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Approach to the Solitary Liver Lesion: Imaging and When to Biopsy

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Abstract

The characterization and management of focal liver lesions is a commonly encountered problem in radiology. While the imaging findings will often be diagnostic, in equivocal cases the decision of how to proceed may be challenging. The primary modalities for liver lesion characterization are multiphase contrast-enhanced computed tomography and magnetic resonance imaging. Most lesions have typical imaging features, and when taken in conjunction with patient demographics and biochemistry the diagnosis can usually be made. Ancillary imaging modalities such as contrast-enhanced ultrasound and hepatobiliary specific contrast agents are also useful. Cirrhotic livers present a challenge due to the spectrum of benign, dysplastic, and malignant nodules that can occur. The report should include information necessary for accurate staging, and published standardized reporting guidelines should be taken into consideration. A decision to proceed to biopsy should be made only after multidisciplinary review of the case. If biopsy is required, fine needle aspiration is usually sufficient, though core needle biopsy may be required in certain circumstances.

Résumé

Les problèmes liés à la caractérisation et à la prise en charge des lésions focales hépatiques sont courants en radiologie. Les examens d'imagerie servent souvent à des fins diagnostiques, mais dans les cas ambigus, il peut être difficile de déterminer la marche à suivre. Les premières techniques utilisées pour la caractérisation des lésions hépatiques sont la tomodensitométrie multiphase avec injection d'un agent de contraste et l'imagerie par résonance magnétique. La plupart des lésions ont des caractéristiques d'imagerie type. En ajoutant celles-ci aux données démographiques et biochimiques du patient, on peut habituellement poser un diagnostic. Les techniques d'imagerie auxiliaires, telles que l'échographie avec injection d'un produit de contraste et l'utilisation d'agents de contraste hépato-spécifiques, peuvent aussi se révéler utiles. Les foies cirrhotiques peuvent poser des difficultés en raison du vaste éventail de nodules (bénins, dysplasiques et cancéreux) qu'ils peuvent présenter. Le rapport devrait comprendre les renseignements nécessaires à une stadification précise et tenir compte des lignes directrices normalisées qui ont été publiées pour orienter sa production. La décision de procéder à une biopsie ne devrait être prise qu'après un examen multidisciplinaire du cas concerné. Pour faire la biopsie, une aspiration à l'aiguille est habituellement suffisante, mais certains cas peuvent nécessiter une biopsie au trocart.

Key Words: Liver neoplasms; Liver cirrhosis; Carcinoma; Hepatocellular; Magnetic resonance imaging; Image-guided biopsy

The characterization and management of the focal liver lesion identified on imaging is a commonly encountered problem in radiology. Often the imaging findings are diagnostic, and after additional consideration of the clinical and biochemical evidence, biopsy is rendered unnecessary. However, in equivocal or complex cases, the decision on how best to proceed may be difficult, particularly at sites without a dedicated hepatobiliary service.

This articles aims to provide a comprehensive approach to the solitary focal liver lesion, including a review of the features of common liver masses, guidance on when to biopsy, and an overview of the current guidelines and staging systems.

Initial Approach to the Solitary Liver Mass

Demographics/Clinical Features

Even before any imaging is reviewed, the demographics and clinical history can provide valuable clues as to the likely diagnosis. Benign lesions such as focal nodular hyperplasia

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(FNH) and adenomas are more common in younger to middle-aged patients, whereas hemangiomas are found in all ages. All 3 lesions also have a female predilection. Exogenous estrogen such as oral contraceptive use can accelerate the development of adenomas and FNH, with the former also increased in prevalence in those using anabolic steroids or in glycogen storage disease. Other information that may be helpful include travel history (parasitic or viral infections) or history of primary malignancy.

Hemangiomas and FNH tend to be incidental findings and asymptomatic, though large lesions may cause right upper quadrant pain from mass effect and capsular distension. Adenomas and hepatocellular carcinoma (HCC) may present with acute symptoms secondary to rupture and subsequent hemoperitoneum.

The list of risk factors for the development of chronic liver disease and HCC is extensive. The most common causes worldwide are viral hepatitis (hepatitis B and C) and alcohol. Other causes include autoimmune liver diseases (autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis), metabolic disorders (hemochromatosis, Wilson's disease, alpha-1 antitrypsin), and, increasingly, nonalcoholic steatohepatitis is seen as a cause that may progress to cirrhosis [1,2].

Alpha-fetoprotein can be used as a biomarker in both primary and secondary liver malignancies, and its clinical utility can range from screening of high-risk patients to monitoring of therapy response and recurrence [3]. Similarly, detection of colorectal liver metastases is aided by monitoring carcinoembryonic antigen levels [4].

Choosing an Imaging Modality

In most cases, liver masses are initially detected on ultrasound or single-phase computed tomography (CT). Magnetic resonance imaging (MRI) is the best modality for characterizing liver masses, due to its improved sensitivity and temporal and contrast resolution. MRI is also preferred in cases when iodinated contrast is contraindicated due to allergy, or in young adults or pediatric patients. In cases of limited resource availability, however, multiphasic CT (arterial, portal venous, and delayed phases) can also adequately characterize liver masses. Often the decision of where to send a patient for imaging depends on local expertise and resources, as well as the likelihood of referral to a tertiary care centre for management.

In the case of MRI, either extracellular or hepatocyte-specific contrast agents (eg, gadoxetic acid) can be used. The underlying mechanism of the latter agent involves uptake and retention of the agent by functioning hepatocytes, which peaks at 20 minutes, with excretion into the biliary system.

Benefits of hepatocyte-specific agents include functional assessment of liver and biliary excretion; improved sensitivity and accuracy for the detection of HCC and hypovascular metastases compared to CT and extracellular agents, respectively [5,6]; and ability to differentiate between lesions with hepatocytes that retain the agent (eg, FNH) from those that do not (ie, most adenomas) that have overlapping imaging features otherwise.

Hepatocyte-specific agents are not without its limitations. They are more expensive and require a longer imaging time. Arterial phase enhancement of lesions is less intense than with extracellular agents, and non−hepatocyte-containing lesions will become hypointense on equilibrium phase (3-5 minutes postinjection) resulting in a pseudowashout appearance, which limits the assessment of lesions such as hemangiomas. The utility of hepatocyte-specific agents in cirrhosis is controversial; as uptake of the agent is reduced as liver function is compromised, lesion conspicuity decreases. Well-differentiated hepatocellular carcinoma may retain contrast on hepatocyte phase imaging and overlap in appearance with high-grade dysplasia [6−8].

Positron emission tomography CT (PET-CT) has limited utility in the diagnosis of hepatic lesions, with its primary role to look for sites of extrahepatic disease. A negative PET scan does not exclude malignancy (in particular, HCC with reported sensitivities of only 60%) and a positive PET cannot differentiate among HCC, cholangiocarcinoma, or metastases [9]. In addition, heterogenous background liver activity makes detection of small lesions challenging [10]. Benign lesions such as FNH and hemangiomas tend to uptake fluorodeoxyglucose similarly to normal liver [11,12], thus increased uptake in a hepatic lesion in a patient with known primary malignancy and no clinical features of infection is suggestive of metastases.

Contrast-enhanced ultrasound (CEUS) is a well-established modality for the evaluation of focal liver lesions and is a useful adjunct or alternative to CT/MRI. It requires the injection of an intravascular microbubble agent as contrast, and has benefits including real-time observation of enhancement patterns, no ionizing radiation, safety in renal impairment, and is relatively easy to use. Sensitivity and specificity may be reduced in livers that are highly attenuating or coarsened, as well as in deeply located lesions (>8 cm from the skin surface). Contrast-enhancement patterns in arterial, portal venous, and late phases are similar to that on CT or MRI with some exceptions. Features such as early arterial enhancement and washout may be easier to appreciate on CEUS due to improved temporal resolution and the purely intravascular localization of the microbubbles [13,14].

Size Matters

Lesions larger than 1 cm can be characterized in most cases. Small hepatic lesions (<1 cm) are difficult to characterize and biopsy, but have a high probability of being benign (>80% even in patients with known malignancy) [15,16], thus close clinical follow-up and monitoring for progression may be the next most appropriate step. In most cases these lesions represent cysts, hemangiomas, or biliary hamartomas.

Lesions <0.5 cm in patients without risk factors (ie, no known malignancy, hepatic dysfunction, hepatic malignancy