Chapter 7
Hemangiomas and Other Vascular Tumors

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Introduction

The liver consists primarily of hepatocytes and cholangiocytes, while endothelial cells, Kupffer cells, stellate cells, and immune cells all serve ancillary roles. There are several types of hepatic masses or mass-like lesions which may arise from the endothelial cells that line the hepatic arteries, sinusoids, portal veins, and hepatic venous system. These entities span the spectrum from rare and aggressive lesions such as angiosarcoma to common benign masses such as hemangiomas. Knowledge of the various vascular tumors of the liver may allow accurate differentiation based on a combination of clinical and imaging features. Tables 7.1 and 7.2 summarize the clinical, histologic, and imaging features of these entities.

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Table 7.1 Overview of vascular tumors of the liver

Lesion	Cell of origin	Incidence and demographics	Clinical features	Gross appearance	Microscopic appearance	Differential diagnosis
Angiosarcoma	Endothelial cells	Rare. Age 50–60. M:F ratio of 3:1	Pain, systemic symptoms such as weight loss and fatigue. Rarely cases may present secondary to tumor hemorrhage	Numerous ill-defined nodules. Hemorrhage and central thrombosis are often seen	Hypercellular tumor exhibiting pleomorphic and spindle to epithelioid cells with minimal stroma	Epithelioid hemangioendothelioma Kaposi sarcoma Carcinoma
Hepatic epithelioid hemangioendothelioma (HEHE)	Endothelial cells	Very rare. Age 10–80. F:M ratio of 2:1	Pain, palpable abdominal mass, constitutional symptoms	Firm gray-white, red or tan tumor with irregular borders	Cords and nests of tumor cells in an abundant myxoid stromal background	Angiosarcoma Intrahepatic cholangiocarcinoma Atypical hemangioma
Cavernous hemangioma	Venous malformation (not technically a neoplasm)	Affect 2–7% of the population. F:M ratio of 4–6:1	Typically encountered incidentally. Symptoms such as pain, bleeding, or consumptive coagulopathy are rare and seen only in the largest lesions	Measure from 3 mm up to greater than 20 cm and are seen throughout the liver. Spongy cystic tissue, with areas of involution depending on age. Calcifications may be seen	Dilated vascular channels lined by bland endothelial cells. May contain areas of thrombus and scarring	Metastases Hereditary hemorrhagic telangiectasia Infantile hemangioma Peliosis hepatis Angiosarcoma Epithelioid hemangioendothelioma

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Table 7.2 Summary of imaging features of vascular tumors of the liver

Lesion morphology	US	NCCT	T1	T2	DWI	Extracellular contrast	Hepatobiliary contrast	FDG PET
Angiosarcoma Single or multiple masses.	Heterogeneous echogenicity	Hypoattenuating masses. Some may be dense due to hemorrhage	Heterogeneous. Increased signal	Heterogeneous increased signal	Heterogeneous increased signal	Arterial phase enhancement in various patterns. Hemangioma or reverse hemangioma patterns	No uptake	Intensely FDG avid
Hepatic epithelioid hemangioendothelioma (HEHE) Single or multiple nodules, or confluent disease	Heterogeneously hypoechoic to liver parenchyma. May be hyperechoic	Hypoattenuating. May contain calcifications	Hypointense core. Hyperintense rim and hypointense halo "dark-bright-dark ring sign" is classic	Hyperintense centrally. May have alternating layers of targetoid high/low T2 signal peripherally	Variable. Can be influenced by T2 shine through	Mild central enhancement of stroma. Possible progressive peripheral enhancement. Washout is not seen	"Trapping" phenomenon of retained central contrast on delayed images has been described, but is not uniformly seen	Variable uptake
Cavernous hemangioma	Hyperechoic to background liver	Hypo to isodense to liver	Hypointense	Hyperintense	Mild diffusion restriction, may be complicated by T2 shine through	Classical pattern of nodular discontinuous arterial enhancement followed by progressive fill-in on delayed phase images. Atypical variants may show either diffuse early enhancement (flash filling) or incomplete fill-in on delayed imaging (sclerosed type)	No uptake	Not FGD avid

Modified, with permission: Ehman et al. [53]
NCCT Noncontrast CT

Hemangioma

Epidemiology and Manifestations

Hemangiomas are the most common benign hepatic tumors with a reported prevalence of 1.4–3% based on surgical or ultrasonographic series [1, 2]. Hemangiomas are more common in women between 30 and 50 years of age with a 2:1 female-to-male ratio although a hormonal effect has not been proven. The majority of cases are asymptomatic and the tumors are often incidentally found on abdominal imaging obtained for other indications. A small proportion of patients with giant hemangiomas greater than 8 cm in size may present with vague symptoms, including abdominal distention, right upper quadrant abdominal pain, and early satiety due to extrinsic gastric compression. Subcapsular hemangiomas may also present with acute severe abdominal pain resulting from thrombosis or bleeding within the tumor and consequent irritation of the hepatic capsule; however, given the high prevalence of hepatic hemangiomas and the rarity of reports of bleeding from pathologically confirmed hemangiomas, this complication appears to be exceedingly rare [3]. Chronic, recurrent fevers have also been reported in the setting of large hemangiomas, likely related to intratumoral necrosis [4].

Giant hemangiomas, particularly in children, have been associated with high-output heart failure [5], hypothyroidism, and Kasabach–Merritt syndrome, a consumptive coagulopathy presenting with thrombocytopenia and hemolytic anemia [6, 7].

Pathology

Hemangiomas are benign vascular tumors. They have no malignant potential and are not precursor lesions for angiosarcoma. Based on the size and morphology of the blood vessels, hemangiomas are subdivided into cavernous hemangiomas, capillary hemangiomas, and anastomosing hemangiomas.

The most common type of hemangioma is the cavernous hemangioma (>95% of all cases), which consists of a generally well-circumscribed and unencapsulated cluster of large caliber and thin-walled vessels (Fig. 7.1). The vessels are closely approximated, with little intervening stroma. The vessels are lined by bland endothelial cells. Over time, hemangiomas can become sclerosed and sometimes partially calcified.

Cavernous hemangiomas in rare cases grow large enough to be called giant cavernous hemangiomas—there is no universally applied size criterion for using this term, but a common criterion is greater than 8 cm. Giant cavernous hemangiomas overall look similar to smaller hemangiomas histologically, but often have somewhat infiltrative borders at the interface with the background liver, a finding called

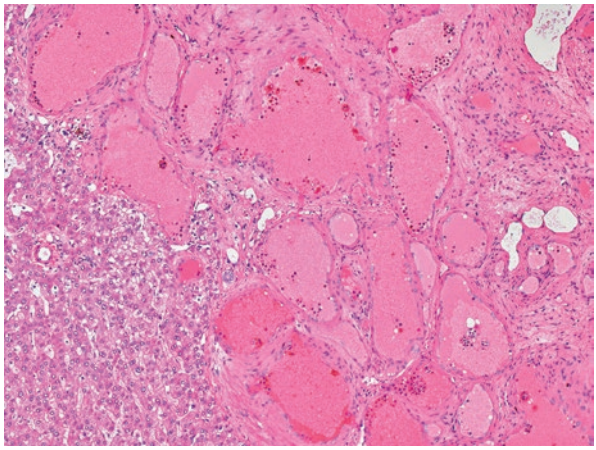

Fig. 7.1 Hemangioma, cavernous. The tumor is composed of large dilated blood vessels. Normal liver is seen in the lower left of the image

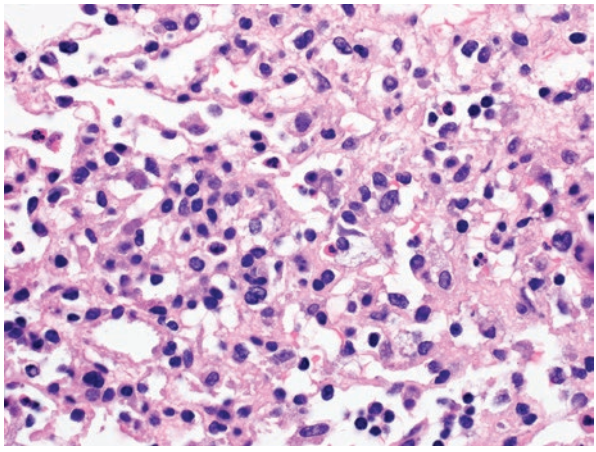

Fig. 7.2 Hemangioma, anastomosing. Small-sized and interconnecting vessels are seen, lined by plump endothelial cells

"hemangiomatosis" or "hemangioma-like vessels" [8]. They are also more likely to have areas of fibrosis.

The rare capillary hemangioma is composed of small thin-walled vessels with a lobular arrangement. The lumens are lined by plump but cytologically bland endothelial cells. In some cases, the vascular lumens can be compressed and inconspicuous, obscuring the vascular nature of the lesion. Rare cases with capsules have been reported [9].

The anastomosing hemangioma is composed of interconnecting small- to medium-sized vascular spaces (Fig. 7.2). The lining endothelial cells can be plump or "hobnailed," often with mild cytological atypia, sometimes causing confusion with angiosarcoma [10]. About 70% of anastomosing hemangiomas have GNAQ mutations [11]. Similar histological and molecular findings have been reported under the term "hepatic small vessel neoplasm" [12].

Imaging Features

Hemangiomas most often occur with a set of classic imaging features which typically results in an unequivocal diagnosis; however, atypical variants may lack classic features and therefore present a more difficult diagnosis.

Classically, hepatic hemangiomas appear hyperechoic at ultrasound, isodense or hypodense to liver parenchyma at noncontrast CT, hypointense to liver at T1 precontrast MRI and moderately T2 hyperintense, with variable diffusion restriction. With the administration of contrast at either US, CT, or MRI, there should be initial nodular, discontinuous, peripheral contrast enhancement with progressive central fill-in over time [13, 14, 15].

Atypical hemangioma variants based on imaging appearance have been described as giant, flash filling, calcified, hyalinized, cystic, and pedunculated. Giant hemangiomas are described as those measuring greater than 8 cm and usually show peripheral nodular enhancement, but delayed phase fill-in may be incomplete, possibly owing to their very large size [16, 17]. The so-called flash-filling hemangiomas are often small and follow the aorta on each vascular phase of imaging [18, 19]. Based on their enhancement pattern, these lesions may serve as mimics for other small hypervascular lesions such as metastases. Because they are slow-flow vascular lesions, hemangiomas sometimes contain calcifications or phleboliths. Hyalinized or sclerotic hemangiomas may mimic hypoenhancing metastases due to their low density/signal intensity and mild peripheral enhancement. At MRI, these sclerotic hemangiomas may have mild T2 signal and will not take up hepatobiliary contrast agents. Stability in size or biopsy may be the only ways to tell these from more sinister lesions. Cystic hemangiomas can contain cystic spaces with fluid–fluid levels visible at CT and MRI but not at US [20, 21, 22]. Examples of classic cavernous hemangiomas (Fig. 7.3) as well as several atypical variants are shown (Fig. 7.4).

Natural History and Management

Hemangiomas are associated with a low risk of complications or significant progression and do not carry malignant potential. Therefore, treatment or follow-up of small asymptomatic hemangiomas is not recommended. Tumor growth may be observed in giant hemangiomas, which in turn may lead to symptoms and possible complications, such as rupture and bleeding [23]. Fortunately, spontaneous tumor rupture resulting in intraperitoneal hemorrhage is exceedingly rare and mostly observed in large, peripheral, and exophytic tumors [24]. Percutaneous ultrasound-guided radiofrequency ablation [25], transcatheter arterial embolization [26], or surgical enucleation [27] has been performed for severely symptomatic or complicated giant hemangiomas. Symptomatic improvement postablative therapy or surgery has been reported in 75–96% of patients; however, extensive evaluation to rule out other possible causes of symptoms is imperative [28, 29].

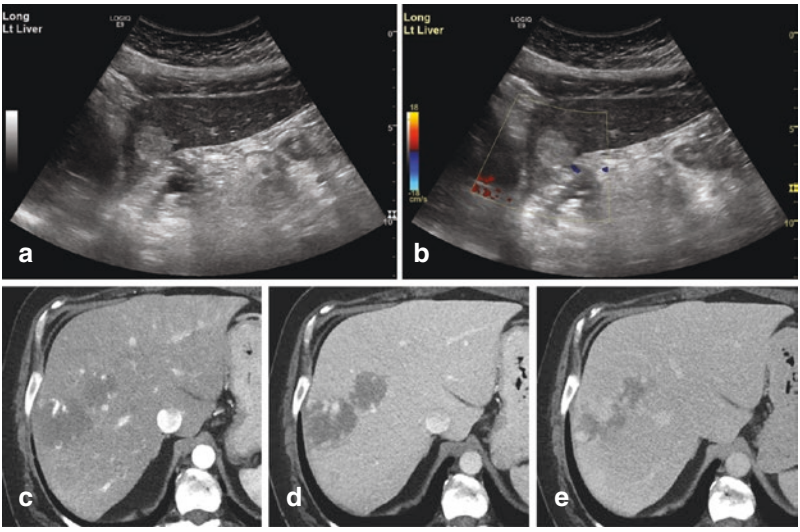

Fig. 7.3 Hemangiomas, classic appearance. Grayscale sonographic images of the left lobe (**a**) show a homogeneously hyperechoic mass with no increased blood on color Doppler (**b**). While the sonographic appearance alone is nonspecific, this mass was later imaged with multiphase CT confirming the diagnosis of a cavernous hemangioma. Axial CT images in the arterial (**c**), portal venous (**d**), and 3-minute delayed (**e**) phases show two adjacent hypodense foci with discontinuous nodular enhancement and progressive fill-in over time, classic features of a cavernous hemangioma

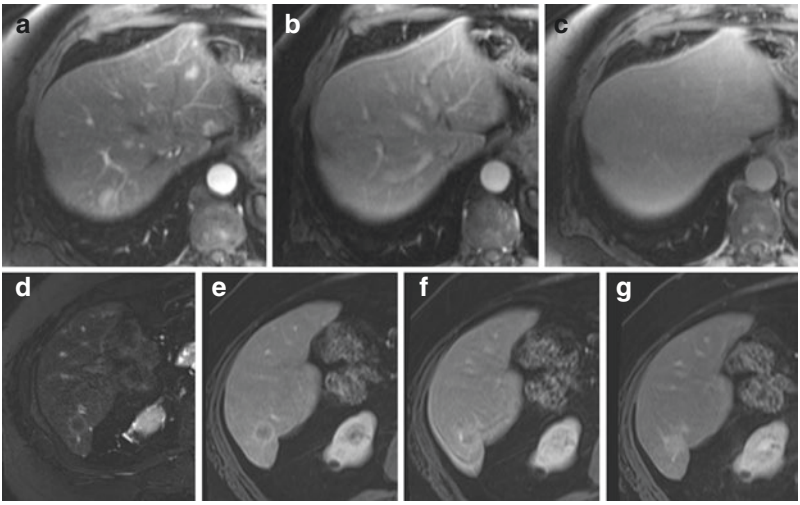

Fig. 7.4 Hemangiomas, atypical appearance. MRI of the liver in a patient with multiple vertebral body and splenic hemangiomas shows an avidly arterially enhancing focus (**a**) which is isointense to liver parenchyma on other phases (**b**, **c**). Several other lesions with similar enhancement pattern were seen throughout the liver, compatible with flash filling hemangiomas. MR images from a patient being followed up after renal mass ablation demonstrate a lesion in the posterior right hepatic lobe with a rim of T2 hyperintensity and a hypointense core (**d**) as well as rim-like arterial enhancement (**e**) with progressive central fill-in on delayed (**f**, **g**) phase images. This finding was stable for greater than 4 years and therefore compatible with a partially sclerosed hemangioma

Hepatic Epithelioid Hemangioendothelioma

Epidemiology and Manifestations

Hepatic epithelioid hemangioendothelioma (HEHE) is a locally aggressive vascular tumor with metastatic potential and shared features between hemangioma and angiosarcoma. The estimated prevalence of HEHE is less than one in 1 million, affecting predominantly females (1:3–4 male-to-female ratio) with a usual age at diagnosis between 20 and 60 years [30]. Patients are often asymptomatic at early stages but are at risk of liver failure with disease progression and extensive organ involvement. Initial symptoms are nonspecific and include upper abdominal pain or fullness, weight loss, fever, jaundice, and fatigue [31].

Pathology

HEHE are vascular malignancies that are clinically lower grade than angiosarcomas. The tumor cells can be epithelioid and dendritic, without well-formed blood vessels, potentially leading to diagnostic challenges. The tumor cells often have intracytoplasmic lumens, leading to a signet ring cell-type morphology. The tumor cells are embedded in a distinctive myxoid or hyalinized matrix (Fig. 7.5). HEHE form mass lesions, but tumor cells can also extend outside the main mass along the sinusoids, portal veins, and central veins, leading to fibro-obliteration of the veins and subsequent parenchymal atrophy with hepatocyte dropout.

Because the tumor has signet ring-type cells and abundant extracellular matrix, the histological findings can mimic cholangiocarcinoma or other adenocarcinomas [32]. In challenging cases, immunostains are used to prove vascular differentiation. At the molecular level, many HEHE have a t(1;3)(p36.3;q25) translocation that leads to a CAMTA1–WWTR1 fusion product.

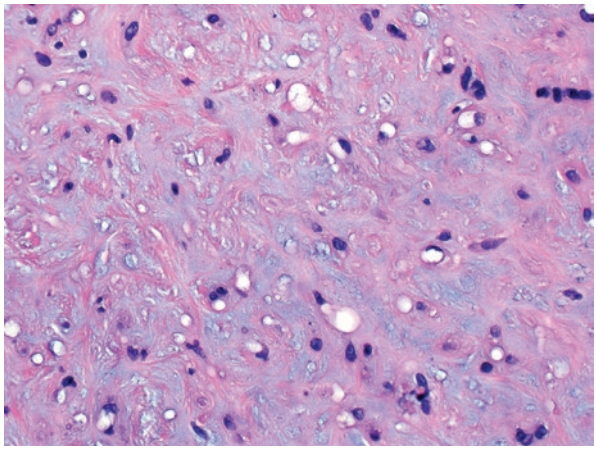

Fig. 7.5 Epithelioid hemangioendothelioma. The tumor cells have small lumens, resembling signet ring cells, and are embedded in a dense myxoid matrix

Imaging Features

The imaging appearance of HEHE is described to follow three subtypes: solitary nodular type, multiple nodular type, and diffuse confluent nodular type. It is theorized that a solitary lesion progresses to multiple nodules which then coalesce over time to form confluent disease. Solitary lesions are classically found in the subcapsular right hepatic lobe, measuring between 1 and 5 cm [33]. Less frequently, solitary lesions can be found in the central liver [34]. Multiple masses tend to be larger, measuring between 1 and 12 cm and may be found either peripherally or in the central liver [35]. Multinodular lesions will most frequently exhibit the classic finding of capsular retraction [34]. This finding should be differentiated from the capsular bulge seen in cholangiocarcinoma. Solitary nodular type (Fig. 7.6) and multinodular type (Fig. 7.7) are shown.

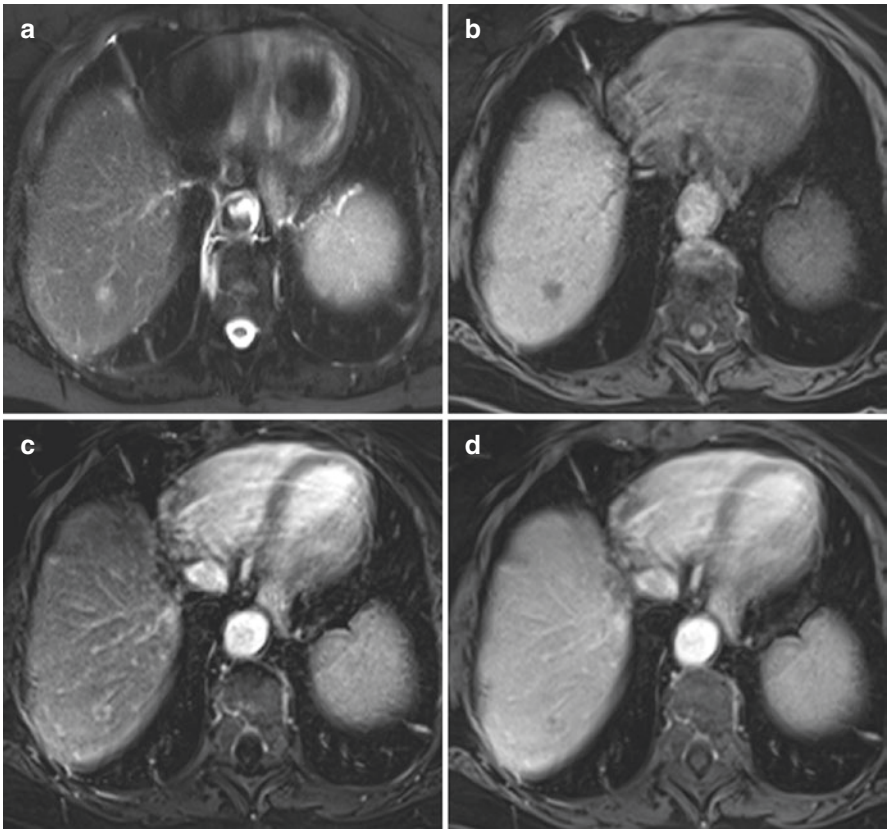

Fig. 7.6 Epithelioid hemangioendothelioma. MRI images from a 76-year-old woman show a solitary lesion in the hepatic dome which was thought to represent cholangiocarcinoma and went on to be resected. Histology confirmed a hepatic epithelioid hemangioendothelioma (HEHE). Note the T2 hyperintense center with intermediate T2 signal rim (**a**), T1 hypointensity (**b**), early peripheral enhancement (**c**), and laminated delayed central fill-in (**d**)

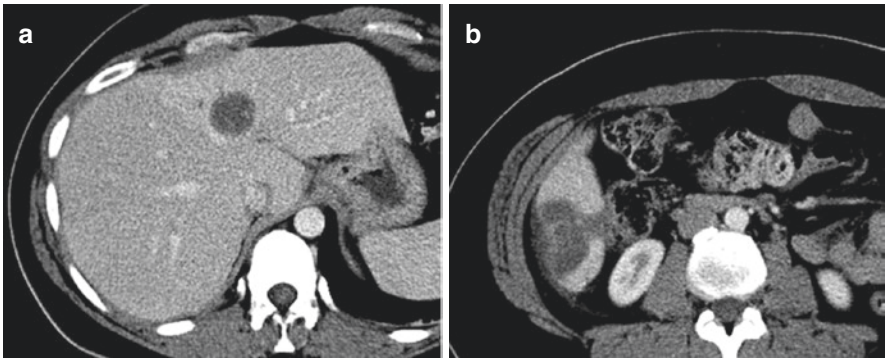

Fig. 7.7 Epithelioid hemangioendothelioma. Single-phase CT images from a 31-year-old woman with biopsy-proven hepatic epithelioid hemangioendothelioma. Multiple hypoenhancing hepatic lesions are seen in the anterior left lobe (**a**) and the inferior right lobe (**b**). Note the presence of capsular retraction adjacent to both lesions. Alternative etiologies with similar single-phase imaging features would be expected to result in capsular bulge

Sonographically, HEHE should show hypoechoic nodules, though a minority of nodules may appear hyperechoic to surrounding liver. As with other modalities, capsular retraction can be seen. At CT, lesions should be hypointense to hepatic parenchyma and at MRI, lesions should be T1 hypointense. T2 appearance is variable, but many lesions are T2 hyperintense centrally due to a core of fibrous stroma. Others may demonstrate alternating rings of T2 signal in the so-called "dark-bright-dark ring" sign [36]. When performed, diffusion-weighted imaging will also show a multicentric pattern of high and low signals. After contrast administration, some lesions show a rim of enhancement followed by fill-in on delayed phase, in a pattern similar to that of cholangiocarcinoma or metastases. In contrast to hemangiomas, globular peripheral enhancement is not seen. There have been reports of HEHE lesions "trapping" hepatobiliary contrast agents and resulting in a hypointense rim with a hyperintense core, though this is not frequently observed [34]. Extrahepatic HEHE has been described in the lung, lymphatic system, peritoneum, bone marrow, and spleen.

Natural History and Management

HEHE is associated with a high risk of metastasis, particularly to the lungs, bone, peritoneum, and lymph nodes. Untreated patients carry a 5-year mortality risk greater than 50% and, therefore, expectant management is not recommended. Surgical resection and liver transplantation are the treatments of choice, while the role of chemotherapy and radiation has not been well established. Unfortunately, surgical resection is an option in only about 10% of cases, as the majority of patients present with multifocal bilobar disease and about a third have extrahepatic involvement at diagnosis. In those with limited disease, surgical resection carries a good prognosis with 75% survival at 5 years [37]. Liver transplantation is the preferred treatment modality

for unresectable HEHE and is associated with 1-year and 5-year survival rates of 96% and 80%, respectively [37, 38, 39]. Extrahepatic metastases do not significantly affect long-term outcomes posttransplant and, therefore, are not a contraindication to transplant. Currently, patients with HEHE do not qualify for automatic MELD exception points, as do patients with hepatocellular carcinoma listed for liver transplantation. However, given the acceptable outcomes with transplant, selected patients with HEHE may be granted exception MELD points upon request to the Regional Review Board of the United Network for Organ Sharing (UNOS).

Angiosarcoma

Epidemiology and Manifestations

Hepatic angiosarcoma (HAS) is a rare and aggressive vascular tumor, which accounts for <1% of all primary liver tumors [40, 41]. HAS is associated with exposure to known carcinogens in 25% of cases, including vinyl chloride monomer, radiocontrast material thorotrast, androgenic steroid use, chronic arsenic ingestion, and exposure to radium [42]. The other 75% of tumors have no known etiology. HAS is more common in men (3:1 male-to-female ratio) in their sixth to seventh decade of life [43]. Patients often present with vague, nonspecific symptoms including fatigue, weight loss, and upper abdominal pain [40]. About half of the patients present with symptoms of liver failure or portal hypertension, such as jaundice, hepatosplenomegaly, ascites, and possibly hepatic encephalopathy [42]. Angiosarcoma has also been associated with Kasabach–Merritt syndrome [44] and spontaneous tumor rupture resulting in hemoperitoneum [45]. In contrast to hemangiomas, the diagnosis of HAS often relies on histopathologic assessment, which in turn depends on adequate tumor sampling. Due to the increased risk of bleeding, percutaneous needle biopsy is not recommended, and rather fine-needle aspiration cytology is preferred [46].

Pathology

Angiosarcomas are high-grade malignant vascular tumors that can be primary to the liver or metastatic. They are composed of malignant cells that have evidence for vascular differentiation by morphology or by immunostains such as CD34, FLi-1, or ERG. In most cases, angiosarcomas form distinct mass lesions, but rarely they grow as a subtle diffuse sinusoidal infiltrate, leading to hepatomegaly without a mass lesion (Fig. 7.8). When forming mass lesions, the tumor cells can be epithelioid (Fig. 7.9), spindle cell, or show irregular poorly formed vascular structures (Fig. 7.10), often with slit-like spaces that contain red blood cells. The tumor cells show cytological atypia and numerous mitotic figures.

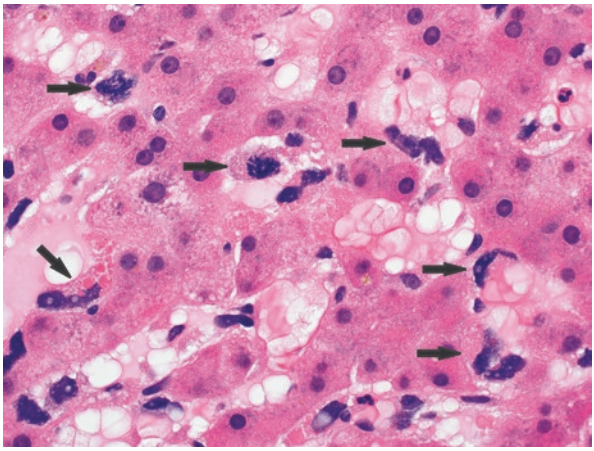

Fig. 7.8 Angiosarcoma, sinusoidal pattern. There was no mass lesion, but a biopsy showed diffuse infiltration of the sinusoids by malignant endothelial cells (arrows). Most of the remaining cells in the image are benign hepatocytes

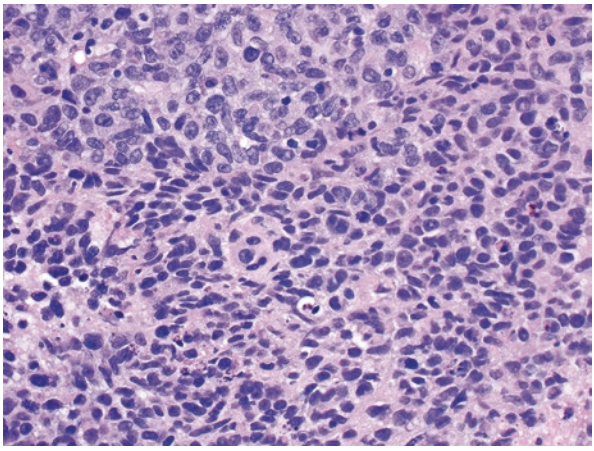

Fig. 7.9 Angiosarcoma, solid pattern. This mass-forming angiosarcoma shows no evident blood vessels, and the diagnosis required immunostains

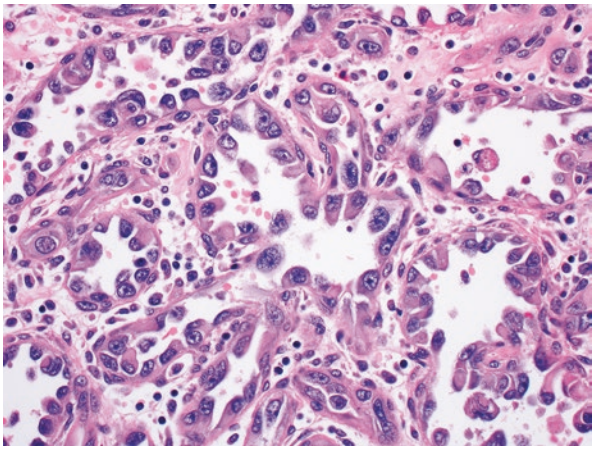

Fig. 7.10 Angiosarcoma, vessel-forming pattern. This mass-forming angiosarcoma had vascular-like spaces lined by highly atypical cells

Imaging Features

Due to their rarity, knowledge of the appearance of angiosarcomas is largely limited to observations published in case series ranging from 7 to 35 patients [47, 48, 49]. At imaging, tumors are found to be multifocal in nearly all patients, and the dominant tumor may range in size from 3 to 20 cm. While most lesions are found to involve both hepatic lobes, a subgroup has been described to involve only the left hepatic lobe. Metastases, most commonly to spleen, peritoneum, lungs, or bone marrow, are seen in 45–60% of patients at presentation.

At multiphase CT, hepatic angiosarcomas should follow the blood pool attenuation. Prior to the administration of contrast, lesions will be hypodense to liver parenchyma, though areas of hemorrhage or blood products may be denser. Several patterns of contrast enhancement have been described, including nodular, rim, branching, and diffuse enhancement. At least one type of arterial phase enhancement is seen in over 90% of tumors [49]. On portal venous and delayed phase images, lesions will enhance progressively in one of two patterns, either hemangioma-like peripheral to central or a reverse hemangioma pattern with central early enhancement with delayed peripheral fill-in [48, 49].

At MRI, angiosarcoma has an overall low T1 signal except for areas of hemorrhage which may have a high intrinsic T1 signal. Angiosarcomas usually have central heterogeneous T2 hyperintensity, and larger lesions may demonstrate serpiginous DWI hyperintensity. Enhancement patterns using extracellular contrast agents mirror those seen at CT. An example of a well-differentiated angiosarcoma is shown in Fig. 7.11.

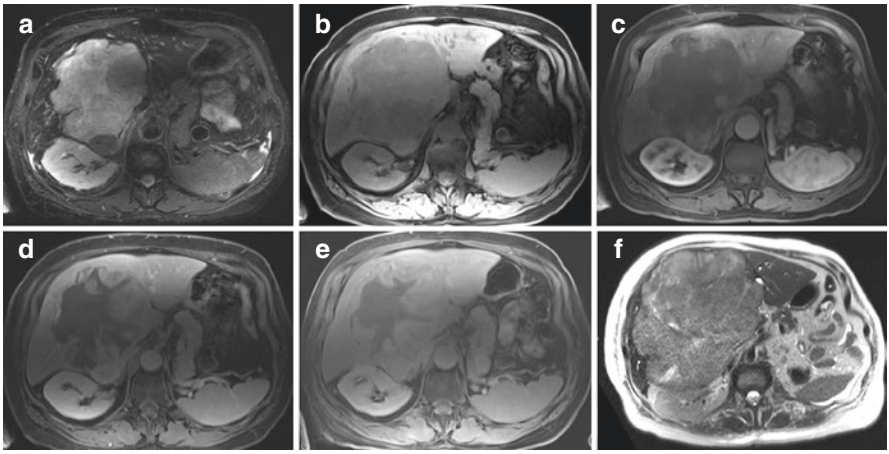

Fig. 7.11 Angiosarcoma. Biopsy-proven angiosarcoma spanning both hepatic lobes (**a**) in a 74-year-old man. The T1 signal is somewhat heterogeneous suggesting internal hemorrhage (**b**). Following administration of contrast there is peripheral arterial enhancement (**c**) followed by progressive fill-in on delayed phase images (**d**, **e**). Although based on enhancement pattern alone, this lesion could be mistaken for a giant hemangioma; rapid growth in 5 weeks seen on a follow-up scan (**f**) is more indicative of an aggressive process such as angiosarcoma

Imaging differentiation of angiosarcoma from other etiologies is difficult, as hemangiomas, epithelioid hemangioendotheliomas, and hypervascular metastases as well as primary hepatic neoplasms such as HCC and intrahepatic cholangiocarcinoma may all have overlapping features. Rapid progression over serial exams is the most reliable differentiator; however, prospective diagnosis is challenging and ultimately may require histologic sampling.

Natural History and Management

Hepatic angiosarcoma carries an extremely poor prognosis with a median survival of only 1 month [50]. Surgical resection of localized tumors may prolong survival, and is the therapy of choice for early solitary tumors. Systemic therapy or transarterial chemoembolization with palliative intent has shown potential benefits in patients with dominant HAS [51]. Additionally, transarterial embolization can be used to achieve hemostasis in ruptured HAS with hemoperitoneum. Liver transplantation is contraindicated in HAS due to aggressive early recurrence posttransplant, observed in up to 80% of patients [52].

Summary

Vascular tumors of the liver span the spectrum from exceedingly rare to very common and from malignant with a dismal prognosis to benign and incidental. While the clinical and imaging features may possess a large amount of overlap, classic findings may allow for noninvasive diagnosis in some cases. Histologic sampling may be required for others.

References

1. Gandolfi L, Leo P, Solmi L, Vitelli E, Verros G, Colecchia A. Natural history of hepatic haemangiomas: clinical and ultrasound study. Gut. 1991;32:677–80.
2. Kaltenbach TE, Engler P, Kratzer W, Oeztuerk S, Seufferlein T, Haenle MM, Graeter T. Prevalence of benign focal liver lesions: ultrasound investigation of 45,319 hospital patients. Abdom Radiol (NY). 2016;41:25–32. https://doi.org/10.1007/s00261-015-0605-7.
3. Tait N, Richardson AJ, Muguti G, Little JM. Hepatic cavernous haemangioma: a 10 year review. Aust N Z J Surg. 1992;62:521–4.
4. Liu X, Yang Z, Tan H, Zhou W, Su Y. Fever of unknown origin caused by giant hepatic hemangioma. J Gastrointest Surg. 2018;22:366–7. https://doi.org/10.1007/s11605-017-3522-y.

5. Smith AA, Nelson M. High-output heart failure from a hepatic hemangioma with exertion-induced hypoxia. Am J Cardiol. 2016;117:157–8. https://doi.org/10.1016/j.amjcard.2015.10.019.
6. Concejero AM, Chen CL, Chen TY, Eng HL, Kuo FY. Giant cavernous hemangioma of the liver with coagulopathy: adult Kasabach-Merritt syndrome. Surgery. 2009;145:245–7. https://doi.org/10.1016/j.surg.2007.07.039.
7. Shimizu M, Miura J, Itoh H, Saitoh Y. Hepatic giant cavernous hemangioma with microangiopathic hemolytic anemia and consumption coagulopathy. Am J Gastroenterol. 1990;85:1411–3.
8. Jhaveri KS, Vlachou PA, Guindi M, Fischer S, Khalili K, Cleary SP, Ayyappan AP. Association of hepatic hemangiomatosis with giant cavernous hemangioma in the adult population: prevalence, imaging appearance, and relevance. AJR Am J Roentgenol. 2011;196:809–15. https://doi.org/10.2214/ajr.09.4143.
9. Jhuang JY, Lin LW, Hsieh MS. Adult capillary hemangioma of the liver: case report and literature review. Kaohsiung J Med Sci. 2011;27:344–7. https://doi.org/10.1016/j.kjms.2011.03.003.
10. Lin J, Bigge J, Ulbright TM, Montgomery E. Anastomosing hemangioma of the liver and gastrointestinal tract: an unusual variant histologically mimicking angiosarcoma. Am J Surg Pathol. 2013;37:1761–5. https://doi.org/10.1097/PAS.0b013e3182967e6c.
11. Bean GR, Joseph NM, Gill RM, Folpe AL, Horvai AE, Umetsu SE. Recurrent GNAQ mutations in anastomosing hemangiomas. Mod Pathol. 2017;30:722–7. https://doi.org/10.1038/modpathol.2016.234.
12. Gill RM, et al. Hepatic small vessel neoplasm, a rare infiltrative vascular neoplasm of uncertain malignant potential. Hum Pathol. 2016;54:143–51. https://doi.org/10.1016/j.humpath.2016.03.018.
13. Johnson CM, Sheedy P 2nd, Stanson AW, Stephens DH, Hattery R, Adson M. Computed tomography and angiography of cavernous hemangiomas of the liver. Radiology. 1981;138:115–21.
14. Tung G, Vaccaro J, Cronan J, Rogg J. Cavernous hemangioma of the liver: pathologic correlation with high-field MR imaging. AJR Am J Roentgenol. 1994;162:1113–7.
15. Yamashita Y, Ogata I, Urata J, Takahashi M. Cavernous hemangioma of the liver: pathologic correlation with dynamic CT findings. Radiology. 1997;203:121–5.
16. Choi B, Han M, Park J, Kim SH, Han M, Kim C. Giant cavernous hemangioma of the liver: CT and MR imaging in 10 cases. Am J Roentgenol. 1989;152:1221–6.
17. Soyer P, Dufresne A, Somveille E, Scherrer A. Hepatic cavernous hemangioma: appearance on T2-weighted fast spin-echo MR imaging with and without fat suppression. AJR Am J Roentgenol. 1997;168:461–5.
18. Hanafusa K, Ohashi I, Himeno Y, Suzuki S, Shibuya H. Hepatic hemangioma: findings with two-phase CT. Radiology. 1995;196:465–9.
19. Quinn SF, Benjamin G. Hepatic cavernous hemangiomas: simple diagnostic sign with dynamic bolus CT. Radiology. 1992;182:545–8.
20. Hihara T, Araki T, Katou K, Odashima H, Ounishi H, Kachi K, Uchiyama G. Cystic cavernous hemangioma of the liver. Gastrointest Radiol. 1990;15:112–4.
21. Itai Y, Ohtomo K, Kokubo T, Yamauchi T, Okada Y, Makita K. CT demonstration of fluid-fluid levels in nonenhancing hemangiomas of the liver. J Comput Assist Tomogr. 1987;11:763–5.
22. Soyer P, Bluemke D, Fishman E, Rymer R. Fluid–fluid levels within focal hepatic lesions: imaging appearance and etiology. Abdom Imaging. 1998;23:161–5.
23. Jing L, Liang H, Caifeng L, Jianjun Y, Feng X, Mengchao W, Yiqun Y. New recognition of the natural history and growth pattern of hepatic hemangioma in adults. Hepatol Res. 2016;46:727–33. https://doi.org/10.1111/hepr.12610.
24. Mocchegiani F, et al. Prevalence and clinical outcome of hepatic haemangioma with specific reference to the risk of rupture: a large retrospective cross-sectional study. Dig Liver Dis. 2016;48:309–14. https://doi.org/10.1016/j.dld.2015.09.016.

25. Park SY, Tak WY, Jung MK, Jeon SW, Cho CM, Kweon YO, Kim KC. Symptomatic-enlarging hepatic hemangiomas are effectively treated by percutaneous ultrasonography-guided radiofrequency ablation. J Hepatol. 2011;54:559–65. https://doi.org/10.1016/j.jhep.2010.07.024.
26. Sun JH, et al. Transcatheter arterial embolization alone for giant hepatic hemangioma. PLoS One. 2015;10:e0135158. https://doi.org/10.1371/journal.pone.0135158.
27. Abdel Wahab M, et al. Surgical management of giant hepatic hemangioma: single center's experience with 144 patients. J Gastrointest Surg. 2018;22:849–58. https://doi.org/10.1007/s11605-018-3696-y.
28. Farges O, Daradkeh S, Bismuth H. Cavernous hemangiomas of the liver: are there any indications for resection? World J Surg. 1995;19:19–24.
29. Yoon SS, Charny CK, Fong Y, Jarnagin WR, Schwartz LH, Blumgart LH, DeMatteo RP. Diagnosis, management, and outcomes of 115 patients with hepatic hemangioma. J Am Coll Surg. 2003;197:392–402. https://doi.org/10.1016/S1072-7515(03)00420-4.
30. Sardaro A, Bardoscia L, Petruzzelli MF, Portaluri M. Epithelioid hemangioendothelioma: an overview and update on a rare vascular tumor. Oncol Rev. 2014;8:259. https://doi.org/10.4081/oncol.2014.259.
31. Lauffer JM, Zimmermann A, Krahenbuhl L, Triller J, Baer HU. Epithelioid hemangioendothelioma of the liver. A rare hepatic tumor. Cancer. 1996;78:2318–27.
32. Makhlouf HR, Ishak KG, Goodman ZD. Epithelioid hemangioendothelioma of the liver: a clinicopathologic study of 137 cases. Cancer. 1999;85:562–82.
33. Miller W, Dodd G 3rd, Federle M, Baron R. Epithelioid hemangioendothelioma of the liver: imaging findings with pathologic correlation. AJR Am J Roentgenol. 1992;159:53–7.
34. Kim EH, Rha SE, Lee YJ, Yoo IR, Jung ES, Byun JY. CT and MR imaging findings of hepatic epithelioid hemangioendotheliomas: emphasis on single nodular type. Abdom Imaging. 2015;40:500–9.
35. Paolantonio P, Laghi A, Vanzulli A, Grazioli L, Morana G, Ragozzino A, Colagrande S. MRI of hepatic epithelioid hemangioendothelioma (HEH). J Magn Reson Imaging. 2014;40:552–8.
36. Economopoulos N, Kelekis NL, Argentos S, Tsompanlioti C, Patapis P, Nikolaou I, Gouliamos A. Bright-dark ring sign in MR imaging of hepatic epithelioid hemangioendothelioma. J Magn Reson Imaging. 2008;27:908–12.
37. Mehrabi A, et al. Primary malignant hepatic epithelioid hemangioendothelioma: a comprehensive review of the literature with emphasis on the surgical therapy. Cancer. 2006;107:2108–21. https://doi.org/10.1002/cncr.22225.
38. Nudo CG, et al. Liver transplantation for hepatic epithelioid hemangioendothelioma: the Canadian multicentre experience. Can J Gastroenterol. 2008;22:821–4.
39. Rodriguez JA, Becker NS, O'Mahony CA, Goss JA, Aloia TA. Long-term outcomes following liver transplantation for hepatic hemangioendothelioma: the UNOS experience from 1987 to 2005. J Gastrointest Surg. 2008;12:110–6. https://doi.org/10.1007/s11605-007-0247-3.
40. Molina E, Hernandez A. Clinical manifestations of primary hepatic angiosarcoma. Dig Dis Sci. 2003;48:677–82.
41. Zocchetti C. Liver angiosarcoma in humans: epidemiologic considerations. Med Lav. 2001;92:39–53.
42. Chaudhary P, Bhadana U, Singh RA, Ahuja A. Primary hepatic angiosarcoma. Eur J Surg Oncol. 2015;41:1137–43. https://doi.org/10.1016/j.ejso.2015.04.022.
43. Bioulac-Sage P, Laumonier H, Laurent C, Blanc JF, Balabaud C. Benign and malignant vascular tumors of the liver in adults. Semin Liver Dis. 2008;28:302–14. https://doi.org/10.1055/s-0028-1085098.
44. Fujii F, et al. Hepatic angiosarcoma with Kasabach-Merritt phenomenon: a case report and review of the literature. Ann Hepatol. 2018;17:655–60. https://doi.org/10.5604/01.3001.0012.0949.
45. Leowardi C, et al. Ruptured angiosarcoma of the liver treated by emergency catheter-directed embolization. World J Gastroenterol. 2006;12:804–8.
46. Wong JW, Bedard YC. Fine-needle aspiration biopsy of hepatic angiosarcoma: report of a case with immunocytochemical findings. Diagn Cytopathol. 1992;8:380–3.

47. Bruegel M, Muenzel D, Waldt S, Specht K, Rummeny EJ. Hepatic angiosarcoma: cross-sectional imaging findings in seven patients with emphasis on dynamic contrast-enhanced and diffusion-weighted MRI. Abdom Imaging. 2013;38:745–54.
48. Koyama T, Fletcher JG, Johnson CD, Kuo MS, Notohara K, Burgart LJ. Primary hepatic angiosarcoma: findings at CT and MR imaging. Radiology. 2002;222:667–73.
49. Pickhardt PJ, Kitchin D, Lubner MG, Ganeshan DM, Bhalla S, Covey AM. Primary hepatic angiosarcoma: multi-institutional comprehensive cancer centre review of multiphasic CT and MR imaging in 35 patients. Eur Radiol. 2015;25:315–22.
50. Groeschl RT, Miura JT, Oshima K, Gamblin TC, Turaga KK. Does histology predict outcome for malignant vascular tumors of the liver? J Surg Oncol. 2014;109:483–6. https://doi.org/10.1002/jso.23517.
51. Park YS, Kim JH, Kim KW, Lee IS, Yoon HK, Ko GY, Sung KB. Primary hepatic angiosarcoma: imaging findings and palliative treatment with transcatheter arterial chemoembolization or embolization. Clin Radiol. 2009;64:779–85. https://doi.org/10.1016/j.crad.2009.02.019.
52. Bonaccorsi-Riani E, Lerut JP. Liver transplantation and vascular tumours. Transpl Int. 2010;23:686–91. https://doi.org/10.1111/j.1432-2277.2010.01107.x.
53. Ehman EC, et al. Hepatic tumors of vascular origin: imaging appearances. Abdom Radiol. 2018;43(8):1978–90.