

Primary Hepatic Epithelioid Hemangioendothelioma: A Case Report and Literature Review

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Case report

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Abstract

Background: Epithelioid hemangioendothelioma (EHE) is a low-grade malignant tumor of vascular origin. The rarity of HEHE make the diagnosis and treatment of this entity very challenging.

Case presentation: We report a case of a 69-year-old female patient suffering from HEHE who complained of "Abdominal distension pain with dizziness, appetite loss more than half a month". Enhanced computed tomography (CT) of the upper abdomen indicated multiple space-occupying lesions in the liver. The pathological results of color ultrasound puncture suggested HEHE. We performed transcatheter arterial chemoembolization (TACE) and relevant examinations according to the patient's condition and the patient choice. Follow-up examinations 18 months after discharge did not demonstrate tumor recurrence.

Conclusions:

HEHE is a relatively rare hepatic malignant tumor derived from vascular endothelial cells, with low incidence, atypical clinical manifestations, difficult diagnosis, and the diagnosis can only be confirmed with pathological results. Currently, appropriate treatment methods should be selected according to the specific conditions of patients.

Background

EHE is a rare malignant tumor originated from vascular endothelial cells^[1], which can occur in all parts of the body, mostly in the soft tissues of the limbs, and can also be seen in other organs such as lung, bone, spleen and brain^[2]. HEHE is rare, with an incidence of about 0.1 in 100,000^[3]. The etiology of HEHE is not yet clear. The possible etiological factors include oral contraceptives, progesterone imbalance, liver injury, alcohol, chloroethylene pollution, viral hepatitis, cirrhosis, long-term use of immunosuppressive agents after liver transplantation, etc^[1]. The CT imaging features of HEHE mainly included: capsular retraction, calcification, halo sign and target sign^[4]. The diagnosis of HEHE was mainly based on pathology. Microscopically, the tumor cells were mostly arranged in a dense and disordered pattern, with a cord-like or nested cord-like distribution, and the cell morphology was mostly epithelioid, fusiform or irregular. Hypertrophy irregular nuclei, uneven chromatin or coarse granular; The positive rates of CD34, CA31 and Vimentin were the highest^[5]. We report an elderly female patient with HEHE who was treated by TACE.

Case Presentation

A 69-year-old woman complained of abdominal distension pain with dizziness, appetite loss more than half a month. Before half a month, without obvious inducement, the patient developed upper abdominal pain, which was gradually relieved after rest, with Jaundice, loss of appetite and fatigue. There were no significant comorbidities at admission. The patient was a non-smoker, without personal or family history of other diseases. Physical examination upon admission: Jaundice, upper abdominal pain, no hepatic

palm, no spider angionma, a 7cm old surgical scar in the right abdomen, Murphy's sign(-), Shifting dullness(-). Laboratory examinations Laboratory studies of serum α -fetoprotein (AFP), carcino-embryonic antigen (CEA), and Glucoprotein antigen 199(CA19-9) revealed that these values were within normal limits. Liver function, renal function, electrolyte, coagulation function, blood routine, urine routine, qualitative analysis of hepatitis B, HAV-IgM/IgG, HCV-IgG, HDV-IgG and HEV-IgG were all normal. Imaging examinations Enhanced computed tomography (CT) of the upper abdomen (figure 1) : the surface of the liver was smooth, and multiple circular low-density shadows were observed in the liver, the larger one was located in the posterior segment of the right lobe of the liver, with a size of about 5.3×2.6cm. Contrast-enhanced scan revealed mild circumferential enhancement and intrahepatic bile duct dilation. Imaging diagnosis: Multiple Liver Space-occupying lesions. Chest high resolution CT plain scan: multiple micro nodules scattered in both lungs, metastasis is not excluded, follow-up review. Pet-ct (figure 2): 1. Multiple intrahepatic space occupying, increased glucose metabolism, malignant lesions were considered. 2. Multiple nodules in both lungs, no increase in glucose metabolism, nature to be determined. We decided to do an ultrasound-guided biopsy of the liver. Ultrasound-guided percutaneous liver biopsy revealed hepatic epithelioid hemangioendothelioma. Immunohistochemical (figure 3): Vim [+] CD31[+] CD34[+] F8 [+] EMA [-] TTF1 [-] Ki-67 [+] 2% - 5%. According to clinical, imaging and pathological findings, it was diagnosed as hepatic epithelioid hemangioendothelioma. We performed transcatheter arterial chemoembolization (TACE) and relevant examinations according to the patient's condition and the patient choice. Follow-up CT showed no tumor recurrence after 18 months.

Discussion

EHE was first reported by Wesis and Enzinger in 1982^[6], and HEHE was first described by Ishak in 1984 [7]. Epithelioid endothelial cell tumor is a rare malignant tumor originated in endothelial cells^[1], can be in each part, with limb soft tissue for many, also seen in other organs such as lung, bone, spleen, brain^[2]. HEHE etiology has not been clearly identified, the possible pathogenic factors include oral contraceptives, progesterone disorders, liver trauma, alcohol, vinyl chloride pollution, viral hepatitis, liver cirrhosis, liver transplantation, long-term use of immunosuppressive agents, etc.^[1]. The commonality of some of the above factors is that they stimulate the proliferation of hepatic vascular endothelial cells at the molecular level^[8]. No other special medical history was found in this patient, and no treatment factors related to this disease were found.

The onset of the disease is relatively insipid, and most of the cases have reached the middle and late stage when the disease is diagnosed. The common symptoms are epigastric discomfort or pain, fatigue, poor appetite and so on. Occasionally, fever and jaundice are seen. Although HEHE is a low-grade malignant tumor, metastasis occurs in 1/3 of the cases due to the rich blood sinus of the liver. Tumor cells are prone to invade the terminal branches of the portal vein, and migrate most commonly to the lung or the abdominal cavity. The patients with metastatic tumor can die from liver and respiratory failure. It is difficult to distinguish polycentric origin from metastasis because it can be transferred from primary organs to other tissues and organs, and also has multiple primary lesions at the same time^[8].

Most HEHE lesions are multiple, and most of them are located under the liver capsule or around the liver. The imaging characteristics of HEHE mainly include: capsular retraction, calcifications, halo sign and target sign [4]. Most plain CT scans were of low density, and some lesions showed a circular shape with lower density. Enhanced CT scans showed progressive enhancement, which was related to the size of the lesions [9]. MRI showed a clearer tumor structure, and MRI plain scan showed hypointense on T1-weighted images and hyperintense on T2-weighted images. The larger lesion (> 2 cm) is prone to liquefaction necrosis, and the lesion density or signal is uneven [10].

The diagnosis of HEHE was mainly based on pathology. The gross appearance of HEHE was mostly nodules with infiltrating growth of grayish-white tough masses. Under the microscope, the tumor cells were mostly arranged in a dense and disordered pattern with a cord-like or nested cord-like distribution, and the cell morphology was mostly epithelioid, fusiform or irregular. Hypertrophy irregular nuclei, uneven chromatin or coarse granular; The cytoplasm is abundant and eosinophilic, and there are often vacuoles containing red blood cells in the cytoplasm. The stroma is rich in collagen and mucous or hyaline degeneration. The positive rates of CD34, CA31 and Vimentin were the highest [5].

Differential diagnosis: (1) Low differentiation adenocarcinoma: Due to the epithelioid morphology and intracytoplasmic vacuoles of EHE, it is easy to be misdiagnosed as adenocarcinoma, especially in a puncture specimen. The heterogeneity of adenocarcinoma cells is more obvious, and the two can be distinguished by using cytokeratin and vascular endothelial markers. (2) Epithelioid angiosarcoma: the cellular heterogeneity is significant, with more nuclear schwannosis and often associated with necrosis. A small number of patients with EHE have some overlap with epithelioid angiosarcoma, and it is presumed that the two have a continuous spectrum of morphology. A combination of immunohistochemical staining can clearly differentiate between the two. [11]

Currently, there is no standard treatment, including surgical resection, liver transplantation, and hepatic arterial chemoembolization. For HEHE detected at early stage, isolated or confined to hepatic segments or lobes, radical resection is the first choice, most of which can achieve a better prognosis, and the 5-year survival rate of patients with radical resection can reach 55% [12]. Liver transplantation is an ideal option for patients without radical resection. Lai [13] summarized 149 HEHE patients registered in the European liver transplantation registration system from November 1984 to May 2014, and found that the 1-year, 5-year and 10-year survival rates of HEHE patients after liver transplantation were 88.6%, 79.5% and 74.4%, and the 1-year, 5-year and 10-year disease-free survival rates were 88.7%, 79.4% and 72.8%, respectively. For HEHE patients without radical resection and without liver transplantation treatment, radiotherapy, chemotherapy and intervention therapy can be selected according to the situation.

Conclusion

In conclusion, HEHE is a relatively rare malignant tumor derived from vascular endothelial cells, with a low incidence, atypical clinical manifestations which resulted in difficulty of clear diagnosis. Currently,

radical resection is the first choice is the of treatment for HEHE. However, in many cases, the appropriate treatment should be selected based on the patient's specific situation.

Abbreviations

EHE Epithelioid hemangioendothelioma

HEHE Hepatic epithelioid hemangio-endothelioma

CT Enhanced computed tomography

TACE Transcatheter arterial chemoembolization

Declarations

Ethics approval and consent to participate☒

Not applicable.

Consent for publication☒

The authors certify that they have obtained patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be published in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Availability of data and material☒

All data of this patient of this case report is included in this published article.

Competing interests☒

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' Contributions:

Dr. JRW, Dr. BL and Dr. YC were involved in compilation of the data and drafting of the article. All authors have read and approved the final manuscript.

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Figures

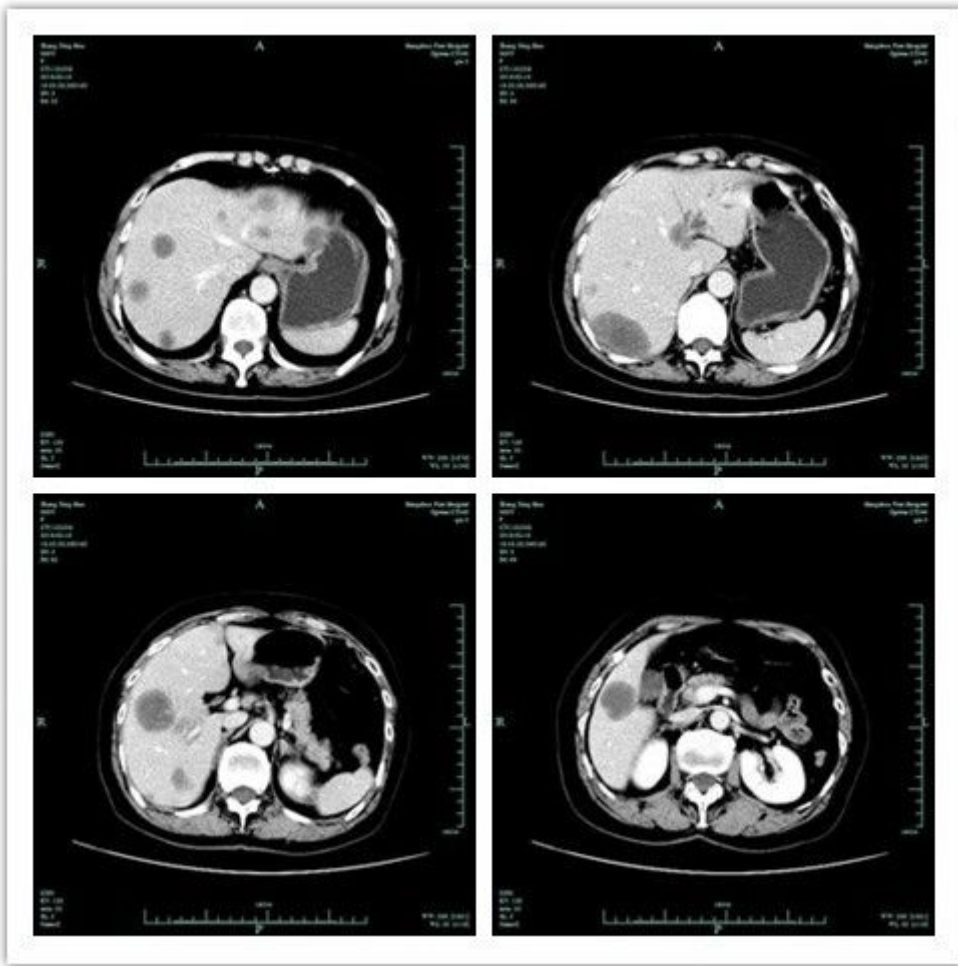


Figure 1

Enhanced computed tomography showing Multiple Liver Space-occupying lesions

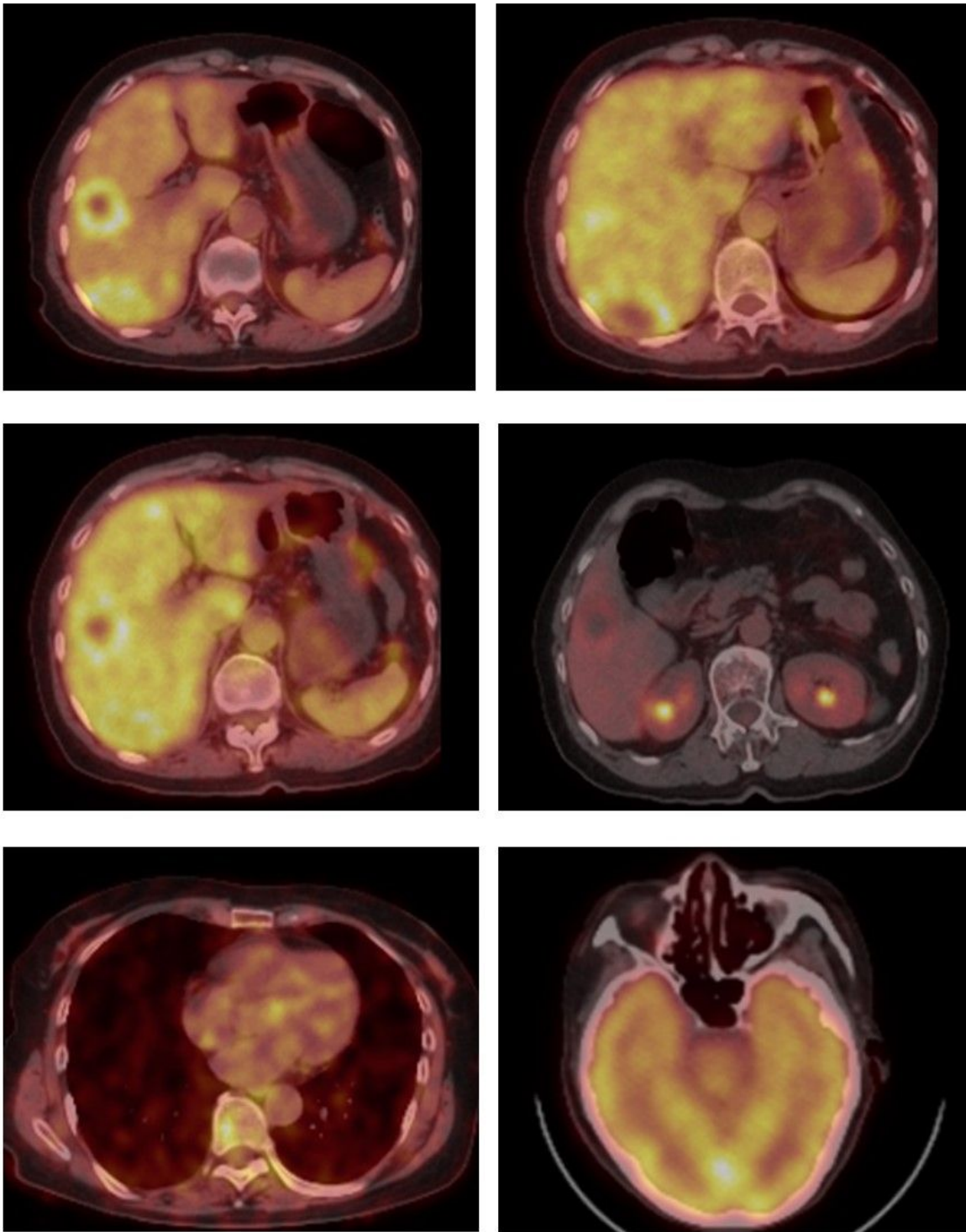


Figure 2

Pet-ct Multiple intrahepatic space occupying, increased glucose metabolism No masses of increased glucose metabolism were seen in the lungs or skull

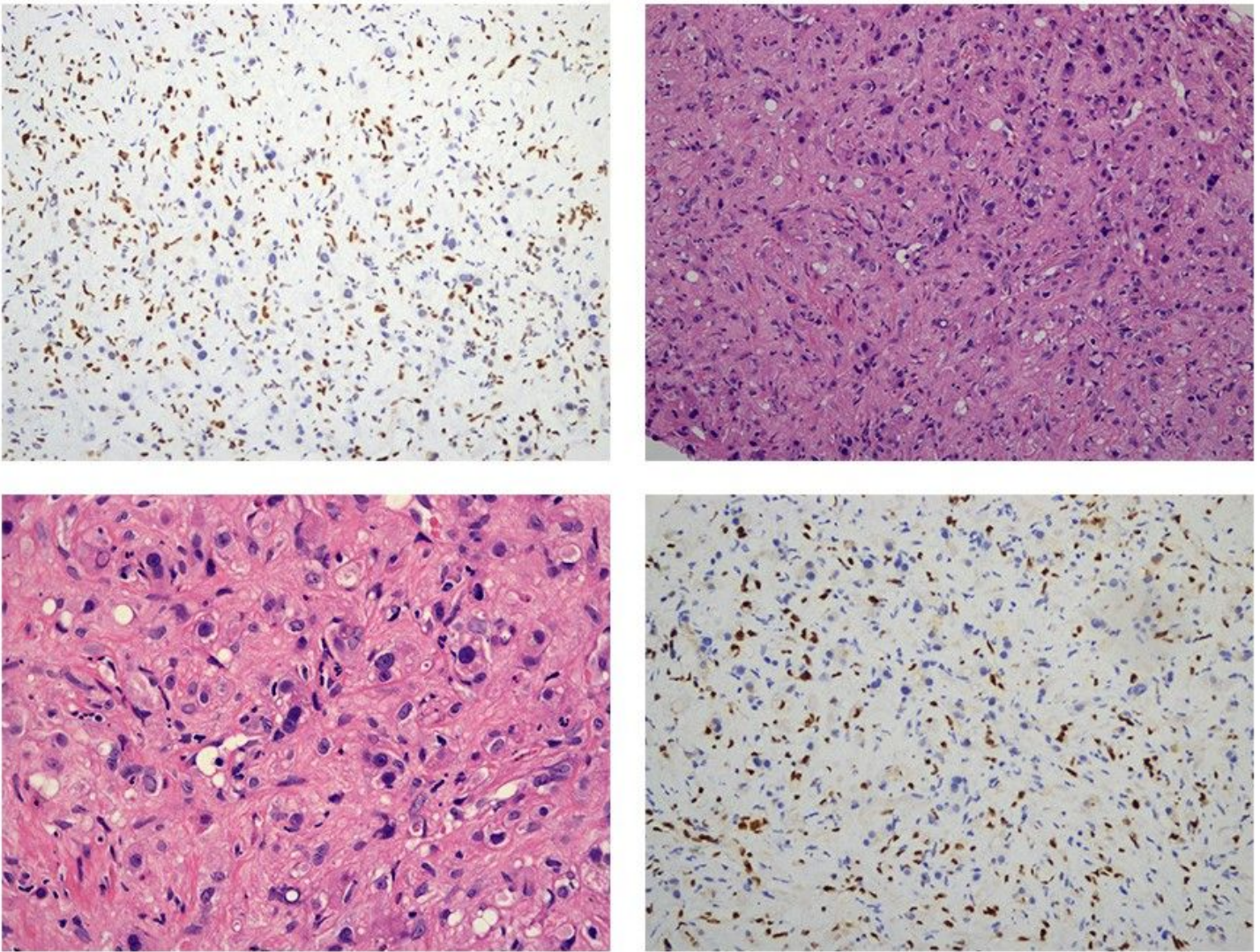


Figure 3

Vim [+] CD31[+] CD34[+] F8 [+] EMA [-] TTF1 [-] Ki-67 [+] 2% - 5%.