Primary Glomangioma of the Liver

A Case Report and Review of the Literature

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• Glomangiomas are a subset of glomus tumors that have a rich vascular network. Although a majority of the glomus tumors occur in the skin of the hand, they have also been reported in the deep soft tissue, bone, lungs, and gastrointestinal tract, especially the stomach. To our knowledge, only one such case has previously been reported primarily occurring in the liver. We report a case of a glomangioma primarily arising in the liver of a 57-year-old man who presented with right flank pain of several months' duration. A 3.0-cm hepatic mass was excised and consisted of numerous, small-to-medium branched vessels with the stroma containing small, round, regular cells with sharply outlined round-to-oval nuclei. Immunostains showed the tumor cells to be diffusely positive for vimentin and smooth muscle actin and to be focally positive for calponin. Collagen IV stained the pericellular matrix. The immunostain for CD34 highlighted the vascular network as well as outlined the tumor cells in many areas. Coexpression of actin and CD34 in glomus tumors, although unusual, has recently been reported in the literature. Despite its bland histology, the large tumor size and deep visceral location were suggestive of aggressive behavior; thus, a close clinical follow-up was recommended. The patient had an unremarkable postoperative course and has no evidence of metastatic disease 12 months after the procedure. An accurate diagnosis and an understanding the biology of this rare disease, especially in an unusual location, are crucial to its management.

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Glomangioma, a subset of glomus tumors originally described by Masson[1] in 1924, is a neoplasm of the glomus apparatus. The glomus body is a specialized arterial-venous anastomosis that controls blood flow for thermal regulation. These bodies are typically located in the skin in the subungual regions of the upper extremities and, less often, in the subcutaneous soft tissue such as the coccygeal soft tissue.[2,3] The individual glomus cells have the ultrastructural features of modified smooth muscle cells.[4] Glomus tumors occur mostly in young adults (aged 20–40 years), typically as exquisitely painful nodules, but can also occur in children. Women and men are equally affected. These tumors are usually solitary, but they can be multiple. When glomus tumors have prominent vascular structures, the tumors are classified as glomangiomas.[2,4] When there is also a prominent smooth muscle component, the tumor is classified as a glomangiomyoma.[2]

A majority of the glomus tumors have been reported to occur in the skin of the hand, particularly in the subungual region. However, they have also been reported in the deep soft tissue, bone,[2] lung,[5] and gastrointestinal tract, especially the stomach.[6–9] It has recently been proposed that deep-seated glomus tumors, especially if larger than 2.0 cm, need a close follow-up, regardless of histology.[6] To our knowledge, only one case of glomangioma has previously been reported occurring primarily in the liver.[10,11] We report the second case of glomangioma primarily arising in the liver and discuss the biologic significance of such a diagnosis.

REPORT OF A CASE

A 57-year-old man presented to a clinic with the chief complaint of right flank pain of several months' duration. The patient's medical history was remarkable for hypertension, gastroesophageal reflux disease, a pacemaker for sick sinus syndrome, and a hiatal hernia. His surgical history was remarkable for a partial gastrectomy. On admission, the patient was discovered to have microhematuria, but there were no other significantly abnormal physical or laboratory findings. The patient underwent a dual-phased helical computed tomographic examination of the abdomen and pelvis, which revealed a 3.5-cm hypervascular mass within the posterior segment of the right lobe of the liver (Figure 1). A prominent feeding artery (Figure 1) and a prominent draining portal vein were identified. A radiologic analysis indicated that the mass could be an atypical hepatoma, a hypervascular metastasis, or an arteriovenous malformation. Because of the possibility of an arteriovenous malformation, an angiography was performed. This analysis demonstrated neovascularity in the mass, and it confirmed the presence of a prominent feeding artery (Figure 2) and a draining portal vein. The angiographic appearance was more suggestive of a hypervascular neoplasm than an arteriovenous malformation. An ultrasound-guided fine-needle aspiration showed only benign hepatic parenchyma. An exploratory laparotomy was performed to remove the hepatic mass. The postoperative course was unremarkable. There was no evidence of recurrence or metastatic disease 12 months after the procedure.

PATHOLOGIC FINDINGS

Pathologic examination revealed that the hepatic mass contained a 9.0-cm irregular segment of hepatic parenchy-

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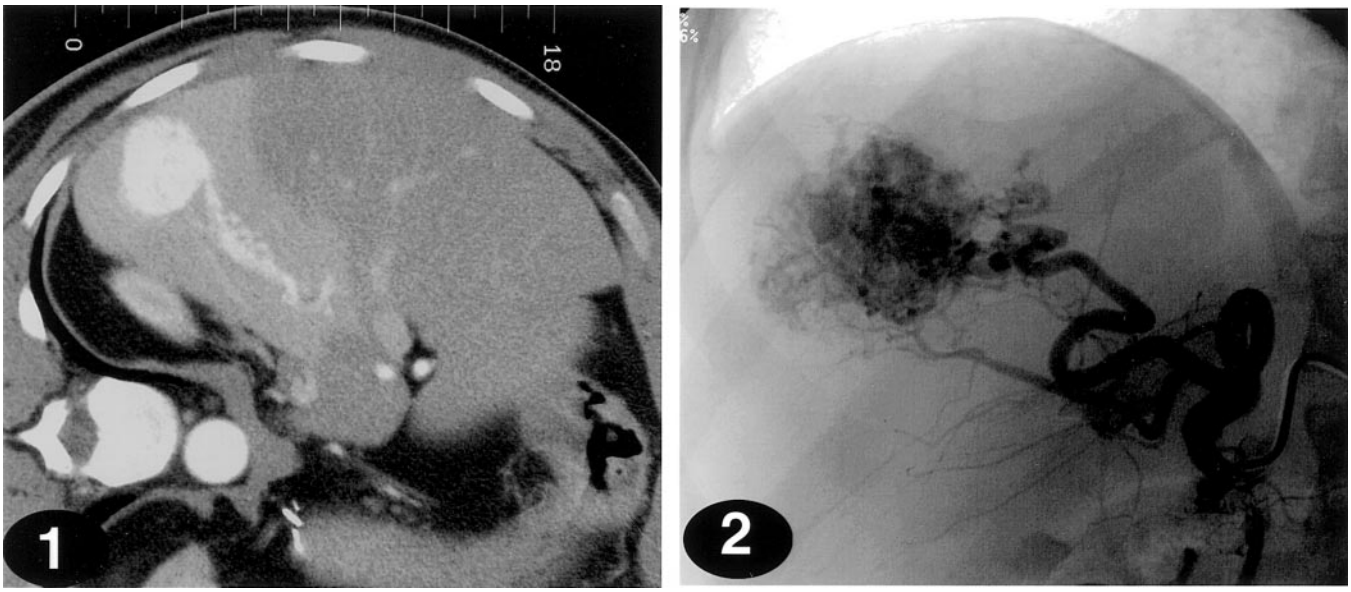


Figure 1. *Arterial-phase helical computed tomographic scan showing a prominent feeding vessel arising from the right hepatic artery and a 3.5-cm hypervascular mass.*

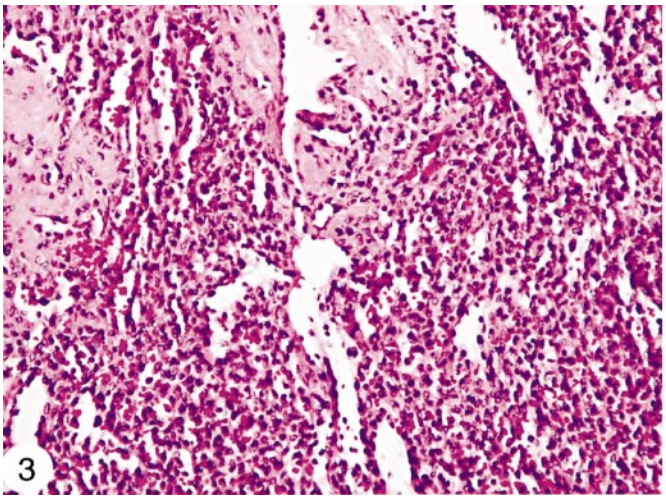
Figure 2. *Hepatic arteriogram confirms a large feeding artery and demonstrates neovascularity within the mass.*

ma with a 3.0 × 2.5 × 1.5-cm, red-brown, hemorrhagic and trabeculated neoplasm. The neoplasm was well demarcated with irregular borders. The surrounding liver parenchyma appeared grossly unremarkable. Microscopically, the tumor consisted of numerous, small-to-medium branched vessels, and the stroma contained small, round, regular cells with sharply punched-out, circular nuclei (Figure 3). These nuclei were centrally located and surrounded by scant-to-moderate amounts of eosinophilic cytoplasm. The individual cells had a bland morphology and contained rare mitotic figures (Figure 4). The tumor had irregular borders; however, no hepatic parenchymal, perineural, or vascular invasion was observed. Immunostains showed the tumor cells to be positive for smooth muscle actin (Figure 5). Vimentin showed diffuse cytoplasmic positivity in the tumor cells. Calponin also showed focal cytoplasmic positivity. Collagen IV immunostaining showed faint extracellular positivity around clusters of tumor cells. CD31 and CD34 immunostains highlighted the vascular network of the neoplasm and in many areas outlined the tumor cells (Figure 6). Immunostains for chromogranin, desmin, S100, cytokeratin AE1/AE3, CD117, and leucocyte common antigen were negative. The p53 immunostain was focally positive in the tumor cells, but Bcl-2 was negative. MIB1 immunostain showed approximately a 7% labeling index in the neoplastic cells.

COMMENT

Tumors derived from the glomus body, a specialized smooth muscle–derived structure that normally regulates blood flow for thermal regulation,[2] are well described in the literature. These tumors typically occur as painful skin nodules in the upper extremities and, less often, in subcutaneous tissue such as coccygeal soft tissues. In addition to soft tissues, these tumors have been described in locations such as the lung, trachea, mediastinum, cervix, vagina, bone,[6,7] and gastrointestinal tract.[8,9] Glomus tumors of the soft tissues most commonly occur in young adults, with men and women equally affected. In contrast, gastrointestinal glomus tumors occur most commonly in older women. Although rare examples of metastatic malignant glomus tumors have been reported in the liver,[12] to our knowledge, only one case of primary glomus tumor of the liver has previously been reported in the literature.[10,11] The reported case was quite similar to the current case. In the reported case, a subcapsular mass was detected on a routine ultrasound examination in a 61-year-old man, and the tumor was excised because of the patient's symptoms, namely a loss of appetite and weight, and because of the suspicion of a vascular neoplasm on radiologic evaluation. In the case of our study, the tumor was excised because of persistent right flank pain and because of the suspicion of a vascular neoplasm on radiologic evaluation. However, in neither case was evidence of malignancy found by histologic examination.

Because of the rarity of glomus tumors in this location, several other tumors were included in the differential diagnosis. Unlike vascular tumors such as hemangiopericytomas, hemangioendotheliomas, and angiosarcomas,[2] the current case had uniformly small, round-to-polygonal tumor cells with scant cytoplasm, bland nuclear features, and very low mitotic activity. The tumor cells were present in ill-defined clusters between the vessels; no well-defined nests, trabeculae, sheets, or spindling was observed. Features typical of hemangioendothelioma, such as intravascular tufting or intracytoplasmic lumina, and those of hemangiopericytoma, such as staghorn vessels, were also lacking in this case. Immunohistochemical evidence of myogenic differentiation and pericellular reactivity for collagen IV[2,6,7,13] further supported the diagnosis of glomangioma. The overall histology and immunohistochemical features were similar to the only other reported case of primary glomangioma of the liver in the literature.[10] An interesting finding in the current case was the intense widespread staining for CD34 that not only marked the vascular network but also marked the individ-



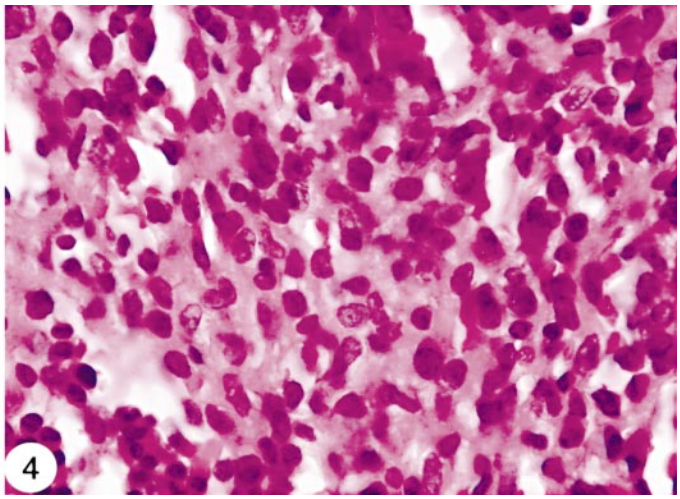
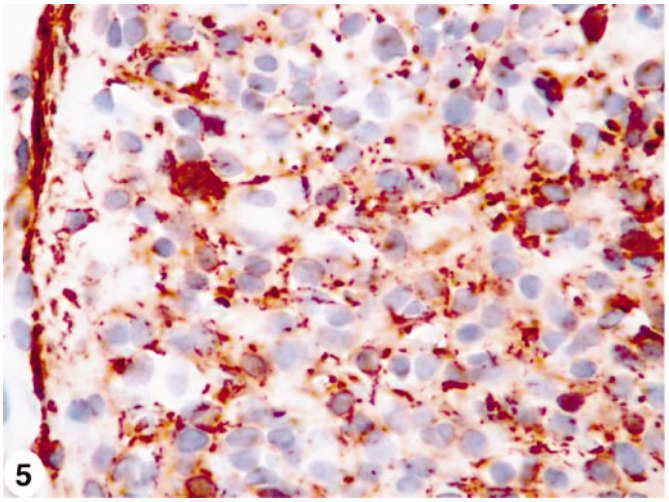


Figure 3. *The neoplasm is composed of a trabeculated network of vessels surrounded by bland, small tumor cells (hematoxylin-eosin, original magnification ×100).*

Figure 4. *The neoplastic cells have sharply outlined round-to-oval nuclei with bland chromatin and scant-to-moderate eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×400).*



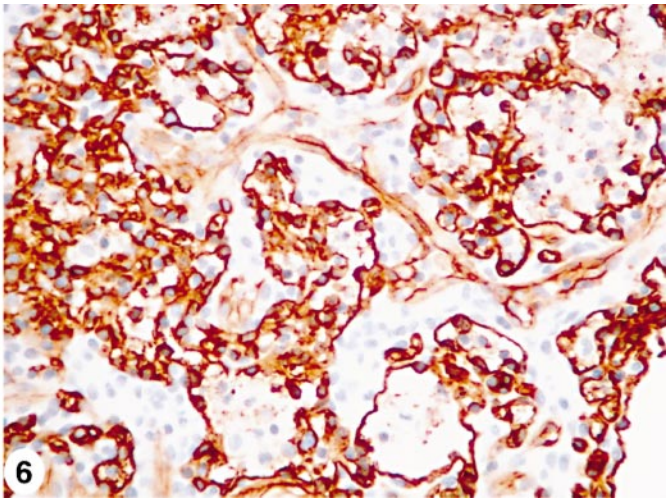


Figure 5. *Immunostaining for smooth muscle actin that shows scattered tumor cells with cytoplasmic positivity (smooth muscle actin, original magnification ×400).*

Figure 6. *CD34 immunostain highlighting the vascular network and the outlining of a few tumor cells (CD34, original magnification ×200).*

ual tumor cells in many areas. Such coexpression of myogenic markers and CD34 has recently been reported in glomus tumors.[14]

The absence of desmin immunopositivity in conjunction with the histologic appearance ruled out a vascular leiomyoma. The absence of S100 and chromogranin staining ruled out a paraganglioma. The lack of CD117 positivity has also been described as a feature of glomus tumors of gastrointestinal origin, and this helps distinguish glomus tumors from gastrointestinal stromal tumors. Our case was negative for CD117 immunostaining. Although we did not observe any areas that displayed the typical characteristics of a glomus tumor, as are sometimes seen at the periphery of atypical glomus tumors,[6] the overall morphology and vascularity in conjunction with the immunopositivity for smooth muscle actin and pericellular collagen IV helped establish the diagnosis of glomangioma in this case.

Most glomus tumors are small, superficially located, and benign.[2] Examples of histologically atypical, malignant, and even rare metastasizing glomus tumors[6,7] have been reported in the literature. There have been recent attempts to separate malignant glomus tumors from those of uncertain malignant potential.[6,7] Gould et al[7] classified the potentially malignant glomus tumors into locally infiltrative glomus tumors, glomangiosarcomas arising in a benign glomus, and de novo glomangiosarcomas. In a large, comprehensive, outcome study of atypical glomus tumors, Folpe et al[6] recently proposed that these atypical tumors be classified by use of the following 4 types: (1) malignant, (2) symplastic, and (3) glomus tumors of uncertain malignant potential, and (4) glomangiomatosis. They suggested that the term malignant glomus tumors be reserved for lesions that fulfill at least one of the following criteria: a deep location and a size that is larger than 2.0 cm, atypical mitotic figures, or a combination of

moderate-to-high nuclear grade and a mitotic activity of 5 per 50 high-power fields or higher. The metastatic rates in these groups were 67%, 100%, and 42%, respectively, and 75% of the patients who developed metastases died of the disease in less than 3 years. They also noted that deeply situated lesions were almost always larger than 2.0 cm. Similarly, high mitotic activity usually occurred in the presence of marked nuclear atypia. The term glomus tumor of uncertain malignant potential was used to describe superficial glomus tumors with mitoses of more than 5 per 50 high-power fields, deep location only, or large size only. Although the current case satisfied the criteria of deep location and size larger than 2.0 cm and had irregular borders, it had a low mitotic count and did not have any histologic atypia or perineural or vascular invasion. The only other reported case of primary glomangioma of the liver was also large (4.0 cm) and showed growth tendency, and the patient reported weight loss, which necessitated surgical excision, although no evidence of histologic malignancy or metastasis was documented.[10] Neither the reported case[10] nor the current case showed the marked nuclear atypia of symplastic or malignant glomus tumors or the diffusely infiltrating growth pattern of glomangiomatosis.[6] Hence, although the current tumor had a bland histology and appeared completely excised, its large size and visceral location suggest aggressive behavior. Because of its uncertain malignant potential, the patient is currently undergoing appropriate clinical follow-up.

In conclusion, we have reported an unusual case of primary glomus tumor of the liver of uncertain malignant potential. To our knowledge, this is the second such reported case in the literature.

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