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# Benign hepatic incidentalomas

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## Introduction

Benign liver lesions are common and are increasingly discovered incidentally on routine abdominal imaging performed for unrelated reasons or vague abdominal symptoms.[1] Patients diagnosed with benign liver masses tend to be female and are often asymptomatic at the time the lesion is identified.[2] Because the diagnosis of a liver lesion can lead to anxiety and uncertainty in patients, it is important for health care providers to understand the clinical presentation, imaging features, and management of benign liver lesions, and what distinguishes them from malignant lesions.[3] The differential diagnosis is broad and encompasses both solid and cystic processes (Table 1). Here, we focus on the clinical and especially radiographic features of nonmalignant liver lesions in order to guide management and follow-up of this increasingly common clinical problem.

### *Clinical evaluation*

As with any new clinical concern, establishing a correct diagnosis is the primary objective, and in the case of liver masses, malignant conditions must be ruled out. A comprehensive patient history should be taken, starting with the presence of symptoms and their duration and character. When detected incidentally, benign liver lesions tend to be asymptomatic, although patients may recall abdominal discomfort or pain, early satiety, and concern for increasing

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**Table 1**
Differential diagnosis of benign incidental liver masses.

| Solid lesions | Cystic lesions |
|---|---|
| Hemangioma* | Simple cyst* |
| Focal nodular hyperplasia (FNH)* | Polycystic liver disease* |
| Hepatocellular adenoma* | Infectious cysts (pyogenic, amebic, |
| Angiomyolipoma* | echinococcal, fungal)* |
| Regenerative nodule | Biliary cystadenoma* |
| Inflammatory pseudotumor | Mesenchymal hamartoma* |
| Focal fatty infiltration | Caroli disease |
| Fibroma | Ciliated foregut duplication cyst |
| Lipoma | Intrahepatic pseudocyst |
| Leiomyoma | Traumatic cysts (biloma, hematoma, seroma) |

* Pathologies covered in the current review.

abdominal girth as a result of the size or location of the tumor(s), or both. Other potential symptoms may include fever, weight loss, fatigue, and jaundice. Next, risk factors for both benign and malignant liver pathologies must be ascertained, including alcohol use, anabolic steroid or oral contraceptive use, history of transfusions or intravenous (IV) drug use, and a history of prior cancers that may metastasize to the liver, including those of the gastrointestinal (GI) tract and breast. A detailed travel history supporting exposure to *Entamoeba histolytica* or members of the *Echinococcus* family should also be elicited.[4] Family medical history should focus on metabolic syndromes including glycogen storage diseases, hemochromatosis, and Wilson's disease. Physical examination should note key findings such as fever, jaundice/scleral icterus, hepatosplenomegaly, and abdominal distention with fluid shift concerning for ascites, all of which may denote chronic liver disease.[4] Although not always necessary for presumed benign liver lesions, basic laboratory studies including complete blood count, basic metabolic panel, and liver function tests may be obtained. An alpha-fetoprotein (AFP) level should only be drawn when hepatocellular carcinoma (HCC) is suspected.

### *Radiographic evaluation*

Imaging may begin with transabdominal ultrasound (US), which is noninvasive and can differentiate lesions into cystic vs solid, solitary vs multiple/diffuse, and may assist in characterizing the surrounding liver parenchyma.[5] However, because benign lesions can sometimes masquerade as malignant lesions, it is often necessary to obtain further imaging once a mass is detected. After US, the standard for radiologic liver evaluation is cross-sectional imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI), which allows for imaging in multiple phases (i.e., delayed, arterial, portal venous) with excellent diagnostic accuracy and may help distinguish benign from malignant lesions due to well-described typical radiographic appearances.[6] Although this review does not cover malignant liver lesions, general imaging features that favor malignancy rather than a benign mass include a tumor with poorly-defined margins, diffuse heterogeneous or rim enhancement, and washout on dynamic imaging; the presence of hepatic or portal vascular invasion; and a peripherally enhanced mass with a surrounding hypoattenuating rim.[7]

Routine US examination of the liver includes real time gray scale and color flow evaluation of the liver parenchyma and vasculature. The technical feasibility of high quality US is highly dependent on the operator, the availability of a good acoustic window (typically between the ribs and in the midline upper abdomen), the ability of the patient to follow instructions, and a relatively normal body habitus. Apart from detecting diffuse and focal liver lesions, US can assess the patency of intrahepatic vessels and evaluate for biliary ductal dilatation. In addition, US elastography is increasingly used to assess liver stiffness in patients with chronic liver disease ultimately leading to cirrhosis.[8] Although not widely available in the United States,

contrast-enhanced US is another emerging technique useful for further characterization of focal liver lesions.[9]

CT is the most widely available and used modality for detection and further characterization of focal and diffuse liver disease, followed by MRI. A multiphase liver protocol CT typically includes a precontrast series of the abdomen, followed by intravenous injection of nonionic water-soluble contrast (120-150 mL of iohexol at 4-5 mL/s) and image acquisition during arterial, portal venous, and delayed phases (at 40 seconds, 50-60 seconds and 180 seconds postinjection, respectively). By contrast, incidental liver lesions are often detected on routine single-phase contrast-enhanced CT of the abdomen that is typically acquired during the portal venous phase. MRI has the advantages of greater soft tissue contrast, multiplanar capabilities, and lack of ionizing radiation. For the liver, it is a remarkably resourceful imaging modality. Liver protocol MRI on 1.5 or 3 T scanner includes single-shot fast spin echo localizers in 3 planes, coronal single-shot fast spin echo, axial gradient echo T1-weighted in and out-of-phase, axial fat suppressed T2-weighted images with respiratory gating, dynamic 3D gradient echo fat saturated dynamic T1-weighted images (in precontrast, arterial, portal venous, and immediate delayed phases), 5-minute delayed axial T1-weighted gradient echo, and diffusion weighted images. Depending on the indication, either an extracellular agent (e.g., gadobutrol at a dose of 0.1 mmol/kg) or hepatobiliary agent (e.g., gadoxetic acid at a dose of 0.025 mmol/kg) are injected at a rate of 2 mL/s, followed by saline flush. When the latter is used as intravenous contrast agent, particularly for the diagnosis of focal nodular hyperplasia, 20-minute delayed axial T1-weighted gradient echo images are also acquired.

### *General management*

In general, because benign liver lesions typically have characteristic findings on abdominal imaging, routine biopsies for most benign appearing lesions are not routinely indicated. However, a percutaneous biopsy may be required in cases where imaging is indeterminate or features are not clear. Once a diagnosis has been established, the majority of benign liver lesions will not require surgical resection. The general exceptions to this rule include progressively worsening symptoms (usually pain) and clinical and/or radiologic suspicion of malignancy or malignant potential.[10,11]

## Benign solid liver lesions

The presence of solid liver lesions on imaging can be especially anxiety-provoking for patients and concerning to physicians, since most malignant conditions in the liver, whether primary or secondary, will appear as solid masses. For this reason, it is crucial for clinicians to have a good understanding of the most common benign solid liver lesions that may be encountered on imaging. Chief among these are hemangiomas, focal nodular hyperplasia lesions, and hepatocellular adenomas. Less common entities include angiomyolipomas and regenerative nodules, which are comprised of regenerating hepatic tissue in response to injury, most often seen in the setting of cirrhosis, and tend to be multifocal. Here, we discuss the first 4 pathologies listed above.

### *Hemangioma*

#### *Clinical features*

The most common benign liver lesion, accounting for nearly three-quarters of all such lesions, is the hemangioma, which has a reported overall prevalence of 5% to 20%.[12,13] Hemangiomas are macroscopically flat and well-circumscribed, with a reddish-blue color.[14] Pathologically, they are composed of vascular channels lined by endothelium covered in loose, supportive fibrous stroma,

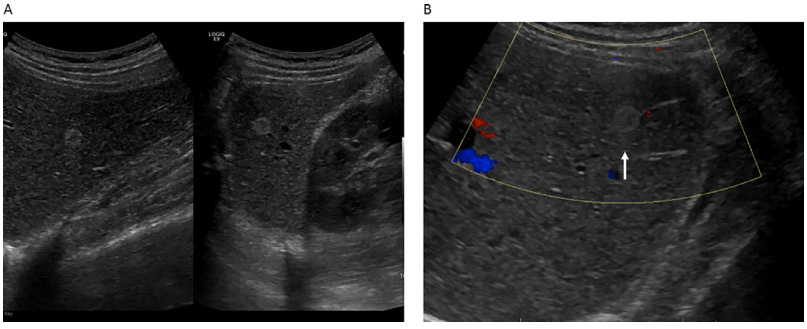


**Fig. 1.** Ultrasound evaluation of a hemangioma in a 41-year-old woman. (A) Longitudinal and transverse ultrasound (US) images show a small homogenously hyperechoic lesion in the right liver, with sharply circumscribed margins. (B) No internal flow is detected within the lesion on color Doppler interrogation.

and may contain septations.[7,14] They are more commonly discovered in women than men, with a female incidence of up to 10%.[15] Hemangiomas have no specific age predilection and are typically smaller than 5 cm, carrying no significant complication risk, although they can range from several millimeters to 20 cm. Those greater than 5 cm are termed "giant hemangiomas."[14-16] Hemangiomas may be found in both the right and left lobes of the liver, although they are more often found on the right side, and have been reported to be multiple in up to 40% of patients.[17]

In general, most hemangiomas are diagnosed incidentally on routine imaging, are asymptomatic, and do not tend to grow in size over time.[7,18] Clinical abdominal examination and laboratory studies including liver function tests are most often normal in patients with hemangiomas, and tumor markers are neither diagnostic nor necessary.[4,14] Occasionally, giant cavernous hemangiomas may cause significant hepatomegaly that can be appreciated on palpation. Moreover, they may cause nonspecific abdominal pain that prompts initial imaging. Rarely, giant hemangiomas can be associated with clinical syndromes necessitating further evaluation and surgical intervention. Kasabach-Merritt syndrome is an uncommon consumptive coagulopathy most frequently seen in children, marked by elevated fibrin degradation products and severe thrombocytopenia.[19] However, adult patients may also experience this syndrome as a result of clotting and subsequent fibrinolysis within the lesion, which in severe circumstances may lead to disseminated intravascular coagulation.[20] Bornman syndrome is an inflammatory reaction induced by partial thrombosis of the lesion and is marked by fever, abdominal pain, weight loss, anemia, and elevated erythrocyte sedimentation rate with normal white blood cell count.[21] Finally, although rare, patients with large hemangiomas have been reported to experience high output cardiac failure due to increased left-to-right arteriovenous shunting, causing exertional hypoxia.[22] All of these clinical scenarios may lead to significant, and potentially lifestyle-limiting, consequences and merit prompt evaluation and intervention in order to reverse these processes.

*Radiographic features*

The imaging features of a hemangioma are determined by the size of the lesion, imaging modality, technique, and protocol utilized. Although hemangiomas can vary greatly in size, typical hemangiomas are usually incidentally found in asymptomatic patients, measuring 3 cm or less in diameter. On US, hemangiomas typically appear as homogenously hyperechoic lesions in relation to the hepatic parenchyma, with sharply circumscribed margins and posterior acoustic enhancement (Fig 1).[23] Usually, no internal flow is demonstrated on color Doppler interrogation as flow within these lesions is typically slow. However, there is significant overlap in the sonographic imaging appearance of hemangiomas and that of HCC and some hepatic metastases, and further evaluation with contrast-enhanced computed tomography (CECT) or MRI is usually required to more definitively establish the diagnosis.

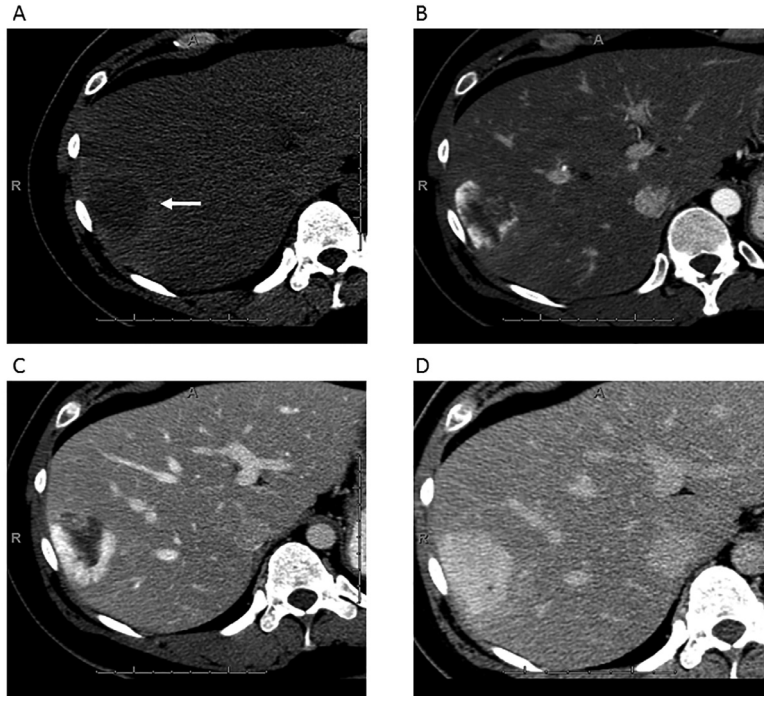


**Fig. 2.** CT evaluation of a hemangioma in a 55-year-old man with melanoma. (A) Axial noncontrast CT scan image shows a mildly lobulated hypoattenuating lesion in the periphery of the right liver (arrow). (B) Axial arterial phase contrast-enhanced CT (CECT) image shows discontinuous peripheral globular enhancement displaying attenuation values similar to that of the abdominal aorta. Axial portal-venous phase (C) and axial delayed equilibrium phase (D) CECT images show progressive centripetal filling of the lesion with attenuation values similar to that of the blood pool.

On CT, hemangiomas typically appear as well-defined hypoattenuating lesions in relation to the hepatic parenchyma on noncontrast scans (Fig 2). After intravenous contrast administration, they typically display a discontinuous peripheral globular or nodular pattern of contrast enhancement with progressive centripetal filling from the arterial phase into the portal-venous and equilibrium phases of contrast enhancement that tends to mirror the contrast attenuation of the aorta or blood pool during each phase.[24] This classic discontinuous globular pattern of contrast enhancement is a very reliable imaging feature, with reported sensitivity of 88% and specificity of 84% to 100%.[25,26] This typical imaging appearance is observed during a multiphasic liver protocol. However, clinicians often have to contend with a single-phase CECT instead, during which these lesions are captured on a single-phase postcontrast acquisition. In this scenario, it is important to try to identify the classic discontinuous peripheral globular enhancement pattern that characterizes hepatic hemangiomas (Fig 3).

On MRI, hemangiomas typically appear as sharply-circumscribed masses which are hypointense to the hepatic parenchyma on T1-weighted sequences and markedly hyperintense on T2-weighted sequences. On post-contrast multiphasic MRI, hemangiomas show the same typical peripheral discontinuous globular enhancement pattern with progressive centripetal filling on delayed phases seen with CECT (Fig 4).[24] Similar to CECT, the signal intensity of the discontinuous peripheral nodular areas of enhancement mirrors that of the aorta and blood pool. MRI utilizing postcontrast multiphasic imaging and T2-weighted series is highly accurate in the diagnosis of hemangiomas, with a reported sensitivity of 98%, specificity of 98%, and accuracy of 99%.[27]

The quality of the bolus and the timing of the imaging acquisition directly affect the appearance of hemangiomas on postcontrast images. It is not unusual for these lesions to vary in size,

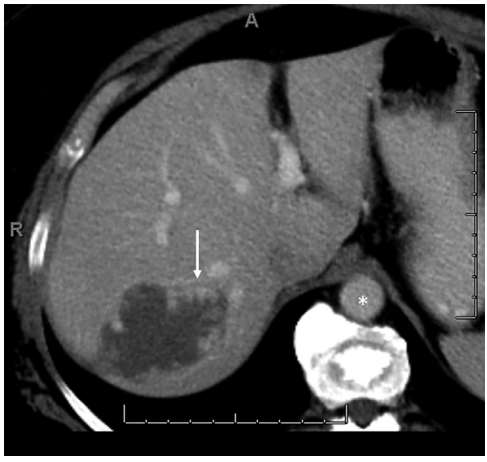


**Fig. 3.** CT evaluation of a hemangioma in a 68-year-old man with history of melanoma. Single phase axial CECT images show a large, mildly lobulated mass in the right posterior liver, displaying the classic discontinuous globular peripheral enhancement. Note that the attenuation of the peripheral enhancing nodules (arrow) matches the attenuation of the aorta (asterisk). These classic imaging findings allowed a confident diagnosis of hemangioma in this patient with a diagnosis of stage IIA melanoma.

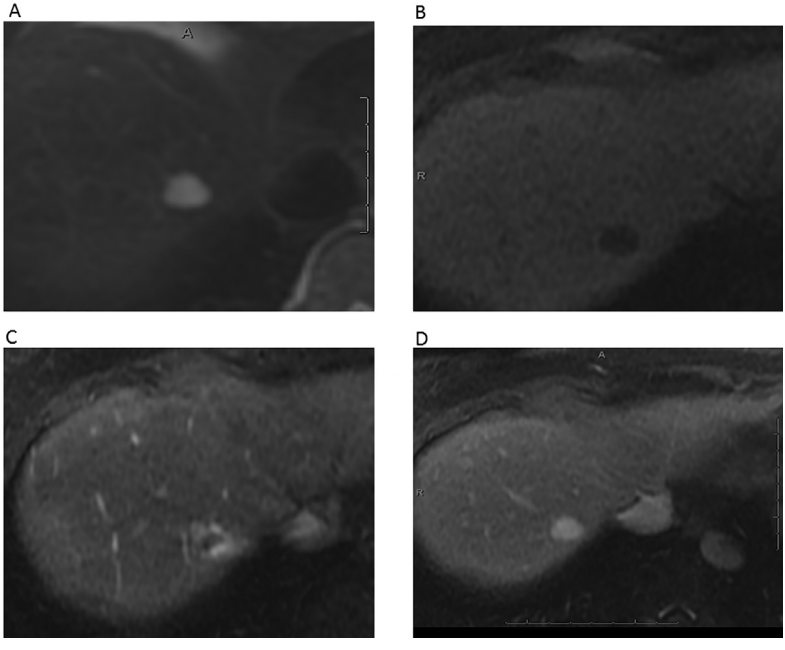


**Fig. 4.** MRI evaluation of a hemangioma in a 65-year-old man with history of lymphoma. (A) Axial T2-weighted Fast Spin Echo (FSE) image with fat saturation (FS) shows a small sharply-circumscribed high signal intensity lesion in segment VII. Axial precontrast (B) and postcontrast multiphasic (C and D) gradient echo (GRE) T1-weighted images show the discontinuous peripheral nodular enhancement pattern with progressive centripetal filling typical of hemangiomas. Note the similar signal intensity of the lesion to the signal intensity of the blood pool.

shape, and degree of enhancement between studies, which may catch them on different phases of contrast enhancement, causing diagnostic confusion. Careful attention to technique used during imaging acquisition is important to correctly interpret apparent changes in size, shape, internal density, or signal intensity between studies, particularly when interpreting examinations obtained at different institutions, in order to avoid potential pitfalls. The imaging diagnosis of hemangioma is relatively straightforward when the above-mentioned classic imaging features are present. When these features are not present, the lesions are named atypical hemangiomas, and the imaging diagnosis can be quite challenging. Several patterns of atypical hemangiomas have been described in the literature.[24,28] A discussion of all atypical appearances is beyond the scope of this article; instead, the ones mostly like to create a diagnostic dilemma in clinical practice are briefly discussed.

Although the size and definition of a giant hemangioma vary among different authors, these lesions can become quite large and symptomatic, causing significant enlargement of the liver. Due to their large size, they may lose their typical homogenous hyperintensity on T2-weighted images and the classic peripheral discontinuous globular enhancement pattern may be difficult to appreciate, confounding the diagnosis (Fig 5). Flash-filling hemangiomas show rapid early complete homogenous enhancement on CECT and MRI that persists on the delayed phase images.[24,28] In these cases, the late phase of contrast enhancement is the most important, as these lesions will retain contrast and display internal attenuation or signal intensity similar to that of the blood pool. Flash-filling hemangiomas are typically small and maintain the classic high signal intensity on T2-weighted sequences (Fig 6). Lastly, sclerosing or hyalinized hemangiomas completely lose the classic imaging features of a hemangioma. Their appearance on CECT and MRI is virtually indistinguishable from that of other malignant hepatic tumors, and histologic diagnosis is required for diagnosis. A noninvasive imaging diagnosis is only possible when prior remote examinations demonstrate the presence of a classic hemangioma in the same location. In our experience, the presence of sharply delineated margins is another useful imaging finding seen in sclerosing hemangiomas that may help distinguish them from malignant liver lesions.

*Management*

Because of the characteristic appearance of typical hemangiomas on imaging, biopsy of these lesions is almost never necessary nor recommended, and may lead to bleeding complications.[7] Additionally, biopsy is relatively low yield and major hemorrhage with potential for transfusion requirement or even death has been reported,[29] although more recent data emphasizing the need to ensure a rim of normal liver between the capsule and the lesion itself support the safety of hemangioma biopsy.[30] Tissue biopsy may be especially helpful in the case of sclerosing or hyalinized hemangiomas, where diagnosis on the basis of imaging findings alone may be challenging. Management of hemangiomas is based on the overall clinical picture. The majority of hemangiomas are small and asymptomatic; these may be observed without intervention and do not require specific follow-up.[14,31] Even giant hemangiomas may not merit treatment or surveillance. In a retrospective analysis of 233 patients with hemangiomas larger than 4 cm in size treated conservatively at the Mayo Clinic over a mean follow-up of 11 years, 20% had persistent or new onset symptoms related to their hemangioma, and only 6% ultimately required some type of intervention.[32] Just as surgical resection for asymptomatic lesions should not be offered routinely, there is also no role for requiring patients to stop oral contraceptives or avoid pregnancy, as hormonal fluctuations have not been associated with regression or outcome of hemangiomas.[14] Moreover, any limitation on physical activity is also unwarranted, as the incidence of traumatic rupture is exceedingly low in the literature.[32]

Although conservative management is the rule of thumb for hemangiomas, there exist a few indications for intervention. First, giant hemangiomas that cause severe symptoms of ongoing pain, abdominal mechanical complications (e.g., stomach compression), high output cardiac failure, Kasabach-Merritt syndrome, or Bornman syndrome may require resection. Additionally, rapid growth in size may be a soft indication for surgery. Indeed, although traumatic or spontaneous rupture of a hemangioma is rarely seen, it is most commonly observed with rapidly expanding lesions and can be associated with a high mortality rate (36%-39%).[33] Although

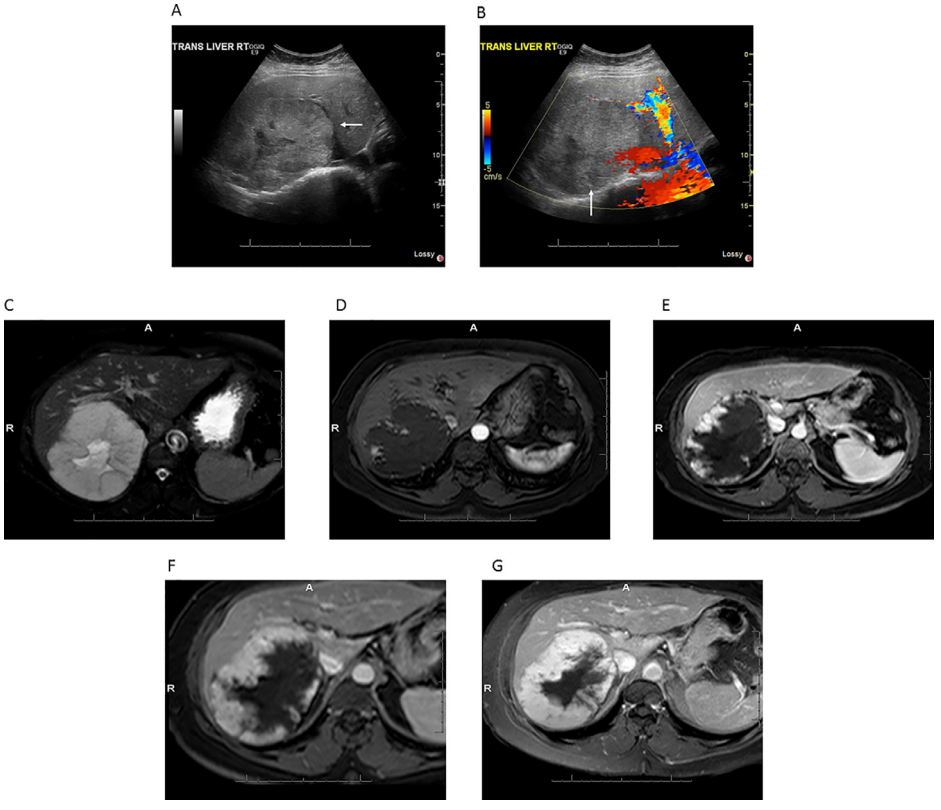


**Fig. 5.** Evaluation of a giant hemangioma in a 54-year-old woman with history of renal cell carcinoma. Transverse grayscale (A) and color Doppler ultrasound images (B) of the right liver show a large lobulated hyperechogenic mass with central hypoechogenicity, corresponding to the central scar that can be seen in giant hemangiomas. Flow is not detected within the lesion on color Doppler interrogation due to slow flow. The ultrasound features are nonspecific and insufficient for the noninvasive diagnosis, requiring confirmation with multiphasic CT or MRI. (C) Axial FSE T2 FAT SAT image shows a lobulated hyperintense lesion in the right liver with a more hyperintense central scar. (D-G) Serial axial GRE T1-weighted postcontrast multiphasic images show a large lobulated hepatic mass displaying the typical discontinuous peripheral globular enhancement characteristic of hemangiomas. Progressive centripetal filling is noted moving from the arterial to delayed equilibrium phase. However, due to its large size, complete filling in of contrast is difficult to demonstrate. The T2-weighted appearance is also atypical. Compare this appearance with the homogenous T2 hyperintensity displayed by a typical hemangioma in Figure 4A.

reports of successful treatment of hemangiomas with nonoperative therapies such as radiation therapy, ablative techniques, and hepatic artery embolization have emerged, data regarding their efficacy are limited and their routine use in the management of symptomatic hemangiomas is not currently endorsed or recommended.[14,34-36] Instead, surgery to remove the hemangioma is the only proven, effective treatment to stop and reverse the associated severe clinical syndromes.[37] Resection of hemangiomas may be accomplished either by enucleation or formal resection, with the former option favored whenever possible to preserve liver parenchyma.[4,38] Studies have demonstrated that both enucleation and resection are curative for this lesion and can be performed safely even for very large hemangiomas, with little difference in morbidity and mortality between the 2 approaches.[39,40] Furthermore, open and minimally invasive techniques (laparoscopy and/or robotics) may both be employed, as they bear similar safety profiles when performed at the hands of experienced surgeons.[41] When dealing with patients with multiple hemangiomas, only the offending lesion – usually a giant hematoma – needs to be removed. Once hemangiomas are resected, recurrence rates are very low, and surveillance is unnecessary.

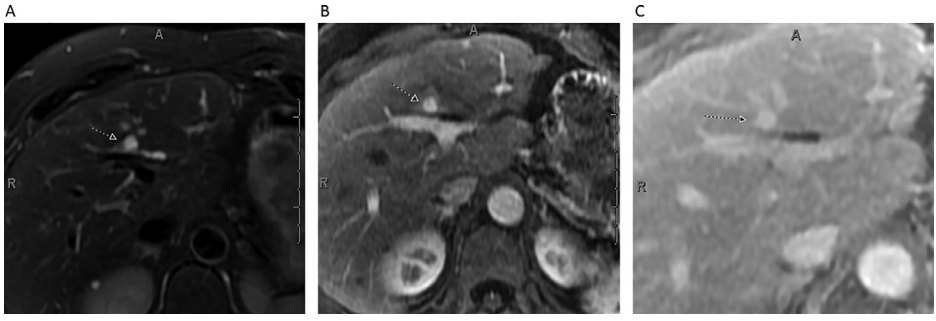


**Fig. 6.** MRI evaluation of a flash-filling hemangioma in a 61-year-old woman with lymphoma. (A) Axial T2-weighted FSE with fat saturation shows a sharply circumscribed homogenously hyperintense hepatic lesion in segment IV (arrow). Axial GRE T1 multiphasic postcontrast images show early homogenous enhancement of the lesion (B) that persists in the delayed phase (C). The persistence of complete homogenous enhancement during the late phase with similar signal intensity to the blood pool is an important imaging feature to characterize it as a flash-filling hemangioma and differentiates it from hypervascular metastases or heptocellular carcinoma, which wash out in the delayed phase.

As is our recommendation for all liver pathologies, surgery should be performed in specialized centers with experience in treating patients with complex hepatobiliary problems and in managing them comprehensively both pre- and postoperatively.

## *Focal nodular hyperplasia*

### *Clinical features*

Following hemangioma, focal nodular hyperplasia (FNH) is the next most common benign liver lesion, with a prevalence of approximately 1% to 3% worldwide.[42,43] Macroscopically, FNHs are typically well-circumscribed and lobulated without a capsule and have a pathognomonic fibrous central scar.[14] Pathologically, they are composed of hepatocytes, Kupffer cells (unlike hepatocellular adenomas), bile ducts, and blood vessels, and their formation results from a hyperplastic hepatocellular reaction to an arterial malformation in the liver, which leads to a characteristic hypervascular central scar, and is characterized by large fibrotic arteries with inflammatory cellular infiltrate and ductal proliferation.[4,14,44] A minority (approximately 20%) will be atypical in that they fail to exhibit some of the classical pathologic findings seen in most FNHs, such as the presence of vascular malformations and/or a nodular appearance as well as the typical central stellate scar.[45]

FNHs occur predominantly in women, with an 8:1 female:male ratio, and tend to be diagnosed in patients from their second to fifth decades.[45,46] Neither anabolic steroid use nor oral contraceptives have been linked to the formation of these tumors.[7,47] FNHs are typically solitary, although multifocal lesions have been described in up to 20% of patients.[48] They are usually less than 5 cm in size with rare lesions measuring greater than 10 cm. FNHs are considered to have no potential for malignant transformation, although isolated case reports of finding an HCC within an FNH lesion have been published.[49] Whether the cancer truly arose from the FNH or was a concomitant finding is unclear, especially since FNHs have been reported to be associated with other liver lesions, particularly hemangiomas, in almost one quarter of the cases.[50] From a genetic standpoint, FNHs may show deregulation of vascular remodeling genes involving angiopoietin, which favors that they are a result of hyperplastic arterial malformation.[51]

Typically, FNHs do not cause symptoms like pain, and rupture and bleeding are very uncommon. Additionally, physical examination and laboratory studies are within normal limits in the vast majority of patients.[4] Therefore, FNHs are most often detected incidentally on abdominal imaging performed for unrelated reasons. Rarely, large FNH lesions may cause abdominal discomfort or mildly increased alkaline phosphatase if they extrinsically compress hepatic veins or intrahepatic bile ducts.[14]

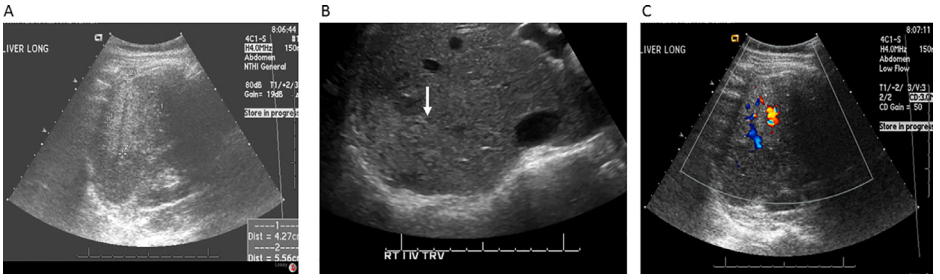


**Fig. 7.** US evaluation of focal nodulor hyperplasia (FNH). Longitudinal (A) and transverse (B) grayscale ultrasound images show a large mildly hyperechogenic lesion in the right liver (arrow). Flow is detected within the lesion on color Doppler interrogation (C). In our experience, the classic "spoke-wheel" pattern of vascularity described in the literature is not very commonly seen in daily clinical practice, but flow is usually demonstrated with FNH on Doppler interrogation. The confident diagnosis of FNH often requires demonstration of their typical imaging features on multiphasic CECT or MRI.

*Radiographic features*

FNHs can be diagnosed on imaging studies based on their morphology, texture, vascularity, and appearance in relation to the surrounding hepatic parenchyma. On grayscale US, FNH is typically homogenous in echotexture and therefore may not be detected very frequently. It is usually slightly hyperechoic or isoechoic to the liver parenchyma, and its scar may be seen as a linear hyperechogenic structure in the center of the lesion (Fig 7).[42,52,53] On color Doppler interrogation, characteristic centrifugal arterial flow from the central scar toward the periphery of the lesion may be seen. On real-time contrast-enhanced US, a typical "spoke-wheel" vascular pattern with homogenous enhancement in the arterial phase that becomes iso- or hypervascular during the portal and late equilibrium phases may be observed.[54]

FNH is typically mildly hypo- or isoattenuating to the surrounding hepatic parenchyma, with gently lobulated margins on nonenhanced CT. Following intravenous administration of contrast, the lesion is classically homogenously hyperattenuating to hepatic parenchyma, with exception of the central scar (Fig 8). It becomes isoattenuating to the hepatic parenchyma in the portal and delayed equilibrium phases while the central scar may show enhancement.[52,53] On MRI, FNH is typically iso- or mildly hypointense to the surrounding hepatic parenchyma on T1-weighted images, and mildly hyper- or isointense on T2-weighted images. The central scar is hypointense on T1 and hyperintense on T2-weighted images. This latter feature is helpful in differentiating the central scar of FNH from that of fibrolamellar HCC, which is classically hypointense on T2-weighted images.[7,55] This is especially useful since the 2 lesions occur in the same patient population and may thus be mistaken for each other. Similar to CECT, intense homogenous enhancement is seen in the arterial phase, with the exception of the central scar. The lesions quickly become isointense to the surrounding hepatic parenchyma in the portal venous and delayed equilibrium phases (Fig 9).[42,52] The presence of a pseudocapsule due to compressed hepatic parenchyma as well as prominent vessels and dilated sinusoids around the lesion may be observed. When these classic imaging features are present, the diagnosis can be confidently made noninvasively. However, atypical features may complicate the diagnosis, and include heterogeneous attenuation, signal intensity, and enhancement pattern on CT and MRI; absence of a central scar; strong T1 hypointensity and T2 hyperintensity; presence of intralesional steatosis fat; calcification of the central scar; and multiplicity of lesions (Fig 10).[42,53]

Conventional MRI is more sensitive and specific than US and CECT for detecting FNH, with sensitivity and specificity of 70% and 98%, respectively.[56] Specific contrast agents with hepatobiliary elimination can be used to demonstrate the hepatocellular origin of these lesions. The hepatobiliary phase (HBP) of gadoxetic acid-enhanced MRI (Gd-EOB-DTPA-MRI) is very helpful for the diagnosis of FNH.[57] A systematic review and meta-analysis of the literature on the diagnostic value of Gd-EOB-DTPA-MRI included 304 patients with FNH and showed that 94% to 97% of FNHs are hyper- or isointense to the surrounding hepatic parenchyma in the HBP of Gd-EOB-DTPA-MRI and was highly accurate for distinguishing FNH from HCC, with an over-

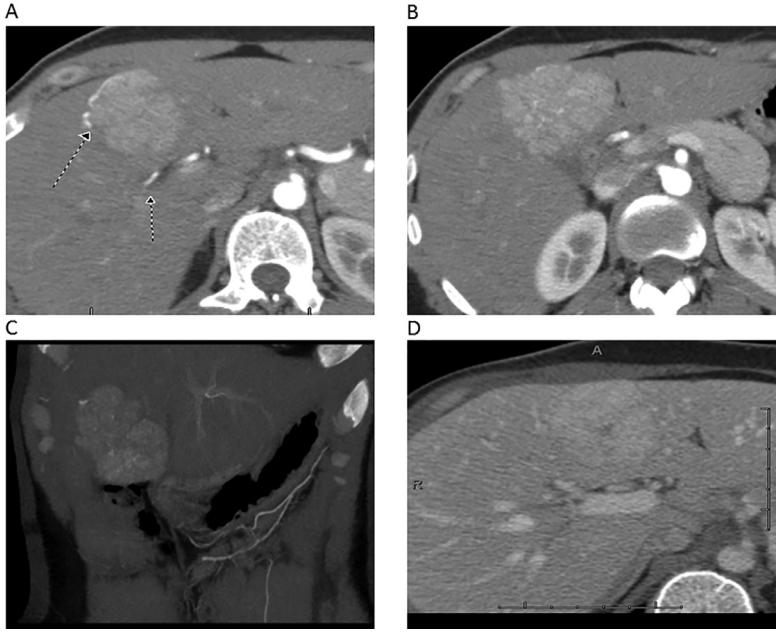


**Fig. 8.** CT evaluation of focal nodular hyperplasia (FNH) in a 39-year-old woman. Axial (A, B) and coronal (C) CECT images in the arterial phase show a gently lobulated lesion in segment IV with homogenous arterial enhancement typical of FNH. The lesion is supplied by branches of the right hepatic artery. In the portovenous phase, it becomes homogenously enhancing and is virtually isodense with the hepatic parenchyma (D), again typical of FNH.

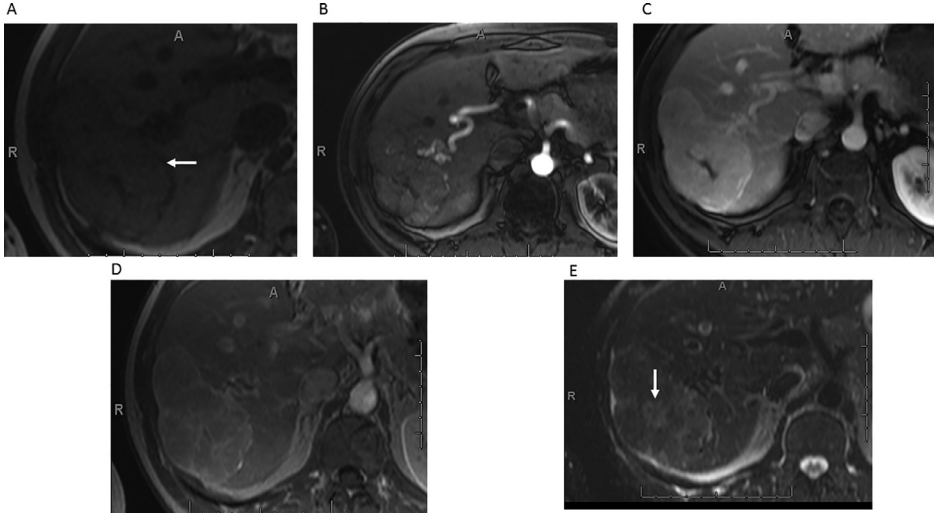


**Fig. 9.** MRI evaluation of a large focal nodular hyperplasia (FNH) in a 65-year old-man. Despite its large size, the mass (arrow) displays similar signal intensity to the liver on T1W GRE images (A). It is supplied by enlarged branches of the right hepatic artery and shows arterial enhancement (B). It becomes homogeneously hyperintense on the portovenous phase (C) and a central hypointense scar is noted. On delayed equilibrium phase (D), the lesion is of similar signal intensity to the remainder of the hepatic parenchyma and a portion of the central scar has filled with contrast. (E) Axial T2 FAT SAT images show a mildly hyperintense large lobulated lesion in the right liver with a hyperintense central scar (arrow). The T2 hyperintense scar of FNH is an important imaging feature to differentiate it from the T2 hypointense scar of fibrolamellar hepatocellular carcinoma.

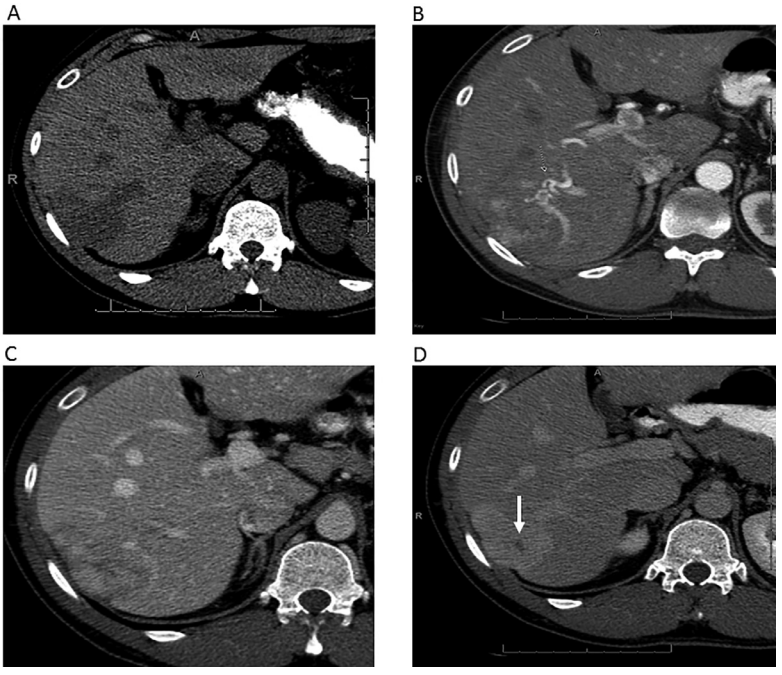


**Fig. 10.** Evaluation of an atypical 5-cm focal nodular hyperplasia (FNH) in a 43-year-old man. (A) A lobulated hypodense lesion is seen in the right liver on noncontrast CT. The lesion shows arterial enhancement (B) that is not homogenously hyperdense as would be typical of FNH. Note an enlarged branch of the right hepatic artery supplying the lesion, which does not become isodense with the hepatic parenchyma on the portovenous (C) or delayed equilibrium (D) phases. A central hypodense scar (arrow) is seen in the delayed phase; this pattern of enhancement of the central scar differs from that of the typical FNH, which usually demonstrates enhancement on the delayed phases, as in Figure 9E.

all sensitivity of 93.9% and specificity of 97%.[58] The main differential diagnosis of FNH is with other hypervascular lesions, such as hypervascular metastases, HCC, hepatocellular adenomas, and flash-filling hemangiomas. In our institution, Gd-EOB-DTPA-MRI is the imaging modality of choice for FNH, particularly in atypical cases in which CECT and conventional MRI results are inconclusive.

*Management*

Because FNH are usually stable in size and many even regress over time, and because they have no malignant potential, patient reassurance should be given and they may be observed with nonoperative management.[4,14] As in the case of hemangiomas, there is no link between estrogen and development or proliferation of FNH, and as such, cessation of oral contraceptives or avoiding pregnancy is not recommended.[14] In a study of 216 women with FNH with various oral contraceptive use patterns (from none to high-dose to pure progesterone) followed over time, Mathieu and colleagues found that neither the intake nor type of contraceptive influenced the size or number of lesions, nor did cessation of oral contraceptives impact their appearance. Twelve of the women became pregnant during the study period, and no increase in lesion size was appreciated during pregnancy.[59] FNHs may be followed clinically with repeat abdominal imaging, keeping in mind that the size of FNH lesions may fluctuate over time, with the lesion appearing larger or smaller across separate studies.[59,60]

Although most FNHs will not require invasive interventions, a biopsy may be necessary when it is not possible to radiographically distinguish FNH from a malignant lesion. This is especially applicable to patients with atypical FNH. The biopsy should include samples from the central scar in order to demonstrate pathognomonic bile ductules, which may only be present in this

area of the lesion.[46] Indications for surgical intervention include instances when atypical features are found such as large lesions causing pain, lesions growing in size over time, those in male patients (which tend to display more severe morphologic atypia), and those that are indistinguishable from malignant tumors.[4,14,61] Similar to the surgical treatment of hemangiomas, enucleation, partial resection, or even anatomic hepatectomy may be required to remove FNHs. However, in contrast to surgery for hemangiomas, resection is favored over enucleation due to the frequent presence of large veins that tend to surround FNH lesions (see Figs 9 and 10).[14] Alternatively, patients with large symptomatic FNH lesions that are otherwise not concerning for malignancy and/or are too risky for resection may be considered for transarterial embolization, which has been reported to shrink the lesion and provide symptomatic relief, although this treatment modality is not routinely recommended.[62] Although some authors advocate follow-up of FNH with US at regular intervals, there are few data to support the need for close surveillance of this benign pathology.

### *Hepatocellular adenoma*

#### *Clinical features*

Hepatocellular adenomas (HCAs), also called hepatic adenomas, are relatively uncommon overall, with an estimated prevalence of less than 0.05%.[63] Pathologically, they are proliferations of normal-appearing benign hepatocytes with collections of thin vessels organized in a trabecular fashion without the characteristic acinar architecture or portal triads of typical liver parenchyma, and macroscopically, the lesions are well-circumscribed and have no capsule.[3,4,64] HCAs occur predominantly in women, with a female to male ratio of 9:1, and are found most commonly in fertile women of child-bearing age. These lesions may be solitary or multiple and range from 1 to 30 cm in size (typically 5-15 cm).[4,65] When more than 10 lesions are present, and in the absence of known risk factors, the condition is termed liver adenomatosis.[4,66] HCAs may be asymptomatic or, alternatively, may cause general abdominal pain and discomfort. Hepatic function studies are usually normal, although large HCAs may lead to elevated gamma-glutamyltransferase, elevated alkaline phosphatase, and/or elevated transaminases on routine laboratory studies.[4,67] Large tumors, especially those larger than 7 cm, may spontaneously rupture and bleed, leading to significant hemorrhage and possible shock.[64,68]

The strongest risk factor for development and subsequent growth of HCA is exposure to estrogen, either by pregnancy or oral contraceptives.[63,64,69] The mechanism of how and why estrogen exposure leads to HCA formation and growth is unclear, although it has been speculated that HCA may be the outcome of a gene mutation in the hepatocyte nuclear factor 1$\alpha$ (HNF1$\alpha$) after estrogen exposure or a germline mutation of CYP1B1 resulting in decreased enzyme activity in estrogen metabolism.[63,70] What is known is that there exists a dose-dependent correlation of HCA development with oral contraceptives, and cessation of oral contraceptives can lead to regression of the lesion.[71,72] Patients exposed to increased androgens in the form of anabolic steroids are also at increased risk of HCA development.[73] In addition, there is also a correlation of HCA formation with obesity and nonalcoholic steatohepatitis.[74] Finally, glycogen storage diseases, especially type Ia glycogenosis, or other genetic metabolic syndromes like McCune-Albright syndrome are additional risk factors for HCA formation.[63,75]

#### *HCA subtypes*

Four main subtypes of HCA have been identified on the basis of molecular and pathologic features.[76-78] Their distinction is important in that they bear different risks for complications, including malignant transformation, and warrant different therapeutic approaches. The first subtype, accounting for approximately 30% to 40% of all HCAs, is the HCA-H subtype, which is associated with HNF1A gene mutations. Pathologically, HCA-H demonstrates cytologic atypia with abundant steatosis and lack of inflammatory changes.[63,64,78] The second and most common subtype (40%-50% of HCAs) is Inflammatory HCA (HCA-I). It is also known as telangiectatic HCA and is associated with activation of the JAK/STAT pathway via mutations of the IL6ST,

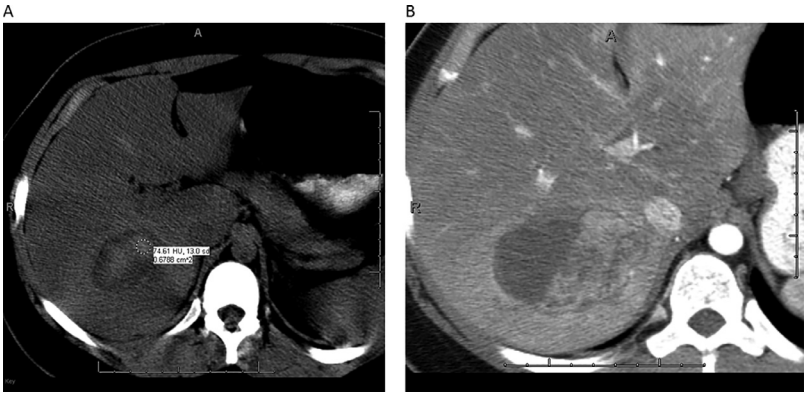


**Fig. 11.** CT evaluation of a segment VII hepatocellular adenoma with spontaneous hemorrhage in a 39-year-old woman. (A) Axial noncontrast CT image shows a hypodense mass in the right liver with internal hyperattenuating material (76 HU) indicative of hemorrhage. (B) Axial CECT image shows heterogeneous enhancement of the mass with attenuation similar to the remainder of the hepatic parenchyma, and lack of enhancement of the hemorrhagic areas. The lesion does not wash out and there are no vascular invasive features.

STAT3, or GNAS genes, and on pathology shows characteristic inflammatory infiltration with sinusoidal dilation and pseudoportal tracts that lack bile ducts and veins but have thick-walled arteries.[63,64,79] HCA-I is associated with obesity and nonalcoholic steatohepatitis.[67] The third HCA subtype is $\beta$-Catenin activated HCA (HCA-B), which accounts for 10% to 15% of HCAs, is associated with $\beta$-catenin gene activating mutations, and exhibits cytologic atypia with steatosis and lack of inflammatory changes with a pseudoacinar pattern on pathology.[64] HCA-B is associated with an increased risk of malignant transformation, especially when the lesion in larger than 5 cm.[67] The final 10% of HCAs are categorized as HCA-U subtypes, which have general morphologic features of a hepatocellular adenoma, but otherwise lack specific genetic or pathologic distinctions that would allow them to fit into any of the other 3 categories.[64]

*Radiographic features*

The imaging features of HCAs vary greatly depending on the size and internal composition of the lesion. Indeed, HCA lesions may contain variable amounts of macroscopic or microscopic intracellular fat, hemorrhage of different ages, calcifications, and internal necrosis, compounding their imaging appearance.[80] On grayscale US, HCAs may appear hyperechogenic in relation to the adjacent hepatic parenchyma due to presence of internal fat and/or hemorrhage. Internal hemorrhage, however, may also appear hypoechogenic or cystic. On color and spectral Doppler US interrogation, HCAs may show peri- and intratumoral vessels with a flat continuous waveform.[80,81] However, the sonographic appearance of HCAs is not characteristic, and most adenomas are not diagnosed on US, requiring further evaluation with CECT and MRI.

On nonenhanced CT, HCAs appear as a well-defined oval mass that is usually isodense or heterogeneously hypodense (due to presence of intratumoral fat) to the surrounding hepatic parenchyma. Hemorrhage will appear as hyperdense areas that may be intratumoral, intraparenchymal, or subscapular (Fig 11). On CECT, they show variable heterogeneous hyperdense enhancement in the arterial phase. HCAs may be hyper-, iso-, or hypoattenuating in relation to the hepatic parenchyma in the portal venous phase, and in the delayed equilibrium phase, they are usually hypoattenuating and may display a hyperattenuating pseudocapsule (Fig 12).[80]

Similarly to CECT, MRI appearances of HCAs vary with size and internal composition of the lesion. On T1-weighted images, HCAs may display high signal intensity (due to fat or recent hemorrhage) in relation to the surrounding hepatic parenchyma, which is easier to appreciate on MRI than CT or US (Fig 13). Low T1 signal intensity may be observed in the presence of necrosis, calcification, or old hemorrhage. On T2-weighted images with fat saturation, HCAs

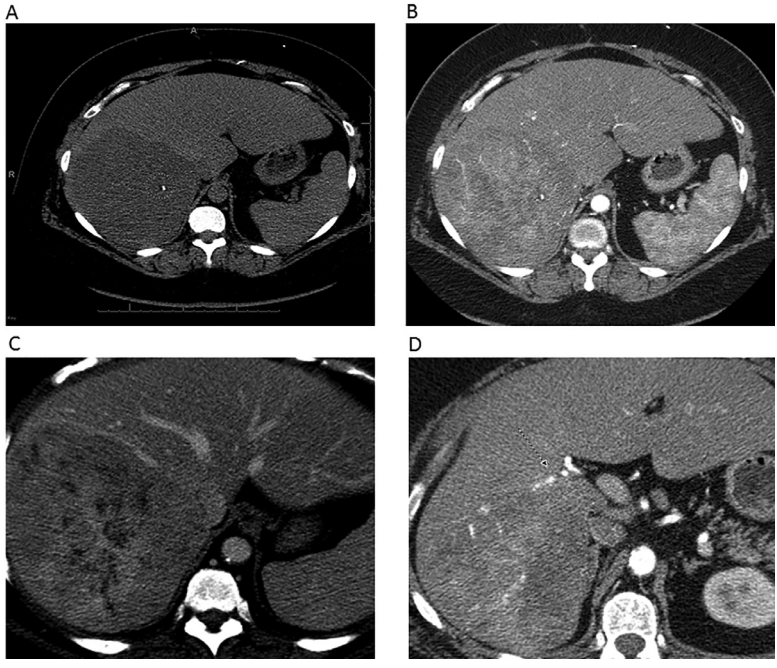


**Fig. 12.** CT evaluation of a large hepatocellular adenoma occupying most of the right liver in a 64-year-old woman. (A) Precontrast CT image shows a large hypodense mass in the right liver, with lobulated margins. A small focus of calcification and fat is appreciated within the lesion. CECT in the arterial (B) and portovenous (C) phases shows that the heterogenous arterial enhancement of the mass persists in the portovenous and delayed phases. Despite the large size of this lesion, there are no foci of internal necrosis and the heterogenous attenuation of the lesion is uniformly present in the center and periphery of the lesion. (D) The lesion is supplied by branches of the right hepatic artery. There is long segment abutment with the right hepatic vein and retrohepatic IVC (C), but no vascular invasion is seen.

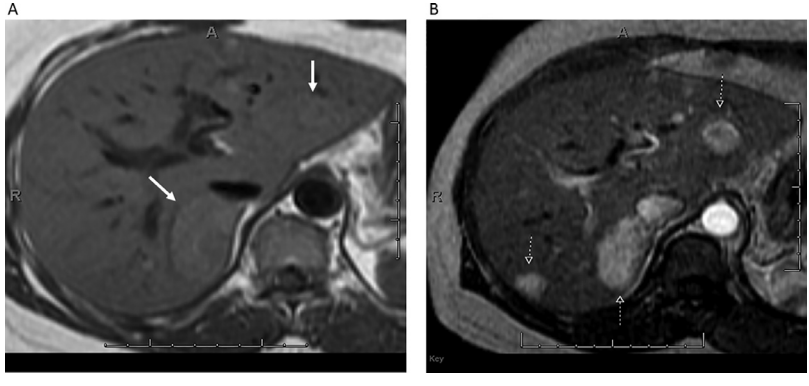


**Fig. 13.** MRI evaluation of multiple hepatocellular adenomas in a 60-year-old woman. (A) Axial T1 image shows a mildly hyperintense lesion in segment VII and suggestion of a subtle lesion in segment II (arrows). (B) Axial T1 postcontrast image shows multiple arterially enhancing hepatic lesions, some of which were not apparent on the noncontrast T1 image. Hepatocellular adenomas may have signal intensity remarkably similar to the hepatic parenchyma, particularly lesions without large amount of fat and no internal hemorrhage, which can make them less conspicuous and easy to overlook on noncontrast examinations.

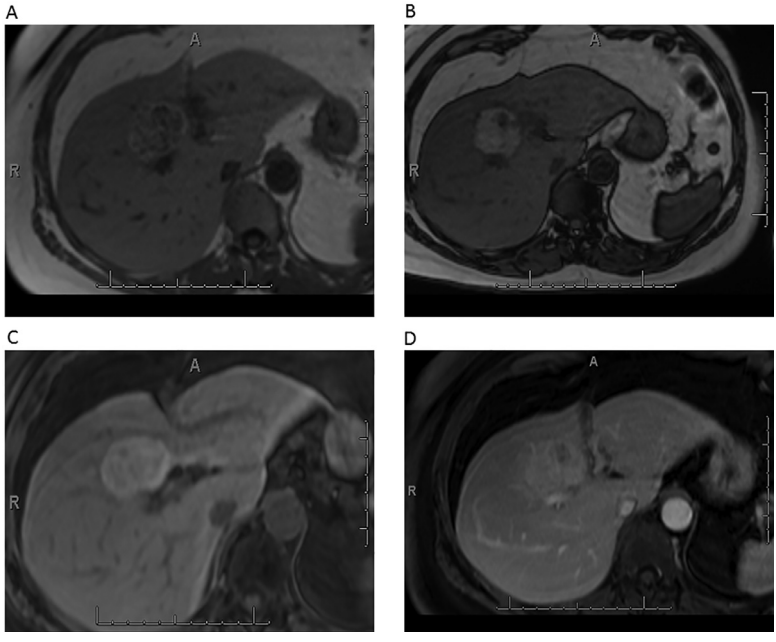


**Fig. 14.** MRI evaluation of a hepatocellular adenoma in a 59-year-old woman. Axial GRE in-phase and opposed phase (A, B) images show a T1 hyperintense liver mass with foci of intravoxel fat. On axial T1 FAT SAT pre- (C) and postcontrast (D) images, the hepatic mass is hyperintense to the liver and shows subtle heterogenous arterial enhancement that persists in the portovenous phase.

display heterogeneous signal intensity, ranging from high T2 signal in areas of necrosis or acute hemorrhage to low T2 signal in the presence of fat or old hemorrhage. Multiphasic MRI with extracellular agents shows heterogeneous enhancement in the arterial and portal phases, and a delayed hyperintense signal of the pseudocapsule relative to the surrounding liver in the delayed equilibrium phase.[80,82] Following the injection of hepatocellular-specific contrast agents, the majority of HCAs do not show significant uptake due to the relative lack of Kupffer cells within the tumor, which thus appears hypointense to the surrounding liver in the HBP. This is in contrast to the typical appearance of a classic FNH, which becomes hyper- or isointense in the HBP; this feature is helpful in differentiating HCA from FNH.[57,58] We find Gd-EOB-DTPA-MRI to be particularly useful in the evaluation of HCAs as it may show specific imaging features that can help differentiate between the subtypes of HCA.[57,83] HNF1$\alpha$-inactivated HCA (HCA-H) typically shows diffuse fat evidenced by loss of signal on gradient recalled echo T1-weighted out-of-phase in relation to in-phase, mild to moderate arterial vascularity on dynamic postcontrast images, and hypointensity in the HBP (Fig 14). HCA-I may show a characteristic “atoll sign” on T2-weighted images, which is a peripheral rim of hyperintensity surrounding the T2-isointense center of the lesion, marked arterial hypervascularity on dynamic postcontrast images, and hypointensity in the HBP. HCA-B typically shows mild to moderate arterial hypervascularity on dynamic postcontrast images, may show the presence of a scar, and iso- or hyperintensity in the HBP. Finally, unclassified HCA does not display specific imaging features.[57,80,83]

Despite the high utility of imaging in establishing a diagnosis, the main difficulty with HCA from a diagnostic imaging perspective remains the difficulty in differentiating it from HCC, which can be indistinguishable from HCA on imaging.

*Management*

Unlike hemangiomas and FNHs, HCAs do carry a significant risk of rupture and hemorrhage in up to 25% of patients.[67,84] They also carry malignant transformation potential, approximat-

ing 4% to 4.5%, although this risk may be overestimated owing to treatment and reporting biases.[14,65,85] Because of these potential complications, and since HCAs may bear a similar appearance to that of other focal benign hepatic lesions as well as that of the malignant HCC, there may be a role for percutaneous liver biopsy to confirm the diagnosis and help distinguish between the subtypes of HCAs.[64,86] This latter piece of information, along with certain clinicopathologic features, can aid in determining the risks of both hemorrhagic complications and malignant transformation associated with the tumor, and thus in directing therapy.

Large tumors (>5 cm), especially those of the HCA-I subtype, are at greatest risk for rupture and hemorrhage. In a multi-institutional series of 124 patients with HCA who underwent treatment, tumors that ruptured averaged 10.5 cm, and no tumor smaller than 5 cm ruptured. In addition, recent hormone use was identified as an independent risk factor for rupture.[84] Tumor size larger than 5 cm has also been identified as a risk factor for malignant transformation, independent of HCA subtype. In a systematic review of the literature covering more than 1600 HCAs, Stoot and colleagues reported a mean size of 10.5 cm for HCAs with features of malignant alteration, with only 3 total cases (4.4%) measuring less than 5 cm in diameter.[65] Beside size, HCA subtype is also a well-recognized risk factor for this complication. In particular, HCA-B, which is associated with activating mutations of the $\beta$-catenin gene, carries the greatest risk of malignant degeneration into HCC, with 1 series reporting presence of invasive disease arising from an adenoma in 46% of HCA-B, but not in HCA-I and only rarely in HCA-H.[76] Additional risk factors for malignant transformation of HCA include male gender, which is associated with a 6 to 10-fold higher risk than women; use of anabolic steroids; and patients with glycogen storage diseases.[65,85,87] Conversely, the number of lesions, including in the setting of adenomatosis, does not appear to pose a risk for rupture, hemorrhage, or malignant degeneration.

Based on this knowledge, an algorithm for managing HCAs is possible.[3] HCAs of any subtype and any size in men should be resected given the significant risk of malignant transformation. On the other hand, the management of HCAs in women can be more selective. Tumors that are smaller than 5 cm may be observed initially with cessation of oral contraceptives and may be followed with biannual or annual evaluations with repeat MRI over at least 5 years.[88] Tumors larger than 5 cm in size may be given an opportunity to shrink after cessation of contraceptives, but should be considered for resection if they persist.[84,85,88] Finally, presence of symptoms may serve as an indication for surgical resection. These same principles apply to patients with multiple HCA, for whom only the largest tumors (those > 5 cm in size) should be resected.

When surgery is considered, a nonanatomic resection is appropriate given the low risk of vascular invasion or nodal involvement. This may be accomplished via either an open or minimally invasive approach, depending on the surgeon's experience and comfort level. If a lesion has been complicated by rupture and hemorrhage, attempt at immediate resection has been associated with mortality risk as high as 8%.[67] Instead, in this clinical scenario, initial treatment should consist of transarterial embolization in order to control bleeding and potentially lead to shrinkage of the tumor.[89] Transarterial embolization has also been used in some series as primary treatment for HCAs, with promising results.[90,91] Likewise, radiofrequency ablation has been used successfully to safely treat HCAs smaller than 4 cm in size.[92] Still, surgery remains the most effective intervention and the gold standard for the treatment of HCAs that cannot be safely observed. Liver transplantation is reserved for patients at high risk for malignancy with unresectable tumors or those with glycogen storage disorders unresponsive to medical therapy.[14] We recommend follow-up of HCAs that are not surgically resected to ensure stability and surveillance of those that are removed, especially in men and patients with $\beta$-catenin activated HCA.

### *Angiomyolipoma*

#### *Clinical features*

Angiomyolipomas are very rare lesions that have been described most commonly in the kidney but are also found in the liver.[93] Hepatic angiomyolipomas most commonly affect women in the third to fifth decades of life and are often larger than 5 cm at the time of diagnosis, with the ability to increase in size.[94] They are usually asymptomatic with normal liver function tests and

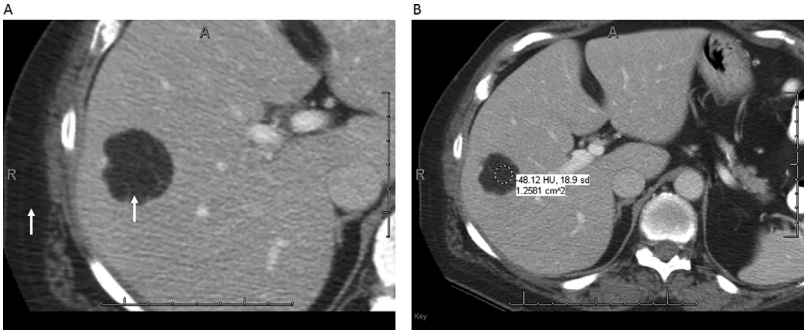


**Fig. 15.** CT evaluation of an angiomyolipoma in a 45-year-old man. Axial CECT images show a gently lobulated hypodense mass in the right liver. The lesion density is visually identical to that of the subcutaneous and retroperitoneal fat (arrows) (A). Note the negative HU in the R.O.I. circle, consistent with macroscopic fat (B).

negative tumor markers, and are found incidentally on routine abdominal imaging. Macroscopically, hepatic angiomyolipomas lack encapsulation but are well-circumscribed with mature adipose tissue and smooth muscle cells.[95] Pathologically, these lesions are mesenchymal in origin and contain blood vessels, smooth muscle cells, and adipose tissue in various proportions and arise from perivascular epithelioid cells.[14] There is an association of hepatic angiomyolipomas with tuberous sclerosis,[96] and although rare, malignant degeneration of hepatic angiomyolipomas has been described in the literature.[97]

*Radiographic features*

The imaging features of hepatic angiomyolipomas will depend on the internal composition of the tumor and specifically on the variable amounts of intralesional fat (from less than 10% to more than 90%), smooth muscle, and proliferating vessels present. The most useful diagnostic feature is the presence of fat within a well-circumscribed hepatic mass in the context of a patient with tuberous sclerosis. Hepatic angiomyolipomas are not readily diagnosed on US, and CT and MRI represent the most useful imaging modalities for this diagnosis. MRI is the most specific imaging technique to detect both macroscopic and microscopic fat. On CECT and MRI, the lesions are usually well-defined, displaying variable amounts of fat attenuation (lipoid component) interspersed with variable amounts of enhancing soft tissue (myoid and angioid components) (Fig 15).[98,99] To compound the issue, there are cases in which the intralesional fat component of angiomyolipomas may be very difficult to recognize on CT and MRI. Moreover, because both HCCs and hepatic angiomyolipomas may contain variable amounts of fat, differentiating between the two can be virtually impossible on imaging. In a study comparing gadoxetic acid-enhanced MRIs of 18 patients with hepatic cystadenomas to those of 36 patients with HCCs and noncirrhotic livers, Lee and colleagues reported that the 2 diseases were indistinguishable on the basis of standard dynamic enhancement profiles. Instead, the authors highlighted the gender distribution and some imaging features that were helpful in differentiating the two, which included isointensity on DWI, washout in the portal phase, early draining veins, intratumoral vessels, and presence of capsule.[99] In addition to HCC, the differential diagnosis for hepatic angiomyolipoma also includes hepatic lipoma (homogenous fat density or signal intensity on all series and sequences), focal steatosis, and liposarcoma and teratoma metastases.

*Management*

Angiomyolipomas may be indistinguishable from hepatic metastases, so current guidelines recommend biopsy with histologic confirmation of diagnosis, which may be aided by staining with melanocytic markers, especially human melanoma black 45.[14] Asymptomatic angiomyolipomas less than 5 cm in size may be observed with close follow-up and serial abdominal imaging. Angiomyolipomas greater than 5 cm in size, on the other hand, should be resected as there is evidence that the risk of malignant transformation increases with tumor size.[100] Although

angiomyolipomas of the kidney are primarily treated with transarterial embolization, there are currently no data to support this treatment approach for hepatic angiomyolipomas.

## Benign cystic liver lesions

Hepatic cysts are commonly seen in clinical practice and encompass a broad spectrum of disease processes with a wide differential, from incidental simple developmental cysts of no or little clinical significance to malignancy. Differentiating clinically significant from insignificant lesions is of utmost importance and imaging usually plays an important role in accomplishing this task. Nonmalignant hepatic cysts covered in this review include simple hepatic cysts, including in the context of polycystic liver disease; infectious cysts of various etiologies (pyogenic, amebic, and echinococcal); biliary cystadenomas, which bear malignant potential; and mesenchymal hamartomas. Other benign cystic liver lesions not covered in this review include Caroli disease, ciliated foregut duplication cysts, intrahepatic pseudocysts, and trauma-related conditions such as bilomas, hematomas, and seromas. Some hepatic cystic lesions have classic imaging findings that allow a confident diagnosis noninvasively and knowledge of these key radiologic features is therefore critical in making the correct diagnosis.[101]

### *Simple hepatic cyst*

#### *Clinical features*

Simple hepatic cysts are the most prevalent liver lesions in the general population. They are found in approximately 2% to 18% of the population, are typically less than 3 cm in size (although they can reach 20 cm), and are most commonly found in women in their fifth to sixth decades.[3,4,102] The female: male ratio is approximately 3:1 for asymptomatic cysts, while it is close to 10:1 for symptomatic cysts.[103] Simple cysts are typically congenital in nature and unilocular (i.e., without septations). They develop from enlargement and dilation of biliary microhamartomas without direct biliary tree communication and are lined with cuboidal epithelium.[103] They are asymptomatic in nearly three-quarters of patients and are often found incidentally on routine abdominal imaging.[3,102] However, depending upon size and location, they may cause significant symptoms, including lower extremity edema from compression of the inferior vena cava or jaundice from compression of the main bile ducts.[104]

#### *Radiographic features*

Simple cysts vary in size and number and are usually round or oval with thin imperceptible walls. On US, the characteristic imaging features are a round completely anechoic structure, with sharply circumscribed margins and posterior acoustic enhancement. No internal nodularity, debris, or septations are present and there should be no internal vascularity on color Doppler interrogation. On CECT, simple cysts are homogenously hypodense lesions with sharply circumscribed margins, displaying internal attenuation values in the range of 0-15 Hounsfield Units (HU). Following intravenous contrast administration, no internal enhancement is seen (Fig 16). It is important to note that a precontrast scan can be very useful, as internal hemorrhage with blood clots and calcifications may compound the interpretation of single-phase contrast-enhanced scans. When present within a cyst, these features may masquerade as solid components or internal enhancement, causing diagnostic confusion with more ominous lesions. This potential pitfall can be easily avoided with the utilization of a precontrast scan of the liver.

On MRI, simple hepatic cysts are homogenously hyperintense on T2-weighted sequences, matching the signal intensity of cerebrospinal fluid, fluid in the biliary tree, and collecting systems. They are homogenously hypointense on T1-weighted sequences and do not show internal enhancement following intravenous administration. The walls are essentially imperceptible

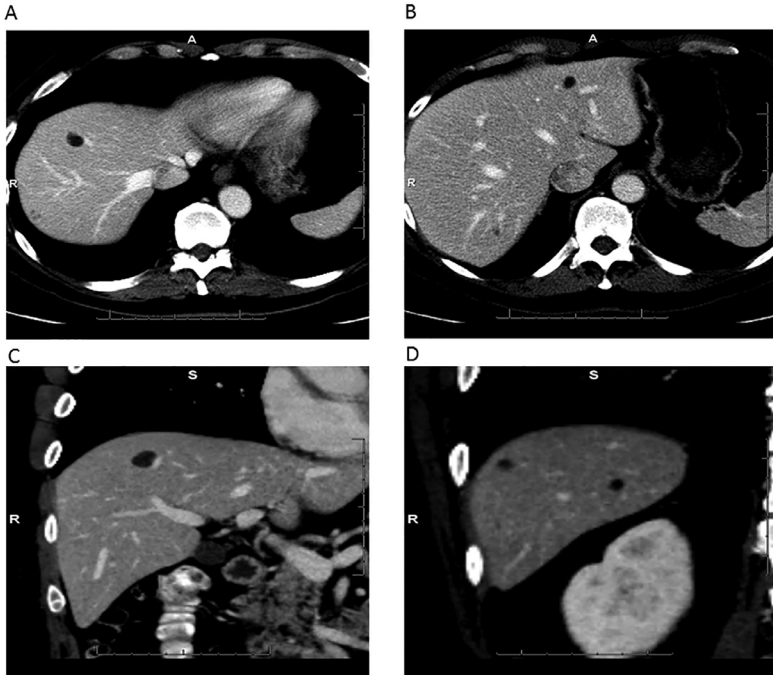


**Fig. 16.** CT evaluation of simple hepatic cysts in a 62-year-old man with a history of angiosarcoma. Axial (A, B) and coronal (C, D) CECT images show scattered incidental small simple hepatic cysts in both lobes of the liver. The lesions are sharply circumscribed and homogenously hypoattenuating in the portal venous phase images, with thin imperceptible walls, and lack internal solid components.

and no internal septations or nodularity is seen. The differential diagnosis mainly includes biliary hamartomas or von Meyenburg complexes. These are benign developmental lesions, usually multiple and less than 15 mm in diameter, that consist of dilated small bile ducts and a surrounding fibrous stroma.[105] On imaging, these lesions typically appear as multiple small simple-appearing cysts, predominantly along the subcapsular region.[101] Subtle rim enhancement, if noted, is thought to be related to enhancement of the compressed hepatic parenchyma adjacent to the small hamartoma.[106] Importantly, these do not show communication with the biliary tree, a feature that is useful to differentiate them from Caroli's disease.[101]

*Management*

Although the majority of simple hepatic cysts are small, they can enlarge and cause compression of hepatic structures such as portal or hepatic veins or bile ducts. Compression of bile ducts may lead to jaundice and elevated serum bilirubin.[107] Intracystic hemorrhage causing pain is rare but may occur in larger cysts.[3] Because they are benign and unlikely to cause any problems, asymptomatic cysts do not require intervention, and no specific serial imaging is required.[108] Moreover, if simple cysts are encountered incidentally during an operation for an unrelated reason, it is not necessary to routinely intervene upon them.[103]

Hepatic cysts that cause abdominal discomfort, on the other hand, do merit intervention. Studies have described percutaneous drainage of these cysts, but this approach will almost always lead to recurrence and therefore does not represent a durable option for the management of hepatic cysts.[103,109] Instead, definitive treatment requires surgical intervention, which can be accomplished by a minimally invasive approach with laparoscopy.[3,110] Formal hepatectomy (e.g., segmentectomy, sectionectomy, hemihepatectomy) is usually not required for this benign process and may pose additional risks without offering any true advantages.[103] Instead, laparoscopic

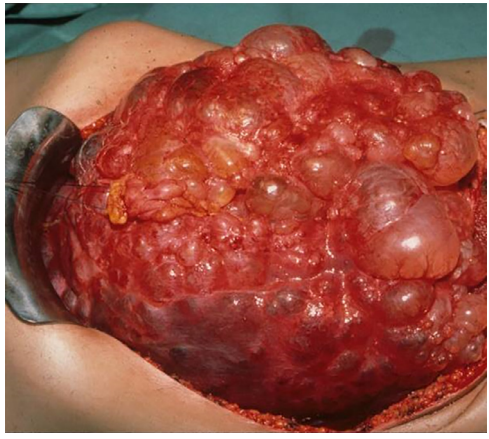

**Fig. 17.** Gross appearance of polycystic liver disease. The liver parenchyma has been diffusely replaced by innumerable cysts of varying sizes, leading to significant hepatomegaly. Surgical treatment of polycystic liver disease is complex, and liver transplantation offers the best chance for definitive management.

drainage with cyst unroofing or fenestration has shown favorable results with low risk of associated complications or recurrence.[111,112] Given the low morbidity and the technical ease with which this procedure can be achieved, laparoscopic cyst unroofing has become the preferred approach in the treatment of symptomatic hepatic cysts. Finally, cyst enucleation presents a reasonable option when diagnostic uncertainty remains and is associated with good reported outcomes.[113]

## *Polycystic liver disease*

### *Clinical features*

Polycystic liver disease (PLD) is a condition marked by the growth of multiple fluid-filled cysts of differing sizes in the liver, and is defined as growth of more than 10 cysts.[114] The number and size of the cysts may be so great as to nearly completely replace the liver parenchyma and cause significant hepatomegaly (Fig 17). PLD is encountered in the context of 2 distinct hereditary disorders, both of which are autosomal dominant: isolated polycystic liver disease, also referred to as autosomal dominant polycystic liver disease, which affects less than 0.01% of the general population, and autosomal dominant polycystic kidney disease (ADPKD), which is more common and has an estimated prevalence of 0.2%.[115,116] Although the morphology and pathophysiology of the cysts is similar between the 2 syndromes, they differ in their genetic profiles, management, and prognosis, with ADPKD patients having to contend with multiple large renal cysts with significant renal function implications that are beyond the scope of this review. Germline mutations in *PKD1* and *PKD2* have been associated with ADPKD, whereas mutations of *PRKCSH*, *SEC63*, and *LRP5* are found in autosomal dominant polycystic liver disease.[117,118] Men and women are affected in overall equal numbers, but women have been described to have worse severity of disease and faster disease progression, pointing to estrogen as a significant contributor to the growth of the cysts.[116,119] Cyst formation in PLD can occur at any age, however patients usually begin to notice symptoms around the fifth decade of life, and symptoms tend to become more severe with increasing age.[114] The most common symptoms of PLD are abdominal pain and fullness in the right upper quadrant, dyspnea, gastroesophageal reflux, and jaundice (from external compression of bile ducts), and physical examination is often significant for hepatomegaly.[116,120] In addition, hepatic function studies may show elevated alkaline phosphatase and gamma-glutamyltransferase.[114]

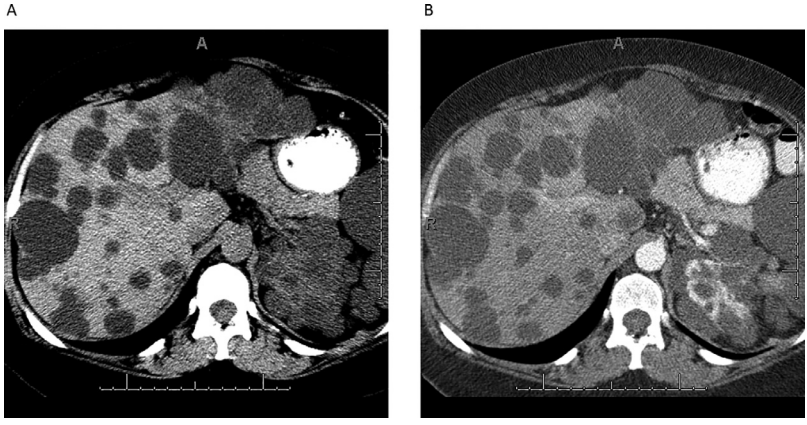


**Fig. 18.** CT evaluation of a 68-year-old man with polycystic liver disease. Axial noncontrast (A) and CECT (B) images show numerous sharply circumscribed masses in the liver of homogenous low attenuation. There are no enhancing nodules or septations within these lesions. Note the numerous cysts in the left kidney.

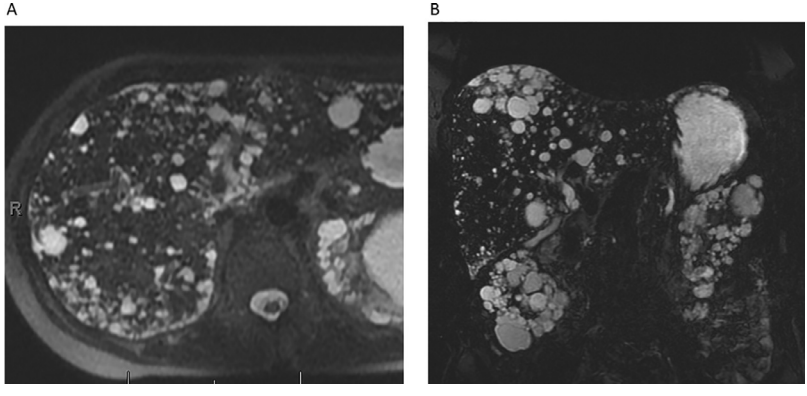


**Fig. 19.** MRI evaluation of polycystic liver disease. Heavily T2-weighted axial (A) and coronal (B) images show innumerable cysts of various sizes in both the liver and kidneys.

*Radiographic features*

Cross-sectional imaging with US, CECT, and MRI typically shows multiple hepatic cysts of varying sizes (less than 1 mm to greater than 12 cm) and location, with the extent of disease varying from limited areas to diffuse involvement of all hepatic sectors. Grayscale US typically shows multiple anechoic cystic masses, with well-defined margins and enhanced through transmission. On nonenhanced CT, PLD is characterized by the presence of multiple hypodense cysts, with some cysts showing internal attenuation higher than water due to internal hemorrhage (Fig 18). Curvilinear calcifications may be seen along the walls, usually the sequela of old hemorrhage. Following intravenous contrast administration, no enhancement should be observed along the cyst wall or its contents. Cysts complicated with hemorrhage and/or infection may display a more heterogenous appearance, with internal debris, septations, and fluid–fluid levels and may show wall enhancement.[101,121] MRI findings of uncomplicated cysts include sharply circumscribed walls, homogenous low T1 signal, homogeneous high T2 signal and lack of enhancement following intravenous contrast (Fig 19). Complicated cysts with hemorrhage and/or infection may show heterogeneous high T1 signal intensity and heterogeneous low T2 signal due to hemorrhage and/or air, may contain internal debris or septations, and show wall enhancement.[101,121]

CECT and MRI are very helpful to identify complicated cysts with hemorrhage and/or infection that may be responsible for patients' symptoms, their exact location, distribution, and relation to adjacent anatomical structures. The differential diagnosis is made primarily with hepatic biliary cysts, bile duct hamartomas, Caroli disease, and cystic metastases, particularly from GI stromal tumors after successful treatment with imatinib and colorectal adenocarcinoma treated with bevacizumab.

*Management*

The majority of patients with PLD will not have symptoms and thus will not require treatment. When symptoms do occur, they may be grouped into 2 main categories: volume-related complications (abdominal pain and discomfort, GERD, obstructive jaundice, portal hypertension, portal vein occlusion, Budd-Chiari syndrome, and IVC compression) and intracystic complications (hepatic cyst hemorrhage, infection, and rupture).[122] In the presence of these complications, intervention is indicated and ranges from medical management to surgical options. Nonoperative options include avoidance of estrogen, which is thought to stimulate cyst fluid production, and the use of somatostatin analogs to reduce fluid secretion and curb the growth of the cysts.[116,123] When medical therapies fail, or in the presence of more severe symptoms, invasive procedures are necessary. Which procedural option is best for individual patients with PLD may be aided by classification systems like the Gigot and Schnelldorfer classifications.[124,125] Symptomatic cysts that are greater than 5 cm may be aspirated and injected with a sclerosing agent that inhibits fluid reaccumulation by damaging the epithelial lining of the cyst. This procedure has been demonstrated to be safe, with good immediate postoperative symptomatic relief, although only 20% of patients will have partial or full regression of their disease.[126,127] For patients in whom aspiration sclerotherapy is not an option or does not offer durable improvement, surgical options include fenestration, resection, and transplantation. As is the case for isolated simple cysts, fenestration is most suitable for cysts that are superficial and situated in the anterior liver sectors. Fenestration is associated with a high rate of immediate symptom improvement (92%), but symptom recurrence and fluid reaccumulation occur in nearly one quarter of patients. Moreover, rates of morbidity of 23% and mortality of 2% have been reported.[126] Although selective hepatic resection for large areas of cyst burden has been described, whether it presents a good option for patients with PLD has long been and remains in question.[116,122,128] Although resection can provide symptom relief, recurrence rates are high, postoperative complications may approach 50% due to distortion of the liver anatomy by the presence of the cysts, and perhaps most importantly, hepatectomy may complicate future orthotopic liver transplantation (OLT), which provides the only definitive therapy for PLD.[125,129] Because liver function tends to be preserved, even in the most advanced settings, patients with PLD will often need Model for End-Stage Liver Disease exception criteria to receive an allograft. In light of the limited availability of organs, OLT is mostly reserved for patients with PLD who have severe symptoms. Nearly one half of patients with PLD in the context of ADPKD will need combined liver and kidney transplantation. Survival after OLT is excellent, and need for re-transplantation has been reported at 3%.[126]

*Pyogenic hepatic cyst*

*Clinical features*

Pyogenic hepatic cysts are infected collections, or abscesses, of the liver and are one of the most common forms of intra-abdominal abscesses. They usually form indirectly as a result of leakage of bowel contents and peritonitis from perforation, as in the case of appendicitis or diverticulitis, or GI malignancy. However, pyogenic liver abscesses may also result from direct bacterial spread from a biliary infection related to gallstones, biliary instrumentation, or biliary tract malignancy.[130] Rarely, they may form from systemic bacteremia related to conditions like infectious endocarditis. Pyogenic cysts have an annual incidence of 3 to 4 cases per 100,000 patients and tend to occur more commonly in men than women.[131,132] Risk factors for development of

pyogenic cysts include GI malignancy (especially hepatobiliary and pancreatic neoplasms), diabetes mellitus, liver transplant, use of proton pump inhibitors, and nonmalignant underlying hepatobiliary or pancreatic diseases.[132,133] The differential diagnosis for pyogenic cysts is broad and includes acute cholecystitis, cholangitis, hepatitis, and right lower lobe pneumonia, as well as primary or metastatic liver tumors and other types of cysts (simple, amebic, and echinococcal).[134]

Patients with pyogenic abscesses typically present with abdominal pain in 50% to 75% of the cases and fevers in up to 90%.[130,132] Other nonspecific symptoms may include weight loss, nausea and vomiting, and general malaise. There should be a high index of clinical suspicion in patients with those symptoms in the setting of a history of known GI malignancy and/or recent hepatobiliary instrumentation. On physical examination, patients may exhibit right upper quadrant abdominal tenderness to palpation, jaundice, and/or hepatomegaly, although these findings may only be present in approximately one half of the cases; therefore, absence of these findings does not rule out a pyogenic cyst. In addition to patient history and physical examination, laboratory studies including complete blood count, liver function test, and blood cultures should be obtained. Leukocytosis and elevated liver enzymes including transaminases, bilirubin, and alkaline phosphatase are common with pyogenic cysts.[130,132] Pyogenic hepatic cysts are usually polymicrobial and include both aerobes and anaerobes. The most common bacteria identified in these infected cysts are *Escherichia coli* and *Klebsiella pneumoniae*, both of which are found in the colon and are often cultured from the bile.[135] One study implicating GI malignancy as the cause of pyogenic cysts reported *Streptococci* and *Candida* species as the most common pathogens.[131] Another study investigating liver abscesses after hepatobiliary instrumentation, in particular after transarterial chemoembolization, found that gram positive cocci including *Streptococcus pyogenes* and *Staphylococcus aureus* accounted for the majority of the pathogens.[136] Due to the variety of different pathogens associated with pyogenic cysts, it is important to obtain both blood and abscess content gram stain and cultures, with either US or CT guidance, in order to direct antibiotic therapy.

*Radiographic features*

The imaging appearance of pyogenic hepatic cysts varies greatly depending on size, number of lesions, degree of reactive inflammatory changes in the adjacent liver parenchyma, and presence of gas.[101,137] The number and size of the lesions tend to correlate with the etiology: pyogenic liver cysts originating from the biliary tract (ascending cholangitis) are usually multiple small lesions involving both lobes of the liver; those from portal venous origin tend to be larger; and those resulting from trauma or surgery tend to be solitary and larger. On US, pyogenic hepatic cysts are usually round or ovoid, with irregularly hypoechoic or mildly echogenic walls, and display variable internal echogenicity, ranging from completely anechoic to hyperechogenic (Fig 20).[137] Gas within the lesions usually appears as irregular, brightly hyperechogenic foci with “dirty” posterior acoustic shadowing. Increased vascularity may be seen along the periphery of the lesion on color Doppler interrogation.

Likewise, on CECT, simple pyogenic hepatic cysts are usually well-defined oval masses with internal attenuation in the range of 0-45 HU. Clusters of small lesions tend to coalesce, forming a large abscess cavity. Rim or continuous capsular enhancement is usually present and there may be hyperenhancement of the adjacent hepatic parenchyma due hyperemia and surrounding inflammatory changes (Fig 21). On T1-weighted images, pyogenic hepatic cysts are hypointense, whereas they are hyperintense on T2-weighted images. Variable amounts of high T2 signal may be seen in the adjacent liver parenchyma due to perilesional edema and hyperemia. On postcontrast T1-weighted images, they usually display rim or capsular enhancement similarly to CECT. Air–fluid levels may be seen on both CT and MRI (Fig 22). In addition to conventional MRI, DWI has been found to be useful in differentiating hepatic abscesses from malignant lesions. In a study of 74 patients with malignant hepatic tumors, hepatic abscesses revealed rims with high apparent diffusion coefficient values when compared to hepatic tumors ($P< 0.001$). Diagnostic performance of the area under the ROC curve of DWI was excellent among 2 independent observers, with values of 0.986 and 0.982.[138]

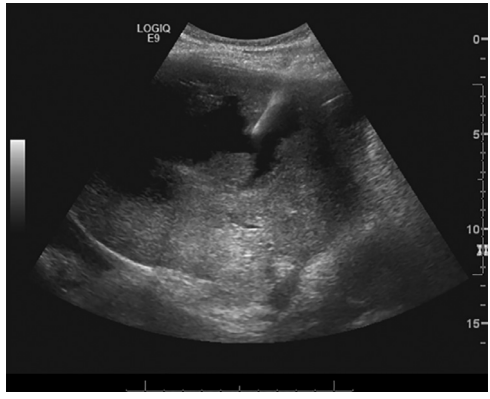


**Fig. 20.** US-guided biopsy of a cystic mass in a 65-year-old man with a history of pancreatic neuroendocrine neoplasm. Longitudinal ultrasound image of this large cystic lesion reveals internal debris and jagged walls. Percutaneous biopsy was consistent with a pyogenic abscess in the setting of ascending cholangitis post-pancreaticoduodenectomy.

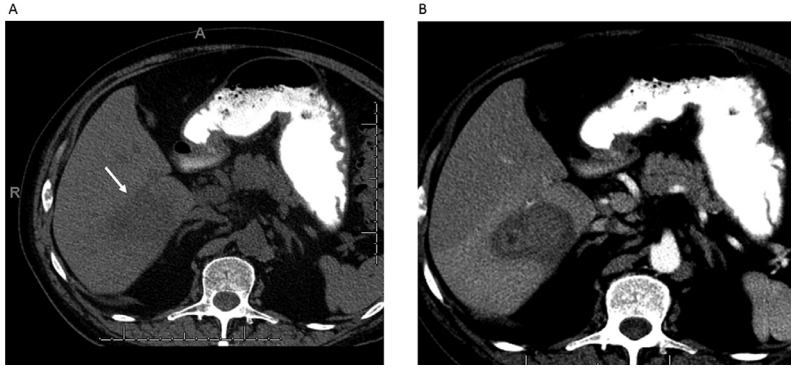


**Fig. 21.** CT evaluation of a pyogenic (due to methicillin-resistant *S. aureus*) abscess in a 45-year-old male leukemia patient. (A) Axial noncontrast CT image shows a vague hypoattenuating area in the right liver (arrow). (B) CECT in the portovenous phase shows a heterogeneously hypoattenuating lesion in the posterior sector of the right liver with hyperemia of the hepatic parenchyma. Hepatic abscesses have a varied imaging appearance depending on many factors including the causative organism, degree of destruction of the underlying hepatic parenchyma, inflammatory immune response of the host, and the age of the abscess among others. The clinical context is crucial to establishing the correct diagnosis.

*Management*

The mainstay of treatment for pyogenic liver cysts is antibiotic therapy and abscess drainage, which has both diagnostic and therapeutic value. Depending upon the size and number of the pyogenic lesion(s), the infection may be drained percutaneously with either US or CT guidance, or surgically. In patients with a solitary abscess that is less than 5 cm in diameter, percutaneous drainage with US or CT guidance with or without drainage catheter placement is recommended.[139] For solitary abscesses larger than 5 cm, percutaneous drainage catheter placement is recommended. A drainage catheter should be left in place until the output is minimal and the patient has improved clinically. A recent meta-analysis noted a significantly higher rate of adequate drainage and resolution of abscess with catheter placement vs aspiration alone for larger abscesses.[140] For multiple or multiloculated pyogenic collections, percutaneous drainage may not be feasible or successful. Although percutaneous drainage may be attempted initially, failure with this technique should prompt surgical drainage, either by laparoscopy or with

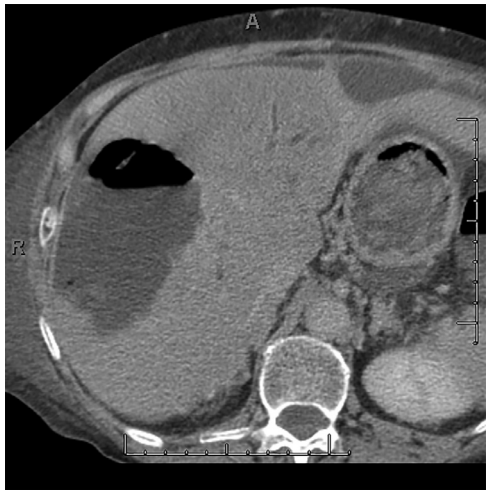


**Fig. 22.** CT evaluation of the pyogenic abscess in the same 65-year-old patient with the history of pancreatic neuroendocrine neoplasm as in Figure 20. On axial CECT imaging, a large cystic lesion with jagged walls and air–fluid level can be appreciated. Both large abscess size and presence of intra-abscess gas are associated with risk for failure of catheter drainage.

traditional open surgery, especially for large abscesses displaying gas formation, both of which are predictors of percutaneous drainage failure.[141]

In addition to drainage, patients with pyogenic liver abscesses should also receive IV antibiotic therapy. The choice of antibiotic may be tailored to culture results; however, in patients who present with sepsis, empiric antibiotics should not be delayed. Because the majority of pyogenic infections stem from GI sources, empiric antibiotic coverage should include streptococcal, gram-negative bacteria, and anaerobic bacteria coverage.[142] Common antibiotic regimens include a third-generation cephalosporin (such as ceftriaxone) or a beta-lactamase inhibitor combination (such as piperacillin-tazobactam) plus metronidazole to provide coverage for *E. histolytica* until amebic abscess is ruled out. In patients with penicillin allergies, a fluoroquinolone like ciprofloxacin or a carbapenem like meropenem plus metronidazole would also be effective. Two to four weeks of IV therapy should precede transition to oral antibiotics for a full course of 4 to 6 weeks of antibiotics, to be determined with clinical judgment based on severity of the infection.[139,142] Once patients are discharged, follow-up imaging to rule out a persistent or new abscess is only recommended in patients with ongoing clinical symptoms despite completion of therapy.

### *Amebic hepatic cyst*

#### *Clinical features*

*E. histolytica* is a parasite that causes amebic infections in humans, with primary intestinal manifestations in the form of amebic dysentery and secondary extraintestinal sequelae, the most common of which is amebic hepatic cysts or abscesses.[143] This amebic infection is transmitted via the fecal-oral route and is more common in men than women. It is rare in the United States, but is endemic in certain developing countries, including those across South and Central America and Africa, Mexico, and India. Liver involvement stems from ascending infection from the intestines to the portal venous system.[144] Once a patient has contracted this amebic infection, clinical manifestations, in particular liver abscesses, may not become apparent until several weeks to months later.

Patients with an amebic hepatic abscess will often present with a few weeks of abdominal pain, fevers, malaise, and weight loss, with less than 10% of patients exhibiting jaundice.[145] Classically, they endorse travel to underdeveloped countries. On examination, right upper quadrant abdominal pain is common. Similar to pyogenic abscesses, amebic abscesses cause leukocytosis without eosinophilia, elevated alkaline phosphatase, and often elevated transaminases. Patient serology should be tested for antibodies to *E. histolytica,* which is positive in more than 90% of infected patients at the time of presentation.[146] Because serology is highly sensitive for infection, routine cyst aspiration for confirmation of diagnosis is not required. However, if obtained, the fluid of an amebic cyst is thick and brown in color, and is classically described as "anchovy paste."[147] If a cystic liver lesion is otherwise indistinguishable from a pyogenic abscess, the fluid may be sent for PCR or antigen testing for *E. histolytica*, but cultures of the abscess are often sterile, as the parasites tend to reside in the outer rim of the abscess.[148] The differential diagnosis for amebic hepatic cyst includes pyogenic cysts as well as echinococcal cysts and hepatic malignancies.

*Radiographic features*

The imaging features of amebic cysts are very similar and essentially indistinguishable from those of pyogenic cysts. The diagnosis relies on clinical findings and serologic markers. Features that may suggest an amebic abscess are presence of extrahepatic disease, such as pleural or pericardial effusions, hydropneumothorax, subcapsular location in the posterior sector, and a ring of edema forming a double-target sign.[101,149] On MRI, the central portion of the lesion is typically cystic, while the periphery displays variable signal intensity on T1 and T2-weighted images.[150]

*Management*

Although they manifest clinically in a similar fashion, amebic abscesses, unlike pyogenic abscesses, are treated with medical management rather than invasive interventions. Once a diagnosis of amebic abscess has been established on the basis of clinical suspicion or serologic confirmation, treatment with metronidazole 500 to 750 mg by mouth 3 times per day for 7 to 10 days should be initiated. This should be followed by 10 additional days of paromomycin 25 to 30 mg/kg divided into 3 doses per day in order to eradicate intraluminal parasitic cysts to prevent reinfection.[151] This regimen by itself yields a cure rate of greater than 90%. Aspiration of the cyst for definitive management is only recommended if the patient does not respond to antimicrobial therapy.[152] The prognosis for patients with amebic hepatic cysts is excellent with prompt initiation of therapy. Although rare, amebic cyst rupture has been described, and surgical drainage and irrigation is only advised in this situation.[152]

*Echinococcal hepatic cyst*

*Clinical features*

Two echinococcal tapeworm species, *Echinococcus granulosa* and *Echinococcus multilocularis*, are known to cause human infections with clinically significant sequelae. Cystic echinococcosis manifests most commonly from *E. granulosa*, although infestation with *E. multilocularis* tends to be more aggressive.[153] Epidemiologically, this type of infection is uncommon in the United States, occurring instead most often in South America, sub-Saharan Africa, China, and in Mediterranean and Middle East areas where sheep – the intermediate hosts – are raised. The definitive animal host, usually a dog or a fox, can carry adult tapeworms in its intestines and shed the eggs, which then infect humans, the accidental hosts, through oral ingestion.[154] Once the eggs are ingested by humans, oncospheres hatch from the eggs and enter the portal venous system via intestinal mucosal penetration. After the oncospheres migrate to the liver, fluid-filled echinococcal (also called hydatid) cysts form after a few days.[155] Pathologically, echinococcal cysts contain an internal endocyst layer containing germinal epithelium surrounded by a parasite-derived exocyst layer surrounded by a host-derived pericyst layer. The cysts grow inter-

nally within the cavity of the cyst, and fragmentation of the innermost layer of the cyst leads to daughter cysts.[154] Over time, echinococcal cysts may also exhibit calcification within their walls.

Clinically, initial infection with *E. granulosa* is asymptomatic, and may not cause symptoms for months to years. Echinococcal cysts that are small or calcified may never cause symptoms in the patient. Because of the way cysts spread in the circulation, they can affect many organs, including the liver, brain, lungs, heart, kidneys, and bones, although the liver is the most commonly affected site, accounting for nearly two thirds of all cases.[156] Hydatid cysts preferentially affect the right lobe of the liver in up to 65% to 85% of cases, and most patients will not have symptoms until cysts have grown to at least 10 cm.[155] Once enlarged, ECs may cause compression or secondary mass effect on other organs, which may cause abdominal pain, early satiety, and nausea and vomiting. Additionally, these cysts can erode into or obstruct lymphatic or venous outflow or the biliary tree, which can cause secondary infection, cyst rupture, or cholangitis, which in turn may lead to fevers and life-threatening anaphylactic reactions.[155,156]

As is the case with other types of hepatic cysts, a full patient history should inquire about travel to or residence in a higher-risk endemic area and/or contact with herds of sheep or dogs that may have ingested sheep remains. Physical examination may reveal right upper quadrant pain or hepatomegaly, although these findings are nonspecific. Additionally, complete blood count, serum chemistries, and liver function tests should be obtained. Patients with echinococcal cysts often exhibit leukocytosis with mild eosinophilia, thrombocytosis, as well as nonspecific elevations in hepatic transaminases.[157] Importantly, when echinococcal infection is suspected, serologic studies, specifically antibodies to echinococcal species, should be tested to confirm the diagnosis.[158] Serology is useful both for initial diagnosis and follow-up.[157] Finally, transabdominal US and axial imaging with CT and MRI may also assist with the diagnosis. Biopsy and/or aspiration of the cysts should be avoided unless diagnosis cannot be achieved by other means, as this increases the risk of free rupture of the cyst and anaphylactic shock.[159,160]

*Radiographic features*

The characteristic imaging appearance of echinococcal cysts is a dominant cyst containing multiple daughter cysts, predominantly along its periphery. There are 4 different types of echinococcal cysts depending on their radiologic appearance: type I – a unilocular simple cyst; type II – a cyst with multiple peripheral daughter cysts, floating membranes, or vesicles; type III – a calcified cyst; and type IV – a complicated cyst (e.g., a ruptured cyst with superinfection).[101,161] The imaging appearance reflects the internal composition and stage of development of each cyst. US findings include simple anechoic cysts, multiseptated cysts with daughter cysts, cysts with floating undulating membrane ("Water Lily sign"), and hyperechogenic cysts with posterior acoustic shadowing (calcified cyst). Likewise, CECT and MRI findings range from simple nonenhancing cysts and cysts with multiple daughter cysts to infiltrative cystic and solid masses of low attenuation, with enhancement of cyst wall and septa (Fig 23). Rupture of the cyst can occur into the biliary tree, peritoneal or pleural cavities with spread of disease to lungs, heart, brain, bone, and bacterial superinfection.[153,161]

*Management*

For most echinococcal cysts, a combination of antihelminthic drug therapy and surgery is the mainstay of treatment. The most common antiparasitic agents used in echinococcal infection are albendazole or the less well-absorbed mebendazole.[162] Either drug should be started at least 4 days prior to surgery, as they help to both inactivate the live parasites to prevent secondary infection and soften the cyst walls for surgical resection.[163] Albendazole should be continued for at least 1 month following surgery, whereas mebendazole should be continued for at least 3 months following surgery.[164] For patients who are not surgical candidates, antihelminthic therapy may be considered as a definitive treatment.

Surgical resection of echinococcal cysts is the central step in the treatment of complicated cysts, including those that have eroded into the biliary tree, caused symptoms through mass effect on other organs, or ruptured, leading to hemorrhage or secondary parasitic infection. Other surgical indications include large cysts measuring greater than 10 cm in diameter, extrahepatic

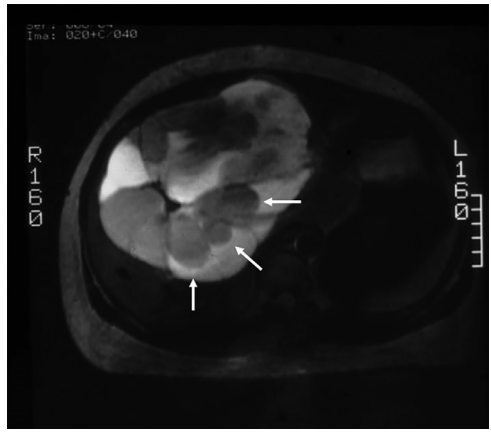


**Fig. 23.** MRI evaluation of an echinococcal cyst in a 56-year-old man. Axial T1-weighted MRI shows a large multiloculated cystic lesion containing T1-hyperintense areas, indicative of hemorrhage or high proteinaceous content. Multiple T1-hypointense daughter cysts are seen within the large multivesicular cyst (arrows). Despite its large size, there is no definitive evidence of biliary communication, transdiaphragmatic migration, exophytic growth outside the liver or direct invasion into the thoracoabdominal wall.

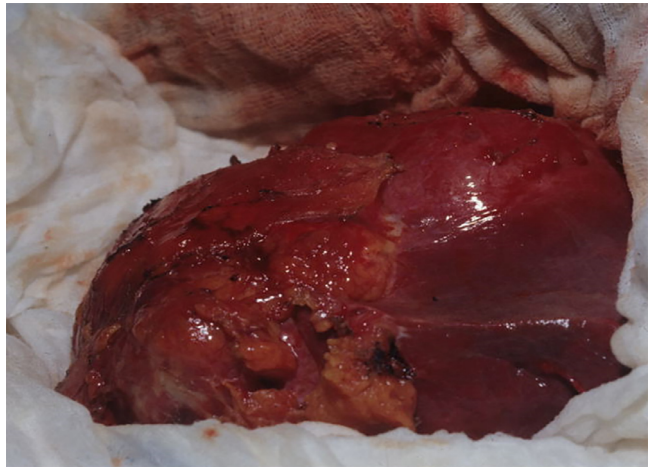

**Fig. 24.** Intraoperative appearance of large echinoccal cyst in the liver of the patient from Fig 23. The cyst size approaches 20 cm and indicates the need for surgical resection due to concern for impending rupture. Care has been taken to cover the surgical field with laparotomy pads to insulate the liver in the event of cyst spillage.

involvement, and cysts at high risk of impending rupture (Fig 24).[165,166] The objective in surgery is to not only remove the cyst(s), but also to obliterate the cyst cavity within the liver while avoiding spillage of cyst contents into the abdomen.[166] Often, before the cyst is resected, it is aspirated or unroofed and injected with a sterilizing agent, most commonly hypertonic saline or ethanol, to decrease the risk of spillage of live parasites (Fig 25).[166] The traditional surgical approach is described as open pericystectomy, whereby the cyst and a small rim of surrounding hepatic parenchyma are resected (Fig 26). However, this may also be accomplished laparoscopically.[165,167] Complications from surgery may occur and include spillage of cyst contents causing anaphylaxis or secondary infection, biliary fistula, cholangitis, intraabdominal abscess, and/or recurrent echinococcal infection.[168]

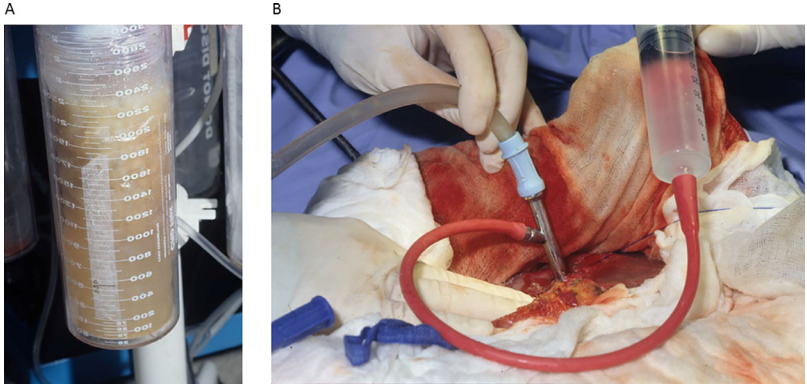


**Fig. 25.** Aspiration of echinococcal cyst content and injection with hypertonic saline. Prior to resection of the cyst, its contents are aspirated (A) and the cavity is infused with hypertonic saline to sterilize the cyst lining and minimize the risk of spillage of live parasites (B).

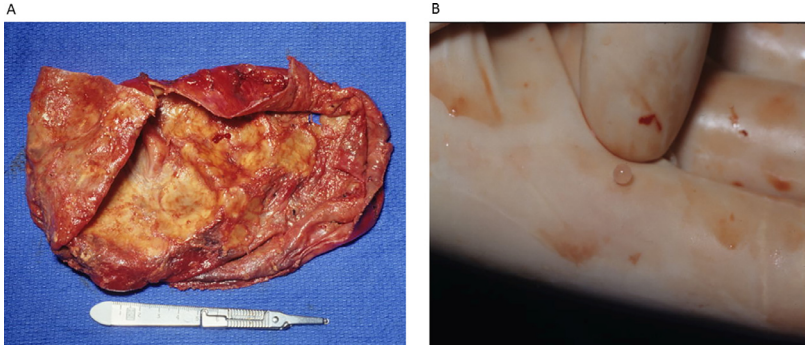


**Fig. 26.** Echinococcal cyst appearance following excision. The echinococcal cyst has been entirely resected. On the back table, the cyst is opened for evaluation (A). Daughter cysts are often found within the parent cyst (B).

Although surgery has historically been the cornerstone of echinococcal cyst treatment, non-surgical options offer effective alternatives, especially for patients who cannot tolerate open or laparoscopic resection and those with simple cysts.[159,160] The percutaneous aspiration-injection-reaspiration procedure has been shown to be effective in treating echinococcal cysts in more than 90% of well-selected patients.[169] The procedure is performed with imaging guidance, usually with US or CT. The cyst is penetrated with a needle and the cyst fluid is aspirated. Following initial aspiration, a sterilizing agent is injected into the cyst space followed by repeat aspiration. The injection and reaspiration steps should be repeated as long as live parasites are present on immediate histopathology.[169] The percutaneous aspiration-injection-reaspiration procedure should not be pursued in patients with superficial cysts with increased risk of rupture into the abdomen, calcified cysts that would be impenetrable with a needle and catheter, cysts with direct biliary erosion, and cysts with nonliquid foci that cannot to be aspirated.[168]

After treatment, because there is a risk of recurrence, patients should be followed clinically in 3- to 6-month intervals with US, CT, or MRI to ensure disease stability. This surveillance should be continued for a period of 5 years to rule out recurrence.

*Biliary cystadenoma*

*Clinical features*

Biliary cystadenomas, or noninvasive cystic neoplasms, are uncommon benign, usually multiloculated cystic lesions of the liver that originate from biliary epithelium but involve hepatic parenchyma, usually without direct connection to the biliary system.[170,171] The vast majority of these lesions are of the mucinous type, with only approximately 5% of these lesions being of the serous type. Pathologically, a thickened fibrous capsule surrounds the entire cystic lesion, which contains internal septations. The cystic compartments are lined with columnar or cuboidal epithelium that usually secretes mucus. Often, a denser mesenchymal stroma will surround the cystic lesion, which is also surrounded by a layer of collagen tissues containing bile ducts, nerves, and vessels.[172,173] Classically, biliary cystadenomas are characterized by the presence of ovarian-type stroma with estrogen and progesterone receptor expression (although absence of this finding does not preclude the diagnosis), which may explain its greater prevalence in women, especially those in their third to fifth decades.[171] The lesions themselves typically grow to a range of 1.5 cm-15 cm, although some become as large as 30 cm in diameter.[170] Smaller lesions tend to be asymptomatic and may be detected incidentally on routine abdominal imaging for another reason. Lesions that are larger in diameter often cause nonspecific abdominal pain with occasional nausea and vomiting. Rarely, large lesions may cause compression of the biliary tree leading to obstructive jaundice or compression of the portal venous system causing portal hypertension and splenomegaly.[174] The differential diagnosis for hepatic cystadenoma includes other hepatic cystic lesions as discussed above, hepatic adenoma, hepatic hamartoma, as well as the malignant version of this process, hepatic cystadenocarcinoma.

Besides a clinical history and physical examination, routine laboratory studies including complete blood count, chemistry, liver function panel, and tumor markers such as CA 19-9, CEA, and AFP should be obtained. Nonspecific right upper quadrant abdominal tenderness or fullness may be present on examination. Routine laboratory studies may be normal, but cystadenomas may cause mild elevation of bilirubin and alkaline phosphatase. AFP and CEA levels are usually within normal limits, while CA 19-9 may be mildly elevated.[173] Imaging with US, CT, and/or MRI is essential for diagnosis. Fine needle aspiration biopsy is warranted to establish a definitive diagnosis and distinguish cystadenoma from cystadenocarcinoma based on grade severity and presence of invasive carcinoma, as the treatment and prognosis differ significantly.[175] On macroscopic evaluation, noninvasive cystadenomas usually have a smooth surface, typically with a thinner wall, whereas invasive cystadenocarcinomas have a thicker wall, potentially with carcinomatous masses protruding from the wall of the lining of the cyst.[176] Additionally, fluid from malignant lesions has been shown to have an elevated CEA level, although this may not be present in all cases.[177]

*Radiographic features*

The typical imaging features of biliary cystadenomas vary according to the size of the primary lesion and their internal composition, and to the presence or absence of calcification and/or internal hemorrhage. US findings will demonstrate a unilocular or multilocular cyst with posterior acoustic enhancement, low-level echoes and/or debris due to internal hemorrhage, mucin, or proteinaceous material. Mural nodularity and papillary projections may be present.[178] CT and MRI findings mirror those on US. The density of the fluid reflects its contents, ranging from simple fluid attenuation, usually due to serous or bilious fluid, to high attenuation in the presence of internal blood products or proteinaceous content (Fig 27). CT is extremely sensitive to calcifications and may better depict septal or cyst wall calcifications compared to US, while the latter may detect thin noncalcified septa that can elude detection on CECT. Tumor nodules and papillary projections typically enhance on CECT and MRI (Fig 28), and magnetic resonance cholangiography can be helpful in demonstrating biliary dilation, obstruction, and communication with the biliary tree.[178] Still, it must be emphasized that there are no consistent imaging findings that can reliably differentiate biliary cystadenoma from cystadenocarcinoma.[175]

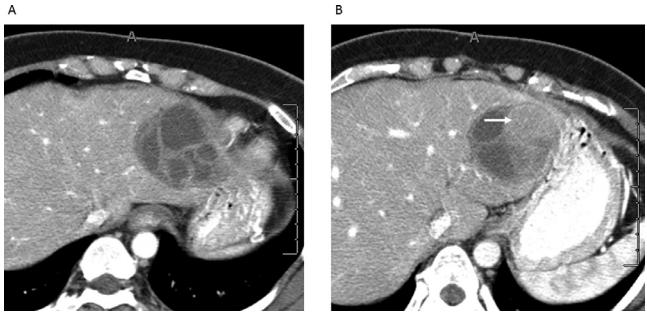


**Fig. 27.** CT evaluation of a biliary cystadenoma in a 62-year-old woman with a history of melanoma. (A) CECT images in the portovenous phase show a cystic lesion in the lateral sector of the left liver. Multiple internal septations are evident. (B) The hyperattenuating density (arrow) within the lesion is consistent with intralesional hemorrhage. There is no significant attenuation difference from the precontrast scan (not shown). Histopathologic evaluation confirmed biliary cystadenoma.

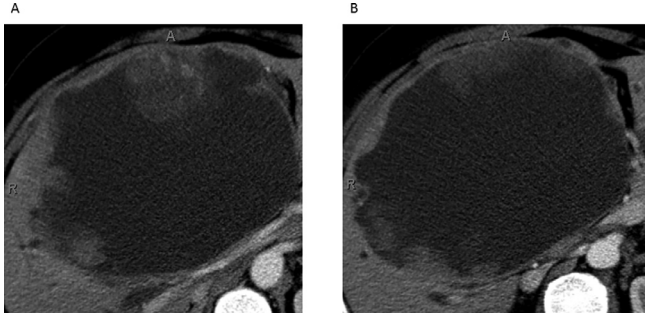


**Fig. 28.** CT evaluation of a biliary cystadenocarcinoma in a 58-year-old man. On axial CECT images, a large cystic lesion in the liver can be seen. Multiple mildly enhancing masses and nodules are noted along the periphery of the cystic mass. In order to accurately determinate the presence of internal enhancement, a precontrast scan is required as internal hemorrhage or high proteinaceous material may appear hyperattenuating on CT and masquerade as enhancing solid tissue. In this case, these nodules were real, and following resection, a diagnosis of cystadenocarcinoma was reached. Although presence of enhancing mural nodules supports a diagnosis of malignancy, their absence does not rule out invasive disease.

*Management*

Although they are considered benign, cystadenomas do bear malignant potential, with risk of malignant transformation estimated at 10% to 20%, and have high rates of recurrence.[172,179] Therefore, definitive management of these lesions consists of surgical resection. Attempts at non-operative management, including aspiration, fenestration, and sclerosis are inappropriate, with high rates of failure and recurrence. For smaller tumors, enucleation of the lesion without additional hepatic parenchyma is acceptable and feasible due to the nature of the thick fibrous capsule, making dissection of the lesion without major blood loss or bile leakage possible. However, larger lesions, and especially those that are preoperatively indistinguishable from malignancy, may require formal hepatectomy. Although resection of these lesions has traditionally been accomplished via open surgery, the laparoscopic approach has been shown to be safe and feasible in well-selected patients.[172,179] Because cystadenomas tend to recur and have malignant potential, patients should be followed clinically with routine CT or MRI. Follow-up intervals start at every 6 months during the first year after resection, and then yearly thereafter.[180]

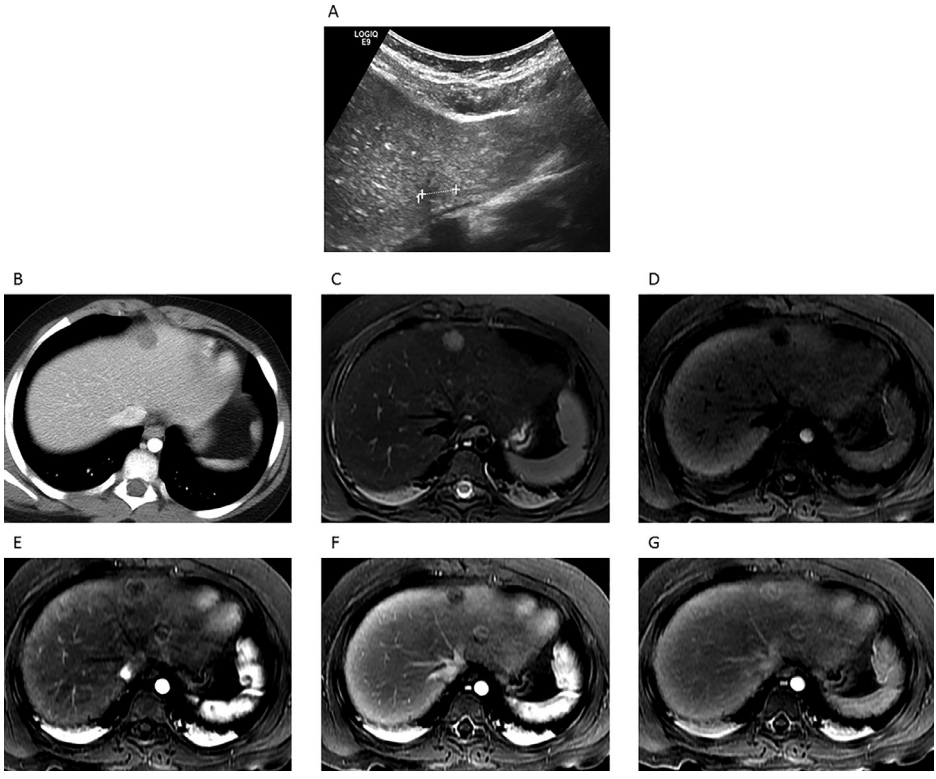


**Fig. 29.** Evaluation of a mesenchymal hamartoma in a 7-year-old child. (A) Longitudinal US image shows a small lesion with heterogenous echotexture in the left liver. (B) CECT shows a 2.5-cm hypodense mass in segment IV, corresponding to the lesion seen on US. On MRI, the lesion is gently lobulated and hyperintense on T2 (C), hypointense on T1 (D), and shows heterogenous enhancement in the multiphasic postcontrast MR images (E-G). The imaging features were nonspecific and the lesion was resected. Pathology was consistent with a mesenchymal hamartoma.

### *Hepatic mesenchymal hamartoma*

#### *Clinical features*

Mesenchymal hamartomas of the liver are uncommon cystic tumors usually found during childhood, although diagnosis in adulthood may occur. Serum AFP and liver functions tests are typically within normal limits. Pathologically, they are made up of normal hepatocytes, bile ducts, and immature mesenchymal cells.[181] Macroscopically, they are well-circumscribed and are composed of a myxoid mass with many fluid-containing cysts. Mesenchymal hamartomas exhibit myxoid stroma with abnormal bile duct architecture.[182] They are most often solitary, but may be multiple, have both cystic and solid components, and typically do not have a formed capsule. The majority of lesions are right-sided, and some may be pedunculated.

#### *Radiographic features*

Mesenchymal hamartomas in children have varied radiologic appearances, with most cases described as a large multiloculated mass with multiple septa and cystic spaces. They are usually solitary lesions.[183,184] In a study of 13 patients with pathologically proven mesenchymal hamartomas, all had a single tumor with a mean diameter of 13 cm. On CT and/or US, 4 patients (31%) had a multiseptated cystic mass, 5 (38%) had a mixed solid and cystic tumor, and the remaining 4 (31%) had a solid tumor.[184] Fluid–fluid levels and echogenic debris may be seen with the cystic spaces on grayscale US and flow may be detected on Doppler interrogation within the septations

and solid components. On CECT and MRI, heterogeneous enhancement can be seen within the septa and solid components of the lesion (Fig 29).[184]

*Management*

Mesenchymal hamartomas can resemble other cystic liver masses, including metastatic tumors, and biopsy may be considered. Current management standards call for surgical resection of these tumors when possible, or marsupialization for unresectable lesions, although some have reported spontaneous resolution with conservative management.[185,186]

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