the left lobe of the liver in a patient who survived 15 years after multimodal treatment of radical resection and postoperative chemotherapy with thalidomide. Our aim is to focus on the recognition of the clinical features and treatment options for this type of HEHE.

2 Case report

A 62-year-old man presented with nonspecific gastrointestinal symptoms, and a liver tumor was fortuitously discovered in a routine health examination. His past medical history was significant for chronic hepatitis B infection over a period of 20 years. Physical examination was unremarkable. Pertinent laboratory investigations (including routine blood and biochemical analyses) were within the normal reference range, except for elevated serum

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tumor markers of carcinoembryonic antigen (23.82 ng/ml; normal, <3.4) and CA19-9 (48.62 U/mL, normal, <22). Magnetic resonance imaging revealed a lesion with inhomogeneous enhancement in the left lateral lobe of the liver, measuring 3.9 cm × 3.8 cm (Figure 1). An initial diagnosis of hepatocellular carcinoma was considered. Positron emission tomography-computed tomography (PET-CT) was then performed to find the possible primary site; however, there was no evidence of extrahepatic disease, thus supporting a diagnosis of a primary liver tumor. Because the patient was anxious for a preoperative diagnosis, fine needle biopsy of the tumor was performed to achieve a definitive diagnosis. Pathological examination of the biopsy specimen revealed uneven pleomorphic epithelioid tumor cells, which spread into the sinusoids. Epithelioid tumor cells were filled with vacuoles, some of which contained erythrocytes (Figure 2A). Immunohistochemically, the tumor cells were positive for endothelial marker CD34 (Figure 2B), CD31 (Figure 2C) and factor VIII-related antigen (Figure 2D), confirming the vascular nature of the tumor and contributing to the final diagnosis of HEHE.

The patient was treated with complete tumor resection. Macroscopically, the tumor appeared as a grey-white, firm, poorly circumscribed mass, measuring 4.7 × 4.0 × 3.6 cm. Subsequently, the patient underwent 6 months of chemotherapy with thalidomide, a kind of anti-angiogenesis drug. The starting dose of thalidomide was 100 mg daily, which was increased to 200 mg per day after a month. It was well tolerated without significant side effects. No radiation therapy was performed. The patient was followed at our outpatient department and survived 15 years free of recurrence after surgery.

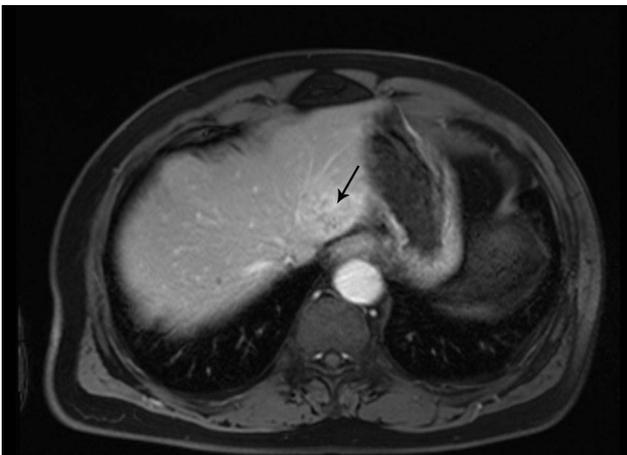


Figure 1: Abdominal magnetic resonance imaging findings. A contrast-enhanced T1W MRI showed a single, round, hypodense lesion with peripheral contrast enhancement in the left lobe of the liver.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from patient whose case was presented in this study.

3 Discussion

Epithelioid hemangioendothelioma is a rare vascular tumor that may occur at various sites such as the skin, bone, stomach, and spleen and was originally described by Weiss and Enzinger in 1982 [8]. The World Health Organization has recognised it as a malignant neoplasm, and its grade of malignancy is unpredictable. HEHE is extremely rare, with an incidence of fewer than 0.1 per 100,000 in the population [9]. In 1984, Ishak et al first reported a series of 32 patients with HEHE, [1] and since then, approximately 200 cases have been reported in the English literature [2].

The pathogenesis of HEHE is still unclear, and oral contraceptives, alcohol, and viruses infection may be risk factors [10, 11]. It usually occurs in women aged 20-40 years [7]. HEHE presents with nonspecific and variable clinical manifestations, ranging from asymptomatic, epi-

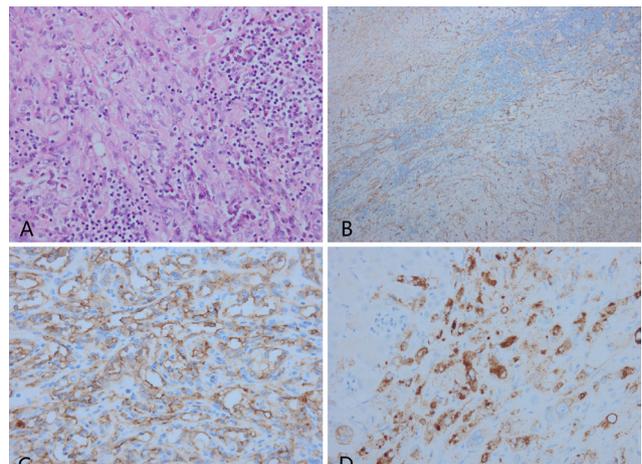


Figure 2: Pathological investigation identified hepatic epithelioid hemangioendothelioma: (A) Tumor cells manifested as epithelioid with rich cytoplasm, some of which revealed intracytoplasmic vascular lumen formation containing erythrocytes (HE×400). (B) immunohistochemistry showed that the tumor was positive for CD34 (HE×100); (C) immunohistochemistry showed that the tumor was positive for CD31 (HE×400); (D) immunohistochemistry showed that the tumor was positive for factor VIII-related antigen (HE×400).

gastric pain, weight loss, and hepatomegaly to liver failure [12, 13]. Imaging examinations such as computed tomography or magnetic resonance scanning may be helpful for making the diagnosis, which typically reveals multiple hepatic nodules with capsular retraction and target-like configuration [14]. However, it is easily misdiagnosed as metastatic carcinoma. PET-CT has been recently shown to be useful for differentiating HEHE from metastatic carcinoma, with the metastatic carcinoma showing hepatic lesions with high glycometabolism. However, PET-CT is very expensive and sometimes only provides a reference, without revealing a definite diagnosis.

Definitive diagnosis of HEHE is dependent on the histopathologic examination, and a fine needle biopsy of the tumor may be performed to achieve an early diagnosis. The characteristic pathological features of HEHE include intracellular vascular lumina formation, sinusoidal infiltration, vessel obliteration, and cellular pleomorphism [7]. Immunohistochemically, positive reactivity to endothelial markers such as vimentin, factor VIII-related antigen, CD31 and CD34 supports the endothelial nature of the tumor cells. The angiogenic vascular endothelial growth factor (VEGF) has also been found positive in HEHE [15].

No consensus exists for a strategy of standardized treatment owing to limited data and the rarity of the disease. However, radical surgical resection or liver transplantation is currently considered the most effective treatment. Most cases are at an advanced tumor stage at the time of diagnosis, and surgical resection is appropriate only for part of the single nodular type of HEHE involving only one lobe of the liver without extrahepatic metastasis. Grotz et al [16] in a study involving 30 patients with HEHE suggested that patients with a nodule smaller than 10 cm should undergo liver resection, while those with single nodules larger than 10 cm or multiple lesions should undergo liver transplantation. Therefore, an early diagnosis is of much importance, so as to prevent the disease from progressing to advanced tumor stages. Other modalities such as chemotherapy, radiotherapy, and thermoablation are also reported, but their benefits are difficult to evaluate owing to a lack of clinical data.

The clinical course of HEHE is variable, ranging from spontaneous regression and long-term survival without any treatment to a rapidly progressive and deadly course. In total, the prognosis of HEHE is considered more favorable than that of other hepatic malignant tumors [17]; the 5-year survival rate of HEHE is 64% after treatment.

Thalidomide is a kind of anti-angiogenesis drug. Chemotherapy with thalidomide has been proposed in the treatment of HEHE. There have been two case reports of HEHE metastatic to the lungs in which the patients were

successfully treated with thalidomide as an anti-angiogenic therapy. In the present case, the patient had a single nodular type of HEHE, and we chose aggressive surgical resection of the tumor followed by 6 months of adjuvant chemotherapy with thalidomide [18, 19]. However, given its extremely rare incidence, the effectiveness and safety of this chemotherapeutic substance needs further examination. In addition, a multicentric prospective study recruiting more patients with resectable HEHE of a single nodule type is needed to evaluate its long-term outcomes.

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Conflict of interests: We declare that we have no any conflict of interests.

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