Case Report

Primary hepatic paraganglioma mimicking hepatocellular carcinoma: a case report

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Background: Primary hepatic paraganglioma (HPGL) originates from sympathetic nervous tissue in the liver. It is one of an exceedingly rare kind of sympathetic paragangliomas. The radiological features and clinical characters of HPGL can be easily confused with hepatocellular carcinoma (HCC). We present a case of HCC that was preoperatively diagnosed as hepatic paraganglioma, however, was pathologically verified as hepatic paraganglioma after surgery.

Case Description: The present case reported a 47-year-old female with a very rare HPGL without any clinical symptoms, except for hyper menorrhagia and paroxysmal hypertension. The Spiegelman lobe of the liver underwent hepatic magnetic resonance imaging, which revealed a 3.2×3.8 cm mass, with uneven arterial phase wash-in and rapid portal and delayed phase wash-out. According to the imaging results, the patient was first diagnosed with hepatocellular carcinoma, and a radical hepatectomy was performed. However, the blood pressure of the patient displayed dramatic changes when the tumor was stimulated in operation. There were no substantial abnormalities found in the bilateral renal and adrenal glands. Therefore, we presumed that the tumor was related to functional pheochromocytoma. The tumor tissue was shown to be positive for chromogranin A, synaptophysin, CD56, and vimentin by immunohistochemical analysis. As a result, the patient was diagnosed with HPGL after this pathologic evaluation.

Conclusions: There are several similarities between HPGL and HCC. For the treatment of hepatic paraganglioma, surgical excision is the recommended practice. Although the majority of paragangliomas are benign, long-term monitoring is required to differentiate benign from malignant paragangliomas.

Keywords: Paraganglioma; liver; hepatocellular carcinoma; surgery; case report

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Introduction

The neural crest Paraganglioma, a rare tumor of the neuroendocrine system, is caused by paraganglia cell clusters. More than half of extra-adrenal paragangliomas had been found in the retroperitoneal area (55.2%), followed by 3.2% in the mediastinum, and 25.6% in the head, and neck, and 5.6% in the bladder (1). Primary hepatic paraganglioma (HPGL) is very rare and can easily be confused with hepatocellular carcinoma in terms of clinical presentation and radiographic features. Although HPGL has been reported previously (2-6), it is still difficult to identify HPGL from hepatocellular carcinoma, hence more relevant cases are required. Herein, we describe a case of HPGL initially diagnosed as hepatocellular carcinoma (HCC). The patient had a hepatectomy after the first diagnosis. Throughout the procedure, her blood pressure was observed to highly fluctuated, particularly after the tumor was removed. The tumor was proven to be paraganglioma after a final pathological investigation. Importantly, this article is presented in accordance with the CARE reporting checklist (available at https://tcr.

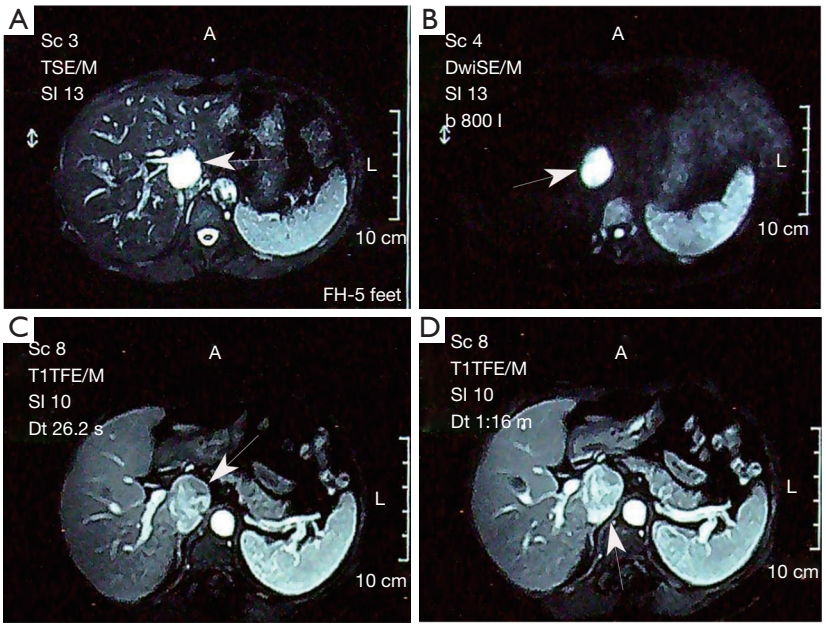

Figure 1 Liver magnetic resonance imaging scans. T2-weighted image (A) showed the mass with high intensity. Diffusion-weighted image (B) revealed the mass with restricted diffusion. Arterial phase (C) displayed the tumor was hyper-enhanced. Portal phase (D) indicated the tumor was de-enhanced. (Shown by the white arrows).

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Case presentation

A 47-year-old female patient with hyper menorrhagia and dizziness was brought to the local hospital. Routine blood examination indicated red blood cells 3.23×10^9 L, hemoglobin 53 g/L, and hematocrit 19.7. Two-dimensional abdominal ultrasound revealed a low echo area in the caudate lobe of the liver with a clear boundary and uniform internal echo. Color Doppler flow imaging showed blood flow signals in the low echo area of the liver. Multiple hypoechoic nodules were also detected in the myometrium of the uterus. Thus, the diagnosis was multiple fibroids of the uterus and caudate lobe of liver mass. Blood transfusion, iron supplement, and other symptomatic treatments were performed. The patient had no history of hypertension. During treatment, the patient's blood pressure increased significantly, up to 169/97 mmHg. Consequently, an Irbesartan hydrochlorothiazide tablet was given to smoothly control blood pressure. Furthermore, segmental curettage of the uterus was performed and no obvious abnormalities were observed in postoperative pathology. Then, the patient came to our hospital for further treatment of a focal liver lesion.

This patient had no history of coronary heart disease, hepatitis, diabetes, and smoking or alcohol abuse. Electrocardiogram, lung function, and chest radiograph were all normal during a routine examination. Additionally, no abnormalities were detected in blood routine, liver and kidney functions, electrolytes, or coagulation function in the laboratory tests. The tumor markers in the patient's blood were similarly found to be at normal concentrations such as carcinoembryonic antigen (CEA) 1.33 ng/mL (normal, <10 ng/mL), alpha-fetoprotein (AFP) 3.84 ng/mL (normal, <20 ng/mL), des-gamma carboxy prothrombin 27 mAU/mL (normal, ≤40 mAU/mL) and carbohydrate antigen 19-9 (CA19-9) 12.19 U/mL (normal, <39 U/mL). Moreover, hepatitis B surface (HBs) antigen, HBV-DNA load, and anti-hepatitis C virus were tested negative.

Liver magnetic resonance imaging (MRI) showed a well-defined 3.8×3.2 cm lesion as T1 hypointense and T2 hyperintense (*Figure 1A*) located at the Spiegelian lobe of the liver. MR with diffusion-weighted images (MR-DWI) revealed the hyperintensity of the tumor with restricted diffusion (*Figure 1B*), whereas MR with perfusion-weighted imaging (MR-PWI) showed the tumor was hyperintense enhanced in the arterial phase (*Figure 1C*) and rapid wash-

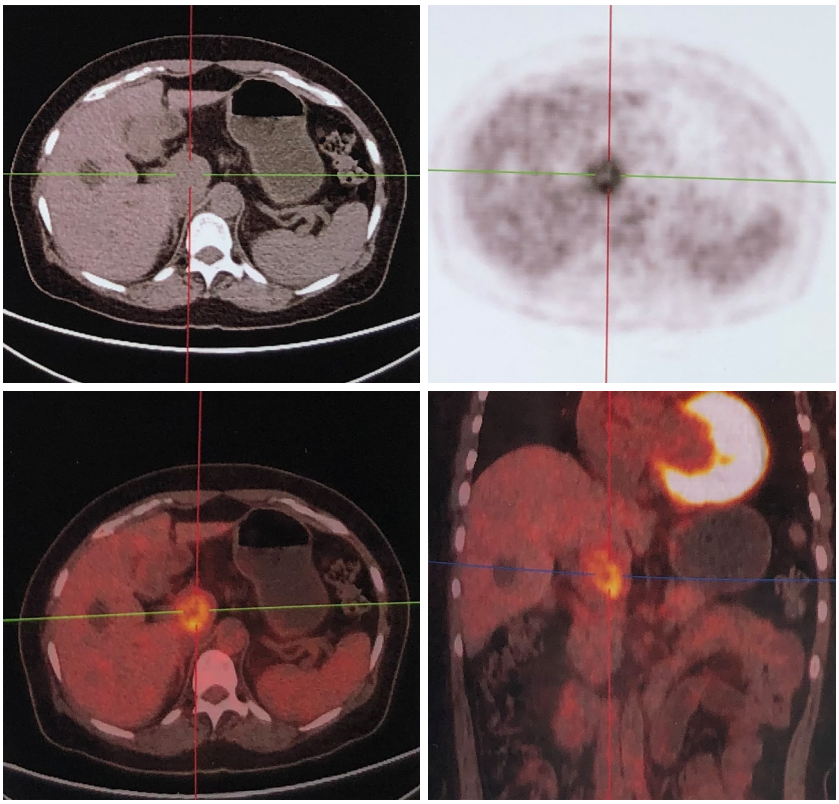

Figure 2 Positron emission tomography-computed tomography scans showed a low-density mass in the Spiegelman lobe with increased fluorodeoxyglucose metabolism.

out in the portal phase (*Figure 1D*). A whole body ^{18}F fludeoxyglucose positron emission tomography CT scan (PET-CT) showed focal avid increased uptake (SUVmax =5.20) in the Spiegelman lobe of the liver (*Figure 2*). Furthermore, no evident anomalies in uptake were seen in the other organs. As a consequence, these findings show that liver mass metastases from other organs should be ruled out and that the patient is most likely suffering from atypical HCC.

We conducted an excision of the focal hepatic tumor after thorough preoperative tests and evaluations. An intraoperative examination indicated that the tumor was 4×3 cm in size and close to the inferior vena cava in the Spiegelman lobe of the liver. In the abdomen, no further abnormalities were observed. The caudate lobe tumor was entirely disclosed when the first portal was blocked. The patient's blood pressure went to 260/180 mmHg after the tumor was detached from the inferior vena cava space. We immediately halted the procedure, within about 5 minutes, the blood pressure had returned to normal. During the second procedure, the blood pressure spiked again, which we found was due to the tumor's stimulation. Re-examination of the bilateral renal and adrenal glands indicated no substantial abnormalities. As a result, we assumed that this tumor was associated with a functional pheochromocytoma. We used a strong dosage of nitroglycerin and quick tumor removal to keep the patient's blood pressure under control. Blood pressure plunged to 60/30 after the tumor was surgically removed. Following the use of noradrenaline, the patient's blood pressure was steadily restored to normal levels. With no antihypertensive medication, the blood pressure ultimately normalized at 110/80 mmHg. Postoperative histopathologic examination showed a yellow tumor measuring 5×3.2 cm in a segment of the liver material, surrounded by a thin intact capsule with a small degree of hemorrhage and necrosis (*Figure 3*). The tumor tissues were found to be arranged in acinous or nest shapes having round or cuboidal tumor cells with nuclear vacuolated without nuclear division respectively. There were no microvascular tumor thrombus

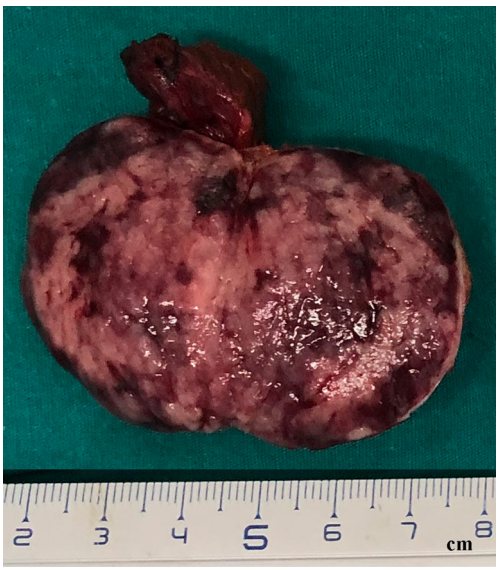

Figure 3 Gross appearance of the mass.

or false lobular structures in the liver observed under the microscope. Immunohistochemical analysis revealed that the tumor tissue was positive for chromogranin A (CgA), synaptophysin (Syn), CD56, and vimentin. Additionally, the patient tested negative for the following markers: Ki-67, CD 34, CD 117, HMB-45, ethidium monoacide (EMA), S-100, smooth muscle actin (SMA), cytokeratin 5.2, dog-1, and melanA. Subsequently, the final pathologic diagnosis of the patient was HPGL.

The patient was successfully discharged from the hospital seven days after the procedure, and no difficulties arose during her stay. The patient's blood pressure remained normal after surgery, even without the use of hypotensive medications. She was instructed to receive liver MRI or CT scans every three months following surgery. During the one-year follow-up period, no recurrences were identified.

All procedures performed in this study were in accordance with the ethical standards of the Clinical Research Ethics Committee of Eastern Hepatobiliary Surgery Hospital and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Paraganglioma, also known as extra-adrenal pheochromocytomas, is a rare neuroendocrine neoplasm. According to the World Health Organization (WHO), tumors associated with adrenal sympathetic tissue should be termed pheochromocytomas, while tumors associated with extra-adrenal sympathetic tissue should be called sympathetic paragangliomas (sPGLs) (7). These are often found along the body's axis and in close proximity to the sympathetic nerve distribution (8). The retroperitoneal cavity is the most prevalent location of disease, followed by the mediastinum, neck, skull base, and other areas of the body. Infrequently, it may also occur in the non-paraganglia distribution. However, paraganglioma occurring primarily in the liver is extremely rare and may be associated with heterotopic pheochromocytes in the liver.

Most sPGLs appear as slow-growing painless masses, and a few functional patients can be diagnosed by symptoms due to excessive catecholamines, such as paroxysmal hypertension, palpitation, dizziness, and hyperhidrosis (9). However, approximately 10–15% of cases of paragangliomas are asymptomatic (10) they are often discovered during physical exams, which makes diagnosis challenging. In the present cases, the patient had no history of hypertension or diabetes, no stomach discomfort or palpitation however, the liver lesion was discovered after excessive menorrhagia followed by dizziness during physical examination. These symptoms can be possibly associated with catecholamine hypersecretion. However, menorrhagia in this patient was considered to be related to uterine fibroids due to the history of multiple uterine fibroids. Nevertheless, hepatic paraganglioma has also been reported to be associated with menstrual irregularities (2). The patient also had paroxysmal hypertension during hospitalization, however, the specific reason for hypertension was not investigated further. Thus, a detailed medical history is important for the diagnosis of paraganglioma.

According to the CT imaging, hepatic paraganglioma characteristically showed liver with low attenuation lesion in the plain scan, obvious uneven wash-in in the hepatic artery phase, and rapid wash-out in the portal vein phase and delayed phase, which is similar to the typical enhancement pattern of hepatocellular carcinoma (11). Hepatic paraganglioma has a comparable increased MRI manifestation to CT scans. Although PET-CT provides a major diagnostic advantage for cancer, it is not specific for hepatic paraganglioma. The most significant test for PGL is ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) scintigraphy with high sensitivity (77–95%) and specificity (95–100%) (12). However, it is important to identify suspected cases in

combination with clinical diagnosis before being used as a means of further diagnosis. Therefore, an accurate diagnosis of primary PGL based only on imaging characteristics is difficult yet challenging.

Pathology is one of the gold standards for paraganglioma diagnosis. The histopathological appearance of paraganglioma is such that the epithelioid host cells are arranged in the form of nests with fibrous vascular or sinusoidal stroma. The cytoplasm is abundant, acidophilic, vacuolar, with fine red-stained particles. Individual cells have heteromorphic nuclei that are circular or oval with small nucleoli. Immunohistochemical staining is helpful for pathological diagnosis and differential diagnosis that is usually manifested as CD56 (+), Syn (+), Cg A (+), EMA (–), SMA (–), AFP (–), CD34 (–) and S-100 (–). The immunohistochemical results of the present case were consistent with the above-mentioned manifestations.

The majority of abdominal paragangliomas are benign; however, at least 10–20% of cases are malignant (8). Nonetheless, even pathological testing is insufficient to distinguish between benign and malignant paragangliomas in most cases. Long-term follow-up, usually over five years, is required to make the distinction (13). As the follow-up duration, in this case, was just half a year, a longer period is required to discover metastases. The most common treatment for HPGL is complete surgical resection, however, radiation therapy and chemotherapy may also play an essential role.

In conclusion, HPGL is extremely rare, while the clinical characters and imaging findings are quite similar to those of HCC except for different etiologies. Surgical resection is the preferred method for the treatment of hepatic paraganglioma. Additionally, long-time follow-up post-operation is the most effective method to distinguish benign from malignant.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-314/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-314/coif). All authors report that this study was supported by the program of Science and Technology Commission of Shanghai Municipality (Grant No. 19ZR1400100). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the Clinical Research Ethics Committee of Eastern Hepatobiliary Surgery Hospital and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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