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REVIEW

Indeterminate liver lesions in cancer

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Abstract

It is important to distinguish liver metastases from incidental benign liver lesions which may be present in patients with cancer. In a minority of cases, sonography or CT may be sufficient to characterise benign lesions, but the range of sequences and contrast media available for liver MRI provides the opportunity for more specific diagnosis in the great majority of cases. Biopsy is rarely needed.

Keywords: *Liver; tumors; differential diagnosis.*

Introduction

Liver imaging is used not only for staging cancer patients, but also for assessment of response to treatment, for re-staging after treatment or with suspected recurrence, and for surveillance during remission. If liver abnormalities are shown, the differential diagnosis of metastatic disease from benign or incidental lesions may have a critical influence on the subsequent management of the patient. Since the widespread introduction of liver imaging for routine clinical investigation, it has become clear that incidental benign liver lesions are not rare. One useful practical guideline is that small (<15 mm) lesions discovered incidentally in patients with no known primary malignancy are virtually always benign. However, in patients with known malignant disease there is a small incidence of metastases whose CT appearances overlap with those of benign lesions. Larger benign lesions are less problematic, but at all sizes the MR appearances are more characteristic.

Liver cysts

Simple cysts are round unless deformed by more rigid adjacent structures. Their contents are anechoic on ultrasound, show watery attenuation on CT, low signal on T1w MRI and bright signal on conventional T2, which is maintained on more heavily T2w sequences. Contrast enhancement produces no change—an enhancing rim raises the suspicion of necrotic metastasis, or in the appropriate clinical context, abscess.

Haemangiomas

Characteristic appearances of haemangiomas are well established—they are hyper-echoic on sonography and show geographic shape with low attenuation on unenhanced CT and on T1w MRI. Their intense signal on conventional T2w MRI is maintained with more heavy T2 weighting (TE = 180 msec or HASTE). With contrast-enhanced CT or gadolinium-enhanced MRI, the lesions show intense nodular enhancement at the periphery, followed by centripetal infilling over the next 5–10 min. Some larger lesions contain a central nodule of hyalinized scar tissue which never enhances. The discontinuity of the peripheral nodular enhancement is a specific feature, and peripheral wash-out does not occur. In contrast, metastases with necrotic centres are usually round in shape and although they may show peripheral enhancement, the ring is more uniform. Whilst delayed enhancement of the necrotic centre of such lesions is not

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uncommon, the brightly enhancing peripheral ring fades fairly rapidly. Some small haemangiomas show uniform and rapid enhancement starting in the arterial phase, similar to the appearance of small hepatocellular lesions, but they show the distinguishing feature of intensely bright signal on T2w MRI, in contrast to the iso-intense or mildly hyper-intense appearance of small benign hepatocellular lesions. Other atypical haemangiomas include small lesions with centrifugal enhancement from a single vascular nodule (central dot sign) and in other cases the lesion may be predominantly fibrous, so enhancement is patchy and delayed, with little of the typical peripheral nodular vascularity.

Fatty change

Fatty infiltration is often heterogeneous and sometimes focal; in other cases small focal areas of liver parenchyma may be spared from fatty change. On sonography, either focal fatty change or focal sparing can produce lesions which are difficult to distinguish from metastases. One helpful feature with focal fatty change or sparing is that there is usually no mass effect—vessels run normally through the apparently abnormal areas. Focal fat may be recognisable on CT by its geographic distribution, normal contrast enhancement, and the lack of a mass effect, but a more reliable diagnosis can be made on MRI. In patients with diffuse fatty change, metastases may be obscured on CT because their low attenuation is matched by the low attenuation of the surrounding liver. Occasionally, a ring of liver tissue immediately surrounding the lesion may be spared from fatty change, producing an irregular halo of denser tissue within an otherwise homogeneous liver. This appearance can be seen with haemangiomas in a fatty liver, as well as with metastases. Using in-phase and opposed-phase T1w sequences, MRI offers a rapid and reliable approach for the recognition of focal fat, and reveals metastatic lesions in the diffusely fatty liver. Where any diagnostic doubt remains, liver-specific contrast agents may be given.

Focal nodular hyperplasia (FNH)

With the widespread use of dual-phase CT, multi-phase contrast-enhanced MR, and the recent introduction of vascular contrast agents in sonography has come a realisation that focal nodular hyperplasia (FNH) is not rare. Larger lesions typically show a rounded or lobulated shape with clear-cut margin, a mass effect displacing adjacent vessels, and a central scar sometimes with radiating spokes towards the periphery. Their echogenicity, attenuation and signal characteristics are little different to those of normal liver tissue. The lesions show marked arterial phase contrast enhancement which usually fades rapidly to become iso-intense in the portal phase, although occasionally increased enhancement lasts for several minutes. Delayed enhancement of the central scar is characteristic. Lesions smaller than about 2 cm are often homogeneous with no central scar, but show the same enhancement characteristics. It is not rare for these small lesions to be multiple, and they may co-exist with other benign lesions. When found in patients with known malignancy, a confident diagnosis of FNH requires the demonstration of intact liver function within the lesion. The most effective method is to use superparamagnetic iron oxide (SPIO) enhancement. Some FNH lesions will take up as much SPIO as normal liver, so the lesion appears black on the post-contrast T2w images. In other cases the lesion may take up some SPIO, but less than the surrounding liver, so that the lesion becomes more apparent after contrast. In these cases it is important to use the same T2w sequence before and after SPIO, and to measure the change in signal intensity in both liver and lesion. If the lesion shows substantial SPIO uptake (more than 40–50% of that taken up by the liver), it may be regarded as benign. Metastases do not take up SPIO, but well-differentiated hepatocellular cancers may take up just a little. Another approach is to use one of the hepatocellular MR contrast agents (mangafodipir, gadobenate, or gadoxetic acid). All of these agents are taken up by the functioning hepatocytes present in FNH lesions (and also in well-differentiated HCC), but because there is no biliary excretory pathway, the lesions retain the contrast for much longer than the normal liver, so becoming brighter on delayed T1w images.

Focal perfusion artefacts

Peripheral wedge-shaped areas of abnormal perfusion, usually seen only in the arterial dominant phases of enhanced CT and MRI, are probably caused by segmental portal vein occlusion, which in some cases is associated with parenchymal tumour deposits; in other cases no cause can be found. Such transient hepatic attenuation defects (THADs) may also be associated with parenchymal oedema within the liver, which appears hyper-intense on T2w MRI. Around the periphery of segment 4, particularly just to the right of the falciform ligament anteriorly, and also anterior to the bifurcation of the portal vein, small areas of liver parenchyma may receive non-portal venous supply from the parabiliary venous plexus and from anomalous drainage of gastric, duodenal and pancreatic veins. This can produce small nodules of focal fatty change in these areas, or more commonly may result in small areas of altered enhancement after contrast.

Other benign malformation

Biliary microhamartomas (von Meyenburg complexes) show imaging characteristics which overlap between cysts and haemangiomas. These biliary malformations

are often irregular or even angular in shape, and usually only a few millimetres in diameter.

Conclusions and key points

(1) Incidental benign lesions are relatively common in patients with malignant disease, and must be distinguished from metastatic disease in order to avoid erroneous management.

(2) Focal fat, focal sparing and haemangiomas may be diagnosed on sonography or CT if they are typical, but in other cases MRI is usually decisive.

(3) FNH can be diagnosed with confidence using liver-specific MR contrast agents.

(4) Discriminating small cysts and haemangiomas from metastases is best done with MRI, using a heavily T2w sequence followed by dynamic gadolinium-enhanced T1.

(5) Tiny lesions which appear on CT to have an angular shape and low attenuation will usually be biliary microhamartomas.

Further Reading

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