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Use of Imaging Studies to Aid in the Diagnosis of Benign Liver Tumors

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G&H What types of benign liver tumors can imaging studies detect?

BLM All benign liver tumors can be seen on imaging, including hepatic hemangiomas, focal nodular hyperplasia, hepatocellular adenomas, liver pseudotumors, focal steatosis, and focal fibrosis. However, the ability to discriminate among these lesions based on their imaging characteristics varies depending on the imaging method; certain methods outperform others because of differences in their ability to determine the tissue composition of the mass (ie, fat, arteries, veins, fibrotic tissue, etc).

G&H Why is accurate diagnosis of benign liver tumors important for guiding clinical management?

BLM The high prevalence of benign liver lesions—including hemangiomas, focal nodular hyperplasia, hepatic adenomas, and shunts—combined with the essential role that imaging studies play in their diagnosis require that clinicians have reliable discriminators to identify which hepatic masses should be watched and which require resection, ablation, or biopsy. To accurately triage patients for expectant watching, surgery, ablative therapy, or transplantation, clinicians must first be able to accurately diagnose the condition.

G&H How do benign liver tumors differ from each other? How do they differ from malignancies?

BLM Characteristics of hepatocellular carcinomas that can be seen on imaging include arterial blood supply, contrast washout (clearing), and lesion capsular enhancement. Hypervascular metastases are uncommon but can include carcinoid tumors, renal cell cancer, and thyroid cancer; they are characterized by heterogeneous enhancement, no washout, and absence of capsular enhancement. In contrast, the most common liver metastases are supplied by the portal veins and, therefore, do not exhibit enhancement by the hepatic artery.

In terms of benign liver tumors, hepatic hemangiomas exhibit a typical, peripheral, discontinuous, nodular enhancement pattern that corresponds to the presence of peripheral venous lakes around the tumor's margins. Centripetal enhancement gradually occurs in these vascular venous lesions, with filling-in of the hemangioma and retention of contrast on delayed imaging studies that use vascular (extracellular) contrast agents. On ultrasound, a typical hemangioma is homogeneous and hyperechoic. They become atypical when hyalinization (scars) develop, which usually occurs when they are larger than 4 cm.

Another type of benign liver tumor is focal nodular hyperplasia. On imaging, focal nodular hyperpla-

sia have a central hypertrophied hepatic artery with branches that radiate to the periphery of the lesion. With the exception of its characteristic central scar, focal nodular hyperplasia enhance homogeneously during the arterial phase of contrast-enhanced imaging studies. Focal nodular hyperplasia are unencapsulated lesions and, therefore, have nodular contours that become isoattenuating or isointense on delayed computed tomography (CT) or magnetic resonance imaging (MRI), respectively.

Finally, hepatocellular adenomas have a heterogeneous enhancement pattern on vascular studies due to their arterial blood supply, which comes from multiple arteries that enter the lesion at different sites on its periphery. The lipid content of hepatocellular adenomas often allows them to be accurately identified on opposed-phase MRI sequences; specifically, these adenomas show signal loss on out-of-phase sequences when fat molecules are separated from water molecules. However, diagnosis of lipid-poor hepatocellular adenomas is more challenging; in these cases, the patient's age, oral contraceptive use, and lack of risk factors must be used to discriminate lipid-poor hepatocellular adenomas from neoplasms.

G&H What imaging technologies can be used to detect benign liver tumors?

BLM The US Food and Drug Administration recently approved liver-specific contrast agents for MRI; one such agent is gadoxetate disodium (Eovist, Bayer). These combination contrast agents have both a vascular extracellular phase that lasts 5 minutes postinfusion and a delayed hepatocyte-specific intracellular phase that lasts 30 minutes postinfusion; after the delayed phase, the agent undergoes biliary excretion. Such contrast agents can determine whether lesions have functioning hepatocytes.

G&H How can use of a gadolinium-based contrast agent aid in the diagnosis of benign liver tumors?

BLM As imaging study refinements have become available in clinical practice, the enhancement characteristics of liver lesions can be identified with greater accuracy both by CT and MRI. Currently, however, the availability of liver-specific combination MRI agents, which have a metabolic pathway similar to that of bilirubin during the delayed phase, has made MRI more useful than CT for characterizing benign hepatic masses. Also, the lack of radiation exposure with MRI has given this technology a further edge over CT.

G&H What are the risks of using a gadolinium-based contrast agent?

BLM Nephrogenic systemic fibrosis (dermal fibrosis) has been recognized since approximately 2005. This condition occurs when patients with renal impairment are unable to clear gadolinium by renal excretion; as a result, this high-density metal is deposited in the dermis. Because of this risk, any patient with an estimated glomerular filtration rate below 30 cannot receive a gadolinium injection. In addition, patients with a known allergy to iodine can only receive a gadolinium infusion if their reactions to iodine were mild (urticaria) and these patients have been prepared with steroids and antihistamines.

G&H What are the advantages and disadvantages of these agents?

BLM Compared to an extracellular contrast agent (vascular contrast), a combination contrast agent has the advantage of being able to offer an assessment of liver function, since the combination agent follows the metabolic pathway of bilirubin during the hepatocyte-specific phase. A disadvantage of liver-specific magnetic resonance (MR) agents is that, at their presently approved dose, they do not offer enough detail for the assessment of the biliary tree.

G&H What is the benefit of using diffusion-weighted MRI for the detection of benign liver tumors?

BLM Diffusion-weighted imaging (DWI) is an established technique in neuroimaging that assesses the presence or absence of the movement of water molecules (Brownian movement). In principle, DWI works because tissues with high cellular density, such as neoplasms, have restricted water molecular motion, while tissues with low cellularity allow for free motion of water particles.

DWI of the liver is an accessory sequence in the characterization of focal liver lesions that can discriminate true lesions from pseudolesions, such as shunts, focal fatty infiltrations, or focal fibrosis. However, DWI is performed while the patient breathes freely; thus, small lesion size and location on the diaphragmatic surface can limit DWI's application for hepatic evaluation.

G&H Are there any other new technologies that can aid in the diagnosis of benign liver tumors?

BLM MR elastography is becoming more important as a tool for assessing the stiffness of tissues or masses. This noninvasive method, which is now available for

both MRI and ultrasound, will be important in the identification and follow-up of hepatic fibrosis, as well as for assessing response to therapy in the prevention of hepatic cirrhosis.

Another technology that is being developed is MR proton spectroscopy (MRS). By offering information about the biochemical composition of the liver parenchyma and masses, this technology will hopefully allow for the detection of hepatic steatosis and neoplasms. Specifically, this novel noninvasive technique can assess tissues for the presence or absence of chemical compounds such as choline peaks in neoplasms (hepatocellular carcinoma) or lipid peaks in hepatic steatosis. MRS could thus allow for characterization of lesions, determination of loss of metabolic activity (response to therapy), and other assessments.

G&H What research questions in this area need to be addressed further?

BLM Imaging studies have become very sensitive to focal liver abnormalities, which often are not masses but rather hepatic pseudolesions, such as focal fatty infiltrations or fibrosis. Focal steatosis can be characterized by its echogenic appearance on sonography, low attenuation on CT, and loss of signal intensity on out-of-phase sequences (opposed-phase imaging). On the other hand, fibrosis exhibits more protean imaging characteristics: Vascular enhancement is present in the acute phase, but the subacute phase lacks fibrotic-retraction features. Thus, fibrosis can mimic focal hepatic masses. These benign processes (pseudolesions) will hopefully become better characterized with newer techniques such as MR spectroscopy, ultrasound elastography, and MR elastography.

Suggested Reading

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