Hepatic Scintigraphy in the Evaluation of Solitary Solid Liver Masses

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CASE PRESENTATION

A 37-yr-old female was referred for evaluation of an asymptomatic mass in the left lobe of her liver. Although she denied jaundice, pruritis, right upper quadrant pain or constitutional symptoms, a gradually rising and elevated alkaline phosphatase level had been noted over the previous 48 mo.

Her medical history was significant for a stable "cold" thyroid nodule. She had received no blood transfusions. She underwent cholecystectomy for symptomatic cholelithiasis 5 yr prior to this referral. Common bile duct exploration was not performed during surgery. There was no mention of a liver mass at the time of this surgery. She had taken oral contraceptives for the preceding 6 yr. She neither drank alcohol nor used intravenous drugs. There was no family history of liver disease.

Physical examination revealed an obese white female without stigmata of chronic liver disease. By percussion, the liver span was 10 cm in the mid-clavicular line. No hepatic or abdominal masses, splenomegaly, or ascites were noted. Laboratory values, including viral hepatitis serologies and α-1-fetoprotein, were normal except for a serum alkaline phosphatase of 397 U/liter (nl 35–125 U/liter) and a g-glutamyl transpeptidase of 65 U/liter (nl 0–40 U/liter).

Ultrasound of the right upper quadrant (Fig. 1) demonstrated an 8-cm hypoechoic mass in the left lobe of the liver without ductal dilatation. Magnetic resonance imaging demonstrated a mass with a heterogenous signal intensity on the T2-weighted images (Fig. 2). A CT portogram showed a low intensity lesion without a central scar (Fig. 3). These findings were felt to be most consistent with hepatocellular carcinoma, although metastatic disease, focal nodular hyperplasia or a hepatic adenoma could not be entirely excluded.

A liver spleen scan, following the administration of 5.1 mCi of ^{99m}Tc-sulfur colloid, showed a large mass in the lateral aspect of the left lobe of the liver with increased activity when compared to the normal right lobe (Fig. 4). Within the mass was a central area of decreased activity. A SPECT scan of the liver following intravenous administration of 5 mCi ^{99m}Tc confirmed a focal area of increased activity in the anterior aspect of the lateral segment of the left lobe (Fig. 5). These findings were felt to exclude malignancy and to suggest focal nodular hyperplasia or, less likely, hepatic adenoma. Limited angiography was performed because of an allergic dye reaction, but this demonstrated branches of the left hepatic artery draped over a hypervascular mass in the left lobe of the liver.

At laparotomy, a soft brown 8 × 6 × 5 cm mass was found in the left lateral lobe of the liver. Multiple vessels covered the anterior and posterior surfaces of the lesion. A left hepatic lobectomy with extended segmentectomy was performed. Intraoperative ultrasound failed to reveal a mass lesion in the right lobe of the liver. Pathological examination of the left lobe lesion revealed hepatic adenoma.

DISCUSSION

Imaging of Intrahepatic Mass Lesions

This case illustrates the importance of utilizing radiologic techniques to characterize liver masses. These lesions come to attention when they are discovered by the patient, palpated by the physician or screened because of constitutional complaints or abnormal liver function tests. Occasionally, they are incidentally noted on imaging techniques obtained to evaluate unrelated complaints.

A careful history may provide clues as to the most likely etiology for an intrahepatic mass lesion. For example, if the patient is an otherwise healthy young woman taking oral contraceptives, hepatic adenoma and, less likely, focal nodular hyperplasia (FNH) merit strong consideration. On the other hand, if a patient with cirrhosis presents with constitutional symptoms, a rising α-fetoprotein and a palpable abdominal mass, hepatocellular

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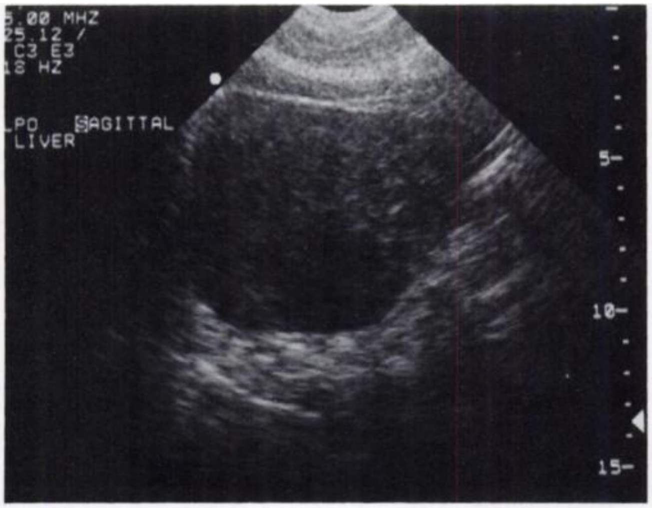

FIGURE 1. A T2 MR image of the liver in the coronal plane shows a low intensity lesion in the left lobe of the liver without a central scar.

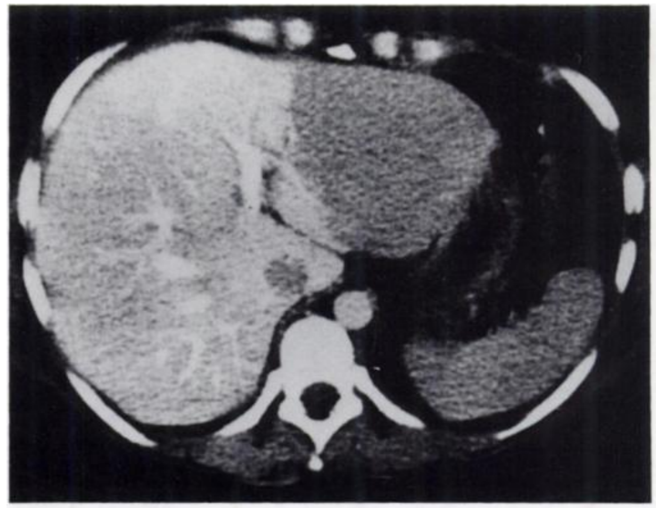

FIGURE 3. Technetium-99m-sulfur colloid scan demonstrates an area of increased activity with a central photopenic area in the lateral aspect of the left lobe of the liver.

carcinoma (HCC), and less likely metastatic disease, need to be considered. Alternatively, hepatic abscess is suggested if a patient has right upper quadrant pain, chills, fever and leukocytosis.

While currently available imaging techniques are quite sensitive for identifying the presence of mass lesions in the liver, they generally fail to show specific patterns for various underlying pathologies. Given the complementary information provided by these different imaging modalities, several studies may be required to establish a diagnosis.

Once a liver mass has been detected, further work-up should proceed with safe and efficient studies which will lead to a specific diagnosis. With this in mind, the purpose of this review article is threefold:

1. To review the utility of different imaging techniques, with emphasis on radionuclide scanning.
2. To characterize the radiologic findings of liver masses, focusing on radionuclide imaging.
3. To suggest a rational approach to the radiologic evaluation of noncystic liver masses in particular clinical settings.

Radionuclide Scanning

Unlike most other imaging techniques, radionuclide scanning takes advantage of the liver's physiologic function. The conventional liver scan is performed following the administration of ^{99m}Tc-labeled sulfur colloid. The particles in this preparation are phagocytized by reticuloendothelial (RE) cells of the liver, allowing visualization of areas with various degrees of RE activity. The liver scan has been useful in the characterization of FNH, focal fatty infiltration of the liver (FFIL), and cavernous hemangioma (CH). It has been less helpful in the diagnosis of hepatic adenoma, HCC, and macroregenerating nodules.

Hepatobiliary imaging is performed utilizing radiophar-

FIGURE 2. CT portagram shows a low intensity left lobe of the liver lesion without a central scar.

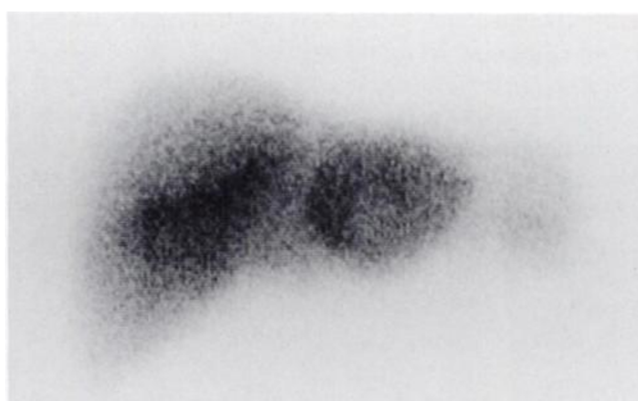

FIGURE 4. Technetium-99m-sulfur colloid coronal SPECT scan shows a focal area of increased activity in the anterior aspect of the lateral segment of the left lobe of the liver.

FIGURE 5. SPECT scan confirms a focal area of increased activity in the anterior aspect of the lateral segment of the left lobe of the liver.

maceuticals which are cleared by the hepatocytes and secreted into the biliary system. This type of imaging will not be discussed in this article.

Since its introduction in 1964, ^{99m}Tc-sulfur colloid has become the most widely used radionuclide for liver scanning. Technetium-99m has a relatively short physical half-life and the radiation dose delivered to the liver and other organs is within an acceptable range.

Usually, planar images are obtained using a gamma camera equipped with a high-resolution collimator for initial evaluation of suspected mass lesions. "Uptake" is due to the presence of normal RE cells, as well as to a normal vascular supply. Photopenic "defects" can be seen with focal masses and in diffuse liver diseases such as cirrhosis.

False-positive radionuclide planar scans may be caused by extrahepatic tumors, the right kidney, inferior vena cava, porta hepatis, gallbladder and by anatomic variations in the size, shape and position of the liver (*1*). Cirrhosis, diffuse fatty infiltration of the liver, biliary obstruction and passive congestion of the liver due to heart failure may be mistaken for multiple space occupying intrahepatic lesions (*2*).

As with any large organ, resolution of intrahepatic lesions decreases gradually as a function of the distance from the surface to the center of the liver. Therefore, relatively superficial lesions can be detected with a higher sensitivity than those lesions found deep within the liver. In general, superficial lesions smaller than 2 cm and deep lesions (especially those within the right lobe) of even 3 to 4 cm are poorly detected.

Red blood cells tagged with ^{99m}Tc can be used to evaluate liver masses. Not only does this labeling assess the vascularity of a lesion, but it also provides important diagnostic information regarding the pattern and timing of filling of the vasculature.

In patients with defects already seen on sulfur colloid studies, radionuclide scanning with ^{67}Ga may add more specificity in certain clinical situations, especially with HCCs and liver abscesses.

The sensitivity of radionuclide imaging with ^{99m}Tc-labeled pharmaceuticals may be increased by the use of single-photon emission computerized tomography (SPECT). The specificity of SPECT, however, is limited by its difficulty in differentiating small lesions from normal vessels and the biliary tree and by variations in normal contour.

Hepatic arterial perfusion scintigraphy (HAPS) is performed following the administration of ^{99m}Tc-macroaggregated albumin into a hepatic artery catheter at a slow delivery rate. Images are obtained using either planar scintigraphy or SPECT (*3*). This is especially useful for lesions such as HCCs which, unlike normal liver, derive their blood supply primarily from the hepatic artery.

In many centers, radionuclide scanning has been displaced by newer, more expensive technologies, despite the fact that scintigraphy remains useful in several specific clinical situations.

Other Imaging Techniques

Ultrasound (US) produces images by transmitting a sound pulse through tissues and then detecting the amplitude and depth of the reflected sound. The reflection of sound waves is dependent on the interfaces between tissues with different acoustical properties. The degree of echogenicity depends on the amount of reflected versus absorbed ultrasound waves. Echogenicity is always compared with the normal surrounding parenchyma. Cystic changes are easily detected with ultrasound.

Sonography is the simplest radiologic test for evaluating liver lesions. Other advantages include its relative low cost, versatility and availability. Similar to computerized axial tomography (CT), it can easily be used to guide percutaneous aspiration or biopsy. Disadvantages of US include operator dependence for optimal results and interference from adipose tissues and overlying bowel gas.

The data obtained by CT are derived from differences in tissue densities and the related attenuation of transmitted x-rays. Intravenous iodinated contrast is used to determine the vascularity of lesions compared to that of normal liver.

Successful CT of the liver can be obtained in spite of significant obesity, overlying bowel gas or ascites. It provides considerable information about extrahepatic anatomy, which may offer additional clues to the etiology of a hepatic lesion. CT is slightly less sensitive than US at detecting small (1 to 2 cm) liver lesions. Other disadvantages of CT include its cost and the risks of intravenous contrast and radiation exposure. Additionally, lesions may be obscured by an artifact caused by surgical clips and by "volume averaging" with normal tissues.

Dynamic incremental bolus CT maximizes differences in the appearance of the vascular supply of hepatic lesions versus normal liver. The liver is rapidly scanned at 10-mm intervals shortly after intravenous iodinated contrast is injected (*4*). The contrast in the vascular system and liver parenchyma equilibrates about 2 min after the bolus is completed. If the liver is scanned after this time, the contrast difference between tumor and normal tissue will no longer be apparent.

In addition to dynamic CT, the liver parenchyma may be densely enhanced by using CT portography. This obligates the additional risk and expense of a percutaneously placed vascular catheter so that contrast can be injected while scanning.

The use of angiography is based on the fact that certain hepatic masses are supplied primarily by the hepatic artery. It is invasive and expensive. With the introduction and refinement of other imaging techniques, angiography is being used less frequently for diagnosis of hepatic masses. Instead, its role has shifted more to preoperative evaluation to assess vascular invasion and anatomical anomalies.

Magnetic resonance imaging (MRI) demonstrates abnormal signal intensity of hepatic masses compared to normal parenchyma. The degree of signal intensity is dependent on the water and fat contents in tissues, as well as to the presence of certain substances, such as hemosiderin. The T1 relaxation time is the time required for protons to realign themselves with an external magnetic field after a radio wave pulse. The T2 relaxation time describes the rate at which protons get out of phase owing to the effects of adjacent protons. Both T1 and T2 images are obtained to demonstrate various lesions in the liver. Gadolinium-DTPA can be used as a contrast agent to obtain further information about the vascular supply of a lesion.

The advantages of MRI include excellent contrast resolution, multiplanar imaging, reproducibility and safety. The size of the lesions that can be resolved parallel those of CT. With MRI, however, motion artifact may preclude optimal assessment of the details of various hepatic lesions. Other disadvantages of MRI include cost, availability and the claustrophobia experienced by some patients.

RADIOLOGIC APPEARANCE OF LIVER MASSES

Neoplasms

Adenoma. Hepatocellular adenomas are benign tumors of the liver which occur almost exclusively in women of childbearing age. Their occurrence has been associated with the use of oral contraceptives (*5*). Adenomas are typically located in the right lobe and are usually well circumscribed by at least a partial capsule (*6,7*). Morbidity is attributed to bleeding, infarction, necrosis and rupture (*5,6*). Progression to malignancy has rarely been described (*8*).

Adenomas usually appear as photopenic defects on sulfur colloid radionuclide scans, making it difficult to differentiate them from HCC, metastases or hemangioma by this technique (*5*). However, as this case demonstrates, the accumulation of activity by a lesion on a sulfur colloid scan does not exclude a hepatic adenoma (*6*).

The typical photopenic appearance of adenomas has been attributed to their supposed lack of reticuloendothelial cells. However, Kupffer cells have been documented in pathologically proven adenomas (*6,9*). Altered blood flow (secondary to infarction and hemorrhage and lack of portal tracts) or decreased phagocytic activity of Kupffer cells within the lesion may explain why an adenoma usually accumulates less colloid than normal liver (*6*).

The US appearance of adenomas may show a mixed pattern of hyper- and hypoechogenicity, depending on whether there is intralesional hemorrhage. On CT, adenomas are hypodense initially, with a wide range of densities seen after contrast infusion (*10*). Angiographically, adenomas appear hypervascular, often with small hypovascular areas, representing hemorrhage or necrosis (*5,7*). Typically, there is no arteriovenous shunting or vascular invasion seen with adenomas. The signal characteristics of adenomas are similar to those of HCC on MR scans (*10*).

FNH. This is another typically solitary lesion found primarily in women. This tumor's association with oral contraceptives, however, is controversial (*5*). While patients with adenomas may have complications of bleeding, the majority with FNH come to medical attention incidentally (*11*). Pathologically, FNH often has a thin capsule and a fibrous central scar with peripherally radiating septae. Negative defects on radionuclide scanning may be seen in up to 30% of cases (*7,11*), however, normal or increased uptake by a hepatic mass suggests FNH (*11*). Intense concentration of colloid, seen in 10% of cases, is specific for FNH (*12*).

Radionuclide imaging appears to be more specific for the diagnosis of FNH than US, CT or angiography (*7*). On ultrasound, a majority appear either isoechoic (visible by a change in normal hepatic contour) or hypoechoic, but they may also be hyperechoic (*11*). Eighty-five percent of FNH lesions are detected with unenhanced CT, while the density of contrast enhancement compared to surrounding normal liver is variable (*7*). On dynamic CT, FNH may be slightly hypodense, showing a transient hyperdensity after bolus infusion (*7*). A central scar visualized on CT, while characteristic of FNH, is uncommon (*7*).

A "classic" angiographic appearance of a hypervascular, septated lesion with a central vascular supply is seen in 36%–78% of cases of FNH (*11*). In fact, the angiographic features in some cases of FNH may incorrectly suggest a diagnosis of hepatoma (*11*). Centrally hypovascular FNH lesions with peripheral vascular blood supplies have been reported (*7,11*).

In MRI, FNH is suggested by a homogenous lesion which is isointense on T1- and T2-weighted sequences with a hyperintense central scar. This constellation of findings is, however, only present in fewer than 10% of cases (*13*).

HCC. This is the most frequent cancer worldwide. It occurs two to four times more commonly in males than in females. Current evidence strongly links the hepatitis B (*13,14*) and C (*15*) viruses as etiologic agents. HCC usually presents at an advanced stage with a poor prognosis. Early detection, when lesions are small (<5 cm) and amenable to surgical cure, is therefore important (*16*). HCCs may be solitary, multifocal or diffuse. Unfortunately, the common, but not necessary, association of this tumor with cirrhosis hinders its radiologic diagnosis.

As was previously stated, the sensitivity of sulfur colloid scanning for detecting lesions smaller than 2 cm in diameter is limited. Moreover, a focal defect in a patient with cirrhosis is not specific for HCC. Radionuclide imaging with gallium, however, confers increased specificity in patients clinically suspected of having HCC. Most HCCs have gallium uptake equal to or greater than that of the adjacent liver in areas corresponding to photopenic defects on sulfur colloid scans (*17*). Lymphoma, metastases and hepatic abscesses, however, may also demonstrate this pattern. Additionally, in 10%–20% of cirrhotics, both the sulfur colloid and gallium scans demonstrate defects, which incorrectly argues against a diagnosis of HCC (*18*).

While inferior to ultrasound in detecting HCCs smaller than 2 cm in size, SPECT's sensitivity is identical to US's for detecting larger tumors. SPECT and US appear to complement each other, each identifying lesions not detected by the other technique (*18*). Some authors consider increased blood-pool activity on a delayed SPECT scan of a ^{99m}Tc-RBC study to be pathognomic of hemangioma, however, small HCCs have demonstrated this pattern (*3*).

Even though the various radiologic modalities are sensitive in detecting lesions which are eventually determined to be HCCs, there are no pathognomic features of HCC on radiologic imaging. US is the most sensitive modality for detecting small tumors; its use is therefore advocated in screening patients at increased risk for HCC (*19*). The demonstration of HCCs by US, however, may be limited by fibrosis of the liver in and around the tumor (*17*). The echogenicity of HCCs may be increased, mixed or even anechoic.

HCC has a variable appearance on CT, often manifesting as an isodense mass surrounded by a low density, contrast enhancing ring (*20*). Angiographically, HCC may demonstrate a tumor blush and early filling of the hepatic veins. Arteriovenous anastamoses may result in retrograde filling of portal vein branches.

Vascular invasion and thrombosis may be determined using angiography or MRI. This information and the extrahepatic extent of tumor help to determine the "resectability" of HCC in individual cases.

Fibrolamellar Variant. Fibrolamellar HCC is a unique variant of hepatoma that was first reported in the United States. Patients are more equally distributed between the sexes and are younger than those with nonfibrolamellar HCC (*21*). Moreover, fibrolamellar HCCs occur in noncirrhotic livers and elevated α-fetoprotein levels are uncommon (*22*). Fibrolamellar HCC is more frequently resectable and carries a better prognosis than usual HCC.

There is limited information regarding the use of radionuclide studies in the evaluation of fibrolamellar variant. Unlike typical HCCs, almost all fibrolamellar HCCs are solitary and may demonstrate a central scar and punctate calcifications on US or CT (*23*). The echogenicity of the tumor is variable on US. On angiography a hypovascular zone may correspond to the central scar. Little has been written about the MRI appearance of this variant.

While it may be difficult to differentiate fibrolamellar HCC pathologically from adenoma and FNH, histology is the only means for making a definitive diagnosis.

Angiosarcoma. Hepatic angiosarcomas are rare malignant neoplasms of vascular origin. The majority occur in males between 50 and 60 yr old. The prognosis is poor with few patients surviving longer than two years.

Angiosarcomas have been associated with exposure to thoratrast, vinyl chloride, arsenicals and radium, and with a history of hemochromatosis (*24*). Pathologically, the tumors may have poorly defined margins and central areas of necrosis and hemorrhage. They tend to produce multiple hemorrhagic nodular masses within the liver.

In those patients in whom the tumor is related to exposure to thorium dioxide, radiopaque material may be seen in the liver and spleen on plain films of the abdomen. While a tagged red blood cell scan characterized by slow early filling and continued delayed activity is felt to be very specific for hemangioma, this appearance has also been described in one case of angiosarcoma (*25*). On angiography, angiosarcomas, unlike hemangiomas, typically have large feeding vessels, arteriovenous shunts, vascular invasion and neovascularization.

Cholangiocarcinoma. Although it is only one-tenth as common as HCC, intrahepatic cholangiocarcinoma (ICAC) is the second most common primary malignancy of the liver. Small centrally located lesions may have obstructive jaundice. Patients with peripheral tumors present in a similar way to those with primary HCC.

ICAC may be very difficult to distinguish from HCC or hypovascular hepatic metastases by radiographic means (*26*). On sulfur colloid scanning, ICAC typically appears as a photopenic defect against a background of normal liver (*27*). However, when associated with sclerosing cholangitis, choledochal cysts or hepatolithiasis, the sulfur colloid scan may be diffusely abnormal. Unlike HCC, ICAC does not accumulate gallium.

On US, ICAC typically appears homogenous and hyperechoic, while on CT, irregularly bordered masses, sometimes surrounded by small satellite lesions, may be seen (*27*). Unlike HCC, ICAC may contain tumor calcifications (*27*). US, CT and MRI may demonstrate dilated intrahepatic ducts with centrally located ICACs. The pattern of contrast enhancement on CT and arteriographic findings of ICAC are variable and therefore not specific.

Metastases. In the United States, metastases are the most common malignant hepatic tumors. Since treatment for various malignancies often hinges on the documentation or exclusion of distant metastases, it is important to determine the sensitivity and specificity of imaging techniques for hepatic metastases. Often, unequivocal diagnosis of suspected metastatic disease requires liver biopsy.

As has been stated, defects on sulfur colloid scanning are not specific for metastatic disease. False-negative sulfur colloid scans have been reported for metastases as large as 3 to 6 cm in size, regardless of their location within the liver (*1*).

It seems reasonable that SPECT should increase the sensitivity of radionuclide scanning for metastases, however, this may not be the case (*28*). An exciting development that may improve both the sensitivity and specificity of radionuclide imaging for metastases is the use of SPECT combined with tumor-specific monoclonal antibody labeling (*29*).

Hepatic arterial perfusion scintigraphy (HAPS) is a refinement of radionuclide scanning used to detect early intrahepatic metastases. HAPS takes advantage of the fact that, unlike normal liver tissue, metastases and tumors derive their blood supply from the hepatic artery. Tumors and metastases therefore show up as hyperperfused masses.

In evaluating surgical candidates for liver metastases, HAPS has been shown to have a sensitivity of 97% and specificity of 50%, which is superior to either CT or MR (*3,30*). In one center's experience, half of the patients with supposed "false-positive" HAPS were later proven to have metastatic disease.

In prospective evaluation of patients clinically suspected of having breast or colon cancer metastases, enhanced CT yields a slightly higher sensitivity than liver-spleen scan or US (*31*). Metastases have a variable sonographic appearance. Intraoperatively, however, US may be extremely sensitive for metastases not detected on preoperative testing (*32*).

On CT scanning, metastases appear as low attenuation areas, often with irregular margins and a necrotic center. Improper delay in scanning after contrast injection may result in metastases appearing isodense with normal liver parenchyma (*33*). A significant advantage of CT in patients with suspected metastatic disease is the ability to demonstrate extrahepatic pathology. This may aid in the location of the primary tumor and may alter staging, prognosis and therapy. Dynamic CT may better demonstrate hypervascular metastases to the liver which can be seen with breast carcinoma, hypernephroma, choriocarcinoma, sarcoma and endocrine tumors. Metastases to the liver from lung, esophagus, stomach, pancreas and colon carcinomas often appear hypovascular (*33*).

On MR scanning, metastases are demonstrated as areas of low signal on T1-weighted and high signal on T2-weighted images, similar to the appearance of HCC. The ability of MRI to image the mesentery and the gastrointestinal tract is inferior to that of CT, owing to motion artifact and the lack of enteral contrast used with MR scans.

Other Lesions

Focal Fatty Infiltration. FFIL may present as a mass or several masses in obese, diabetic, malnourished patients, or, more commonly, in those with a history of excessive alcohol ingestion.

Since the pathological process in FFIL spares the RE cells, sulfur colloid images are typically unaffected by the fatty change, resulting in normal uptake in an area corresponding to a mass seen on US or CT (*34*). Xenon-133 radionuclide scanning takes advantage of the high preferential solubility of this radioisotope for fat. Following inhalation of the ^{133}Xe, the radionuclide is characteristically retained in the area of the liver corresponding to FFIL.

SPECT scanning has been used infrequently in suspected FFIL. In acute alcoholic hepatitis, multiple hot spots, corresponding to areas of low attenuation on CT, have been demonstrated early in the course of the disorder. These have been observed to resolve over a span of several weeks (*3,5*).

While FFIL appears highly echogenic on US, the lesions are poorly circumscribed and are of distinctly low attenuation on CT (*36*). There have been only a few reports describing the MR appearance of FFIL (*37*). More importantly, enhanced CT and MRI are able to document the nondisplacement of normal hepatic vasculature by FFIL, thus differentiating this benign process from a malignant leison.

Liver Abscess. Scintigraphy is uncommonly used to diagnose hepatic abscesses, although sulfur colloid scanning is essentially diagnostic in the appropriate clinical setting. Pyogenic abscesses appear as "hot spots" on more than 80% of gallium scans (*38*).

US, CT and MRI are also extremely effective in the detection of abscesses (*39,40*). While abscesses are usually hypoechoic, with varying degrees of internal debris, gas produced by bacteria may cause them to be hyperechoic (*41*). Amebic abscesses tend to have a round appearance and fine internal echoes. If necessary, US and CT offer the ability to guide diagnostic and therapeutic aspiration.

The ability of CT to demonstrate extrahepatic pathology, specifically the appendix and colon, may help to identify the origin of nonparasitic abscesses. Most abscesses are of low density with rim enhancement when contrast is given.

Hemangioma. Although metastases are the most common malignant hepatic tumor, cavernous hemangiomas are the most common benign tumor of the liver (*42*).

RADIOLOGIC APPROACH TO THE PATIENT WITH A SOLID HEPATIC MASS

The differential diagnosis of solitary, solid hepatic masses is a relatively common clinical challenge. The ability to discriminate benign from potentially malignant lesions is of critical importance. While history and physical examination provide important diagnostic clues, clinicians also rely heavily on imaging techniques.

This article has described the radiologic characteristics of specific hepatic mass lesions using different imaging modalities. In past reviews, sensitivity determinations have usually been calculated not on a prospective basis, but rather on the ability of a test to detect a hepatic lesion in a patient in whom a particular diagnosis is ultimately made.

When confronted with a patient with a hepatic mass lesion, one needs to construct a differential diagnosis, including the likeliest diagnoses given the specific clinical context. Additionally, one needs to incorporate diagnoses which, although less likely, would have profound clinical consequences if missed. Guided by these two principles, it is important to perform safe, inexpensive, and efficient diagnostic testing. Given the complementary information provided by different imaging techniques, more than one radiologic study, frequently supplemented by biopsy, is often necessary to uncover the etiology of a hepatic mass lesion.

This can be illustrated by reviewing the diagnostic approach which might be pursued in three different clinical settings.

Incidentally Discovered Solid Hepatic Mass

In a young, noncirrhotic patient in whom a hepatic mass is incidentally discovered, the likeliest diagnoses are adenoma, FNH or hemangioma. Hemangioma is the most commonly encountered benign lesion, but because of association with malignancy, adenoma warrants the most concern.

In this clinical situation, the hepatic mass has already been identified by a radiologic study. Further work-up depends on the specific findings of that examination. If initial US or enhanced CT show evidence of bleeding or a central scar, this would suggest adenoma or FNH, respectively. Calcifications may indicate hemangioma. Unfortunately, these are uncommon findings.

If the clinical and radiologic data (Table 1) suggest either adenoma or FNH, a sulfur colloid scan is a logical next step. Increased concentration of the radiopharmaceutical would be pathognomonic for FNH. Normal uptake, while strongly suggestive of FNH, does not exclude adenoma. A cold defect would prompt further diagnostic testing.

If the etiology of an incidental hepatic mass is still not evident, angiography or biopsy are the remaining options. Angiography is very sensitive and relatively specific for these diagnoses. Although percutaneous biopsy may be associated with increased risk of bleeding in these vascular lesions, fine needle biopsy has been shown to be safe. However, this is more useful for confirming a suspected malignancy rather than for diagnosing, for example, hemangioma (*43*).

If after the above radiologic evaluation there is still a reasonable concern for adenoma, surgical biopsy and/or excision should be planned. Oral contraceptives should be discontinued preoperatively. This may shrink the adenoma and render it less vascular, thus facilitating its resection (*44*).

Hepatic Mass in a Patient with a Known Extrahepatic Primary Carcinoma or Suspected Primary Hepatic Carcinoma

The emphasis in this situation is on both locating the primary malignancy (if it is not already known) and ruling out hepatic or other metastases. The superiority of CT for evaluating extrahepatic tissues and comparable sensitivity to MRI, US and SPECT in assessing the liver itself make CT the preferred diagnostic tool. Comparison of pre- and post-contrast scans will help to distinguish tumor from normal liver parenchyma (*45*). For patients in whom intravenous contrast poses a significant risk, MRI or, if available, HAPS are diagnostic alternatives.

Whether an extrahepatic malignancy has already been diagnosed or a specific histology is suspected based on clinical or radiographic data (Table 2), tissue documentation of hepatic malignant disease is mandatory. CT, as well as US, can be used to guide percutaneous biopsy of accessible focal lesions. Otherwise laparoscopy or lapa-

TABLE 1
Clinical Features of Hepatic Adenoma, Focal Nodular Hyperplasia and Cavernous Hemangioma

	HA	FNH	CH
Age	20–40 yr old	20–40 yr old	All ages
Sex	90% female	80% female	60%–80% female
Associated with oral contraceptives	Yes	No	Probably
Symptoms associated with bleeding or rupture	Yes	No	Yes
Calcifications	No	No	Yes
Central scar	No	Yes	No
Associated with malignancy	Yes	No	No
Radionuclide scan	Typically photopenic; rarely may show normal uptake	10% intense concentration; 30% increased uptake; 30% normal uptake; 30% photopenic	Cold on sulfur colloid scan; "perfusion/blood-pool mismatch" on serial planar blood-pool scintigraphy
US	Mixed hyper/hypoechoic	Often isoechoic	50%–60% hyperechoic
CT	Hypodense initially	30% change density with i.v. contrast; 15% with central scar	Classic dynamic CT: hypodense on unenhanced, enhance peripherally, centripetal filling in 60%
Angiography	Hypervascular with hypovascular areas (if hemorrhage)	Hypervascular septated lesion with central vascular supply in 35%–80%	Rapid filling of vascular spaces in arterial phase with contrast persisting in venous phase
MRI	Characteristics similar to HCC	Homogenous, isointense on T1 and T2; hyperintense central scar	Smooth, rounded mass with high T1 and T2 signals

rotomy may be required. For patients with suspected hilar cholangiocarcinoma, endoscopic retrograde cholangiography, supplemented by brush cytology, may be diagnostic.

Since the presence of vascular invasion influences the management of malignant disease, arteriography and, less commonly, MRI may be used to exclude vascular involvement and thrombosis (Table 3). Intraoperative ultrasound has been extremely sensitive in localizing metastases unsuspected by preoperative studies (*32*).

Incidentally Discovered Mass in a Patient with Cirrhosis

FFIL, or other benign lesions, can present as focal masses in patients with cirrhosis. Still, it must be remembered that regardless of the etiology, cirrhosis is associated with an increased risk of developing HCC. The scintigraphic appearance of the cirrhotic liver may be partly obscured by decreased uptake of sulfur colloid in the liver or fibrosis around the mass (*2,17,18*). Small foci of HCC may be present in regenerative nodules in cirrhotic livers (*4,6*).

A sulfur colloid, CT or MR scan can be used to diagnose FFIL if there is a low clinical suspicion of malignancy. For HCC, however, there are no pathognomonic features on radiologic imaging. In the appropriate clinical setting, gallium scanning may support the diagnosis of HCC.

In a patient with a mass in a cirrhotic liver, there should be a very low threshold for definitively excluding HCC as a diagnostic possibility. US or CT may be used to

TABLE 2
Clinical Features Typical for Hepatic Malignancies

	HCC	Fibrolamellar HCC	Angiosarcoma	ICAC
Male:female	4:1	1:1	4:1	2:1
Mean age (yr)	60	30–40	50–60	60
Associated with cirrhosis	Yes	No	No	No
α-fetoprotein	High	Normal	Normal	May be slightly elevated

TABLE 3
Vascularity of Intrahepatic Metastases

Hypervascular	Hypovascular
Hypernephroma, breast carcinoma, neuroendocrine tumors, choriocarcinoma and sarcomas	Esophageal, gastric, pancreatic, colon and lung carcinomas

guide a percutaneous biopsy of a lesion. Laparoscopy or laparotomy may be indicated if the pathology obtained is equivocal and the suspicion of malignancy is still high.

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