Angiosarcoma of the Liver

Clinicopathologic Features and Morphologic Patterns

Saba Yasir, MD and Michael S. Torbenson, MD

汇 报 人：张微晨

指导教授：李增山

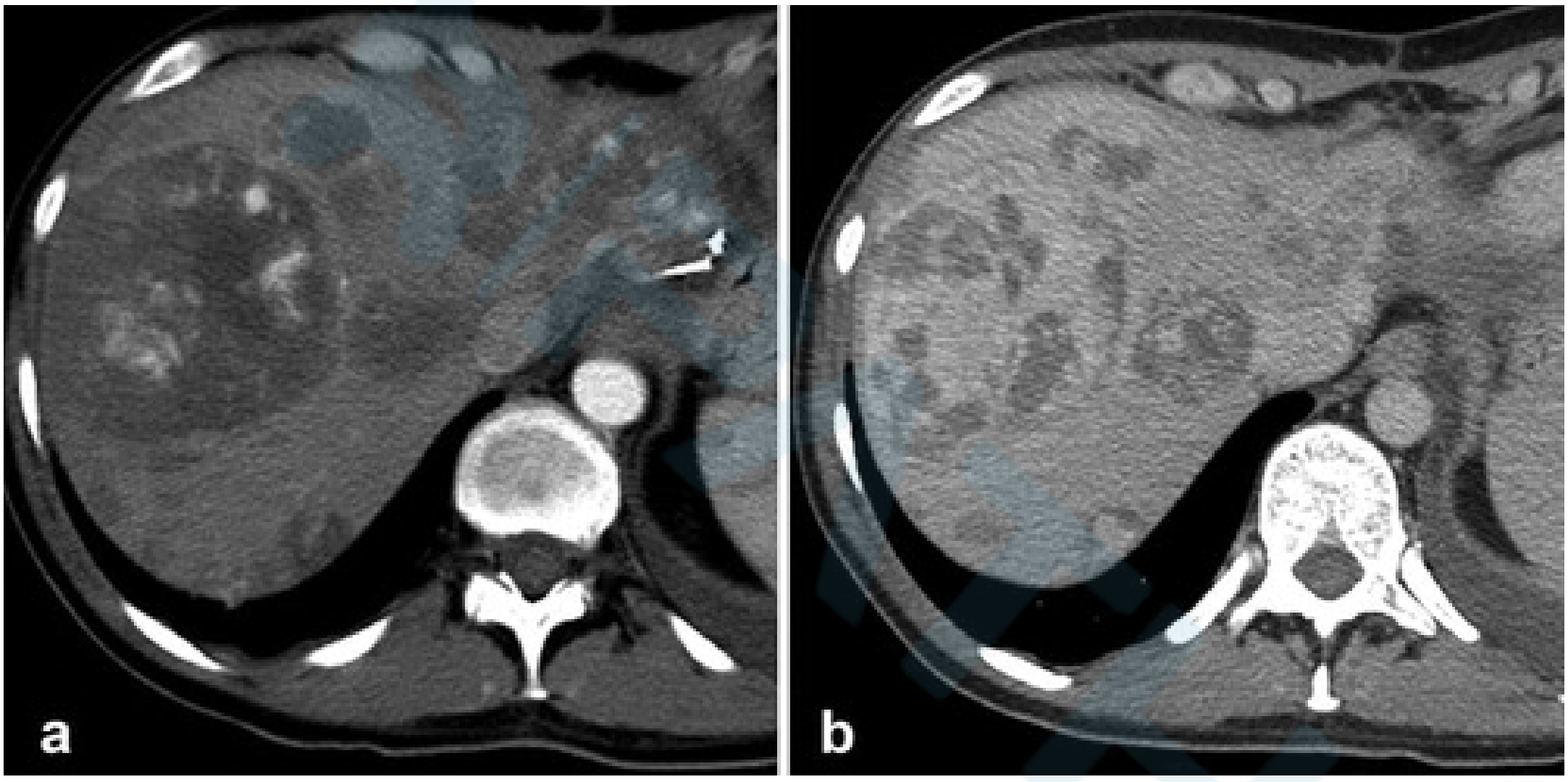
原发性肝脏血管肉瘤

起源于血管内皮细胞，约占全部肝肿瘤的2%。

病因不明，可能与接触某些致癌物质（氧化钍、砷剂、氧化乙烯等）有关。好发于男性，年龄多为50-70岁。

临床表现无特异性，腹痛、发热、体重下降为常见症状。体检可见肝大、腹水、黄疸等。

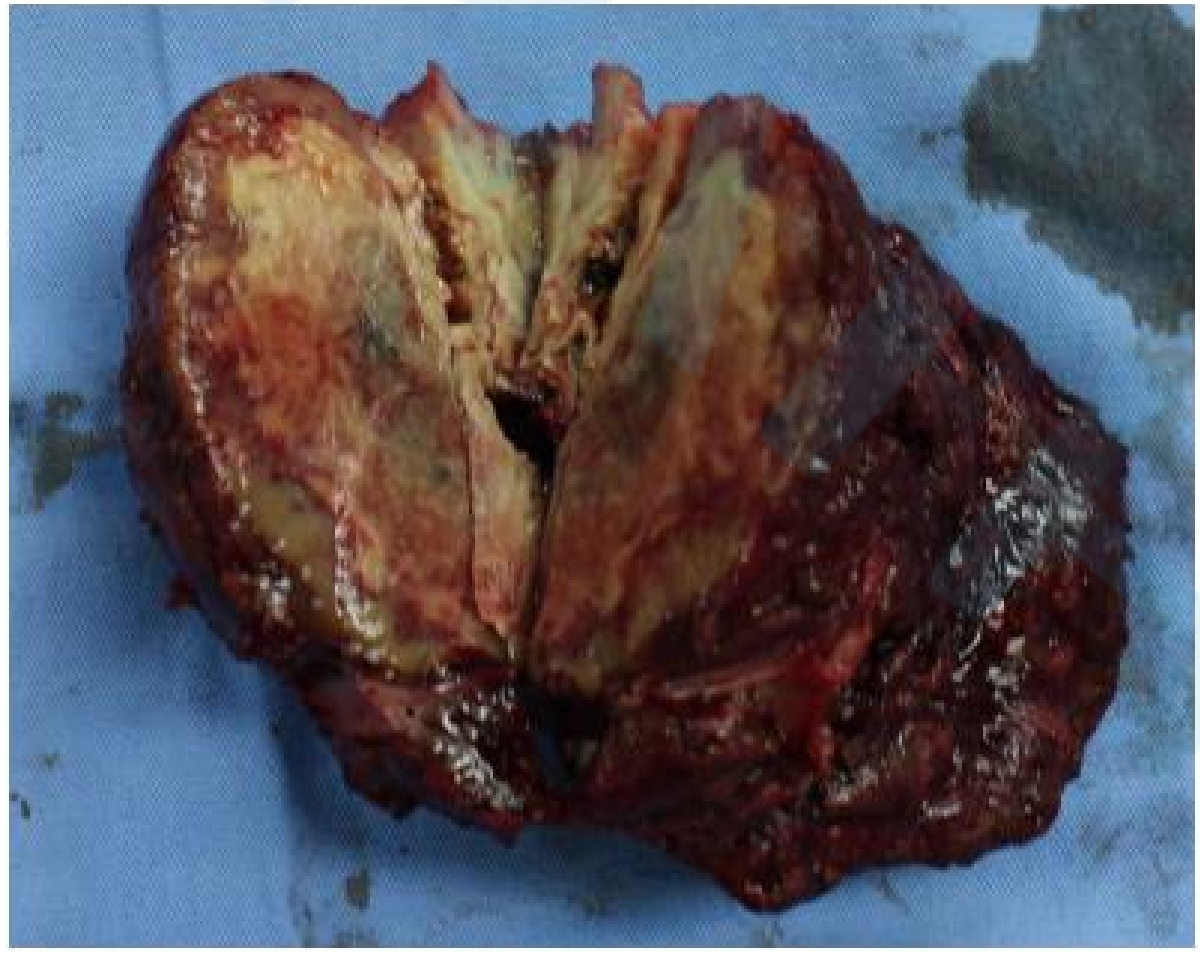
肝血管肉瘤CT表现



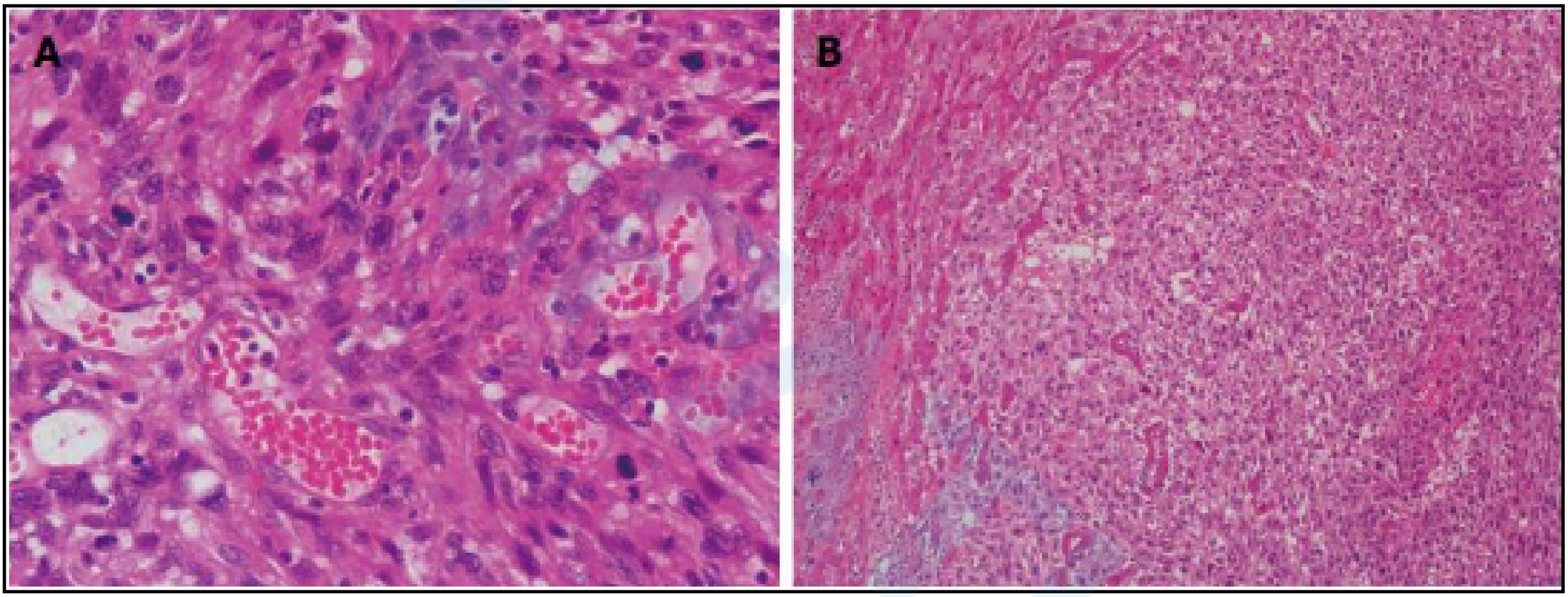
动脉期结节状、不规则强化，门静脉及延迟期渐进性充填

肝血管肉瘤组织学特点

大体观：单个肿瘤病灶大小差别很大，从针尖大至5cm不等，边界不清，多无完整包膜。



肝血管肉瘤组织学特点



肿瘤由大小不等的血管腔隙及肿瘤细胞组成。腔隙相互吻合成复杂的筛网状窦隙，肿瘤细胞沿血窦扩展，瘤细胞异型性明显，甚至可见多核瘤巨细胞。

免疫组化：CD31、CD34、F8因子。

Ref.	*n*	Age (yr) (median)	Sex (M/F)	Clinical manifestations	Tumor characteristics (*n*)	Extrahepatic metastasis	Tumor rupture	Treatment	Surgical margin	Survival time
Kim *et al*[10]	5	41-69 (45)	5/0	Right upper abdominal pain, leg edema, hemoptysis, ascites, chest discomfort, DOE	Multiple nodules (5)	Spleen (2), lung (1), pericardium (1), bone (1)	1	Palliative chemotherapy (4)	/	86 d (m)[1]
Yin *et al*[11]	7	34-71 (52)	6/1	Abdominal pain, jaundice, ascites, anemia, chest pain, edema, weight loss	NS	Spleen (1), lung (2), bone (1)	None	Hepatectomy + chemotherapy (3), chemotherapy (2)	NS	89.9 d (m)[1] (13-238 d), of hepatectomy + chemotherapy: 94 d (m)[1]
López *et al*[36]	2	20, 31	2/0	Acute liver failure	Diffuse micronodules (1), multiple nodules (1)	NS	None	Transplantation + chemotherapy (1), Conservative therapy (1)	/	2 mo, 17 d
Egea Valenzuela *et al*[15]	2	65, 73	2/0	Jaundice, abdominal distension, bleeding tendency	Multiple nodules (2)	None	None	Conservative therapy	/	36 h, several days
Matthaei *et al*[13]	5	20-80 (56)	3/2	NS	Dominant mass (5)	Lung (3), peritoneum (1)	None	Hepatectomy	R0 (4), R (1)	30 mo (m)[1], 1 alive with recurrence (R0), 1 no evidence of recurrence (R0)
Yang *et al*[37]	1	70	1/0	Asymptomatic	Multiple nodules	None	None	Conservative therapy	/	6 mo
Park *et al*[12]	6	29-80 (59.5)	5/1	Abdominal pain, fever, abdominal distension, hematuria, anemia	Dominant mass and/or intrahepatic nodules(6)	Spleen (1)	3	TACE (4), TAE (2)	/	3.5 mo (m)[1]
Bruegel *et al*[14]	7	51-78 (65)	4/3	Abdominal pain, weight loss, fatigue, jaundice	Dominant mass (1), multiple nodules (6)	Spleen (1), bone (3), lung (2), cerebellum (1) retroperitoneum (2)	1	Hepatectomy + chemotherapy(1), hepatectomy (1), chemotherapy(4)	NS	16 mo (m)[1]

[1]Represents median survival time. DOE: Dyspnea on exertion; NS: Not specified; R0: No residual tumor; R1: Microscopic residual tumor; M: Male; F: Female.

蛇 ？　非蛇 ？

材料 & 方法

1996年至2016年经复核最终诊断为原发肝血管肉瘤共21例。

按大体表现分为“肿块形成组”及“非肿块组”。

IHC：CD31、ERG。

TABLE 1. Clinicoradiographic and Histomorphologic Findings in Primary Hepatic Angiosarcomas

Case	Age (y)	Sex	Tumor Size (cm)	Specimen Type	No. Lesions	Histologic Growth Pattern	Margin Status
1	77	M	8.0	Resection	Single	Vasoformative	Negative
2	52	M	Not known	Biopsy	Innumerable	Vasoformative	NA
3	42	F	4.4	Biopsy	Multiple	Vasoformative	NA
4	70	M	Not known	Biopsy	Multiple	Vasoformative	NA
5	64	M	5.0	Biopsy	Multiple	Vasoformative	NA
6	26	F	5.8	Biopsy	Multiple	Vasoformative	NA
7	57	M	2.0	Biopsy	Multiple	Vasoformative	NA
8	71	M	15.0	Biopsy	Multiple (2)	Spindled	NA
9	85	M	12.0	Resection	Single	Spindled	Negative
10	52	M	10.0	Biopsy	Multiple	Spindled	NA
11	71	M	5.0	Biopsy	Single	Epithelioid	NA
12	70	F	Not known	Hepatectomy	Multiple	Epithelioid	Negative
13	51	F	2.4	Resection	Multiple	Epithelioid	Negative
14	89	M	3.8	Biopsy	Multiple	Peliotic	NA
15	65	F	Not known	Wedge biopsy	Not known	Peliotic	NA
16	60	M	NA	Biopsy	Diffuse enhancement	Sinusoidal	NA
17	71	M	6.0	Biopsy	Innumerable	Sinusoidal	NA
18	55	M	10.5	Resection	Multiple (3)	Vasoformative Infantile Hemangioma-like areas	Negative
19	27	F	6.4	Hepatectomy	Innumerable	Vasoformative Numerous background vascular lesions with varying degree of atypia transitioning to angiosarcoma	Negative
20	72	F	2.1	Lobectomy	Multiple (2)	Whorls of spindled cells	Negative
21	63	F	28.0	Resection	Single	Mixed vasoformative, epithelioid and spindled	Negative

F indicates female; M, male; NA, not applicable.

结果

13例为男性，8例为女性，发病中位年龄是61.4岁。

13例为细针穿刺活检，1例为楔形活检，7例为手术切除标本，包括1名肝移植病例。

21例病例中16例可得到肿瘤尺寸，平均肿瘤直径为7.9cm（2.0cm至28cm）。

15例患者表现为多结节样病变，4例表现为单一肿块，1例患者肉眼未见明确结节，但影像表现为弥漫性的不均匀强化。

TABLE 2. Clinical and Outcome Information on Patients With Primary Hepatic Angiosarcoma

Case	Clinical Presentation	Treatment	Recurrence/Metastasis	Follow-up (mo)	Outcome
1	Right upper quadrant pain	Surgery	None	36	AWOD
2	Hepatic venous congestion and cirrhosis	Chemotherapy	Bone	24	DOD
3	Abdominal and chest pain	Chemotherapy	Lung	12	DOD
4	Chest pain and A. fibrillation	Chemotherapy	Bone	12	DOD
5	NASH, cirrhosis	Chemotherapy	Lung	4	DOD

16例病例诊断时仅表现为肝脏受累，但其中5例后续随访表现为病情恶化、肝脏复发或者发生远处转移。

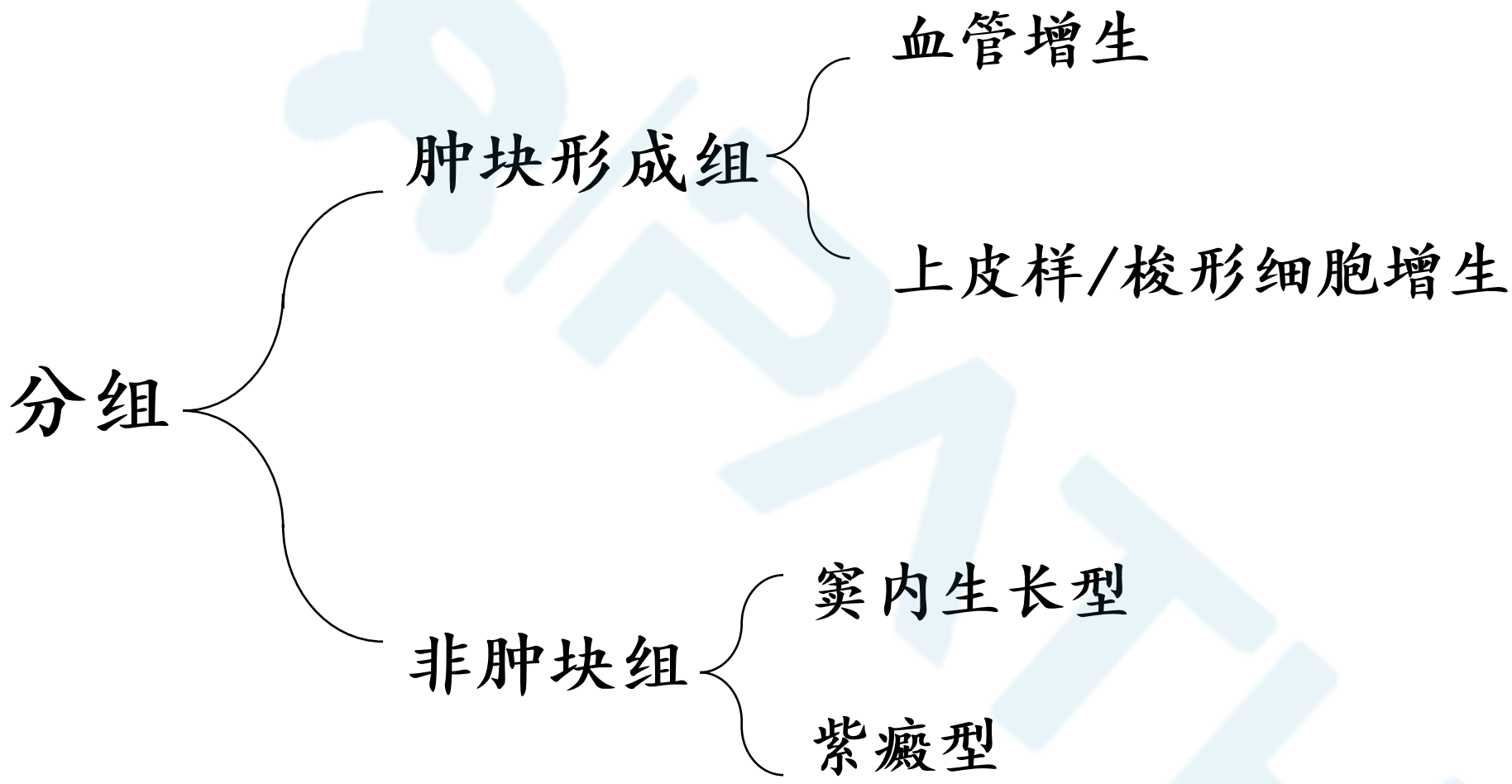
还有5例诊断时已出现转移。

20例患者有随访资料，其中14例患者死于该疾病，死亡中位时间为1个月。

	hypertension				
17	Fulminant hepatic failure and portal hypertension	Palliative care	None	1	AWD
18	Blue rubber bleb nevus syndrome; Gastrointestinal bleeding	Surgery and chemotherapy	Progressive liver disease with metastasis to spleen and GI tract	60	DOD
19	Alcoholic cirrhosis	Liver transplant and postop chemotherapy	Recurrent liver disease	6	DOD
20	Poorly controlled diabetes	Neoadjuvant chemotherapy and surgery	None	24	AWOD
21	Right abdominal pain and weight loss	Chemotherapy	Progressive liver disease	7	DOD

AWD indicates alive with disease; AWOD, alive without disease; DOD, dead of disease.

结果



窦内生长型

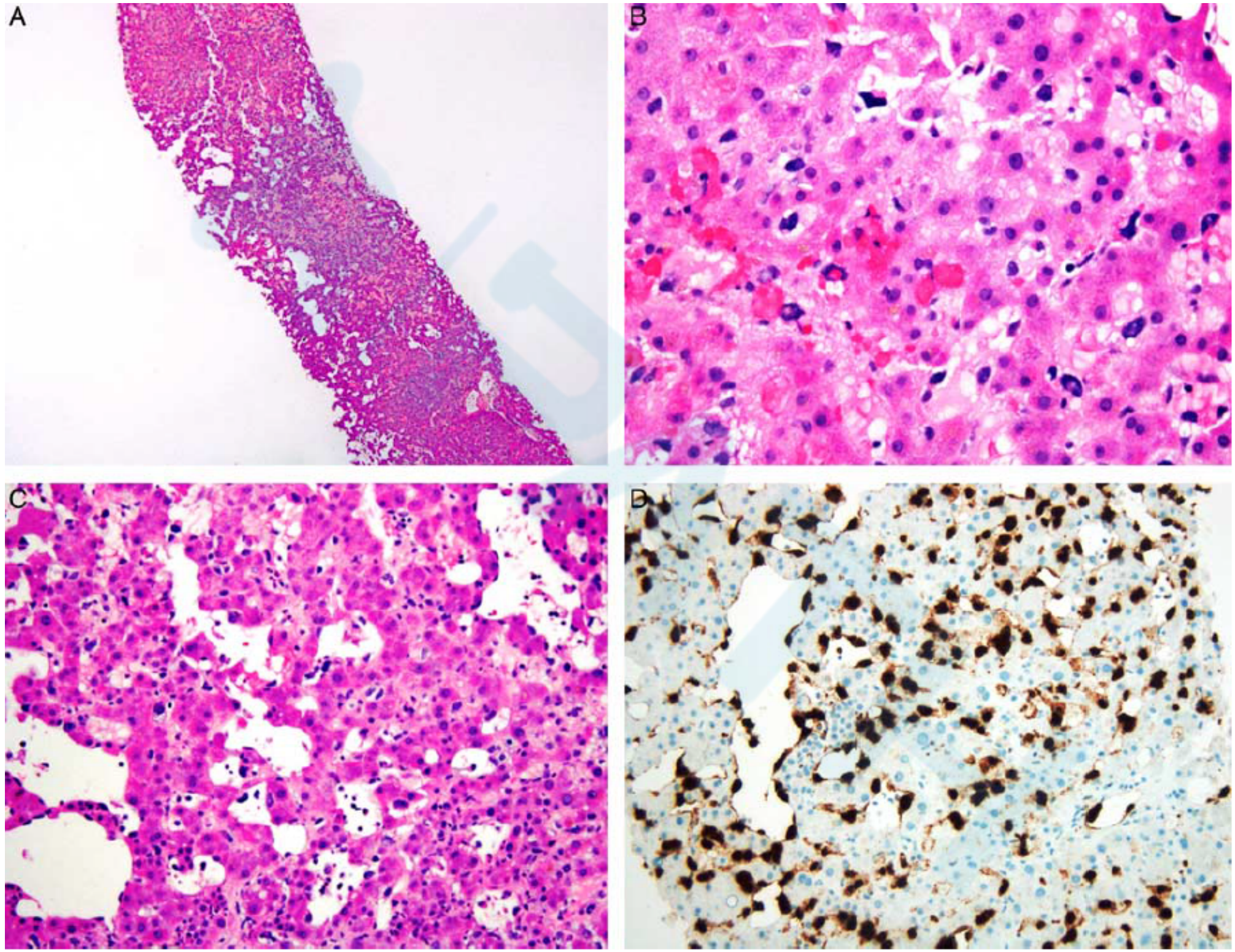


FIGURE 1. Sinusoidal pattern angiosarcoma (case 16). A, Liver parenchyma with sinusoidal dilatation and congestion. B and C, The dilated sinusoids are lined by atypical cells with enlarged hyperchromatic nuclei. D, The atypical cells demonstrate strong positivity for ERG.

紫癜型

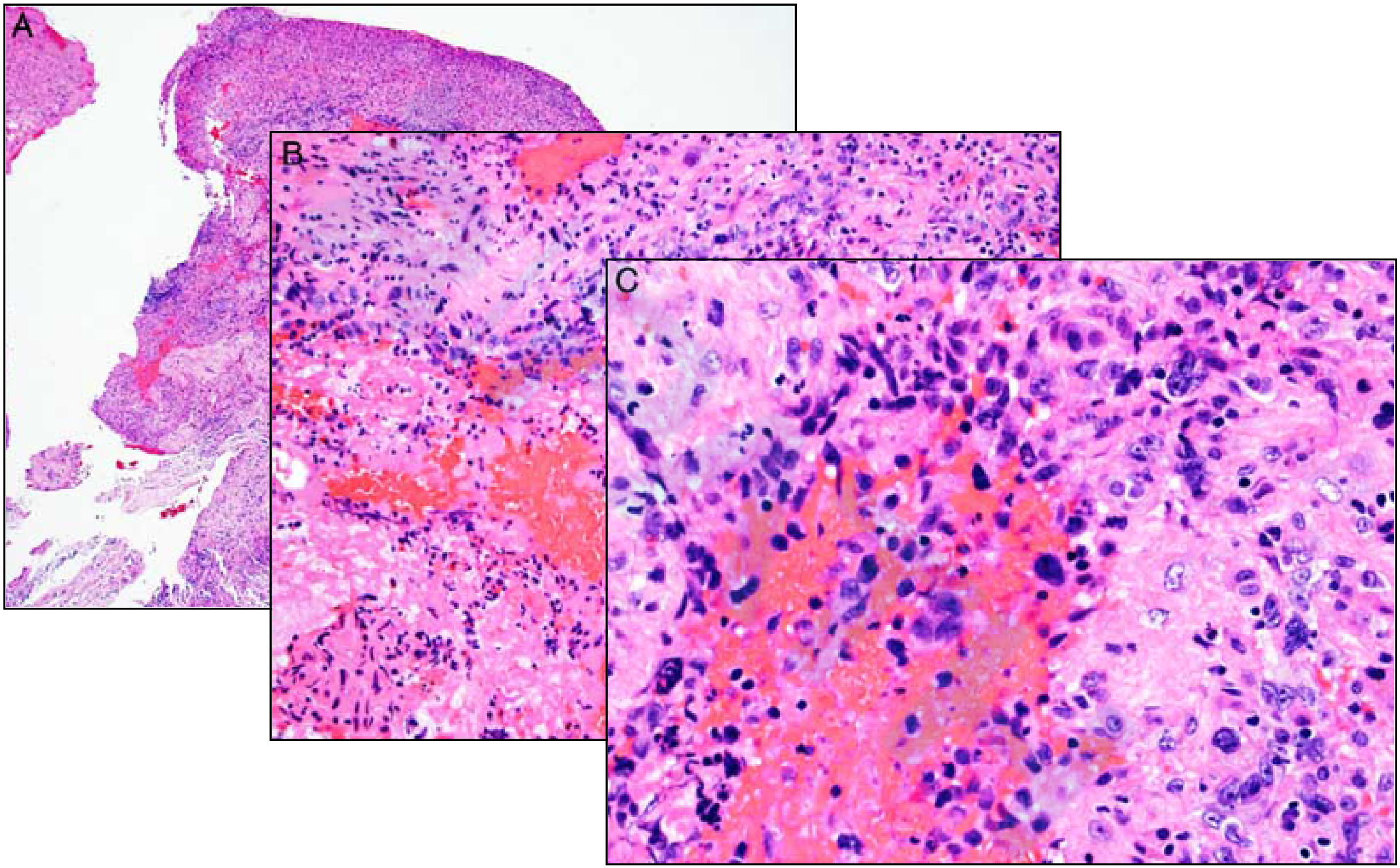
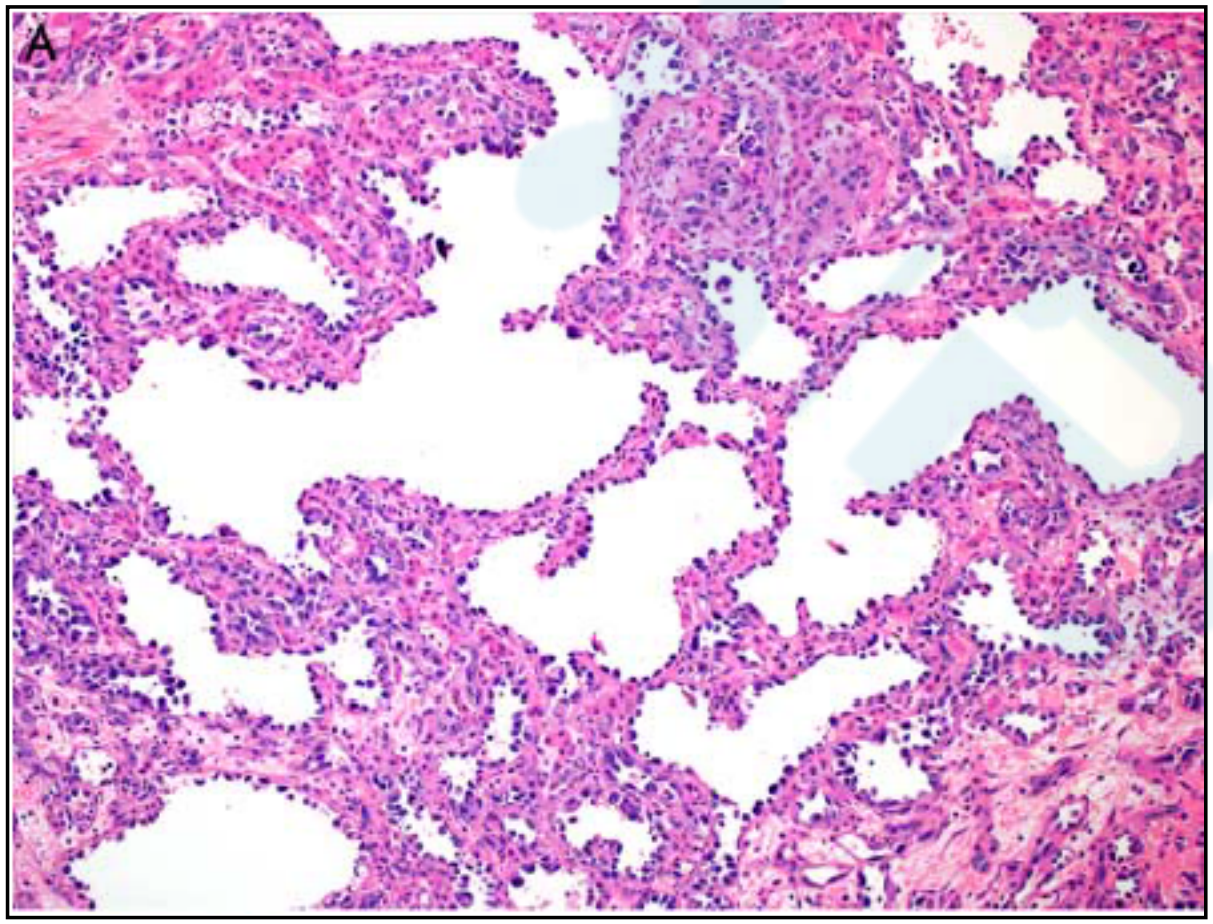


FIGURE 2. Angiosarcoma with peliotic changes (case 15). A, Liver parenchyma with ill-defined peliotic areas containing pooled blood and fibrin. B, The peliotic areas are surrounded by scattered atypical cells admixed with reactive lymphohistiocytic infiltrate. C, There is marked cytologic atypia characterized by nuclear enlargement and hyperchromasia, and nuclear pleomorphism. Mitotic figuresare noted.

血管形成为主型



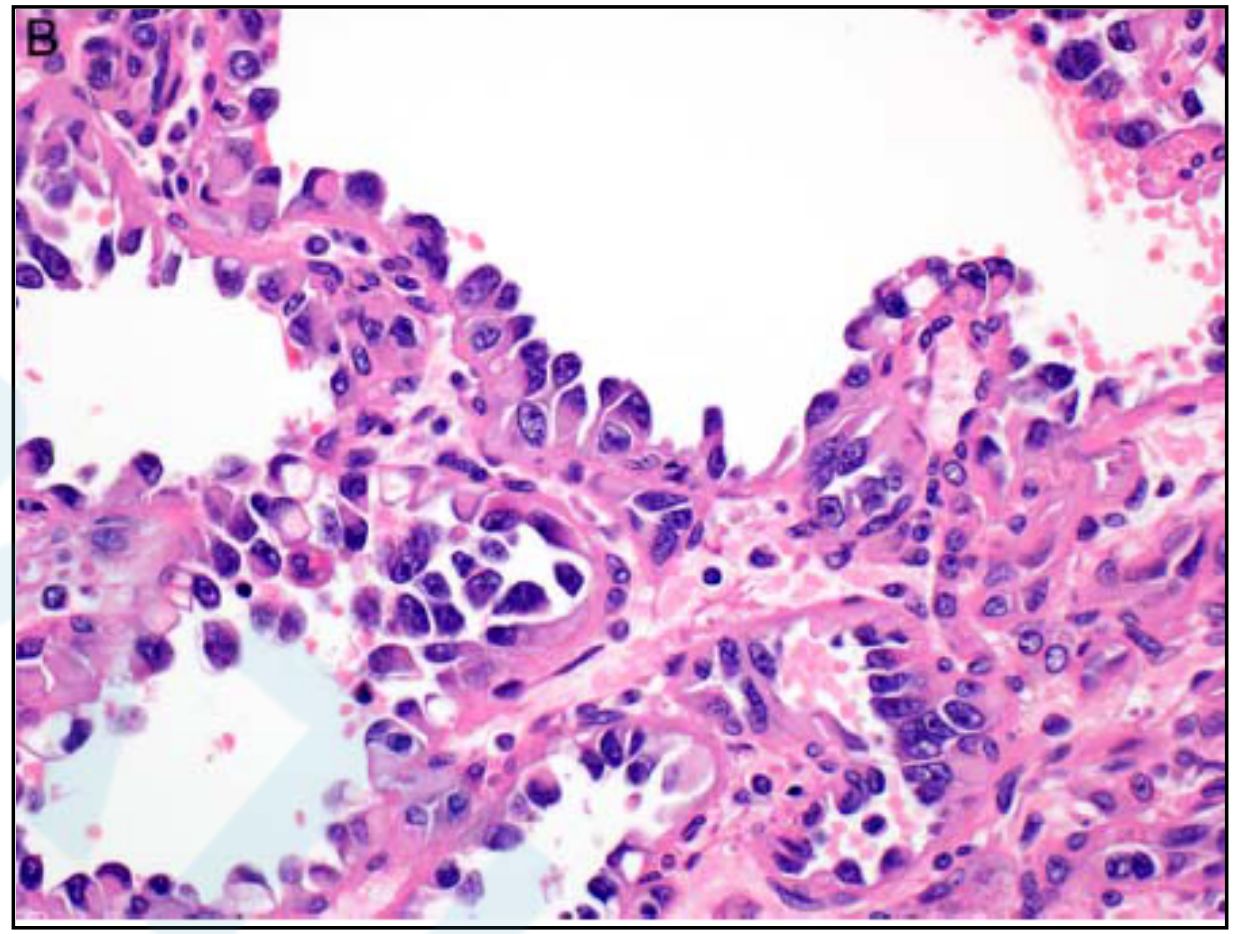


FIGURE 3. Vasoformative angiosarcoma (case 1). A, Architecturally complex interconnecting vascular spaces. B, The endothelial cells demonstrate striking nuclear atypia and tufting.

上皮样型

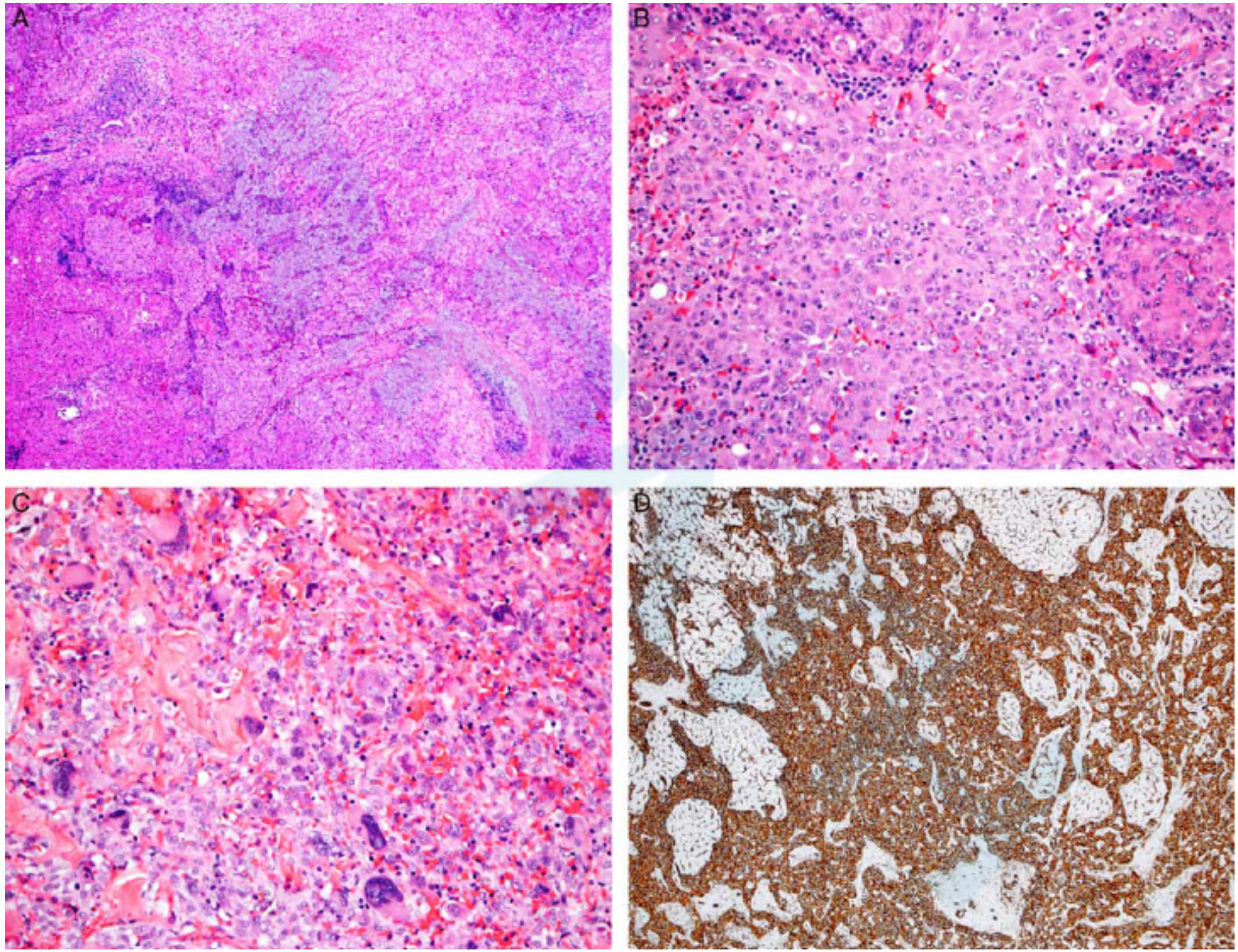


FIGURE 4. Angiosarcoma with epithelioid morphology (case 12). A, Solid nests and sheets of tumor cells infiltrating into the surrounding liver parenchyma. B, Cohesive group of neoplastic cells with epithelioid morphology. The cells have eosinophilic cytoplasm and oval vesicular nuclei. C, Multinucleated tumor giant cells are prominent. D, A CD31 immunostain shows strong staining, supporting endothelial differentiation.

梭形细胞型

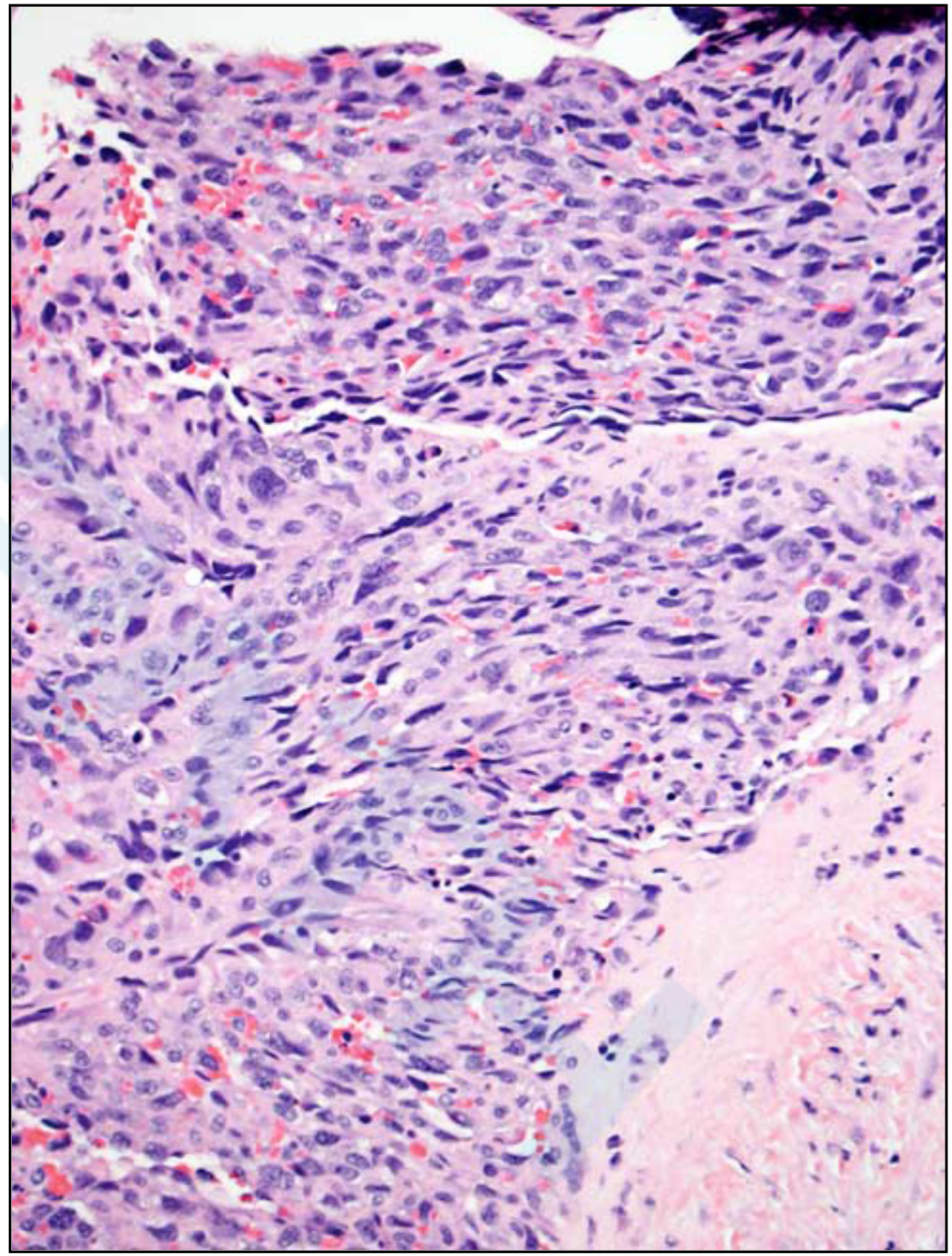


FIGURE 5. Angiosarcoma with spindled morphology (case 9). Spindle cell neoplasm with vaguely stroriform architecture. The tumor cells demonstrate high grade cytologic features.

结果

肿块形成组（17例）
- 血管增生（9）
- 上皮样/梭形细胞增生（3例为上皮样，4例为梭形，1例为混合型）

非肿块组（4例）
- 窦内生长型（2）
- 紫癜型（2）

特殊类型（旋涡状）

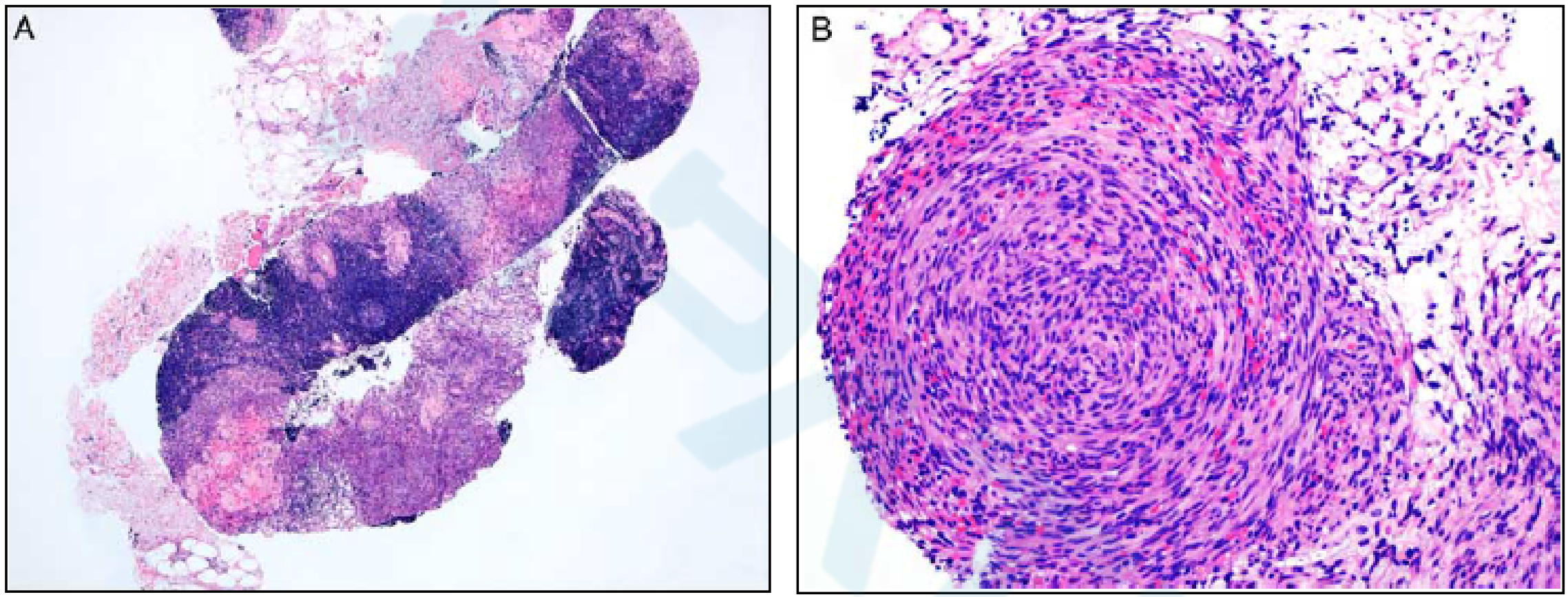


FIGURE 6. Whorling pattern angiosarcoma (case 20). A, The biopsy core is involved by multiple tights whorls of spindle cells in a background of brisk reactive inflammatory infiltrate. B, A single whorl is composed of bland appearing spindle cells.

特殊类型（婴幼儿血管瘤样）

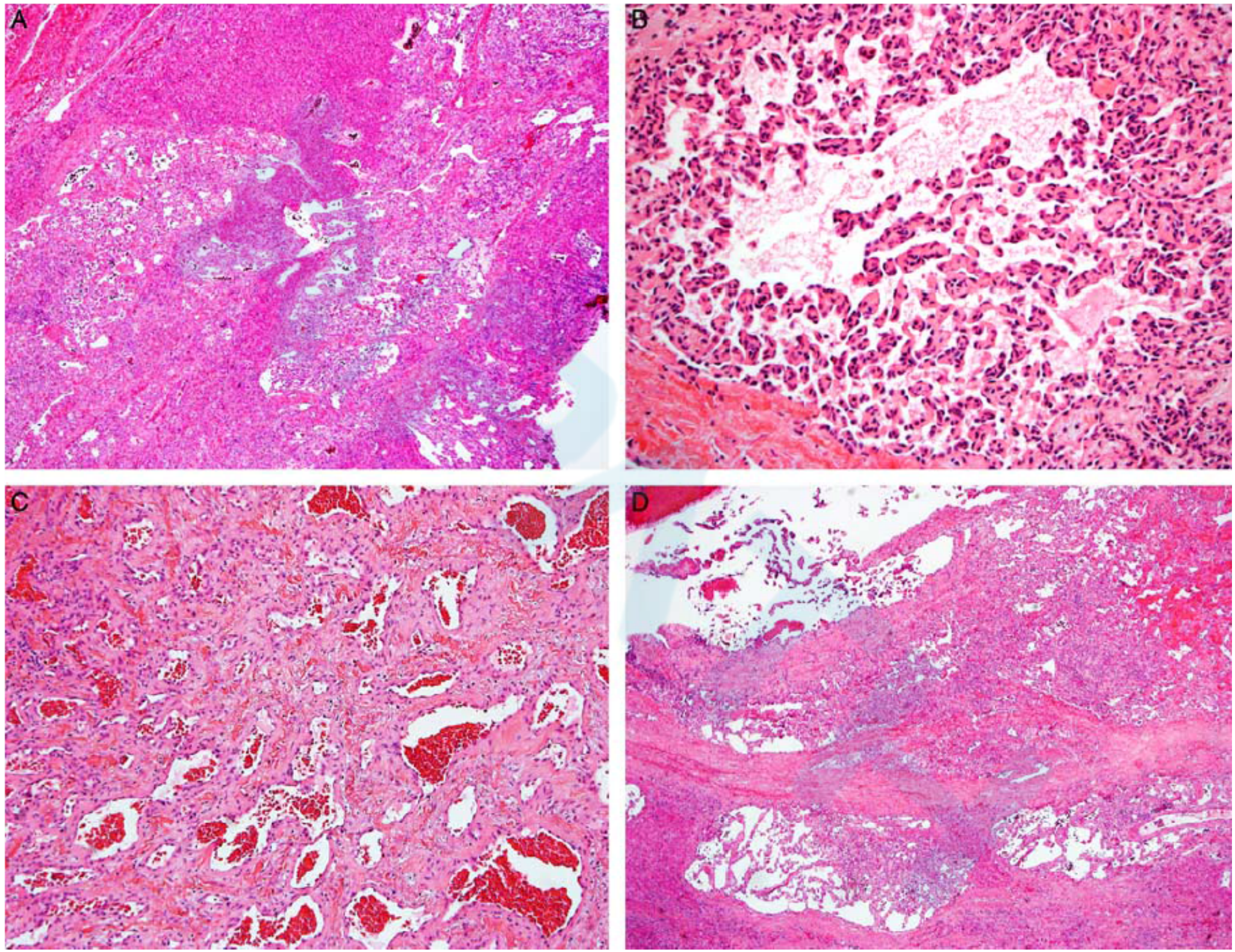


FIGURE 7. Infantile hemangioma-like angiosarcoma (case 18). A, Vasoformative neoplasm containing hemangioma-like areas and infiltration into the liver parenchyma. B, Complex architecture with endothelial tufting and micropapillary fronds. The endothelial cells have mild to moderate nuclear atypia. C, Variable sized benign appearing vascular spaces in a background of fibrous stroma. These areas close resemble infantile hemangioma. D, Marked architectural complexity and widely infiltrative tumor borders.

特殊类型（血管瘤样）

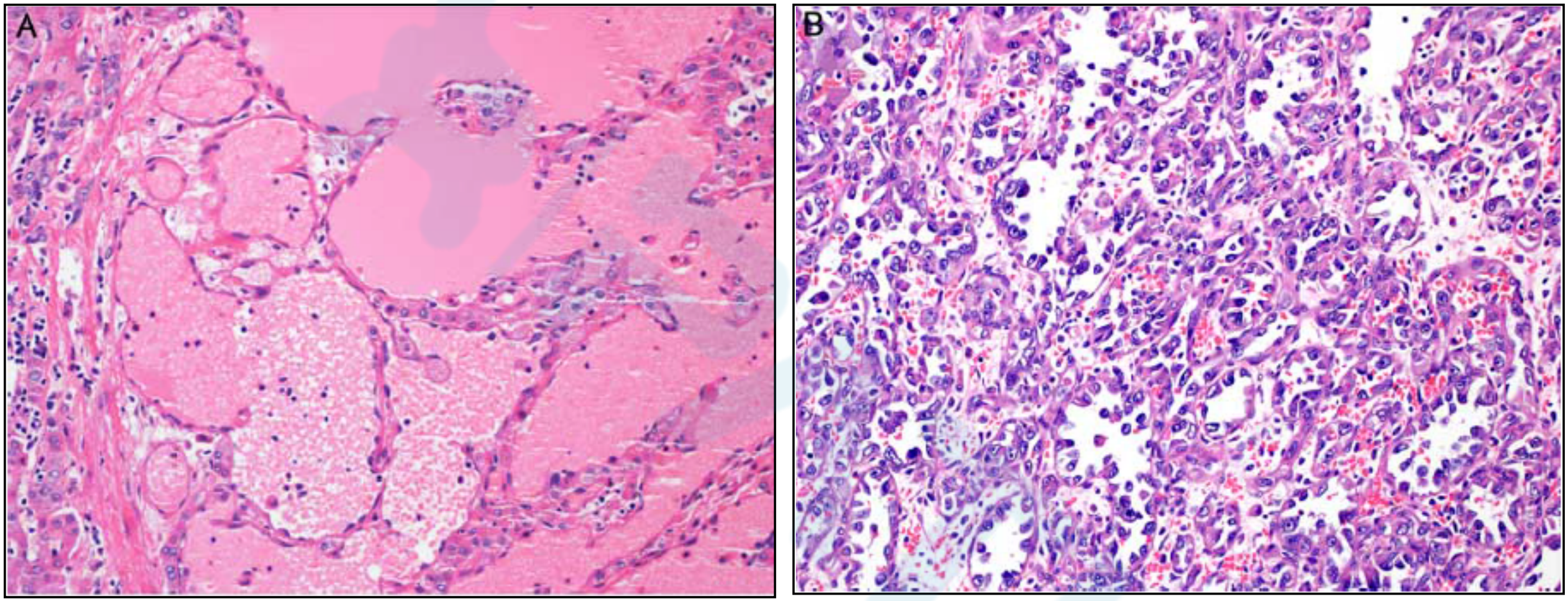


FIGURE 8. Hemangioma-like areas and frank angiosarcoma (case 19). A, A well circumscribed hemangioma without architectural complexity and cytologic atypia. B, A nodule of frank angiosarcoma with interconnecting complex vascular channels and overt cytologic atypia.

讨论

（1）根据原发性肝血管肉瘤的形态学改变，将其分为4组：A：肿块+血管增生型；B：肿块+上皮/梭形细胞为主型；C：非肿块+窦内生长型；D：非肿块+紫癜型。

（2）3例形态特殊的病例，包括旋涡状、婴幼儿血管瘤样、血管瘤样。

（3）由于肝血管肉瘤形态变化多样，诊断难度很大，尤其在细针穿刺活检方面，更具挑战性。所以识别这些形态学特点对于诊断这类罕见类型的肿瘤具有重要意义。

谢谢！

毛毛虫

Hemeroplanes：是天蛾科家族一种飞蛾的幼虫，分布于南美洲、非洲和中美洲很多地区。