

Primary Hepatic Angiosarcoma: A Rare and Very Aggressive Liver Tumour

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ABSTRACT

Primary hepatic angiosarcoma (PHA) is a sporadic and aggressive tumour of the liver that originates from mesenchymal cells and represents less than 2% of all primary liver tumours. It is known to be associated with several environmental and industrial carcinogens; however, in 75% of cases, aetiology remains unclear. Patients generally present with nonspecific symptoms and laboratory findings. Imaging has a limited role in the diagnosis.

We herein present a case of a 52-year-old man with a history of hepatitis B-related cirrhosis who was referred to our hospital for liver transplantation assessment. Magnetic resonance imaging (MRI) revealed two small nodular lesions of 5 and 6 mm in segment IV of the liver, categorised as Liver Imaging Reporting and Data System (LI-RADS) category 3. The patient was discussed at a multidisciplinary tumour meeting, and an MRI follow-up in three months was planned. Three months later, MRI depicted a substantial increase in the lesion size measured 8.5 cm. An ultrasound-guided tru-cut biopsy was performed, and the diagnosis of PHA was confirmed by pathology.

In this report, we aim to highlight PHA's MRI features and underline this rare entity's rapid and fatal progression.

Key Words: Liver, Hepatic angiosarcoma, Magnetic resonance imaging.

How to cite this article: Durmaz S, Basak M, Ozguven BY, Eken KG, Erturk SM. Primary Hepatic Angiosarcoma: A Rare and Very Aggressive Liver Tumour. *J Coll Physicians Surg Pak* 2022; **32(JCPSPCR)**:CR209-CR211.

INTRODUCTION

Primary hepatic angiosarcoma (PHA) is a sporadic and aggressive tumour of the liver that originates from mesenchymal cells and represents less than 2% of all primary liver tumours.¹ It is associated with several environmental and industrial carcinogens, such as thorotrast (thorium dioxide), polyvinyl chloride, and arsenic. Besides, anabolic steroids, hemochromatosis, and Von Recklinghausen syndrome are also known as potential causes.^{1,2}

PHA generally presents during the sixth and seventh decades of life and has an apparent male predilection with a ratio of 3-4:1. Although rare, there are some reported cases of PHA in children with a female predominance.^{3,4} Most patients present with nonspecific symptoms and laboratory findings. Similarly, imaging has a limited role in the diagnosis. A histopathological examination is frequently warranted to confirm the diagnosis.⁴ To date, a limited number of PHA cases have been reported in the English literature.

Herein, we present a 52-year-old male diagnosed with PHA. We aim to emphasise the MRI features of PHA and highlight this rare entity's rapid and fatal progression.

CASE REPORT

A 52-year-old man with a history of hepatitis B-related cirrhosis and hypertension was referred to our hospital to be assessed for liver transplantation. On admission, he had abdominal distension and fatigue. Physical examination revealed diffuse abdominal tenderness and ascites.

The laboratory tests showed elevated liver function tests including liver enzymes (aspartate transaminase: 175 U/L (normal range: <50 U/L), alanine aminotransferase: 134 U/L (normal range: 30-50 U/L), alkaline phosphatase: 301 U/L (normal range, 30-120 U/L), γ -glutamyl transpeptidase: 262 U/L (normal range: 0-55 U/L)) and bilirubin levels (total bilirubin (TB): 3.75 mg/dL, direct bilirubin (DB): 1.59 mg/dL (normal ranges: TB: 0.3-1.2 mg/dL, DB: 0-0.2 mg/dL)). Thrombocytopenia (platelet count: $105 \times 10^9/L$ (normal range: $150-400 \times 10^9/L$)) was also detected. Tumour markers, including α -fetoprotein (AFP) (2.88 ug/L (normal range: 0-9 ug/L)), were within normal ranges.

Magnetic resonance imaging (MRI) revealed two adjacent nodular lesions of 5 and 6 mm in the segment IV of the liver (Figure 1) that were hypointense on T1-weighted, hyperintense on T2-weighted images, and showed diffusion restriction. The

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Received: October 12, 2020; Revised: February 08, 2021;

Accepted: February 08, 2021

DOI: <https://doi.org/10.29271/jcpsp.2022.JCPSPCR.CR209>

arterial enhancement of lesions was not apparent because of numerous arterioportal shunts. The lesions did not demonstrate wash-out and were isointense on hepatobiliary phase images. Both lesions were categorised as Liver Imaging Reporting and Data System (LI-RADS) category 3. The patient was discussed at a multidisciplinary tumour meeting. Because of the diffusion restriction and the lesions' tiny size, an MRI follow-up in three months was planned. Three months later, MRI depicted a substantial increase in the lesion size measuring 8.5 cm (Figure 2).

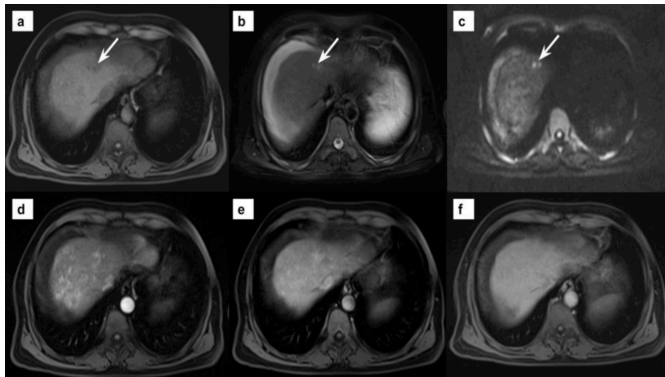


Figure 1: MR images showing two adjacent nodular lesions of 5 mm and 6 mm in segment IV of the liver (arrows). The lesions are hypointense on T1- (a) and hyperintense on T2-weighted images (b) and demonstrate diffusion restriction (c). Note the arterioportal shunts on the arterial phase T1-weighted image (d) that obscure the lesions' arterial enhancement. On the late phase contrast-enhanced T1-weighted image (e), no wash-out is visible, and the lesions are almost isointense with the liver parenchyma on hepatocyte-specific phase image (f).

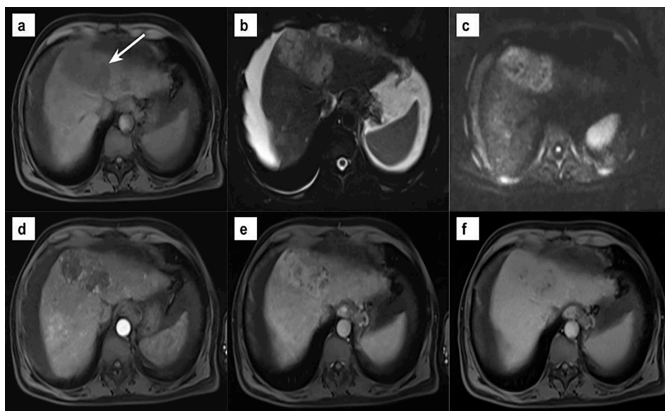


Figure 2: Follow-up T1- (a), T2- (b), diffusion-weighted (c) arterial phase contrast enhanced T1- (d), late-phase T1- (e), and hepatocyte-specific phase images (f) obtained three months later from the first scan demonstrate a very rapid increase in the size of the lesion (arrow) that now measures 8.5 cm in the segments IV and VIII of the liver.

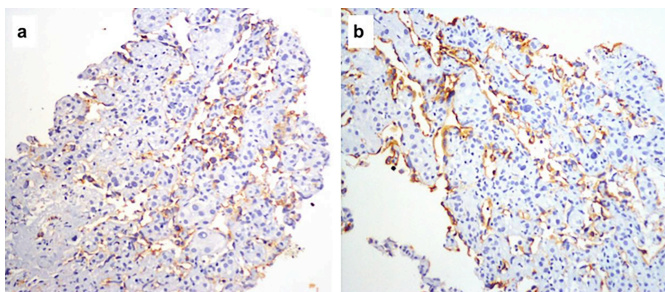


Figure 3: Cytoplasmic immunoreactivity with CD 31 (a) and CD34 (b) in atypical endothelial cells lining vascular structures (CD31 and CD34, x200).

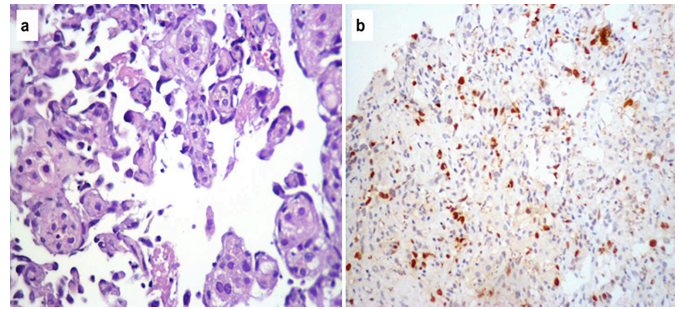


Figure 4: (a) Vascular structures lined by atypical endothelial cells with enlarged hyperchromatic nuclei (H&E, x400). (b) Increased nuclear proliferation marked with Ki-67 in atypical endothelial cells (Ki-67, x200).

On T1-weighted images, the lesion was heterogeneous hypointense and contained hyperintense portions consistent with haemorrhage. On T2-weighted images, it was heterogeneous hyperintense with focal areas of low signal intensity and hypointense septal structures. After IV contrast administration, the lesion showed early peripheral enhancement on the arterial phase images that demonstrated a heterogenous, progressive increase in later phases. It showed restricted diffusion with variable apparent diffusion coefficient (ADC) values and was isointense on hepatobiliary phase images. An ultrasound-guided trucut biopsy was performed. In the histopathological examination, extensive parenchymal necrosis with vascular proliferation lined by atypical cells with large pleomorphic hyperchromatic nuclei was detected. Tumour cells showed strong CD31 and CD34 immunostaining. Ki-67 proliferation index was 30% (Figures 3 and 4). The diagnosis of PHA was confirmed by pathology.

The patient had no history of chemical or industrial exposure and died due to spontaneous rupture and massive intraperitoneal bleeding.

DISCUSSION

Angiosarcoma is a malignant neoplasm of endothelial cell origin, accounting for 2-3% of all soft tissue sarcomas in adults.⁵ While breast and skin are the most common sites, hepatic angiosarcoma represents less than 5% of all cases.⁵ PHA has rarely been seen in clinical practice; however, it is the liver's most common mesenchymal tumour. Despite the risk factors mentioned above, aetiology remains unclear in 75% of cases.⁵

The clinical behaviour of this tumour is highly aggressive, and long-term survival is rare in these patients. Because of nonspecific and variable clinical and laboratory findings, most patients are diagnosed in the advanced stages. Moreover, PHA has a resistance to traditional radiotherapy and chemotherapeutics. Without treatment, the median survival time is less than six months, and despite treatment, only 3% of cases survive more than two years.⁴

Although we did not detect any metastasis in our patient at the first presentation, 60% of the cases are metastatic, and the most common sites of metastasis are the lungs, spleen, and bone marrow, respectively. The spleen is an unusual site for metastatic disease; however, splenic metastasis is common in PHA and is a clue to the diagnosis.^{1,6}

Clinically, patients may be asymptomatic or present with nonspecific symptoms, including abdominal pain, fatigue, fever, and weight loss. Physical examination is also nonspecific, and findings include hepatomegaly, splenomegaly, jaundice, and ascites. Spontaneous massive intra-abdominal bleeding and acute hepatic failure are well-known PHA complications, and patients may also present with these fatal complications in the first presentation.⁷

The laboratory tests reveal elevated liver function tests, including liver enzymes and bilirubin levels. Hematologic abnormalities such as anaemia and thrombocytopenia generally accompany PHA, and tumour markers, including AFP, are within normal ranges in the majority of cases.^{7,8}

Depending on the histopathological composition, PHA may show various CT and MRI appearances; specific imaging features have not been described yet. In cross-sectional imaging, four morphological patterns of PHA, including multiple nodules, a large dominant mass, a mixed pattern of dominant mass and multiple nodules, and diffuse infiltrating tumour, have been described in case reports and a few case series.^{1,8} MRI is a good diagnostic tool to show the heterogeneous, hemorrhagic, and hypervascular nature of PHA. On T1-weighted images, dominant masses generally appear heterogeneous and contain hyperintense portions that represent haemorrhage. On T2-weighted images, these lesions appear as focal areas of high signal intensity and septum-like or rounded areas of low signal intensity, which indicate marked heterogeneous internal architecture of tumours. Dynamic-contrast enhanced series reveal heterogeneous enhancement patterns on early and portal-phase images related to histopathological composition and progressive but incomplete enhancement patterns on delayed-phase images. On diffusion-weighted images, PHA shows diffusion restriction with variable ADC values.⁶⁻⁸ In this report, not only late-stage but also early-stage MRI findings of PHA are available. In our case, PHA first presented as millimetric nodular lesions and rapidly progressed to a dominant heterogeneous mass in three months. Although the last MRI findings correlated with previously described cases in the literature, the first radiological presentation was atypical and confusing. Furthermore, the rapid progression observed in a three-month later MRI highlights the importance of early diagnosis of PHA and how aggressive it is.

Hypervascular liver metastases (such as neuroendocrine tumours), hepatocellular cancer (HCC), cholangiocarcinoma, and mixed HCC-cholangiocarcinoma can show the same imaging features as PHA and cause a diagnostic dilemma. Some benign entities including giant cavernous hepatic hemangioma and hemangioendothelioma may also simulate PHA.^{5,8} The treatment options are limited. Complete surgical resection is the best choice to improve patients' survival; therefore,

PHA's diagnosis in the early stage is essential. Chemotherapy and radiotherapy are other treatment choices without significantly impacting the patient's survival.^{2,6}

In conclusion, the diagnosis of PHA is challenging, especially if the patient does not report any history of chemical or industrial exposure. In rapidly growing hypervascular hepatic lesions with a heterogeneous appearance, angiosarcoma should be considered in the differential diagnosis.

ACKNOWLEDGEMENT:

We thank Dr. Selin Gokcenoglu for providing the photomicrographs and related figure legends.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTIONS:

SD: Design of the work, data acquisition and interpretation, drafting, and final approval.

MB: Interpretation, critical revision and final approval.

BYO, KGE: Data acquisition, critical revision, and final approval.

SME: Data analysis and interpretation, editing and critical revision, and final approval.

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