

World Journal of *Clinical Cases*

World J Clin Cases 2022 June 26; 10(18): 5934-6340



MINIREVIEWS

- 5934** Development of clustered regularly interspaced short palindromic repeats/CRISPR-associated technology for potential clinical applications
Huang YY, Zhang XY, Zhu P, Ji L
- 5946** Strategies and challenges in treatment of varicose veins and venous insufficiency
Gao RD, Qian SY, Wang HH, Liu YS, Ren SY
- 5957** Diabetes mellitus susceptibility with varied diseased phenotypes and its comparison with phenome interactome networks
Rout M, Kour B, Vuree S, Lulu SS, Medicherla KM, Suravajhala P

ORIGINAL ARTICLE**Clinical and Translational Research**

- 5965** Identification of potential key molecules and signaling pathways for psoriasis based on weighted gene co-expression network analysis
Shu X, Chen XX, Kang XD, Ran M, Wang YL, Zhao ZK, Li CX
- 5984** Construction and validation of a novel prediction system for detection of overall survival in lung cancer patients
Zhong C, Liang Y, Wang Q, Tan HW, Liang Y

Case Control Study

- 6001** Effectiveness and postoperative rehabilitation of one-stage combined anterior-posterior surgery for severe thoracolumbar fractures with spinal cord injury
Zhang B, Wang JC, Jiang YZ, Song QP, An Y

Retrospective Study

- 6009** Prostate sclerosing adenopathy: A clinicopathological and immunohistochemical study of twelve patients
Feng RL, Tao YP, Tan ZY, Fu S, Wang HF
- 6021** Value of magnetic resonance diffusion combined with perfusion imaging techniques for diagnosing potentially malignant breast lesions
Zhang H, Zhang XY, Wang Y
- 6032** Scar-centered dilation in the treatment of large keloids
Wu M, Gu JY, Duan R, Wei BX, Xie F
- 6039** Application of a novel computer-assisted surgery system in percutaneous nephrolithotomy: A controlled study
Qin F, Sun YF, Wang XN, Li B, Zhang ZL, Zhang MX, Xie F, Liu SH, Wang ZJ, Cao YC, Jiao W

- 6050** Influences of etiology and endoscopic appearance on the long-term outcomes of gastric antral vascular ectasia

Kwon HJ, Lee SH, Cho JH

Randomized Controlled Trial

- 6060** Evaluation of the clinical efficacy and safety of TST33 mega hemorrhoidectomy for severe prolapsed hemorrhoids

Tao L, Wei J, Ding XF, Ji LJ

- 6069** Sequential chemotherapy and icotinib as first-line treatment for advanced epidermal growth factor receptor-mutated non-small cell lung cancer

Sun SJ, Han JD, Liu W, Wu ZY, Zhao X, Yan X, Jiao SC, Fang J

Randomized Clinical Trial

- 6082** Impact of preoperative carbohydrate loading on gastric volume in patients with type 2 diabetes

Lin XQ, Chen YR, Chen X, Cai YP, Lin JX, Xu DM, Zheng XC

META-ANALYSIS

- 6091** Efficacy and safety of adalimumab in comparison to infliximab for Crohn's disease: A systematic review and meta-analysis

Yang HH, Huang Y, Zhou XC, Wang RN

CASE REPORT

- 6105** Successful treatment of acute relapse of chronic eosinophilic pneumonia with benralizumab and without corticosteroids: A case report

Izhakian S, Pertzov B, Rosengarten D, Kramer MR

- 6110** Pembrolizumab-induced Stevens-Johnson syndrome in advanced squamous cell carcinoma of the lung: A case report and review of literature

Wu JY, Kang K, Yi J, Yang B

- 6119** Hepatic epithelioid hemangioendothelioma after thirteen years' follow-up: A case report and review of literature

Mo WF, Tong YL

- 6128** Effectiveness and safety of ultrasound-guided intramuscular lauromacrogol injection combined with hysteroscopy in cervical pregnancy treatment: A case report

Ye JP, Gao Y, Lu LW, Ye YJ

- 6136** Carcinoma located in a right-sided sigmoid colon: A case report

Lyu LJ, Yao WW

- 6141** Subcutaneous infection caused by *Mycobacterium abscessus* following cosmetic injections of botulinum toxin: A case report

Deng L, Luo YZ, Liu F, Yu XH

- 6148** Overlapping syndrome of recurrent anti-N-methyl-D-aspartate receptor encephalitis and anti-myelin oligodendrocyte glycoprotein demyelinating diseases: A case report
Yin XJ, Zhang LF, Bao LH, Feng ZC, Chen JH, Li BX, Zhang J
- 6156** Liver transplantation for late-onset ornithine transcarbamylase deficiency: A case report
Fu XH, Hu YH, Liao JX, Chen L, Hu ZQ, Wen JL, Chen SL
- 6163** Disseminated strongyloidiasis in a patient with rheumatoid arthritis: A case report
Zheng JH, Xue LY
- 6168** CYP27A1 mutation in a case of cerebrotendinous xanthomatosis: A case report
Li ZR, Zhou YL, Jin Q, Xie YY, Meng HM
- 6175** Postoperative multiple metastasis of clear cell sarcoma-like tumor of the gastrointestinal tract in adolescent: A case report
Huang WP, Li LM, Gao JB
- 6184** Toripalimab combined with targeted therapy and chemotherapy achieves pathologic complete response in gastric carcinoma: A case report
Liu R, Wang X, Ji Z, Deng T, Li HL, Zhang YH, Yang YC, Ge SH, Zhang L, Bai M, Ning T, Ba Y
- 6192** Presentation of Boerhaave's syndrome as an upper-esophageal perforation associated with a right-sided pleural effusion: A case report
Tan N, Luo YH, Li GC, Chen YL, Tan W, Xiang YH, Ge L, Yao D, Zhang MH
- 6198** Camrelizumab-induced anaphylactic shock in an esophageal squamous cell carcinoma patient: A case report and review of literature
Liu K, Bao JF, Wang T, Yang H, Xu BP
- 6205** Nontraumatic convexal subarachnoid hemorrhage: A case report
Chen HL, Li B, Chen C, Fan XX, Ma WB
- 6211** Growth hormone ameliorates hepatopulmonary syndrome and nonalcoholic steatohepatitis secondary to hypopituitarism in a child: A case report
Zhang XY, Yuan K, Fang YL, Wang CL
- 6218** Vancomycin dosing in an obese patient with acute renal failure: A case report and review of literature
Xu KY, Li D, Hu ZJ, Zhao CC, Bai J, Du WL
- 6227** Insulinoma after sleeve gastrectomy: A case report
Lobaton-Ginsberg M, Sotelo-González P, Ramirez-Renteria C, Juárez-Aguilar FG, Ferreira-Hermosillo A
- 6234** Primary intestinal lymphangiectasia presenting as limb convulsions: A case report
Cao Y, Feng XH, Ni HX
- 6241** Esophagogastric junctional neuroendocrine tumor with adenocarcinoma: A case report
Kong ZZ, Zhang L

- 6247** Foreign body granuloma in the tongue differentiated from tongue cancer: A case report
Jiang ZH, Xu R, Xia L
- 6254** Modified endoscopic ultrasound-guided selective N-butyl-2-cyanoacrylate injections for gastric variceal hemorrhage in left-sided portal hypertension: A case report
Yang J, Zeng Y, Zhang JW
- 6261** Management of type IIb dens invaginatus using a combination of root canal treatment, intentional replantation, and surgical therapy: A case report
Zhang J, Li N, Li WL, Zheng XY, Li S
- 6269** Clivus-involved immunoglobulin G4 related hypertrophic pachymeningitis mimicking meningioma: A case report
Yu Y, Lv L, Yin SL, Chen C, Jiang S, Zhou PZ
- 6277** De novo brain arteriovenous malformation formation and development: A case report
Huang H, Wang X, Guo AN, Li W, Duan RH, Fang JH, Yin B, Li DD
- 6283** Coinfection of *Streptococcus suis* and *Nocardia asiatica* in the human central nervous system: A case report
Chen YY, Xue XH
- 6289** Dilated left ventricle with multiple outpouchings – a severe congenital ventricular diverticulum or left-dominant arrhythmogenic cardiomyopathy: A case report
Zhang X, Ye RY, Chen XP
- 6298** Spontaneous healing of complicated crown-root fractures in children: Two case reports
Zhou ZL, Gao L, Sun SK, Li HS, Zhang CD, Kou WW, Xu Z, Wu LA
- 6307** Thyroid follicular renal cell carcinoma excluding thyroid metastases: A case report
Wu SC, Li XY, Liao BJ, Xie K, Chen WM
- 6314** Appendiceal bleeding: A case report
Zhou SY, Guo MD, Ye XH
- 6319** Spontaneous healing after conservative treatment of isolated grade IV pancreatic duct disruption caused by trauma: A case report
Mei MZ, Ren YF, Mou YP, Wang YY, Jin WW, Lu C, Zhu QC
- 6325** Pneumonia and seizures due to hypereosinophilic syndrome – organ damage and eosinophilia without synchronisation: A case report
Ishida T, Murayama T, Kobayashi S
- 6333** Creutzfeldt-Jakob disease presenting with bilateral hearing loss: A case report
Na S, Lee SA, Lee JD, Lee ES, Lee TK

LETTER TO THE EDITOR

- 6338** Stem cells as an option for the treatment of COVID-19
Cuevas-González MV, Cuevas-González JC

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Cristina Tudoran, PhD, Assistant Professor, Department VII, Internal Medicine II, Discipline of Cardiology, "Victor Babes" University of Medicine and Pharmacy Timisoara, Timisoara 300041, Timis, Romania. cristina13.tudoran@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*, Production Department Director: *Xu Guo*, Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

June 26, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Hepatic epithelioid hemangioendothelioma after thirteen years' follow-up: A case report and review of literature

Wei-Fang Mo, Yu-Ling Tong

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Mohey NM, Egypt; Yang M, China

Received: November 25, 2021

Peer-review started: November 25, 2021

First decision: January 12, 2022

Revised: January 24, 2022

Accepted: April 22, 2022

Article in press: April 22, 2022

Published online: June 26, 2022



Wei-Fang Mo, Yu-Ling Tong, Department of General Practice, The 2nd Affiliated Hospital of Zhejiang University, School of Medicine, Hangzhou 310009, Zhejiang Province, China

Corresponding author: Yu-Ling Tong, Doctor, Assistant Professor, Department of General Practice, The 2nd Affiliated Hospital of Zhejiang University, School of Medicine, No. 88 Jiefang Road, Hangzhou 310009, Zhejiang Province, China. tongyl0313@zju.edu.cn

Abstract

BACKGROUND

Hepatic epithelioid hemangioendothelioma (EHE) is a rare vascular endothelial cell tumor of the liver, consisting of epithelioid and histiocyte-like vascular endothelial cells in mucus or a fibrotic matrix. Immunohistochemistry is usually positive for vascular markers, such as factor VIII-related antigen, CD31, and CD34. Hepatic EHE can have a varied clinical course; treatment includes liver transplantation, liver resection, chemotherapy, and radiation therapy.

CASE SUMMARY

A 46-year-old woman with abdominal discomfort and elevated serum carcinoembryonic antigen was found to have multiple low-density lesions in the liver and lung on computed tomography (CT) evaluation. An ultrasound-guided fine needle aspiration biopsy revealed a fibrous stroma with dendritic cells, containing intracellular vacuoles. Immunohistochemical staining found that the tumor cells were positive for CD34, CD31, and factor VIII-related antigen. The patient received four courses of combined chemotherapy and was followed-up for 13 years, at which time the patient was in stable condition without disease progression and a confined neoplasm, as evidenced by CT scans.

CONCLUSION

The histology and immunohistochemical characteristics of hepatic EHE are well described. Chemotherapy may be effective in patients with extrahepatic lesions.

Key Words: Epithelioid hemangioendothelioma; Liver neoplasm; Immunohistochemistry; Antineoplastic combined chemotherapy protocols; Treatment; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The gold standard diagnosis for hepatic epithelioid hemangioendothelioma includes epithelioid and histiocyte-like vascular endothelial cells in mucus or a fibrotic matrix, and positive vascular markers. Chemotherapy may be an effective treatment; close follow-up is necessary.

Citation: Mo WF, Tong YL. Hepatic epithelioid hemangioendothelioma after thirteen years' follow-up: A case report and review of literature. *World J Clin Cases* 2022; 10(18): 6119-6127

URL: <https://www.wjgnet.com/2307-8960/full/v10/i18/6119.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i18.6119>

INTRODUCTION

Hepatic epithelioid hemangioendothelioma (EHE) is a rare malignant tumor of vascular origin, with an incidence of 0.1-0.2/100000[1,2]. Oral contraceptives, polyvinyl chloride, asbestos, thorotrast contrast medium, hepatic trauma, and viral hepatitis have been identified as risk factors for subsequent development of disease[3]. While laboratory findings always reveal abnormal liver function, tumor markers are always at normal levels. The patient described in this case report had a history of hepatitis A and normal liver function, but with a mildly elevated tumor marker [carcinoembryonic antigen (CEA) at 6.9 ng/mL]. The patient received four courses of chemotherapy and was found to remain in stable condition after 13 years of follow-up.

CASE PRESENTATION

Chief complaints

A 46-year-old woman with no significant past medical history presented at the hospital with a 1-mo history of epigastric discomfort and asthenia.

History of present illness

The patient had no other symptoms.

History of past illness

The patient had a history of acute hepatitis that had resolved without complications 20 years previously.

Personal and family history

The patient had no personal or family history of other diseases.

Physical examination

Physical examination revealed no remarkable findings.

Laboratory examinations

Laboratory testing on admission showed no abnormalities in markers of inflammation or abnormal liver function, or in peripheral blood panel or biochemical tests. Hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb) and hepatitis C virus antibody (HCVAb) were negative. Tumor markers were in the normal ranges, except for a mildly elevated CEA (6.9 ng/mL; normal range: 0-5.0 ng/mL).

Imaging examinations

Abdominal ultrasound revealed multiple irregular hypoechoic lesions in the liver. Color doppler flow imaging showed spots of avascular reflective material. Contrast-enhanced computed tomography (CT) showed multiple low-density lesions in the right lobe of the liver. The largest was located in segment 8 and was 2.9 cm, 2.3 cm. Some lesions had mild-moderate enhancement during the arterial contrast-enhanced phase. The density was lower than the normal liver parenchyma during the portal vein and lag phase (Figure 1). Magnetic resonance (MR) T1-weighted images showed multiple low signal ovoid lesions in the right lobe of the liver that had a high signal on T2-weighted images (Figure 2). Chest X-rays yielded no remarkable findings. Ultrasound revealed enlarged bilateral lymph nodes in the neck, axilla, and groin.

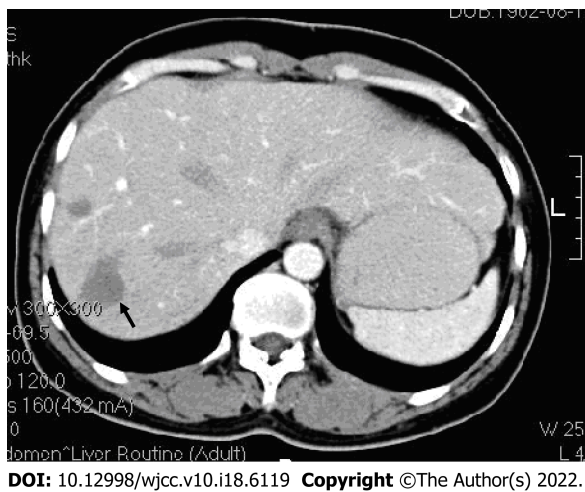


Figure 1 Contrast-enhanced computed tomography. Multiple low-density lesions (black arrow) with mild-moderate peripheral enhancement are seen in the right lobe of the liver.

LABORATORY EXAMINATIONS

Laboratory testing on admission showed no abnormalities in markers of inflammation or abnormal liver function, or in peripheral blood panel or biochemical tests. HBsAg, HBcAb and HCVAb were negative. Tumor markers were in the normal ranges, except for a mildly elevated CEA (6.9 ng/mL; normal range: 0-5.0 ng/mL).

FINAL DIAGNOSIS

An ultrasound-guided fine needle aspiration biopsy revealed few hepatocytes and fibrous tissue with mildly heteromorphic spindle cell (dendritic cell) infiltration. The neoplastic cells were medium to large, with eosinophilic cytoplasm and vesicular nuclei having small, inconspicuous nucleoli. Signet ring cell-like structures were seen with intracytoplasmic lumina, occasionally containing red blood cells (Figure 3). Immunohistochemical staining indicated that the tumor cells were positive for CD31 (H12164PD590, EuroBioscience), CD34 (H12166F, EuroBioscience), and factor VIII-related antigen (FVIII-RAG, BH0012044, Goybio) (Figure 4A-C), while cells were negative for Pan Cytokeratin (CK+AFs-AE1/AE3+AF0-) (PD00330, Dako) (Figure 4D). Other results were lysozyme+, P53+/-+ACY-ndash+ADs-, vimentin+, EMA+, CK8+ACY-ndash+ADs-, AFP+ACY-ndash+ADs-, CK18+ACY-ndash+ADs-, hepatocyte+ACY-minus+ADs-, CK20+ACY-minus+ADs-, and CD68+ACY-minus+ADs-, which weren't been shown in this article. Immunohistochemical staining results revealed evidence of+ACY-nbsp+ADs- endothelial differentiation, and consistent with hepatic epithelioid hemangioendothelioma (EHE).

TREATMENT

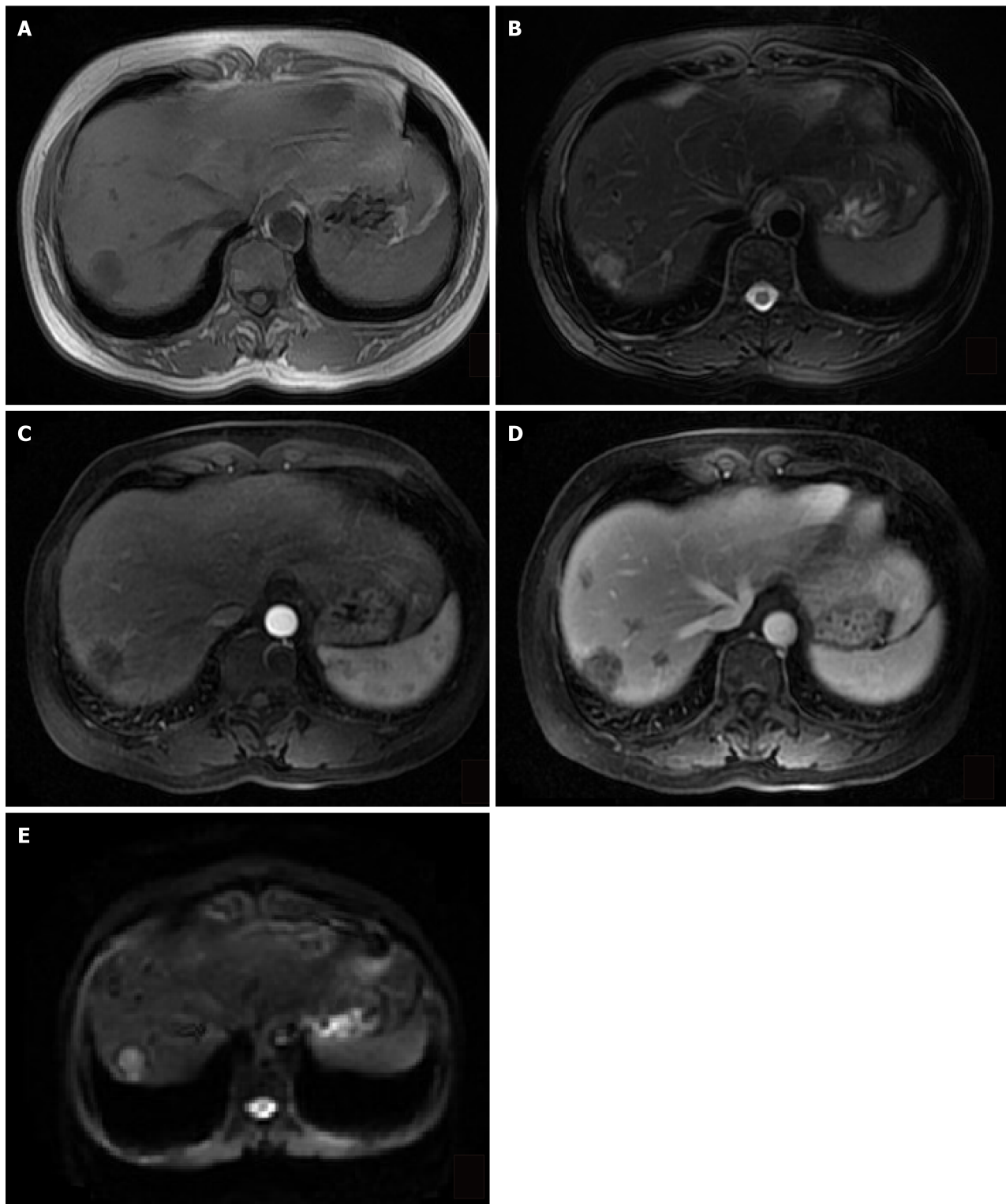
During the patient's hospital stay, she was given four cycles of combined chemotherapy with ifosfamide, cisplatin, epirubicin and recombinant human (rh) endostatin (Endostar; Simcere, Nanjing, China) injection.

OUTCOME AND FOLLOW-UP

After 13 years of follow-up, the patient remains in stable condition. A repeated CT scan found that the size of the lesions had not changed (Figure 5) and her liver function was normal.

DISCUSSION

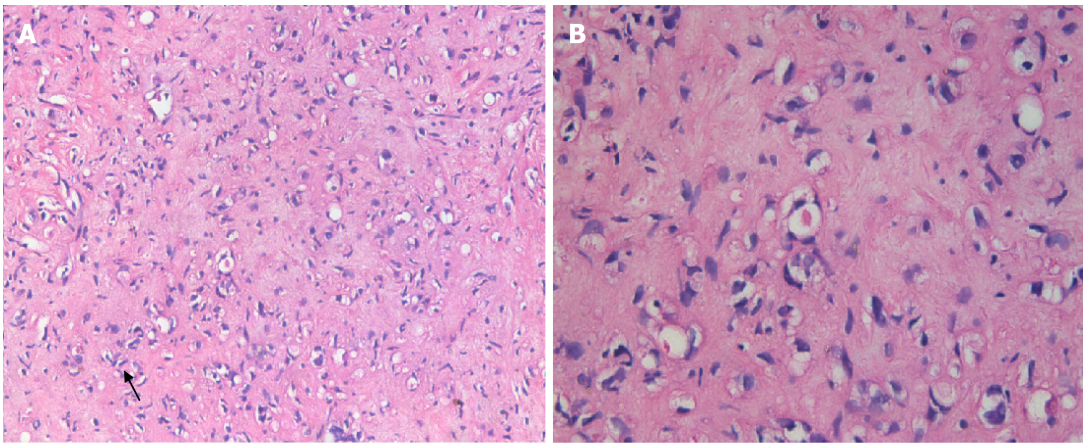
Hepatic EHE is a rare tumor of vascular origin, with an incidence of 0.1-0.2/100000[1,2]. Fewer than 600 cases involving the liver are available in the literature, and it was first reported by Ishak *et al*[4] in 1984.



DOI: 10.12998/wjcc.v10.i18.6119 Copyright ©The Author(s) 2022.

Figure 2 Magnetic resonance weighted image. A: T1-weighted image shows low signal ovoid lesions in the right lobe of liver; B: The lesions have a heterogeneous high signal in the T2-weighted image; C: The largest lesion in the right lobe is mildly heterogeneous with peripheral enhancement and an arterial contrast enhancement pattern; D: Peripheral enhancement of lesions is increased in spots visible in a venous contrast enhancement pattern; E: Lesions show diffusion restriction on a diffusion-weighted image.

Hepatic EHE is as a low-to-moderate grade tumor with a malignant potential intermediate between hemangioma and hemangiosarcoma[4]. Its metastasis rate is 27%-45% and the most common tissues of origin are the lungs (81%) and celiac lymph nodes (39%)[1]. The median age has been reported as 41.7 years, with a female predominance of 3:2[3], and the clinical manifestations are variable. The most frequent symptoms are right upper quadrant pain (48.6%), hepatomegaly (20.4%), and a constitutional syndrome with progressive liver damage and weight loss (15.6%)[3]. Some patients present with Budd-



DOI: 10.12998/wjcc.v10.i18.6119 Copyright ©The Author(s) 2022.

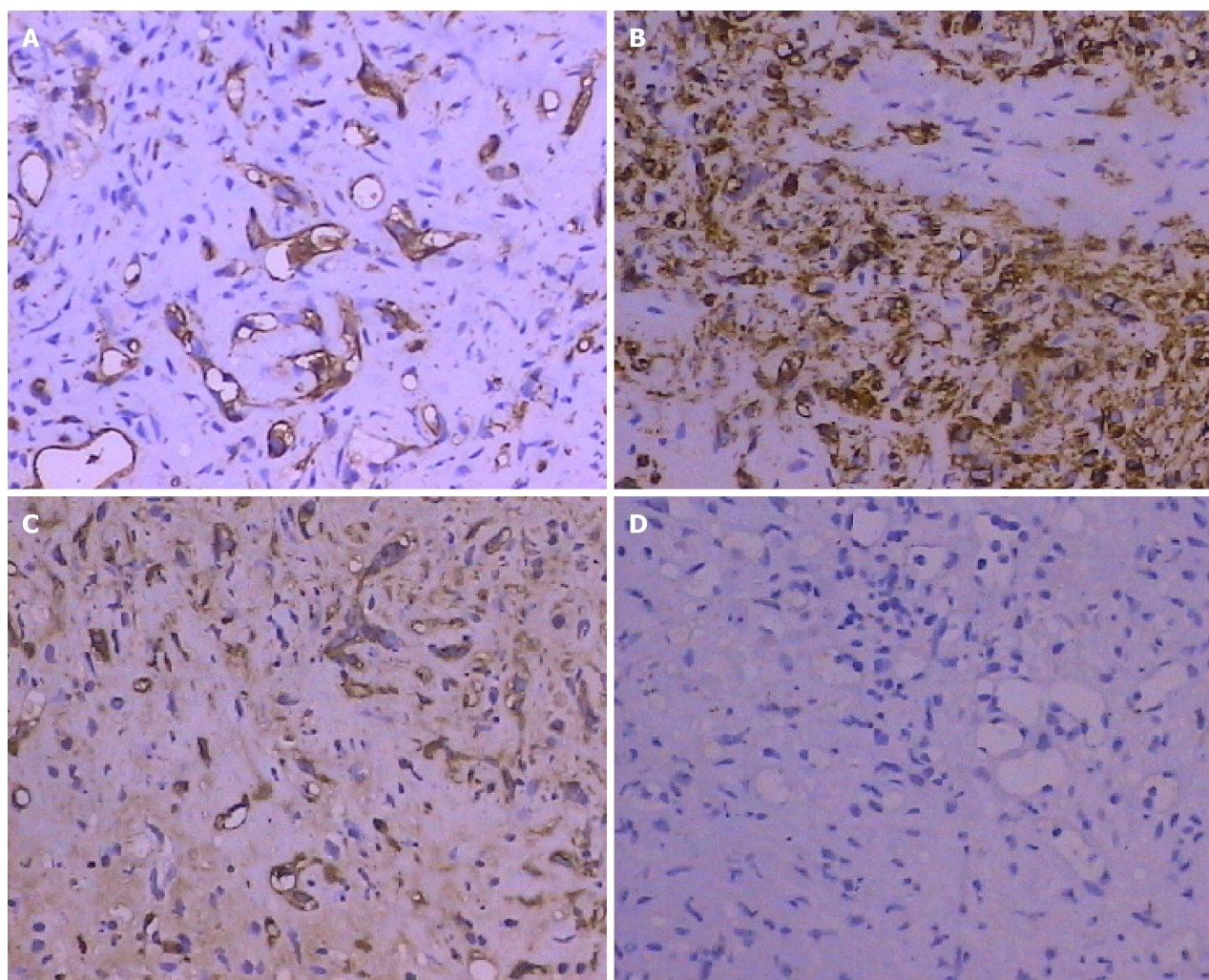
Figure 3 Liver biopsy. A: Mildly heteromorphous spindle cells (dendritic cells) with interdigitating processes (hematoxylin and eosin, 200 ×); B: Intracellular vascular lumina containing a red blood cell (black arrow) (hematoxylin and eosin, 400 ×).

Chiari syndrome or liver failure, while others present with incidental findings[1,5]. Laboratory findings may reveal abnormal liver function. Nearly 75% of patients have elevated alkaline phosphatase (AKP), 2.7% have elevated alpha-fetoprotein (AFP), and 18.8% have elevated serum CEA[1,3]. Our patient had good liver function, with normal AKP, AST, ALT, and AFP. Her CEA was elevated but other markers were in their normal ranges. Oral contraceptives, polyvinyl chloride, asbestos, thorotrast contrast agent, and hepatic trauma have been identified as risk factors for subsequent disease development[3], and viral hepatitis is considered as an etiology[1,4,6]. This patient had a history of viral hepatitis A, but it had resolved without complication 20 years before she presented with hepatic EHE, making a viral etiology implausible. Because of its nonspecific manifestation, the diagnosis of hepatic EHE depends mainly on radiology and histopathology.

Most lesions are peripheral, extending to the capsular margin and are frequently hypoechoic with heterogeneous internal architecture on sonography[7,8]. On CT, lesions are almost hypodense with peripheral contrast enhancement[7,9-11]. Capsular retraction adjacent to the mass is seen in fewer than 25% of patients[9,12]. On MR, T1-weighted images of lesions frequently have a low signal and T2-weighted images have heterogeneous-increased signals. Peripheral enhancement with a thin nonenhancing rim corresponding to a narrow vascular zone can be seen with arterial contrast[7,11-13]. A lollipop sign, which is indicative of hepatic or portal veins terminating at or just within the periphery of lesions, seems to be specific for hepatic EHE[14]. The mean apparent diffusion coefficients of lesions were found to be high compared with other hepatic malignancies, which may be helpful in suggesting the diagnosis[15]. MR appears to be superior to CT, and MR with contrast may be important.

Pathologic diagnosis depends on the vascular nature of the tumor. Histologically, it is comprised of a fibrous stroma with myxohyaline areas including dendritic and epithelioid cells, often with intracellular vacuoles[1,4]. Immunohistochemical staining is positive for the expression of endothelial antigens, such as FVIII-RAG (98%), CD34 (94%), or CD31 (86%), and negative for epithelial markers[1,6]. This tumor was CD34+, vimentin+, and CD31+, and negative for epithelial markers like CK (AE1/AE3) and CK18. Podoplanin was shown to be specifically expressed in hepatic EHE (78%), and may be useful as a diagnostic marker of EHE in liver tumors[9]. Characteristic ultrastructural features include investing basal lamina, cytoplasmic intermediate filaments, Weibel-Palade bodies, and pinocytotic vesicles[4]. High cellularity, more than mitotic count, predicts an unfavorable prognosis[1,3,4]. A recent study reported that these tumors often have t(1;3) (p36.3; q25) translocations, resulting in WWTR1-CAMTA1 fusion[16]. YAP 1-TFE3 fusions have also been identified in about 10% of patients[17].

Treatment options are limited by the rarity of the tumor and currently include liver transplantation (44.8%), chemotherapy or radiotherapy (21.0%), and liver resection (9.4%), with 24.8% of patients receiving no treatment[3]. Complete liver resection should be performed if possible, but the multicentric origin of the tumor and multinodular growth make that difficult to accomplish[18]. Liver transplantation is an effective treatment for patients who are not candidates for resective surgery and those with extrahepatic manifestations or progressive liver failure[19,20]. Hepatic EHE is not sensitive to radiotherapy or chemotherapy, but some studies have found that 5-fluorouracil, doxorubicin, thalidomide, and interferon were effective[14,21,22]. One-year survivals following liver transplantation, without treatment, radiotherapy or chemotherapy, and liver resection have been reported as 96%, 39.3%, 73.3%, and 100%. The corresponding 5-year rates were 54.5%, 4.5%, 30%, and 75%[3]. Hepatic EHE is of vascular origin, vascular endothelial growth (VEGF) receptors have been detected in EHE tumor cells, and VEGF has a role in tumor growth[23]. Combination treatment anti-VEGF drugs and cell cycle inhibitors, such as bevacizumab and capecitabine[24,25], pegylated liposomal doxorubicin[26], and metronomic cyclophosphamide[27] have been effective. For patients with extrahepatic lesions, it has



DOI: 10.12998/wjcc.v10.i18.6119 Copyright ©The Author(s) 2022.

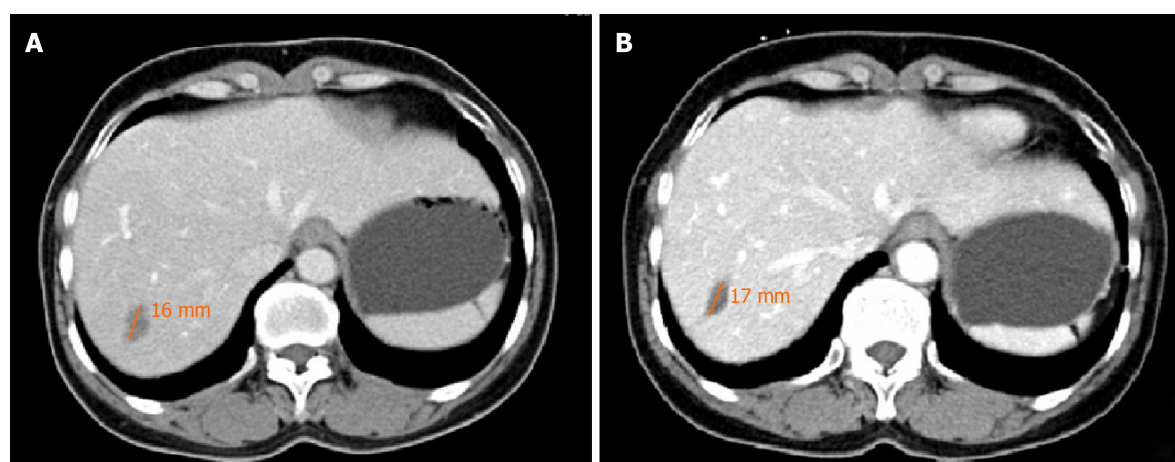
Figure 4 Histopathology, immunostaining of tumor cells. A: Anti-CD31+ (200 ×); B: Anti-CD34+ (200 ×); C: Anti-factor VIII-related antigen+ (200 ×); D: Anti-CK- (Pan) (200 ×).

been reported that adjuvant chemotherapy may prevent recurrence[28].

Because the disease was multifocal in our patient, orthotopic liver transplantation may have been justified as a curative procedure. Unfortunately, a donor shortage and cost limitations made immediate transplantation unrealistic. Consequently, we choose to treat her with combined chemotherapy that included ifosfamide, cisplatin, epirubicin and rh-endostatin. rh-endostatin is purified in an *Escherichia coli* system, with an additional nine amino acid sequence of soluble protein[29]. It targets neovascular endothelial cells and has antiangiogenetic and antitumor activity. Preclinical and clinical studies showed synergistic effects of rh-endostatin and other agents that inhibit the growth of malignant tumors, with minimal toxicity[30-32]. A review by Xu *et al*[33] suggests that the combination of rh-endostatin with chemotherapy, radiotherapy, and biotherapy (*i.e.* fusion protein, or molecular-targeted therapy on cancers, *etc.*) may be the optimal strategy for cancer treatment[33]. Ling *et al*[34] reported that the antiangiogenic activity of rh-endostatin was mediated *in vitro* and *in vivo* by blocking VEGF-induced tyrosine phosphorylation of KDR/Flk-1 in endothelial cells. The vascular nature and endothelial origin of our patient's tumor led us to choose rh-endostatin for her treatment. To date, the size of her lesions has not increased, and the patient is in stable condition with normal liver function. The patient is followed-up regularly, and liver transplantation is still recommended.

CONCLUSION

In conclusion, hepatic EHE is a rare tumor, and its atypical symptoms and varied radiographic appearance make it hard to differentiate from other tumors. Diagnosis depends on histopathology. Liver resection is the treatment of choice in patients with resectable lesions, and liver transplantation is justified as a curative procedure for multinodular disease. Donor shortage and a long waiting time,



DOI: 10.12998/wjcc.v10.i18.6119 Copyright ©The Author(s) 2022.

Figure 5 Contrast-enhanced follow-up computed tomography scans. A: After 4 years, diameter of the low-density lesion was 16 mm; B: After 12 years, diameter of the low-density lesion was 17 mm.

among other reasons, limit the use of liver transplantation. Chemotherapy including rh-endostatin may increase the effectiveness of hepatic EHE treatment. The focus is on its therapeutic efficacy while awaiting a suitable donor liver and for patients with extrahepatic manifestations. Further research is needed.

FOOTNOTES

Author contributions: Mo WF collected the data and wrote the manuscript; Tong YL designed the report; all authors have read and approve the final manuscript.

Supported by Zhejiang Medical and Health Science and Technology Project, No. 2021429795; and Scientific Research Project of Zhejiang Education Department, No. Y202043306.

Informed consent statement: Consent was obtained from the patient, who signed a written informed consent for publication of this case report.

Conflict-of-interest statement: The authors declare that they have no competing interests.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Wei-Fang Mo 0000-0003-4286-3229; Yu-Ling Tong 0000-0002-3772-9327.

S-Editor: Xing YX

L-Editor: A

P-Editor: Xing YX

REFERENCES

- Makhlouf HR, Ishak KG, Goodman ZD. Epithelioid hemangioendothelioma of the liver: a clinicopathologic study of 137 cases. *Cancer* 1999; **85**: 562-582 [PMID: 10091730 DOI: 10.1002/(sici)1097-0142(19990201)85:3<562::aid-cnrc7>3.0.co;2-t]
- Elleuch N, Dahmani W, Aida Ben S, Jaziri H, Aya H, Ksaa M, Jmaa A. Hepatic epithelioid hemangioendothelioma: A misdiagnosed rare liver tumor. *Presse Med* 2018; **47**: 182-185 [PMID: 29373279 DOI: 10.1016/j.lpm.2017.10.026]

- 3 **Mehrabi A**, Kashfi A, Fonouni H, Schemmer P, Schmied BM, Hallscheidt P, Schirmacher P, Weitz J, Friess H, Buchler MW, Schmidt J. Primary malignant hepatic epithelioid hemangioendothelioma: a comprehensive review of the literature with emphasis on the surgical therapy. *Cancer* 2006; **107**: 2108-2121 [PMID: [17019735](#) DOI: [10.1002/encr.22225](#)]
- 4 **Ishak KG**, Sesterhenn IA, Goodman ZD, Rabin L, Stromeyer FW. Epithelioid hemangioendothelioma of the liver: a clinicopathologic and follow-up study of 32 cases. *Hum Pathol* 1984; **15**: 839-852 [PMID: [6088383](#) DOI: [10.1016/s0046-8177\(84\)80145-8](#)]
- 5 **Uchimura K**, Nakamuta M, Osoegawa M, Takeaki S, Nishi H, Iwamoto H, Enjoji M, Nawata H. Hepatic epithelioid hemangioendothelioma. *J Clin Gastroenterol* 2001; **32**: 431-434 [PMID: [11319317](#) DOI: [10.1097/00004836-200105000-00015](#)]
- 6 **Demetris AJ**, Minervini M, Raikow RB, Lee RG. Hepatic epithelioid hemangioendothelioma: biological questions based on pattern of recurrence in an allograft and tumor immunophenotype. *Am J Surg Pathol* 1997; **21**: 263-270 [PMID: [9060595](#) DOI: [10.1097/00000478-199703000-00001](#)]
- 7 **Lyburn ID**, Torreggiani WC, Harris AC, Zwirewich CV, Buckley AR, Davis JE, Chung SW, Scudamore CH, Ho SG. Hepatic epithelioid hemangioendothelioma: sonographic, CT, and MR imaging appearances. *AJR Am J Roentgenol* 2003; **180**: 1359-1364 [PMID: [12704052](#) DOI: [10.2214/ajr.180.5.1801359](#)]
- 8 **Radin DR**, Craig JR, Colletti PM, Ralls PW, Halls JM. Hepatic epithelioid hemangioendothelioma. *Radiology* 1988; **169**: 145-148 [PMID: [3420251](#) DOI: [10.1148/radiology.169.1.3420251](#)]
- 9 **Amin S**, Chung H, Jha R. Hepatic epithelioid hemangioendothelioma: MR imaging findings. *Abdom Imaging* 2011; **36**: 407-414 [PMID: [21079951](#) DOI: [10.1007/s00261-010-9662-0](#)]
- 10 **Miller WJ**, Dodd GD 3rd, Federle MP, Baron RL. Epithelioid hemangioendothelioma of the liver: imaging findings with pathologic correlation. *AJR Am J Roentgenol* 1992; **159**: 53-57 [PMID: [1302463](#) DOI: [10.2214/ajr.159.1.1302463](#)]
- 11 **Fulcher AS**, Sterling RK. Hepatic neoplasms: computed tomography and magnetic resonance features. *J Clin Gastroenterol* 2002; **34**: 463-471 [PMID: [11907365](#) DOI: [10.1097/00004836-200204000-00019](#)]
- 12 **Hayashi Y**, Inagaki K, Hirota S, Yoshikawa T, Ikawa H. Epithelioid hemangioendothelioma with marked liver deformity and secondary Budd-Chiari syndrome: pathological and radiological correlation. *Pathol Int* 1999; **49**: 547-552 [PMID: [10469398](#) DOI: [10.1046/j.1440-1827.1999.00906.x](#)]
- 13 **Van Beers B**, Roche A, Mathieu D, Menu Y, Delos M, Otte JB, Lalonde L, Pringot J. Epithelioid hemangioendothelioma of the liver: MR and CT findings. *J Comput Assist Tomogr* 1992; **16**: 420-424 [PMID: [1592925](#) DOI: [10.1097/00004728-199205000-00014](#)]
- 14 **Alomari AI**. The lollipop sign: a new cross-sectional sign of hepatic epithelioid hemangioendothelioma. *Eur J Radiol* 2006; **59**: 460-464 [PMID: [16644166](#) DOI: [10.1016/j.ejrad.2006.03.022](#)]
- 15 **Bruegel M**, Muenzel D, Waldt S, Specht K, Rummeny EJ. Hepatic epithelioid hemangioendothelioma: findings at CT and MRI including preliminary observations at diffusion-weighted echo-planar imaging. *Abdom Imaging* 2011; **36**: 415-424 [PMID: [20730424](#) DOI: [10.1007/s00261-010-9641-5](#)]
- 16 **Doyle LA**, Fletcher CD, Hornick JL. Nuclear Expression of CAMTA1 Distinguishes Epithelioid Hemangioendothelioma From Histologic Mimics. *Am J Surg Pathol* 2016; **40**: 94-102 [PMID: [26414223](#) DOI: [10.1097/PAS.0000000000000511](#)]
- 17 **Lotfalla MM**, Folpe AL, Fritchie KJ, Greipp PT, Galliano GG, Halling KC, Mounajjed T, Torres-Mora J, Graham RP. Hepatic *YAP1-TFE3* Rearranged Epithelioid Hemangioendothelioma. *Case Rep Gastrointest Med* 2019; **2019**: 7530845 [PMID: [31341686](#) DOI: [10.1155/2019/7530845](#)]
- 18 **Haydon E**, Haydon G, Bramhall S, Mayer AD, Niel D. Hepatic epithelioid haemangioendothelioma. *J R Soc Med* 2005; **98**: 364-365 [PMID: [16055903](#) DOI: [10.1258/jrsm.98.8.364](#)]
- 19 **Lerut JP**, Orlando G, Sempoux C, Ciccarelli O, Van Beers BE, Danse E, Horsmans Y, Rahier J, Roggen F. Hepatic haemangioendothelioma in adults: excellent outcome following liver transplantation. *Transpl Int* 2004; **17**: 202-207 [PMID: [15114438](#) DOI: [10.1007/s00147-004-0697-4](#)]
- 20 **Nissen NN**, Cavazzoni E, Tran TT, Poordad FP. Emerging role of transplantation for primary liver cancers. *Cancer J* 2004; **10**: 88-96 [PMID: [15130268](#) DOI: [10.1097/00130404-200403000-00004](#)]
- 21 **Bancel B**, Patricot LM, Caillon P, Ducerf C, Pouyet M. [Hepatic epithelioid hemangioendothelioma. A case with liver transplantation. Review of the literature]. *Ann Pathol* 1993; **13**: 23-28 [PMID: [8489646](#)]
- 22 **Galvão FH**, Bakonyi-Neto A, Machado MA, Farias AQ, Mello ES, Diz ME, Machado MC. Interferon alpha-2B and liver resection to treat multifocal hepatic epithelioid hemangioendothelioma: a relevant approach to avoid liver transplantation. *Transplant Proc* 2005; **37**: 4354-4358 [PMID: [16387119](#) DOI: [10.1016/j.transproceed.2005.11.022](#)]
- 23 **Kou K**, Chen YG, Zhou JP, Sun XD, Sun DW, Li SX, Lv GY. Hepatic epithelioid hemangioendothelioma: Update on diagnosis and therapy. *World J Clin Cases* 2020; **8**: 3978-3987 [PMID: [33024754](#) DOI: [10.12998/wjcc.v8.i18.3978](#)]
- 24 **Treska V**, Daum O, Svajdler M, Liska V, Ferda J, Baxa J. Hepatic Epithelioid Hemangioendothelioma - a Rare Tumor and Diagnostic Dilemma. *In Vivo* 2017; **31**: 763-767 [PMID: [28652454](#) DOI: [10.21873/invivo.11128](#)]
- 25 **Lau A**, Malangone S, Green M, Badari A, Clarke K, Elquza E. Combination capecitabine and bevacizumab in the treatment of metastatic hepatic epithelioid hemangioendothelioma. *Ther Adv Med Oncol* 2015; **7**: 229-236 [PMID: [26136854](#) DOI: [10.1177/1758834015582206](#)]
- 26 **Grenader T**, Vernea F, Reinus C, Gabizon A. Malignant epithelioid hemangioendothelioma of the liver successfully treated with pegylated liposomal doxorubicin. *J Clin Oncol* 2011; **29**: e722-e724 [PMID: [21788568](#) DOI: [10.1200/JCO.2011.35.5891](#)]
- 27 **Lakkis Z**, Kim S, Delabrousse E, Jary M, Nguyen T, Manton G, Heyd B, Lassabe C, Borg C. Metronomic cyclophosphamide: an alternative treatment for hepatic epithelioid hemangioendothelioma. *J Hepatol* 2013; **58**: 1254-1257 [PMID: [23402747](#) DOI: [10.1016/j.jhep.2013.01.043](#)]
- 28 **Tan Y**, Yang X, Dong C, Xiao Z, Zhang H, Wang Y. Diffuse hepatic epithelioid hemangioendothelioma with multiple splenic metastasis and delayed multifocal bone metastasis after liver transplantation on FDG PET/CT images: A case report. *Medicine (Baltimore)* 2018; **97**: e10728 [PMID: [29851777](#) DOI: [10.1097/MD.00000000000010728](#)]
- 29 **Han Q**, Fu Y, Zhou H, He Y, Luo Y. Contributions of Zn(II)-binding to the structural stability of endostatin. *FEBS Lett* 2007; **581**: 3027-3032 [PMID: [17544408](#) DOI: [10.1016/j.febslet.2007.05.058](#)]

- 30 **Hanna NN**, Seetharam S, Mauceri HJ, Beckett MA, Jaskowiak NT, Salloum RM, Hari D, Dhanabal M, Ramchandran R, Kalluri R, Sukhatme VP, Kufe DW, Weichselbaum RR. Antitumor interaction of short-course endostatin and ionizing radiation. *Cancer J* 2000; **6**: 287-293 [PMID: [11079167](#) DOI: [10.1007/s002620000128](#)]
- 31 **Plum SM**, Hanson AD, Volker KM, Vu HA, Sim BK, Fogler WE, Fortier AH. Synergistic activity of recombinant human endostatin in combination with adriamycin: analysis of *in vitro* activity on endothelial cells and *in vivo* tumor progression in an orthotopic murine mammary carcinoma model. *Clin Cancer Res* 2003; **9**: 4619-4626 [PMID: [14555538](#) DOI: [10.1093/carcin/bgg164](#)]
- 32 **Sun L**, Ye HY, Zhang YH, Guan YS, Wu H. Epidermal growth factor receptor antibody plus recombinant human endostatin in treatment of hepatic metastases after remnant gastric cancer resection. *World J Gastroenterol* 2007; **13**: 6115-6118 [PMID: [18023113](#) DOI: [10.3748/wjg.v13.45.6115](#)]
- 33 **Xu F**, Ma Q, Sha H. Optimizing drug delivery for enhancing therapeutic efficacy of recombinant human endostatin in cancer treatment. *Crit Rev Ther Drug Carrier Syst* 2007; **24**: 445-492 [PMID: [18197781](#) DOI: [10.1615/critrevtherdrugcarriersyst.v24.i5.20](#)]
- 34 **Ling Y**, Yang Y, Lu N, You QD, Wang S, Gao Y, Chen Y, Guo QL. Endostar, a novel recombinant human endostatin, exerts antiangiogenic effect via blocking VEGF-induced tyrosine phosphorylation of KDR/Flk-1 of endothelial cells. *Biochem Biophys Res Commun* 2007; **361**: 79-84 [PMID: [17644065](#) DOI: [10.1016/j.bbrc.2007.06.155](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

