



Case Report

A primary paraganglioma of the liver mimicking hepatocellular carcinoma

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ABSTRACT

Paragangliomas occurring primarily in the liver parenchyma are extremely rare. The radiological features mimic hepatocellular carcinoma. Herein, we describe a case with a presurgical diagnosis of hepatocellular carcinoma, which was pathologically confirmed as hepatic paraganglioma after surgery. A 41-year-old woman visited our hospital for evaluation of a hepatic mass detected incidentally in a health examination 7 years previously. Triple-phase computed tomography of the liver showed a homogeneous and strongly arterial enhancing mass, followed by portovenous washout at the posterior segment of the right lobe. In view of the enhancement pattern and highly vascular nature, the hepatocellular carcinoma was included in the differential diagnosis. Anatomical resection of segment VII was carried out. Grossly, the mass was encapsulated and soft. Microscopically, it had a typical “Zellballen pattern.” Immunohistochemical staining for CD56 was positive, and sustentacular cells at the periphery of the tumor cell nests were also demonstrated by S-100 protein. Therefore, the diagnosis of primary paraganglioma of the liver was confirmed. In conclusion, hepatic paraganglioma should be considered in the differential diagnosis in cases of hepatic masses displaying “early enhancement, early washout.”

KEYWORDS: *Paraganglioma, Sustentacular cell, Zellballen*

INTRODUCTION

Paragangliomas may arise in paraganglia in extra-adrenal sites including the retroperitoneum, neck, and bladder. A tumor arising within the liver parenchyma is extremely rare. The clinical imaging features of paraganglioma of the liver mimic those of hepatocellular carcinoma.

Herein, we describe a case of primary hepatic paraganglioma.

CASE REPORT

A 41-year-old woman was referred to our hospital for further evaluation of an enlarged hepatic mass that had been initially detected incidentally in a health examination 7 years previously. She had no symptoms, such as palpitations, headache, or sweating. As she lived in China most of the year, she had not received any treatment or regular follow-up.

She did not have a history of hypertension or medication history of oral contraceptives. She did not drink alcohol and had been generally healthy. Physical examination found no abnormalities, and her blood pressure was normal. Routine laboratory studies revealed her a complete blood count, leukocyte differential count, coagulation profile, and hepatic and renal function were all within normal limits. Her alpha-fetoprotein was 6.5 ng/mL, and carcinoembryonic antigen <0.5 ng/mL. Hepatitis B surface (HBs) antigen, anti-HBs antibody,

anti-hepatitis B core antibody, and anti-hepatitis C virus tests were negative.

Triple-phase computed tomography of the liver showed a homogeneous and strongly arterial enhancing mass, followed by portovenous washout at the posterior segment of the right lobe. The mass was hypervascular and enhanced by computed tomography hepatic angiography and showed a perfusion defect on computed tomography arteriography [Figure 1]. She did not undergo liver ultrasonography, liver magnetic resonance imaging, or percutaneous liver tumor biopsy. In view of the enhancement pattern and highly vascular nature, the differential diagnosis included hepatocellular carcinoma, focal nodular hyperplasia, hepatic adenoma, and neuroendocrine carcinomas, such as paragangliomas. Several hypervascular metastatic hepatic lesions were also considered, including metastatic renal cell carcinoma, thyroid carcinoma, leiomyosarcoma, choriocarcinoma, and breast cancer, which also display hyperenhancement during the arterial phase on computed tomography. However, the abdomen, liver triple-phase computed tomography in this patient revealed no other mass lesions in the kidneys, uterus, cervix, ovaries, stomach, small

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intestine, colon, or retroperitoneal space. Sonography of the bilateral breasts showed normal glandular and fatty tissue without apparent microcalcification. Physical examination found no palpable thyroid nodule or cervical lymph node. Due to the above findings, the liver metastasis from other primaries could be ruled out.

Anatomical resection of segment VII was carried out according to the imaging studies showing suspected hepatocellular carcinoma. During surgery, a solitary 3.5 cm × 4.5 cm × 4.0 cm mass was found. Grossly, it was an encapsulated soft mass without a central scar [Figure 2]. Microscopically, it was a well-defined, hypervascular lesion with nests of polygonal cells with eosinophilic granular cytoplasm and salt-and-pepper nuclei, separated by fibrovascular septae, the typical “Zellballen pattern” [Figure 3]. The neoplastic cells showed negativity for glypican-3 and hepatocyte paraffin 1, so hepatocellular carcinoma and hepatic adenoma were excluded. Furthermore, the immunohistochemical staining for CD56 was positive [Figure 4]. Sustentacular cells at

the periphery of the tumor cell nests were also demonstrated by S-100 protein [Figure 5]. On the basis of the histopathological morphology and results of immunohistochemical staining, the final diagnosis was primary paraganglioma of the liver.

Postoperatively, the patient had a smooth recovery, was discharged from the hospital, and continued follow-up in outpatient department at 4–6-month intervals. Ultrasound examination 6 months postoperatively showed the liver had a mildly coarse texture, but no hypoechoic lesion.

DISCUSSION

Extra-adrenal paraganglioma occurring primarily in the liver parenchyma is extremely rare. The etiology of a primary hepatic paraganglioma is associated ectopic chromaffin tissues in the liver [1]. However, hepatic metastasis of pheochromocytomas from the adrenal medulla is more common [2]. The patient’s bilateral adrenal glands were intact on computed tomography, so this possibility could be ruled out.

Preoperative diagnosis of sympathetic paraganglioma can be confirmed by biochemical testing, such as evaluation of 24-h urinary catecholamine levels or – the fractionated

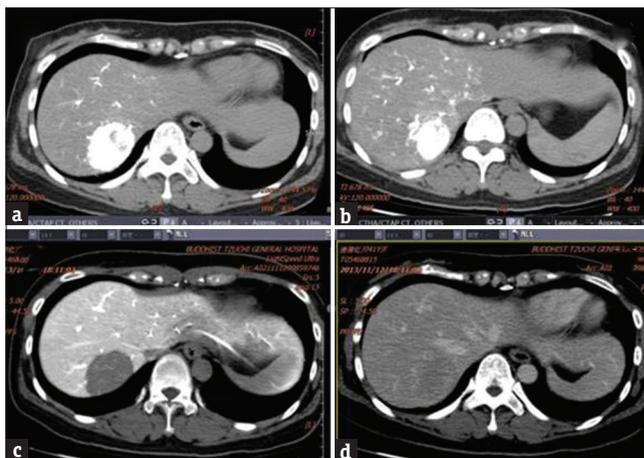


Figure 1: A hypervascular liver mass enhanced by computed tomography hepatic angiography (a and b). A perfusion defect shown on computed tomography arteriography (c and d)

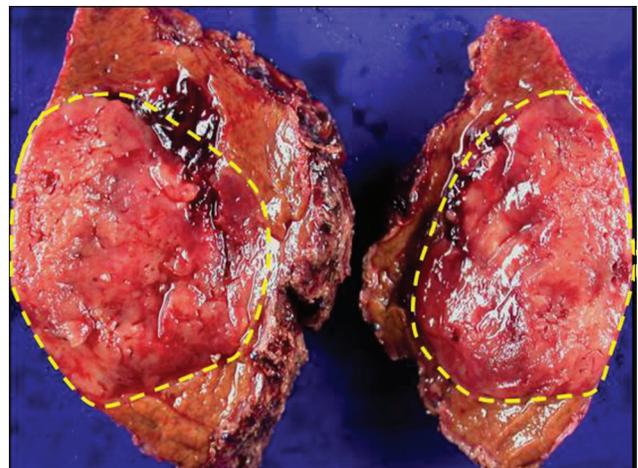


Figure 2: Grossly, the mass is encapsulated and soft

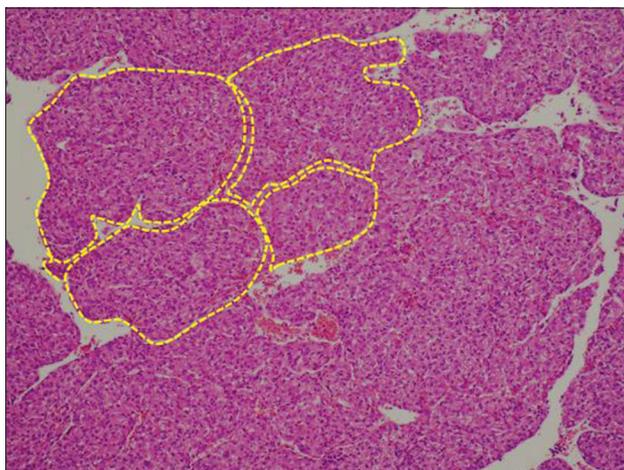


Figure 3: Microscopic examination shows a hypervascular lesion with nests of polygonal cells with eosinophilic granular cytoplasm and salt-and-pepper nuclei, separated by fibrovascular septae, the typical “Zellballen pattern”

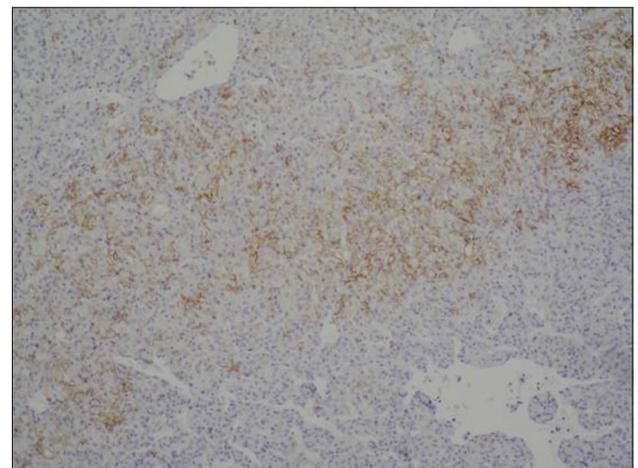


Figure 4: Immunohistochemical staining for CD56 is positive

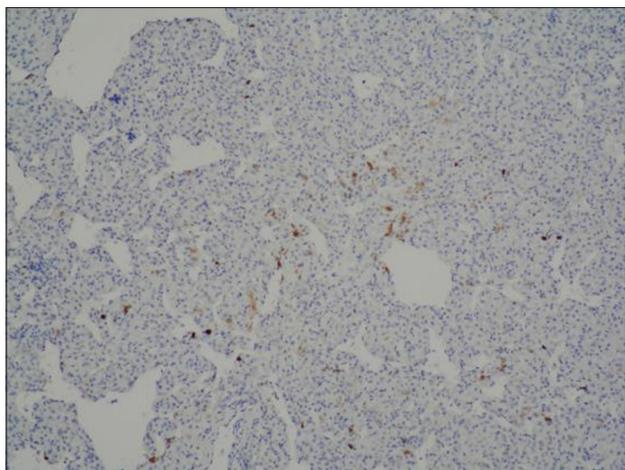


Figure 5: Sustentacular cells at the periphery of the tumor cell nests are demonstrated by S-100 protein

plasma metanephrine level, which is a more sensitive test [3]. However, up to 10%–15% of cases of paraganglioma are entirely asymptomatic, which makes the diagnosis a big challenge for clinicians [4].

On computed tomography, the typical appearance of a paraganglioma is a mass with an unenhanced density >10 Hounsfield units, avid contrast enhancement due to a rich capillary network, and delayed washout [5]. In the present case, the mass displayed very strong arterial enhancement followed by portovenous washout on triple-phase computed tomography, similar to the typical enhancement pattern of hepatocellular carcinoma. Therefore, based on the imaging findings, a preoperative diagnosis of hepatocellular carcinoma was made. However, on histopathological examination, the mass was finally confirmed as a hepatic paraganglioma. Previous studies have indicated it is impossible to make a diagnosis of primary hepatic paraganglioma solely through radiologic measures due to its rarity and nonspecific radiologic characteristics [6].

The histopathologic picture of a paraganglioma is characterized by polygonal cells with salt-and-pepper nuclei, granular eosinophilic cytoplasm, the classic “Zellballen pattern,” which are nests of tumor cells separated by peripheral capillaries. Sustentacular cells can be highlighted at the periphery of the nests by immunohistochemical staining for S-100 protein [7].

The treatment of choice for a primary hepatic paraganglioma is complete surgical resection. However, data on clinical behavior are currently lacking. In this case, the clinical course was benign, and the patient was discharged uneventfully.

A limitation of the present case was the lack of preoperative biochemical evaluation for paraganglioma, such as urinary or plasma catecholamines, free metanephrines, or urinary vanillyl-mandelic acid. These tests were omitted because the patient’s blood pressure had been normal.

In conclusion, the present case shows that hepatic paraganglioma should be considered in the differential diagnosis in cases of hepatic masses displaying arterial enhancement followed by portovenous washout (“early enhancement, early washout”).

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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