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Primary hepatic angiosarcoma manifested as hepatic sinusoidal obstruction syndrome: A case report

Ha H *et al.* Primary hepatic angiosarcoma

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Abstract

BACKGROUND

Primary hepatic angiosarcoma (PHA) is a rare malignancy with a poor prognosis. It is difficult to diagnose PHA because of the lack of specific symptoms or tumour markers, and it rapidly progresses and has a high mortality. To our knowledge, it has not been reported to mimic hepatic sinusoidal obstruction syndrome. Herein, we present a case of PHA manifested as hepatic sinusoidal obstruction syndrome, diagnosed using transjugular liver biopsy, that resulted in the death of the patient.

CASE SUMMARY

A 71-year-old man was admitted with the primary complaint of abdominal distension, decreased appetite, fatigue in the previous month, and loss of 10 kg of weight in the past two years. Both the liver and spleen were enlarged, and the liver had a medium-hard texture on percussion. Laboratory examinations were performed, and abdominal plain CT scans and contrast-enhanced CT images showed hepatomegaly and splenomegaly, as well as diffuse low-density shadows distributed in the liver and spleen. Contrast-enhanced CT scans revealed diffuse hypodensity nodular or flake shadows in the liver and heterogeneous enhancement in the spleen. A transjugular liver biopsy was performed. Based on the pathology results, the patient was diagnosed with hepatic sinusoidal obstruction syndrome secondary to PHA. The patient's status further deteriorated, developing serious hepatic failure. The patient was discharged, and died 3 days later.

CONCLUSION

PHA is rare and has a poor prognosis; however, transjugular liver biopsy can be safely performed to aid in diagnosis.

Key Words: Hepatic angiosarcoma; Hepatic sinusoidal obstruction syndrome; Outcome; Primary cancer; High mortality; Case report

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Core Tip: To our knowledge, PHA has not been reported to mimic hepatic sinusoidal obstruction syndrome. Here, we present a patient who died from PHA, which manifested as hepatic sinusoidal obstruction syndrome, which was diagnosed by transjugular liver biopsy.

INTRODUCTION

Primary hepatic angiosarcoma (PHA) is a rare form of malignancy, accounting for 2% of all primary liver tumours. Despite the low incidence, PHA is still the most common malignant mesenchymal tumour of the liver and the third most common primary liver malignancy^[1,2]. Accurate diagnosis of this tumour is usually difficult because the symptoms and signs are not specific, and tumours are difficult to distinguish radiologically from other hepatic tumours^[3]. In addition, a tissue sample is required for a diagnosis, and very few patients opt to undergo a needle biopsy^[4]. Herein, we report a case of PHA, which was manifested as hepatic sinusoidal obstruction syndrome.

CASE PRESENTATION

Chief complaints

A 71-year-old man was admitted to our hospital with the primary complaint of abdominal distension that commenced a fortnight before presentation.

History of present illness

He had ingested herbal medicine for 20 days prior, to maintain his health, but complained of decreased appetite, fatigue in the previous month, and had lost 10 kg of weight in the past 2 years.

History of past illness

The patient denied any history of hepatitis, diabetes mellitus, or cancer.

Personal and family history

The patient was not a habitual drinker and did not have any significant history of exposure to carcinogenic chemicals such as thorium dioxide, vinyl chloride monomer, or arsenic.

Physical examination

Both the liver and spleen were enlarged, and the liver had a medium-hard texture on percussion.

Laboratory examinations

Laboratory examinations on admission *were as follows* : white blood cell count, $6.57 \times 10^9/\text{L}$; haemoglobin, 88 g/L; platelet count, $45 \times 10^9/\text{L}$; albumin, 32.5 g/L; alanine aminotransferase, 90 U/L; aspartate transaminase, 124 U/L; alkaline phosphatase, 231 U/L; γ -glutamyl transpeptidase, 257 U/L; total bilirubin, 82.6 $\mu\text{mol/L}$; direct bilirubin, 48.2 $\mu\text{mol/L}$; prothrombin time, 18.9 s; international normalised ratio, 1.6; and plasma d-dimer, >10 mg/L. Tumour markers, including α -fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9, were within normal ranges. Screening tests for autoantibodies and viral hepatitis returned negative results.

Imaging examinations

Abdominal plain CT scans and contrast-enhanced CT images showed hepatomegaly and splenomegaly, as well as diffuse low-density shadows distributed in the liver and spleen (Figure 1A). The contrast-enhanced CT scans revealed diffuse hypodensity nodular or flake shadows in the liver and heterogeneous enhancement in the spleen (Figure 1B).

FINAL DIAGNOSIS

The patient presented with abdominal distension, jaundice, ascites, and hepatomegaly, in conjunction with the evidence on enhanced computed tomography; in addition, Budd-Chiari syndrome was ruled out because there were no communicating branches between the narrowed hepatic veins. The patient had a history of herbal medicine intake. After excluding other known causes of liver injury, a preliminary diagnosis of hepatic sinusoidal obstruction syndrome was made; however, there remained some doubts as the herbal medicine that the patient had ingested in its common form does not contain pyrrolidine alkaloid and splenomegaly was significant in the acute phase. The occurrence of splenomegaly during the acute phase of hepatic sinusoidal obstruction syndrome is rare. A transjugular liver biopsy was subsequently performed to improve the diagnosis.

Anticoagulation therapy was administered the following day. Three days later, pathological examination of a liver biopsy sample showed that the hepatic sinusoids were obviously dilated and filled with red blood cells. Hepatocytes around the sinusoid atrophy were found. Significant cytological atypia was observed with anastomosing channels, which was suggestive of angiosarcoma (Figure 2). Immunohistochemically, the specimen was positive for CD31, CD34, and ERG, supporting the diagnosis of PHA (Figure 3). The Ki-67 proliferative index was almost 20%–30%. Based on the pathology results, the patient was diagnosed with hepatic sinusoidal obstruction syndrome secondary to PHA.

TREATMENT

Whole-body PET/CT fusion scanning was performed after administration of ^{18}F -FDG for staging purposes to identify metastatic sites. Diffuse areas of increased uptake were seen in the liver, which corresponded to images on CT (Figure 4A). The maximum standardised uptake value (SUV) in the liver was 4.3. In addition, multiple areas of increased uptake were detected in the spleen and right ilium, suggestive of spleen dissemination (Figure 4A) and bone metastasis (Figure 4B), respectively.

OUTCOME AND FOLLOW-UP

The patient's status further deteriorated, with the development of serious hepatic failure, and progressive reduction in haemoglobin levels and platelet counts. The patient complained of further aggravated abdominal distension. At the family's request, the patient was discharged; he died 3 days later.

DISCUSSION

This case highlights the rarity and complex nature of the diagnosis of PHA. Owing to its rare occurrence, nonspecific symptomatology, nonspecific tumour makers, challenging radiographic findings, and low biopsy rate, confirming a diagnosis of PHA is difficult. The aetiology of PHA remains unclear. According to an epidemiological study, vinyl chloride monomer, thorium dioxide, arsenic, and ¹androgenic anabolic steroids are associated with the development of PHA in 25% of all cases^[5].

¹The symptoms of PHA are variable. Most patients have nonspecific symptoms including abdominal pain, fatigue, weakness, anorexia, weight loss, fever, and low back pain, and these symptoms mimic chronic liver diseases^[6]. Primary hepatic angiosarcoma is more predominantly found in men, with a male to female diagnosis ratio of 3:1, and presents in the fifth or sixth decade of life^[7].

It has been suggested that PHA can be elucidated by counting the number and size of hepatic tumours on CT images. Primary hepatic angiosarcoma can appear ¹as multiple nodules, a dominant mass, or a mixed pattern of a dominant mass and multiple nodules, but rarely manifests as an infiltrative, micronodular subtype^[1]. In our case, the tumour manifested as an infiltrative, micronodular subtype and the findings on contrast-enhanced CT were consistent with hepatic sinusoidal obstruction syndrome. To our knowledge, this is the first reported case of hepatic sinusoidal obstruction syndrome that was diagnosed as PHA.

The history of herbal medicine intake ⁴made this diagnosis more difficult. In China, hepatic sinusoidal obstruction syndrome is often associated with the oral intake of plants that contain pyrrolidine alkaloids. Our case met the 'Nanjing criteria' for the diagnosis of

hepatic sinusoidal obstruction syndrome except that the herbal medicine that the patient had ingested does not contain pyrrolidine alkaloid in its common form^[8]. Budd Chiari syndrome, especially the type with simple hepatic vein obstruction, can be easily misdiagnosed. Communicating branches between the narrowed hepatic veins are seen in Budd Chiari syndrome and are a critical feature that distinguishes Budd Chiari syndrome from other similar conditions^[8].

The patient's condition progressed rapidly. Thus, the diagnosis was questionable. A liver biopsy was necessary to establish a definitive diagnosis. However, because the patient's platelet count continued to decline and coagulation disorders and jaundice could not be controlled, a percutaneous liver biopsy was not performed, due to the associated increased risk of bleeding. There is evidence that transjugular liver biopsy is a highly efficacious, well-tolerated, and safe procedure. It can be safely performed multiple times in the same patient or in critically ill patients with severe coagulopathy and does not significantly increase the rate of complications while maintaining an extremely favourable diagnostic yield^[9]. It is difficult to make a diagnosis of PHA using only a CT scan, and a biopsy might be a reasonable option; however, percutaneous liver biopsy in patients with PHA is not safe because of the vascular nature of the tumour and its tendency to haemorrhage^[2]. Thus, sometimes, transjugular liver biopsy is a good choice.

Microscopic examination could show cytological atypia such as spindle-shaped cells, and immunohistochemical staining positive for CD31, CD34, ERG, and factor VIII in patients with PHA^[10,11].

There is report¹ that F-18 fluorodeoxyglucose positron emission tomography is helpful for distinguishing between PHA and giant cavernous hepatic haemangioma^[8], and it can help to identify metastatic sites for staging purposes. At the time of presentation, most patients with PHA have metastatic lesions, such as lung or spleen lesions. ^[12].

The treatment of PHA has not been defined owing to its rarity and association with high mortality. The median survival duration is 6 mo if the patient does not undergo treatment, and only 3% of patients live longer than 2 years^[2]. There are several choices of

treatment for patients with PHA. Ideal treatment is complete resection, especially when the tumour is limited to one segment of the liver^[13]. The prognoses of these patients depend on the ability to achieve complete tumour resection^[14]. However, more than 80% patients are diagnosed at advanced stage, with only a few patients meeting the criteria for tumour resection, curative surgery is difficult to perform^[15]. PHA is considered to be a contraindication for liver transplantation as survival is poor and recurrence rates are high^[16].

Primary hepatic angiosarcoma is also reported to be radioresistant^[3]. Alternative palliative therapies, including transarterial chemoembolization and systemic chemotherapy are considered to be effective for unresectable PHA^[17,18]. Transarterial chemoembolization is useful to treat acute arterial bleeding from the liver of patients with PHA^[18].

CONCLUSION

PHA is a rare malignancy with a poor prognosis. This case highlights the rarity of the disease, and the difficulty of diagnosis. Transjugular liver biopsy may be a safe choice in patients with PHA to aid in diagnosis.

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