# Primary Hepatic Angiosarcoma: Difficulty in Clinical, Radiological, and Pathological Diagnosis

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**SUMMARY**

**Hepatic angiosarcoma is a rare primary mesenchymal malignancy. Prognosis is poor and mortality occurs early. The diagnosis is challenging. Our case was an asymptomatic 70 year-old man referred, with incidental ultrasonography finding of multiple liver nodules. Diagnostic laparoscopic liver biopsy and the histopathological examination reported a haemangioma. Six months later, he became symptomatic and his health condition deteriorated rapidly.**

**KEY WORDS:**
*Primary liver angiosarcoma*

## INTRODUCTION

Angiosarcoma is a rare mesenchymal malignancy, accounting for less than 2% of all primary liver tumour[1]. We present a case of primary hepatic angiosarcoma which we encounter difficulties in clinical, radiological and pathological diagnosis.

## CASE REPORT

A 70 year-old man was referred, with incidental ultrasonography finding of multiple liver nodules. The ultrasonograph was ordered for investigation of microscopic haematuria. The physical examination was unremarkable. The laboratory data was as follows: hb-17.6g/dL, platelet count-161 x $10^3$, total bilirubin- 17 µmol/L, serum albumin-43g/L, alkaline phosphatase-58U/L, alanine transferase-28U/L. The tumour markers CEA, CA19-9 and AFP were within normal range. Upper and lower gastrointestinal endoscopy studies were done to exclude primary malignancy in the stomach and colon.

Multiple round low attenuation lesions of different sizes were noted in both lobes in the multiphase CT-scan of the liver. These nodules were hypoattenuating in both the arterial and portal venous phases. A differential diagnosis of multicentric hepatoma and liver secondaries were offered by the radiologist. He underwent diagnostic laparoscopy and liver biopsy and the histopathological examination reported haemangioma. Patient was subsequently given outpatient clinic follow up.

Six months later, he returned with complaint of bilateral lower limbs and scrotal swelling, associated with abdominal distension and early satiety. Physical examination revealed tinged of jaundice in the sclera, bilateral pitting oedema and ascites. Repeated laboratory studies were as follows: hemoglobin-11.2 g/dL, platelet count-159 x $10^3$, total bilirubin- 59 µmol/L, serum albumin-22g/L, alkaline phosphatase-138U/L, alanine transferase-40 U/L .A repeat CT-scan of liver showed diffuse nodular involvement of the liver with some irregular arterial enhancement. This enhancement continued into the venous phase. Laparoscopic liver biopsy was repeated. The histopathological examination revealed sinusoidal dilatation and focal ballooning degeneration of the hepatocytes. Some scattered atypical cells present with hyperchromatic and bizarre nuclei, lining the hepatic sinusoids. The specialized stains of vimentin, CD 31, CD 34, CKAE 1/3, CD 3 and CD20 were negative. He developed hepatic encephalopathy and his condition deteriorated. Finally he died of liver failure six weeks after re-admission. The final histopathological diagnosis of hepatic angiosarcoma was made based on the findings of complex dissecting proliferation of thin-walled vascular channels which has resulted in architectural disruption and presence of mild endothelial nuclei hyperchromasia in the first biopsy but has become more striking in the second biopsy specimen.

## DISCUSSION

Hepatic angiosarcoma is a rare disease. But it has generated considerable interest due to the strong association with exposure to industrial and environmental carcinogen. Angiosarcoma is known to associate with exposure to thorotrast (a radiological contrast agent), vinyl chloride, and arsenic. Despite of the known association of chemical carcinogens, majority of hepatic angiosarcoma detected now, are unrelated to the above agents.

Hepatic angiosarcoma predominantly affect male at a rate of 4 to 1, with median age of diagnosis is 50-59 years. The presenting symptoms are non-specific includes: right upper quadrant abdominal pain, anaemia, fever, weight loss, malaise and abdominal mass. Physical findings including ascites, hepatomegaly, jaundice and acute abdominal bleed[1, 3]. Laboratory results are also non-specific. Some cases reported elevated alkaline phosphotase[1]. Thrombocytopenia, DIVC, anaemia (especially microangiopathic haemolytic) was also reported[3]. Tumour markers and hepatitis B and C virus screening were negative. Our case was initially asymptomatic, with incidental ultrasonography findings of multiple hyperechoic liver nodules. Six months later, he became symptomatic and his health condition deteriorated rapidly.

Angiosarcoma is a malignancy of the spindle cells of endothelial cell origin that can form poorly organised vessels, growing along preformed vascular channels. The

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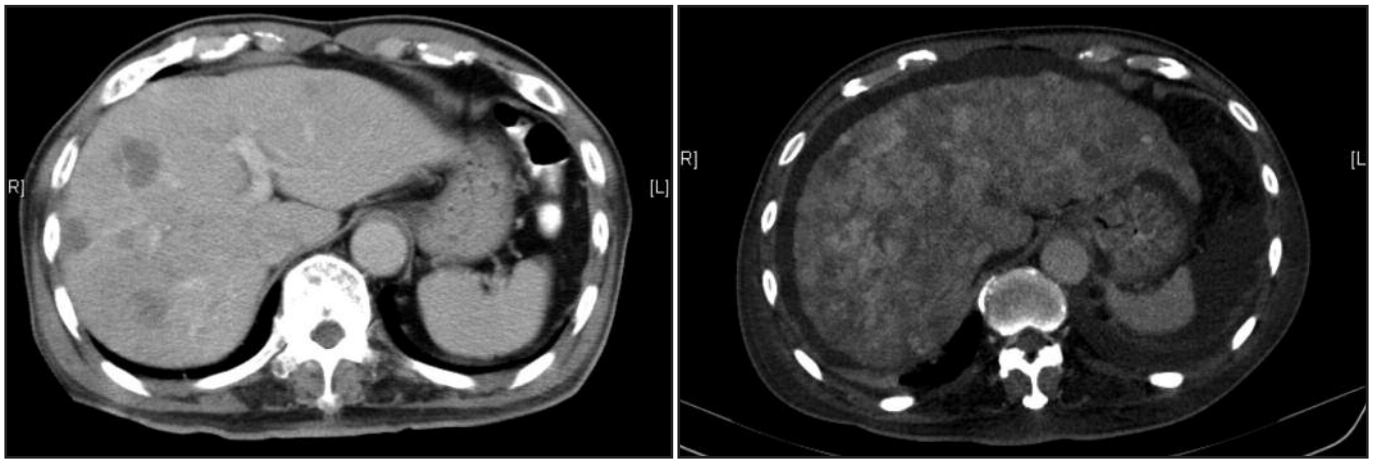


CT-scan of liver at initial presentation (top) shows multiple discrete nodules. Repeated CT-scan six months later (bottom) show diffuse involvement of liver by tumour.

arrangement can be in the sinusoidal or cavernous space, solid nodules or masses. The pleomorphic histopathology has accounted for a variety of pattern of tumour enhancement observed. The gross appearance of angiosarcoma has four patterns: multiple nodules, large dominant mass, mixed patterns of a dominant mass with nodules, and a diffuse infiltrating micro-nodular type. Multinodular and diffuse micronodular are the most common.

Peterson *et al* reported that most angiosarcoma lesion are multifocal and multiple. Many angiosarcoma lesions are hypoattenuating to the liver on both arterial and portal images. A few are hyperattenuating on arterial phase image, with some become isoattenuating on portal phase. But none of these are confused with the typical centripedal nodular enhancement of haemangioma that approximate the density of the contrast opacified blood pool in aorta or the hepatic artery[2]. Koyama *et al* also found that most tumour nodules are hypodense on non-contrast image, with some lesion showing focal areas of enhancement of less attenuation to the aorta. The shape of enhancement may be bizarre, central, or peripheral ring-shaped. The MR imaging demonstrate haemorrhagic, heterogeneous, and hypervascular nature of tumour presented with dominant mass. On dynamic contrast-enhanced MR images, the lesion show heterogeneous enhancement on arterial and portal phase's images and the enhancement are progressive in delayed imaging[3]. MRI study may be helpful in this patient on the subsequent presentation, when contrasted CT-scan show diffuse heterogeneous enhancement. FDG PET-scan was reported useful in detecting malignancy in a case where CT scan shows diffuse hypoattenuation with irregular liver surface, and massive ascites, but no apparent mass lesion. Increased SUV (standardized uptake value) in PET-scan selects patient for liver biopsy.

Our case presented with initial multiphasic CT-scan features of hypovascular liver lesions. Radiological differential diagnosis should include hypovascular liver metastasis (e.g. colonic cancer), hypovascular hepatocellular carcinoma, angiosarcoma and cholangiocarcinoma. A delayed imaging at equilibrium phase can usually exclude hepatocellular carcinoma by demonstrating 'wash out'. Cholangiocarcinoma will show delayed enhancement in the equilibrium phase. A careful clinical examination and investigation would exclude liver metastasis. In the presence of multiple hypoattenuatinng liver lesions, which is not enhanced or show bizarre enhancement atypical of the centripedal nodular enhancement of haemangioma, malignancy should be suspected. Biopsy should be obtained. However, diagnosis should not be based on histological interpretation alone, as hepatic angiosarcoma is difficult to diagnose even with multiple core needle biopsy. Good correlation of the radiological findings and histological interpretation is necessary to avoid error in diagnosis. This patient has also demonstrates morphological changes from initial multiple nodular liver lesions to diffuse infiltrative micro-nodular type of liver lesion in the late state. Such temporal change may represent progress of disease. This feature may also be helpful in the diagnosis of hepatic angiosarcoma.

## CONCLUSION

The diagnosis of hepatic angiosarcoma is challenging. The symptoms and physical findings are unspecific. Multifocal hypovascular liver lesions found in multiphase CT-scan without typical feature of benign haemangioma lesion should prompt suspicious of hepatic angiosarcoma. Histopathological diagnosis should be correlated with radiological findings to avoid error in diagnosis. Early diagnosis is crucial, because once patient become symptomatic, the disease progress is accelerated and treatment cannot be offered.

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