

# Unusual location of the glomus tumour in the liver

## A case report and literature review

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### Abstract

**Rationale:** Liver glomus tumor is very rare, and only 6 cases have been reported. Herein, we report another case of liver glomus tumor and the clinicopathological features are summarized.

**Patient concerns:** An 18-year-old male patient was admitted due to hypertension and arrhythmia for 4 days.

**Diagnoses:** Abdominal enhanced CT revealed a 6.0-cm solid and cystic mass in the left liver lobe. The mass was collected by hepatic lobectomy. Microscopically, the tumor cells were round or oval, and had no malignant features and no evident atypia. Immunohistochemically, tumor cells were positive for SMA and vimentin, but partially positive for syn, CD34 and desmin. He was pathologically diagnosed with liver glomus tumor.

**Interventions:** The patient underwent a left hepatic lobectomy.

**Outcomes:** After surgery, this patient was followed up for 6 months, and metastasis/recurrence was not observed.

**Lessons:** Primary liver glomus tumor has no specific clinical manifestations, and imaging examinations have limitations for its diagnosis. Immunostaining for SMA and vimentin is necessary to prove the diagnosis. Complete resection is strongly advised and it has a favorable prognosis.

**Abbreviations:** CK = cytokeratin, CT = computed tomography, HE = hematoxylin-eosin, HMB-45 = human melanoma black 45, MRI = magnetic resonance imaging, NSE = neuronal specific enolase, PEComas = perivascular epithelioid cell tumors, SFT = solitary fibrous tumor, SMA = smooth muscle actin.

**Keywords:** clinicopathological features, diagnosis, glomus tumor, immunohistochemistry, liver, smooth muscle actin

### 1. Introduction

Glomus tumors are benign growths arising from the normal glomus apparatus located in the subcutaneous tissues and deriving from mesenchymal origin. They account for 1% to 2% of all soft tissue tumors and <5% of all soft-tissue tumors of the hand.<sup>[1,2]</sup> Glomus tumors are encountered most frequently in the digits but can be found rarely in visceral organs. They have been found in the bone, tongue, stomach, lung, rectum, mesentery, mediastinum, and other organs, but glomus tumor in the liver is very rare.<sup>[3]</sup> To date, only 6 cases of glomus tumor in the liver have been reported in available studies.<sup>[3–8]</sup> Herein, we report another case of glomus tumor of the liver in a male patient,

and the clinicopathological characteristics and immunophenotype were evaluated, aiming to provide evidence for the diagnosis of glomus tumor in unusual location.

### 2. Case report

This study was approved by the Institutional Review Board (IRB) of No 1 People's Hospital of Jining City. Informed consent was obtained from the patient. A male patient aged 18 years was admitted due to hypertension and arrhythmia for 4 days. On admission, enhanced computed tomography (CT) of the upper abdomen showed an oval lesion with abnormal enhancement in the left lobe of the liver, which was sized 6.0 cm × 4.6 cm and showed heterogeneous enhancement at the edge of the lesion in early phase of enhancement (Fig. 1A). The inward enhancement was observed in the portal venous phase and delayed phase (Fig. 1). Thus, cystadenoma in the left lobe of the liver was suspected. The patient had no anorexia, nausea, vomiting, chest tightness, shortness of breath, abdominal pain, abdominal distension, diarrhea, fatigue, and xanthochromia, and did not receive treatment before admission. He had no family history of liver disease. Preoperative biochemical examinations showed the levels of alanine aminotransferase (120 U/L; reference: 9–50 U/L), total bilirubin (41.6 μmol/L; reference: 7–23 μmol/L), indirect bilirubin (31.3 μmol/L; reference: 0–15.2 μmol/L), aspartate transaminase (143.8 U/L; reference: 15–40 U/L), lactate dehydrogenase (344.0 U/L; reference: 109–245 U/L), hydroxybutyrate dehydrogenase (214.0 U/L; reference: 72–182 U/L), and glutamate dehydrogenase (166.5 U/L; reference: 0–7.3 U/L) were elevated. Then, an exploratory laparotomy was performed. During the surgery, a tumor was found at the segment III close to

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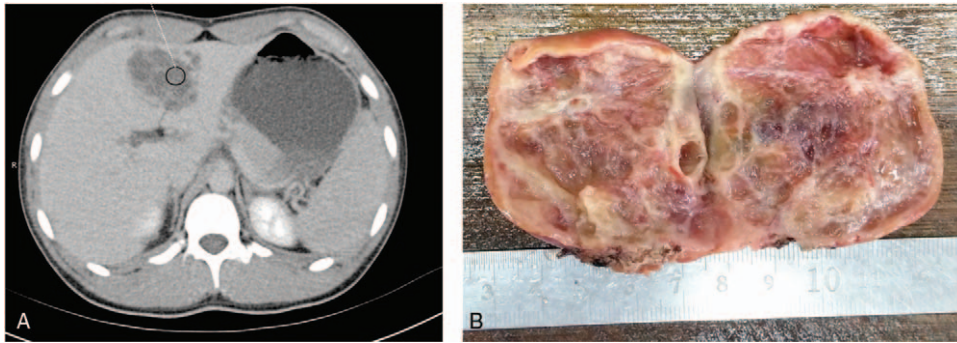
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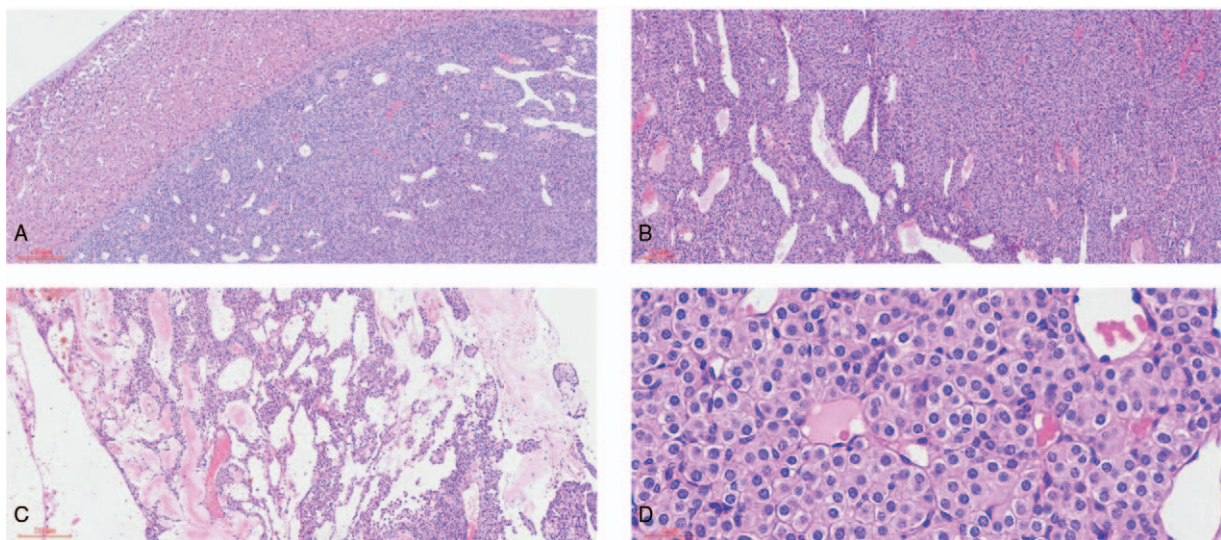
**Figure 1.** Computerized tomography and macroscopic observation. (A) Abdominal computerized tomography (CT) showed a cystic mass in the left lobe of the liver. (B) Macroscopically, the tumor was light red and sized 6.0 cm × 5.5 cm × 4.5 cm with smooth surface and gray section. CT = computed tomography.

the lower edge of the liver and showed exophytic growth; the tumor was red and soft, had irregular border and sized about 8 cm × 7 cm × 6 cm. Then, the liver tumor was resected, and intra-operative pathological examination of the tumor showed small and round tumor cells with possible vascular origin.

The tumor was collected and processed for immunohistochemistry. In brief, tumor tissues were fixed in 10% neutral formalin, dehydrated, embedded in paraffin and sectioned (4 μm). After hematoxylin-eosin (HE) staining, sections were observed under a light microscope. Immunohistochemistry was performed with EnVision 2 step method, and antibodies were from Bei-Jing Golden Bridge Biotech Co., Ltd. Antibodies used for immunohistochemistry included smooth muscle actin (SMA), vimentin, S-100, human melanoma black 45 (HMB-45), melan-A, desmin, calponin, h-caldesmon, glypican-3, CgA, Syn, CD117, DOG-1, cam5.2, CD10, hepatocyte, EMA, cytokeratin (CK), cyclinD1, CD34, and Ki-67.

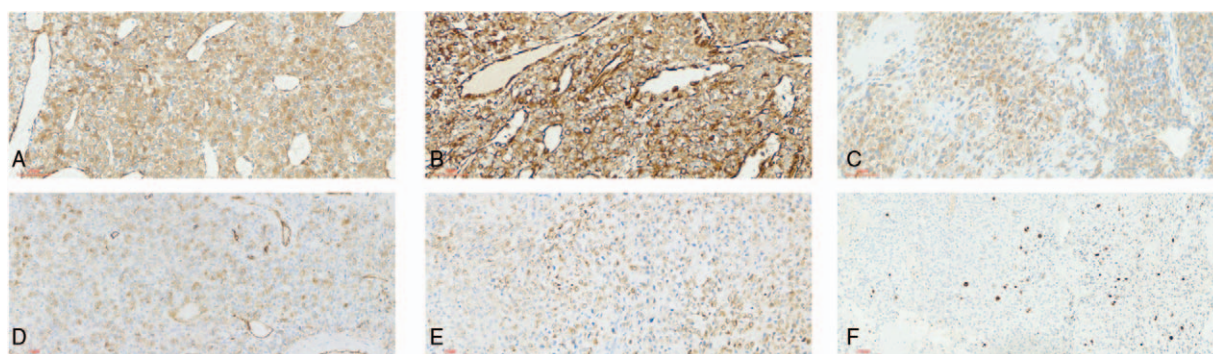
Macroscopically, the tumor was light red and sized 6.0 cm × 5.5 cm × 4.5 cm with smooth surface and gray section. The tumor was honeycomb-like at the cross-section and light yellow liquid was observed in the small cysts (Fig. 1B). Under a light microscope, the tumor had clear borderline (Fig. 2A), tumor

cells surrounded the blood vessels to arrange in solid, nest-like and hemangioperithelioma like manners (Fig. 2B), there were cavernous vessels with focal dilation, tumor cells aggravated besides the blood vessel wall (Fig. 2C), big nerve fibers were noted at the borderline between the tumor and liver tissues, mast cells were occasionally observed in the interstitium, the tumor cells were round to oval, tumor cells had no malignant features and no evident atypia, the chromatin was evenly distributed in cells, cytoplasm was lightly stained and transparent or eosinophilic, perinuclear halo was noted, there was clear cell outline (Fig. 2D), but caryokinesis and necrosis were not observed. Immunohistochemistry showed tumor cells were positive for SMA (Fig. 3A) and vimentin (Fig. 3B); some tumor cells were positive for syn (Fig. 3C), CD34 (Fig. 3D), desmin (Fig. 3E), and cyclinD1, calponin and β-catenin; tumor cells were negative for CD117, DOG-1, Cam5.2, CD10, hepatocyte, EMA, CK, h-caldesmon, glypican-3, CgA, S-100, HMB-45 and Melan-A; Ki-67 proliferation index was <2% (Fig. 3F). According to the above findings, this patient was diagnosed with glomus tumor in the liver. This patient was followed up for 6 months after surgery, and recurrence/metastasis was not observed.



**Figure 2.** Microscopic observation. (A) The tumor had a clear border with normal liver tissues. (B) Tumor cells surrounded the blood vessels to arrange in solid, nest-like and hemangioperithelioma like manners. (C) There were cavernous vessels with focal dilation, and tumor cells aggravated besides the blood vessel wall. (D) The tumor cells were round to oval, tumor cells had no malignant features and no evident atypia, the chromatin was evenly distributed in cells, cytoplasm was lightly stained and transparent or eosinophilic, perinuclear halo was noted, there was clear cell outline.





**Figure 3.** Immunohistochemistry for the tumor. (A) Tumor cells were positive for SMA; (B) tumor cells were positive for vimentin; (C) some cells were positive for syn; (D) some cells were positive for CD34; (E) some cells were positive for desmin; F: Ki-67 staining. SMA=smooth muscle actin.

### 3. Discussion

Glomus tumors are uncommon mesenchymal perivascular tumors with vascular hamartomatous derivative of glomus bodies.<sup>[1,2]</sup> Glomus tumors usually occur in adults (fourth to sixth decades of life) and generally there is no sex predominance, except in digital lesions which affect females more prevalently.<sup>[1]</sup> Glomus tumors are mainly found in the skin of extremities but rarely in visceral organs. Glomus tumors in visceral organs (such as gastrointestinal tract, mediastinum, bladder, kidney, and corpus cavernosum) are frequently diagnosed incidentally or due to vague symptoms. Glomus tumors arising in the liver are extremely rare. To date, 7 reports about glomus tumor of the liver have been published in the English literatures, in which 6 cases were reported.<sup>[3-8]</sup> In this report, we reported another case of glomus tumor in the liver and summarized its characteristics (Table 1).

Of the 7 cases, there were 2 women and 5 men, seeming to a higher incidence in men. In addition, the mean age was  $48.3 \pm 15.6$  years (range: 18–63 years), which was consistent with the

age distribution of general glomus tumors. On the basis of these 7 cases, it is too early to generalize sex and age predominance in the epidemiology of liver glomus tumors. Of note, the patient in our report was the youngest among the available cases, and thus age seems to be not a determinant in the diagnosis of glomus tumor in the liver.

The clinical symptoms of these patients were nonspecific, and gastrointestinal discomforts were the main manifestations such as epigastric pain/discomfort, nausea, loss of appetite and weight loss. Although these manifestations are nonspecific, they may guide the medical examinations, especially the CT or magnetic resonance imaging (MRI) of the liver, which are the commonly used tools in the diagnosis of glomus tumor although the findings may not confirm the diagnosis. Kenn et al reported the imaging findings of glomus tumor in the liver.<sup>[9]</sup> They found that the tumor displayed nodular uptake on enhanced CT; the lesion was moderately hyperintense on a breath-hold T2-weighted image, and dynamic contrast study indicated an early spoke-wheel-like enhancement. In our case, heterogeneous enhancement at the

**Table 1**

**Clinicopathological characteristics of primary liver glomus tumor in available reports.**

Authors	Country	Gender	Age	Clinical manifestations and laboratory tests	Immunohistochemistry	Treatment	Maximum diameter and location
Gassel et al <sup>[4]</sup>	Germany	Male	61	Lack of appetite and weight loss	Desmin (+); actin (+); vimentin (+)	Partial liver resection	3 cm; right lobe
Jaiswal et al <sup>[3]</sup>	USA	Male	57	Right flank pain; microhematuria	Vimentin (+), SMA (+); CD31 (+); CD34 (+)	Resection surgery	3 cm; right lobe
Geramizadeh et al <sup>[5]</sup>	Iran	Female	50	Right upper quadrant bulging	SMA (+); CD34 (+); CD31 (+; endothelial cells)	Left hepatic lobectomy	15 cm; left lobe
Amoueian et al <sup>[6]</sup>	Iran	Female	50	Vague epigastric pain and nausea; an enlarged left liver lobe in physical examination; a mild increase in alkaline phosphatase and bilirubin;	Vimentin (+), SMA (+); CD34 (+); HMB45 (-); CEA (-); synaptophysin (-), chromogranin (-), CK (-)	Hepatic lobectomy	12 cm; left lobe
Kihara et al <sup>[7]</sup>	Japan	Male	63	Epigastric pain and hiccups	Vimentin (+); SMA (+); type IV collagen (+);	Right hepatic lobectomy	20 cm; right lobe
Hirose et al <sup>[8]</sup>	Japan	Male	39	Fullness in the epigastrium; elevated biliary tract enzymes	Vimentin (+), SMA (+); focal positivity for calponin and synaptophysin; Ki-67 proliferative index was less than 3% in cystic lesions and 15% in solid lesions	Left hepatic lobectomy	21 cm; left lobe
Our case	China	Male	18	Hypertension and arrhythmia	SMA (+); vimentin (+); syn (+); cyclinD1 (+); CD34 (±); desmin (±); calponin (±); β-catenin (±)	Hepatic lobectomy	6 cm; left lobe

CEA = carcinoembryonic antigen, CK = cytokeratin, HMB-45 = human melanoma black 45, SMA = smooth muscle actin.

edge of the lesion was found in early phase of enhancement, but the inward enhancement was observed in the portal venous phase and delayed phase. In addition, imaging examinations may also display tumor vessels and cystic lesions.<sup>[8]</sup>

On gross appearance, the mass may be multilocular or monolocular cystic lesion encapsulated with irregular borders. On cross-section, the inner surface is grayish-white or red-brown and slightly rough, and focal hemorrhage may be observed. Kihara et al<sup>[7]</sup> proposed that the sustained hemorrhage and degeneration around the vessels are the main causes of the cystic changes in the glomus tumor. Microscopically, the tumor has numerous, small-to-medium branched vessels, which are surrounded by the epithelioid cells with round-to-oval nuclei and eosinophilic cytoplasm. There is no atypia or mitotic activity. Hepatic parenchymal, perineural, or vascular invasion may not be observed. In the 6 cases reported and our case, the mass was found in the right lobe of 3 patients and the left lobe of 4 patients, and the tumor size ranged from 3 to 21 cm, substantially larger than common cutaneous glomus tumors (typically small, <1 cm).<sup>[10]</sup>

Immunohistochemistry is the most important tool for the diagnosis and differential diagnosis of glomus tumor in the liver. Generally, the tumor cells are positive for desmin, SMA and vimentin, but negative for various cytokeratins, CD117, neuroendocrine markers (neuronal specific enolase [NSE], synaptophysin, chromogranin), S-100 protein, and HMB-45. However, there is still controversy on the reactivity for CD34 and/or CD31 (marker of endothelial cells). In our case and another 2 cases,<sup>[3,6]</sup> some tumor cells were also positive for CD34/CD31; the cases reported by Kihara et al<sup>[7]</sup> and Hirose et al,<sup>[8]</sup> tumor cells were negative for CD34/CD31.

Surgical resection is the recommended treatment for the glomus tumor in the liver. All the patients received lobectomy. The glomus tumor is benign and thus the prognosis of these patients is generally favorable. No recurrence and/or metastasis were observed in these 7 cases after surgical resection.

The glomus tumor in the liver should be differentiated from other vascular tumors (such as hemangioma, epithelioid hemangioendothelioma, and angiosarcoma) in the liver due to the vascular network in the glomus tumor. Histologically, it is easy to distinguish a hemangioma or angiosarcoma from a glomus tumor, but the differentiation between hemangioendothelioma and glomus tumor in the liver is a little bit difficult due to the morphological similarities. Hemangioendothelioma is composed of epithelioid cells, which are arranged in strands, cords, and nests with potential invasive growth. Additionally, histiocytoid and/or fusiform cells may be found in the tumor. Most tumors consist of highly cellular areas with small and prominent nucleoli in vesicular nuclei. Of note, hemangioendothelomas generally express CD34, ERG and vimentin, but lack the reactivity for SMA, S100, and EMA.<sup>[11]</sup> The other 2 differential diagnoses were paragangliomas and perivascular epithelioid cell tumors (PEComas). Paragangliomas are neuroectodermal tumors of the autonomic paraganglia, derived from the chromaffin cells of neural crest origin.<sup>[12]</sup> Its occurrence within the liver is rare. Paraganglioma is pathologically considered as benign lesion with slow-growing mass possessing relatively low proliferative activity although malignant potentials are also occasionally reported.<sup>[13]</sup> The characteristics of paraganglioma are the groups of uniform cells that are surrounded by spindle cells known as “zellballen”; the typical “zellballen” nested cells are pleomorphic and lack the structural organization. However, chief cells have immunopositivity for neuroendocrine markers (chromogranin A, synaptophysin, and NSE) and sustentacular cells show positive reaction

for S-100 protein.<sup>[14]</sup> PEComa is defined as “a mesenchymal tumor composed of histologically and immunohistochemically distinctive perivascular epithelioid cells.”<sup>[15]</sup> The tumor cells consist of epithelioid or spindle-shaped cells which have clear, eosinophilic, or granular cytoplasm. Generally, tumor cells are centrally located and have round to oval nuclei and inconspicuous nucleoli. Immunohistochemically, tumor cells are positive for HMB-45, and occasionally positive for S-100,  $\alpha$ -SMA, and desmin, but negative for epithelial and endocrine markers.<sup>[16]</sup> Hemangiopericytoma may be another disease that should be differentiated from glomus tumor in the liver. It is now considered as the cellular form of solitary fibrous tumor (SFT).<sup>[17]</sup> Hemangiopericytoma is a rare mesenchymal tumour with high vascularity and can be considered as a soft tissue sarcoma with very low-grade malignancy potential. The tumor is subepithelial, well demarcated but unencapsulated. It is composed of uniform tightly packed proliferated round to spindle cells surrounded by an intact reticulin sheaths. Immunohistochemistry shows the tumor cells are positive for SMA, muscle specific actin, nuclear beta catenin, but negative for desmin, keratin, and C-kit (CD117), factor XIIIa, HLA-D related, and vimentin.<sup>[18]</sup>

In summary, primary liver glomus tumor is a new and rare entity in hepatopathology and has unknown histogenesis and origin. It has no specific clinical manifestations, and imaging examinations have limitations for its diagnosis, which may delay the diagnosis of glomus tumor in the liver. Immunohistochemistry is considered essential to confirm the diagnosis. Generally, the tumor cells are positive for desmin, SMA and vimentin, but negative for various cytokeratins, CD117, neuroendocrine markers, S-100 and HMB-45. It seems to be a benign tumor and has a favorable prognosis. Complete resection is strongly advised, and postoperative recurrence and/or metastasis has never been reported in available cases.

## Author contributions

**Conceptualization:** Cuihong Han.

**Methodology:** Qingxia Xu.

**Project administration:** Liang Li, Xiangyu Zhang.

**Software:** Qingxia Xu.

**Supervision:** Xiangyu Zhang.

**Writing – original draft:** Cuihong Han.

**Writing – review & editing:** Liang Li, Cuihong Han.

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