Two case reports of rare diseases occurring in rare parts: Splenic vein solitary fibrous tumor and Liver solitary fibrous tumor

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Case Report

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Abstract

Background

Solitary fibrous tumor (SFT) is a rare soft tissue tumor originating from mesenchyme. Two cases of SFT we report right now occurred in the splenic vein and liver respectively, this primary splenic vein SFT may be the first report case, and also the first report of liver recurrence SFT cured by orthotopic liver transplantation (OLT).

Case presentation

One case was a 37-year-old female patient whose primary tumor site was located in the splenic vein, which resulted in splenomegaly and hypersplenism; its recurrence again and again after surgical resection and eventually transferred to the liver, during 10 years of follow-up, 4 operations were performed, and he is in a good condition right now. The second case was a 54-year-old male patient whose primary tumor site was located in the liver, spleen and left side of the chest wall; however, he had no uncomfortable symptoms. Surgeons performed two operations to remove these tumors, totally. 6 years later, SFT recurrence in the liver, and given that the tumor was so large that it could not be completely surgical resected, we chose orthotopic liver transplantation (OLT), and no tumor recurrence during 12-month follow-up.

Conclusion

The reports of these two cases of SFT are very rare, especially the splenic vein SFT, which expand the understanding of SFT. The main treatment of SFT is still surgical resection, right now, and liver transplantation may be a new option treatment for the huge liver SFT.

Background

Solitary fibrous tumor is an uncommon mesenchymal neoplasm that is characterized by a pattern less histological architecture, an intrachromosomal fusion gene NAB2-STAT6 in chromosome 12, and nuclear immunoreactivity for signal transducer and activator of transcription 6 (STAT6)(1), first described by Klemperer and Rabin in 1931(2), with an incidence of about 0.2/100,000 per years(3). The WHO classified SFT as a tumor derived from fibroblasts or myofibroblasts, rarely metastasizing, in 2013(4). Most SFTs are benign lesions, and the prognosis is good after surgical resection. However, there are still malignant lesions, and the surrounding tissue infiltration, local recurrence, and distant metastasis can be seen(5). Complete surgical resection is still the basis of its treatment. The reports about SFT were mainly concentrated in the pleura, a few reports suggested that it could also appear in any location, including the skin(6), meninges, and thyroid (7), round ligament of the liver(8), pancreas(5), and the liver SFT was first

reported in 1959(9). But there have been no reports of splenic veins SFT, so far, and also the no report of liver recurrence SFT cured by orthotopic liver transplantation (OLT).

Case Presentation

Case 1

A 37-year-old female patient was admitted to the hospital because of abdominal pain for one week. Physical examination upon admission revealed splenomegaly. Laboratory tests, including white blood cell (WBC) (2.70×10^9/L vs. normal range: 4–10×10^9/L), platelet (88×10^9/L vs. normal range: 100–300×10^9/L), and red blood cell (RBC) (3.61×10^{12}/L vs. normal range 3.8–5.1×10^{12}/L); liver function, blood coagulation test, and tumor markers were normal. Computed tomography (CT) scan indicated splenomegaly, splenic vein dilatation, low-density filling defect, no obvious enhancement in arterial and portal phase. The splenic vein tumor and spleen resection were performed in 2009. Grossly, the tumor was yellow-white debris, and the spleen was enlarged (16.0 cm × 5.0 cm), the splenic vein was tortuous and dilated. Histologically, the tumor was composed of spindle cells principally. Immunohistochemically, the tumor cells were positive for vimentin, CD34, and Bcl-2 and negative for smooth muscle actin (SMA), s-100, CD99, and CD117. And we also found Ki-67 (+) > 2%. So, this tumor diagnosed as a malignant solitary fibrous tumor (MSFT).

A month after the operation, CT and positron emission tomography/computed tomography (PET/CT) scan found SFT recurrence, and there was an 8.0cm × 2.5 cm low-density filling defect in the splenic vein, and no signs of tumor and metastasis were found in other sites. We surgically resected the tumor again and, resected the tail of the pancreas and regional lymph nodes too. Histology and immunohistochemistry were the same as before, but this time we found that the tumor broke through the blood vessel wall and infiltrated the surrounding tissues, no tumor tissue infiltration was observed in the remaining parts. After discharge, he was followed up every year without radiotherapy, chemotherapy, or molecular targeted therapy.

Unfortunately, 49 months later (July 2013), magnetic resonance imaging (MRI) revealed two metastatic SFTs in the liver and one tumor in the portal vein, measuring 0.3 cm, 3.0 cm, 8.1cm × 4.8cm × 3.9 cm, respectively (Fig. 1-A, B). Partial liver and portal vein tumor resection were performed. Pathological results confirmed hepatic metastatic MSFT (Fig. 1-C). Immunohistochemistry showed the tumor cells were positive for vimentin, CD34, Bcl-2, epithelial membrane antigen (EMA), and negative for SMA, s-100, STAT-6, CD99, CD117, and Ki-67 (about 5%). However, 39 months later (October 2016), the MRI scan found a local recurrence of the right posterior lobe of the liver and portal vein again, and surgical resection was performed, the pathological examination was the same as before (Fig. 1-D).

At present, the patient is still being followed up in our hospital and is generally in good condition, without symptoms of fatigue, weight loss, abdominal pain et al.

Case 2

A 54-year-old male was admitted to the hospital because of routine medical checkups, with no uncomfortable symptoms (March 2008). Abdominal ultrasonography revealed a 5 cm × 6 cm heterogeneous hypoechoic mass in the right lobe of the liver, without portal vein, hepatic vein, or Inferior vena cava involvement. PET-CT scan revealed multiple neoplastic lesions in the liver, spleen, and left side of the chest wall. The surgeons decided to perform two operations to remove these tumors. In April 2008, left chest wall tumor resection was performed, and in May 2008, partial liver (IV / VI) and partial spleen resection was performed, pathological results confirmed SFT of the chest wall, liver, and spleen (Figure.3).

79 months later (September 2014), she was admitted to our hospital again, because of a mild “heavy” feeling in the abdomen. CT and PET / CT scan demonstrated that the liver had a large solid mass with multiple leaves, and rich blood supply, measuring 23 cm × 18 cm × 11 cm. (Figure.2-A, B). The recurrence of SFT was confirmed by liver biopsy. The huge SFT also caused liver function damage, ALT (186 U/L vs. normal range: 5–35 U/L), and TBIL (53 mmol/L vs. normal range: 3–20 mmol/L). The preoperative evaluation showed that SFT resection may result in insufficient residual liver volume. Therefore, we performed liver transplantation on December 5, 2014. The operation went very well and the patient was also in good condition. Histologically, this tumor was composed of spindle cells with hyper-cellular areas and hypo-cellular areas (Figure.4-A). In hyper-cellular areas there are significant nuclear pleomorphisms and mitotic figures (more than 4 per 10 high-power fields [HPFs]). In other areas many collagen fibers can be observed. We can see the tumor cells infiltrate adjacent tissues. Immunohistochemically, the tumor cells were positive for vimentin, CD34, CD99, and Bcl-2 (Figure. 3-B/C/D) and negative for Syn, chromogranin A (Cg A), anaplastic lymphoma kinase (ALK), SMA, s100, CD117. In addition, focal tumor cells were sporadically positive for CD56, and Ki-67 (+) (5–10%).

The patient was followed up for more than 12 months and was in good condition without recurrence.

Discussion

Clinical characteristics

SFTs grow slowly, and symptoms are often related to the size or site of the tumor, many reports cases are also asymptomatic. Symptoms had been reported in other cases include dyspnea, fatigue, abdominal pain, nausea, vomiting, weight loss and hypoglycemia(2, 10–13). Nausea and vomiting were related to tumor compressing the esophagus and stomach, and hypoglycemia may be associated with IGF-2, while fatigue cannot be explained at present. Two cases of this paper, the first one was hypersplenism; the other one was asymptomatic at first, and at the second hospital admission with a mild "heavy" feeling in the abdomen.

Currently, there is no relevant report on primary splenic vein SFT, only one case of pancreas SFT invading splenic vein has been reported(5), therefore, other clinical characteristics of splenic vein SFT are unknown. But since Nevius and Friedman first described about liver SFT in 1959(9), there have been

reported 96 cases of liver SFT: liver SFTs seem to be more likely to occur in female patients, with a female: male predominance of approximately 1.37: 1, The mean age was 56.3 years old, The tumor can be found in either the right or the left hepatic lobe, The mean tumor size was 16.3 (2.0–35.0) cm(Table 1).

Table 1
Summary of 96 previously reported cases of liver SFT

Characteristics	Value
Age (mean ± SD, years)	56.26 ± 16.5(16–87)
Gender (male / female / NA)	37/51/8
Tumor main location (L/R/R + L/RLig/NA)	36/44/3/1/12
Tumor diameter (mean ± SD, cm)	16.27 ± 7.7(2–35)
IHC($CD34^+$/V^+/$Bcl\text{-}2^+$/$CD99^+$/$STAT6^+$/SMA^+/NA)	76/53/41/17/6/3/15
Treatment(resection / resection + TACE / resection + chemotherapy/TACE/radiation/LT/others)	77/3/3/1/1/1/8

SD, standard deviation; N/A, not available; L, left; R, right; RLig, round ligament; IHC, immunohistochemistry; V vimentin; Bcl-2, B-cell lymphoma 2; STAT6, signal transducer and activator of transcription 6; SMA, smooth muscle actin; TACE, transarterial chemoembolization; LT, liver transplantation.

Diagnosis

Imaging examinations are not specific; however, CT and MRI can find the location, size, and relationship with surrounding tissues of the SFTs, and reflect the internal histology of the tumor. PET/CT can analyze SFTs in both functional metabolism and anatomical location, simultaneous; and can be used to evaluate whether there is a distant metastasis before surgery.

SFTs were usually confirmed by immunohistochemistry, through tissue biopsy or resected specimens. Meanwhile, CD34 expression was the most consistent finding reported to date, present 90–95%, other markers include vimentin, CD99, EMA, and Bcl-2(2, 14). Including two cases in this article, vimentin, CD34, and Bcl-2 were all positive, and only the second case was CD99 positive. However, all these markers may also positive in other soft tissue tumors that mimic SFTs(15). The latest findings suggest that STAT6 is a highly sensitive and almost completely specific immunohistochemical marker of SFT, which helps to distinguish this tumor type(14, 16). Leona *et al*. evaluated whole-tissue sections of 231 tumors, including SFTs and other benign and malignant mesenchymal neoplasms and sarcomatoid mesothelioma. 98% of SFTs showed nuclear expression of STAT6, while STAT6 expression was negative for all other tumor types(14). The first case of immunohistochemistry in this article did not find STAT6 positive, which may be related to the detection method. And the positive rate of CD34 in Table 1 is similar to the above data, while the low positive rate of STAT6 mainly because of the test was not arranged (Table 1).

Treatments

Surgical resection is still the preferred treatment, and the overall 10-year survival in surgical studies with clear margins ranging from 54% and 89%(17, 18), and to achieve clear margins, it is necessary to expand the resection range. Although the first MSFT patient underwent 4 surgical resections, the patient is still in good condition. In addition, some new surgical methods have been reported. Sun *et al*. used liver autotransplantation to treat a large liver SFT patient(19); Zhu *et al*. used endoscopic submucosal dissection to treat a rare esophageal SFT patient(20), and El-Khouli *et al*. used TACE to treat unresectable liver SFT patient(21). For the recurrence of this liver SFT in the paper, we used orthotopic liver transplantation (OLT), and in the 12 months of follow-up, the patient also in good condition with no recurrence and metastasis.

In terms of adjuvant therapy, Bishop *et al*. and Salas *et al*. believed that surgery combined with radiotherapy could get better results than surgery alone(22, 23), however, the sample size is small and need larger sample studies to confirm. Stacchiotti *et al* reported that 8 patients with SFTs were treated with dacarbazine monotherapy and 12 patients were treated with doxorubicin/dacarbazine combination, and doxorubicin/dacarbazine combination caused a max tumor volume inhibition > 80%, the median progression-free survival (PFS) was more longer (24). Martin-Broto *et al*. conducted the first phase 2 trial of pazopanib for SFTs, 58% of patients with typical SFT had a partial response to pazopanib, which suggested that pazopanib has activity in the treatment of SFTs(1).

Prognosis

The benign and malignant tumor affects the survival time of patients.

Most SFTs reported in the literature are benign (> 80%). But some are still malignant, accounting for about 10% -15%(5), for the liver SFT, MSFT accounts for 22.9%, and there is no difference in the ratio of male and female (Table 2).

Table 2
Summary of 22 previously reported cases of liver SFT with malignant features.

Characteristics	value
Age (mean ± SD, years)	61.4 ± 14.8(24–80)
Gender (male / female)	11/11
Tumor main location (L/R/R + L)	7/14/1
Tumor diameter (mean ± SD, cm)	17.41 ± 6.89(3–22)
Treatment(resection / resection + TACE / chemotherapy/portal embolization)	18/1/2/1
SD, standard deviation; L, left; R, right; TACE, transarterial chemoembolization.	

Tumors can be considered as malignant tumors if they have the following points: infiltrative margins, high cellularity, prominent cellular atypia, tumor necrosis and increased mitotic activity (> 4 mitoses per

10 HPF)(4), Marcelo *et al*. also found that ki-67 higher than 5% could as a marker of malignancy, and ki-67 positivity in 5% or less as a marker of benign(11). A long-term follow-up showed that increasing mitotic count correlating with increasing probability of metastases and decreasing overall survival(25). The short-term recurrence of case 2 may be related to mitotic count. Meanwhile, SFT patients with tumors larger than 10 cm have a poor prognosis(26). However, there is one reported case of a malignant SFT measuring only 3 cm in diameter (Table.2). Besides, Martin-Broto *et al*. also suggested that overexpression of CD209 has also been related to poor prognosis in SFTs(1).

Conclusion

This paper is the first reports of splenic vein MSFT with hypersplenism and recurrent liver SFT treated by OLT. Surgical resection is an important choice; radiotherapy, chemotherapy and targeted therapy are used to control local recurrence and distant metastasis may be effective, but further research is needed to confirm it, liver transplantation received in the second case may be a new option treatment for the huge liver SFT. Since splenic vein SFT and other vascular system-related SFT and, liver SFT are very rare, the case reports and further researches on SFTs have great significance.

Abbreviations

SFT
solitary fibrous tumor
MSFT
malignant solitary fibrous tumor
OLT
orthotopic liver transplantation
STAT6
signal transducer and activator of transcription 6
Bcl-2
B-cell lymphoma 2
SMA
smooth muscle actin
EMA
epithelial membrane antigen
Cg A
chromogranin A
ALK
anaplastic lymphoma kinase
WBC
white blood cell (WBC)
RBC

red blood cell (RBC)
CT
computed tomography (CT)
PET/CT
positron emission tomography/computed tomography (PET/CT)
MRI
magnetic resonance imaging (MRI)
PFS
progression-free survival (PFS)
HPS
high-power field
TACE
transarterial chemoembolization
HE
hematoxylin and eosin

Declarations

Ethics approval and consent to participate:

Not applicable

Availability of data and materials:

All data generated or analysed during this study are included in this published article

Consent for publication:

Written informed consent was obtained from the patients for publication of this report and accompanying images.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

Anbin Hu, Xiaofeng Zhu, and Qing Chen provided patients’ information; Banghe Bao analyzed the patients’ data; Wenjing Wang and Banghe Bao were major contributor in writing the manuscript. All

authors read and approved the final manuscript

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Figures

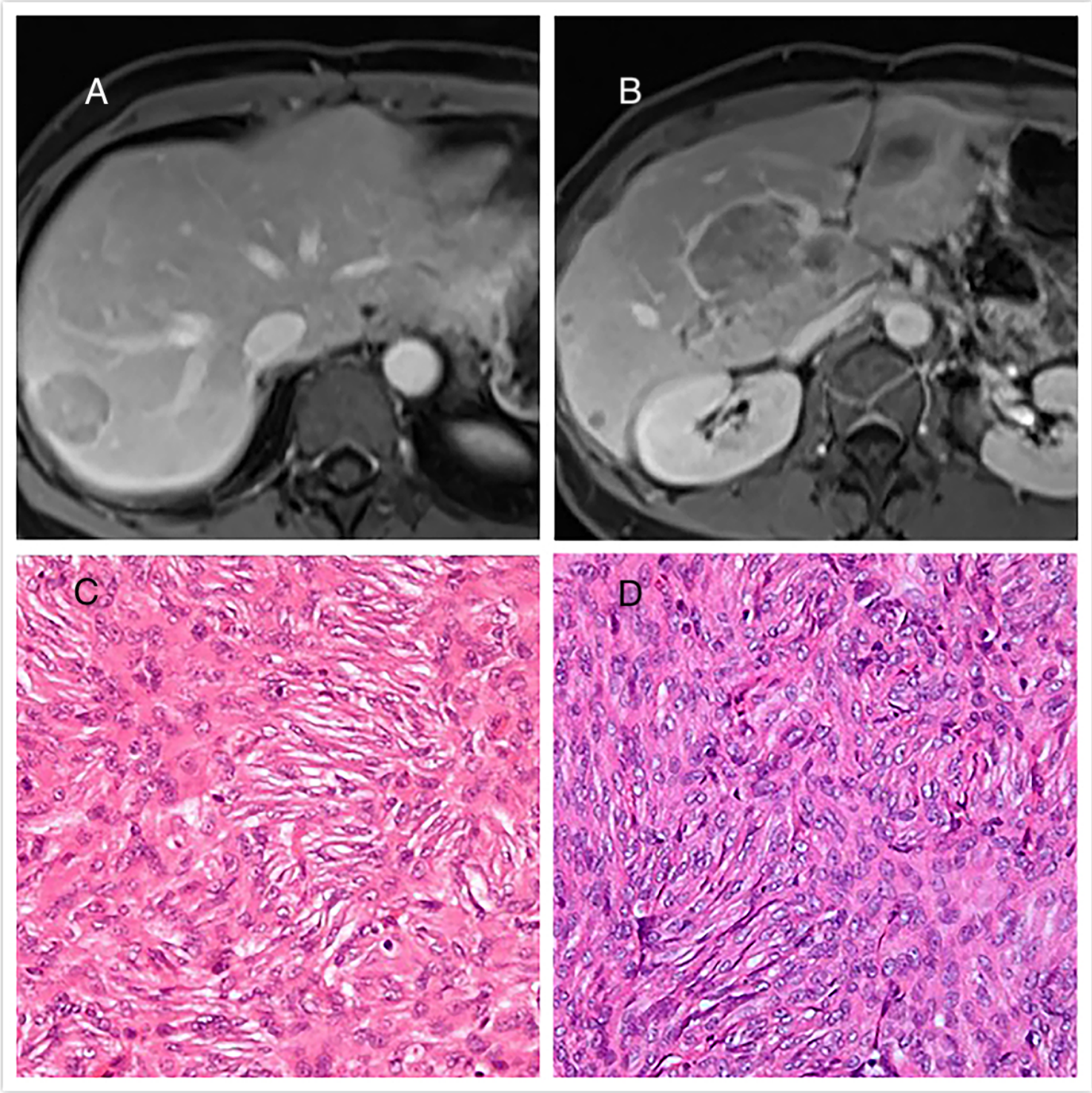

Figure 1

Abdominal magnetic resonance imaging scan prior to the third operation, and postoperative histopathology examination. (A)(B) Abdominal magnetic resonance imaging (MRI) scan about the liver metastatic tumor and portal tumor, measuring 0.3cm, 3.0cm, 8.1cm×4.8cm×3.9cm, respectively. (C)(D) Histological examination showed that the tissues consisted of spindle-shaped cells. The images are of hematoxylin and eosin (HE) staining at (C) x100, and (D) x100 magnification.

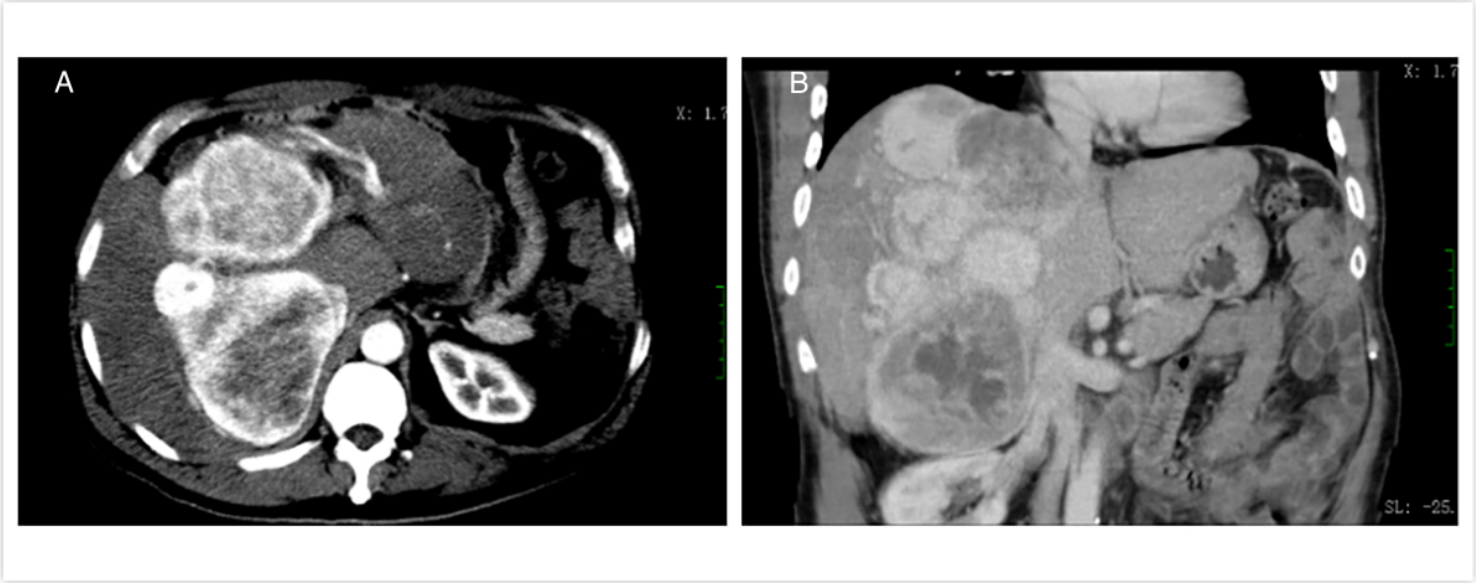

Figure 2

(A)(B) Computed tomography (CT) scan of the abdomen showing a multi-lobed, solitary, large mass (23 cm × 18 cm × 11 cm). The claw sign of hepatic tissue suggests intrahepatic localization. Notable features include hypervascularity, heterogeneous enhancement, and smooth margins.

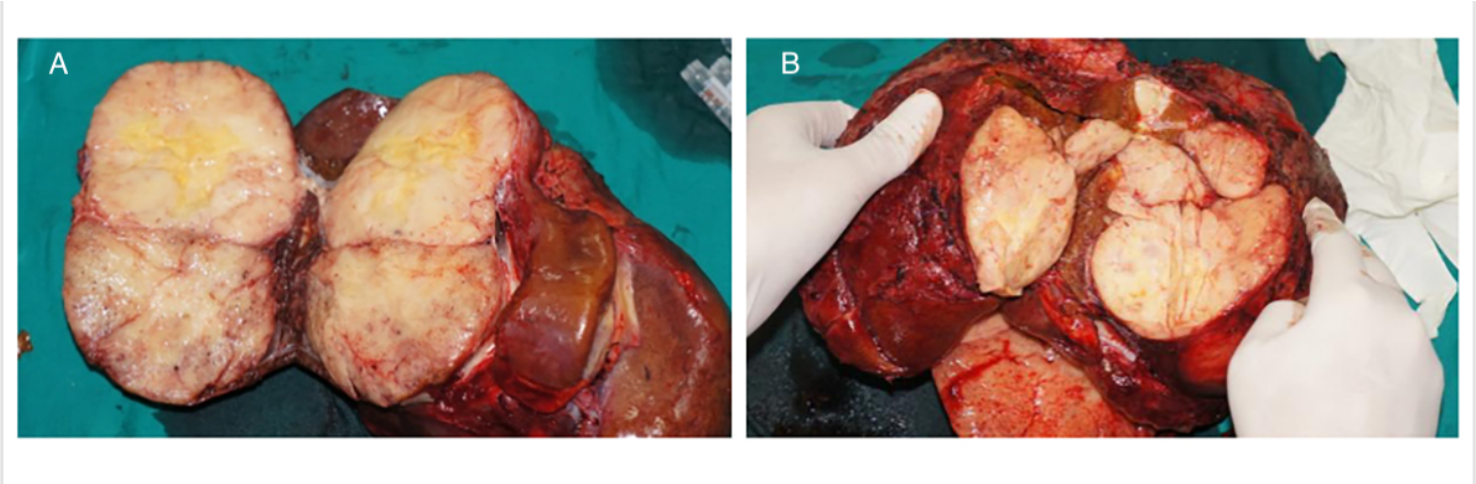

Figure 3

Gross specimen is a bulky, grayish-white neoplasm attached to the liver capsule, having smooth external surface with few congested vessels.

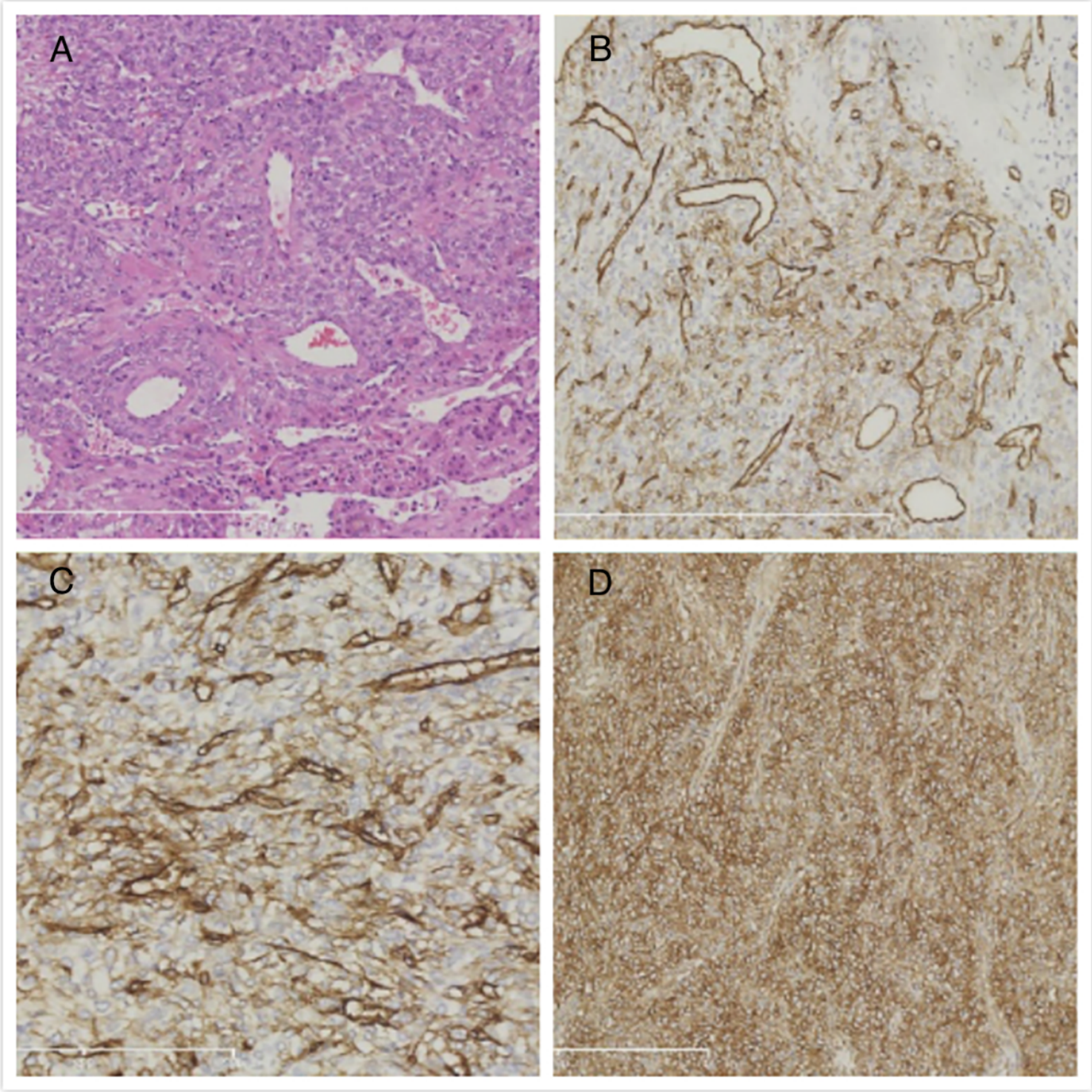

Figure 4

(A) Spindle tumor cells with inconspicuous pleomorphism and rare mitotic figures (approximately 2 per 10 HPF). Hemangiopericytoma-like stag horn blood vessels were observed on the tumor site and scanty hepatocytes are in the lower right corner (HE, × 100). (B)(C) A fraction of tumors are positive for CD34 and vascular endothelial cells are strong positive for CD34. The normal hepatocytes are negative for CD34 (IHC, × 100). (D) The tumors are Positive for CD99 (IHC, × 100).

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