Investigating asymptomatic solitary liver lesions

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Although most patients found to have a single asymptomatic liver lesion will have a benign disease, the possibility of malignancy must be remembered and assessed. Careful consideration is needed to provide a timely diagnosis, weighing up the costs and risks of investigations against the likely pathology.

An asymptomatic liver lesion is usually identified incidentally during abdominal imaging performed for an unrelated reason. In many cases a diagnosis can be established confidently with noninvasive organ imaging. In others, invasive (and risky) investigations or resection of the lesion may be needed to make a confident diagnosis.

The patient's needs and concerns must be considered throughout the diagnostic work up. The aims and limitations of each investigation must be discussed, as the progression from one apparently inconclusive test to another can be difficult for a patient to cope with. Many patients fear malignancy, and in most cases this should be discussed openly and realistically.

History

For patients in whom a liver lesion has been identified, a careful history must be taken to assess the risk of the lesion being malignant. The appearance of a liver lesion in a patient with a past history of malignancy is an ominous finding, and in those with hepatitis C and/or hepatitis B, cirrhosis or haemochromatosis, it should raise concerns of primary hepatocellular carcinoma.

Physical examination

Physical examination of patients with an asymptomatic liver lesion is usually unhelpful, but features of extrahepatic malignancy should be sought. The abdomen should be examined for masses and for the size, shape and tenderness of the liver and spleen. Hepatic bruits or friction rubs may be heard over a hepatic malignancy. The patient should also be examined for signs of chronic liver disease and hepatic decompensation.

Initial investigations

Liver function tests

Standard liver function tests are of limited value when investigating asymptomatic liver lesions. However, elevated gamma glutamyl transpeptidase and alkaline phosphatase levels in the presence of a minimal or absent change in the levels of bilirubin and transaminases suggest a neoplastic or infiltrative process. It is also unusual for liver function tests to be completely normal in the

IN SUMMARY

- **Although most patients with a single asymptomatic liver lesion will have benign disease, the possibility of malignancy must be considered and assessed.**
- **In many cases noninvasive imaging techniques can be used to investigate solitary liver lesions.**
- **Invasive investigations, including angiography, biopsy and resection, may be needed to evaluate some asymptomatic liver lesions.**
- **The appearance of a liver lesion in a patient with a history of malignancy is an ominous finding.**
- **Solid or partially cystic mass lesions of the liver may be malignant and should be investigated further.**

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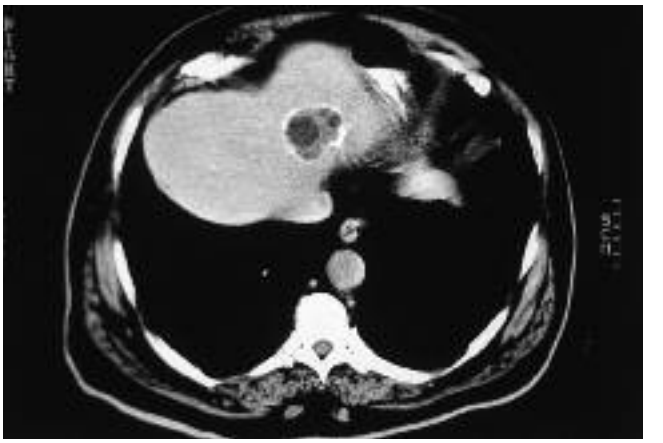

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Figure 1a and b. Hepatic cysts. a (left). CT scan of a simple hepatic cyst. b (right). CT scan of a complex hepatic cyst. The internal structure of this lesion indicates the need for further investigation, which revealed that this was a hydatid cyst.

presence of hepatic malignancy. Estimation of alpha fetoprotein levels can be useful in identifying hepatocellular carcinoma, especially for patients from populations with a high prevalence of this tumour (e.g. those with chronic viral hepatitis or haemochromatosis).

Chest x-rays

A chest x-ray can be useful to identify pulmonary metastases or hydatid cysts. A raised right hemidiaphragm may be seen in association with a hepatic abscess or hepatocellular carcinoma, but these conditions are unlikely to be asymptomatic.

Abdominal ultrasound

Abdominal ultrasound is a safe, noninvasive, and relatively cheap investigation that can be very useful in the assessment of hepatic lesions, particularly in differentiating cystic from solid lesions. If, on ultrasound, the lesion has a typical appearance of a simple cyst or haemangioma, no further investigation is required. Lesions of a complex cystic appearance, on the other hand, require further investigation. Although most asymptomatic solid lesions are benign, they should be investigated further.

Further investigations

Lesions that appear solid or partially cystic on ultrasound may be malignant and should be imaged by computed tomography (CT) and/or magnetic resonance imaging (MRI). If uncertainty remains, invasive investigations, such as angiography, biopsy and resection, must be considered. Laparoscopy, with or without biopsy, can also be a powerful diagnostic tool.

Patients with a past history of malignancy or with a lesion of variable echogenicity, an irregular shape or a mass effect should have a biopsy.

It should be remembered that although a high level of diagnostic certainty can be achieved in many cases by finding typical appearances on imaging, there is no ideal imaging technique. Moreover, a definitive diagnosis of many solid lesions requires histological examination.

Types of liver lesions

Cystic lesions

Simple cysts

On abdominal ultrasound, simple cysts have clearly defined thin walls with an interior devoid of echoes (Figure 1a). Asymptomatic patients with lesions of this appearance need no further tests (Table). Simple cysts may be single or multiple and rarely cause morbidity. They vary in size from less than 1 cm to more than 20 cm in diameter. Liver function tests for patients with these lesions are normal. Large lesions may be associated with right upper quadrant discomfort.

Hydatid cysts

Patients with hydatid cysts (Figure 1b) may present asymptomatically, especially in areas where hydatid disease is endemic (i.e. pastoral areas). The presence, on abdominal ultrasound, of daughter cysts occurring within or outside the primary cyst strongly suggests active hydatid disease. Nonviable cysts may appear heavily calcified with little cystic component. Patients in whom viable hydatid cysts are suspected should be referred to a surgeon experienced in the management of hydatid disease.

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Table. Assessment of asymptomatic liver lesions

Type of lesion	Diagnosis	Management/further investigations
Cystic lesions		
Simple cysts	Confirmed by typical appearance on ultrasound or computed tomography (CT)	Reassure patient; generally no need for further investigation
Complex cystic lesions	Confirmed by any imaging modality	Refer patient for further assessment
Solid lesions		
Haemangiomas	Confirmed by typical appearance on ultrasound or CT	Reassure patient; generally no need for further investigation
Other solid lesions, including adenomas, focal nodular hyperplasia, malignant lesions	Biopsy often required to confirm diagnosis	Refer patient for further assessment

Partially cystic lesions

Partially cystic lesions may be malignant and require histological assessment.

Solid lesions

Haemangioma

Hepatic haemangiomas (Figure 2) are common; they are found in more than 5% of the population. Most are small and asymptomatic. They are usually echogenic on ultrasound and often have a typical pattern of enhancement with dynamic CT. MRI can be useful for detecting small lesions, but angiography may be needed. Needle biopsy of these lesions is contraindicated because of the risk of bleeding.

Giant haemangiomas (those greater than 4 cm in diameter) may be associated with symptoms, particularly upper abdominal pain. The pain experienced by patients with these haemangiomas is not always directly related to the lesion, with resection easing the pain in only about half the cases. Thrombosis within the haemangioma can be painful, and large lesions may be associated also with thrombocytopenia. Malignant change does not occur in haemangiomas.

Hepatic adenoma

Hepatic adenomas are often incidental findings. These solid lesions are usually seen, but not definitively diagnosed, on ultrasound, CT and MRI. Angiography is useful preoperatively to identify them; but, needle biopsy may appear normal.

Most hepatic adenomas are solitary and 1 to 30 cm in diameter. They may occur in relation to and/or enlarge under the influence of the oral contraceptive pill or pregnancy and carry a risk of malignant transformation. There may be mild upper abdominal pain in about one-quarter of cases. Hepatic adenomas should be resected and patients advised to avoid the oral contraceptive pill.

Focal nodular hyperplasia

Focal nodular hyperplasia, while unusual, is more common than adenomas. The lesion is well circumscribed, usually solitary, and typically has a central scar and

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Figure 2. The ultrasound of this lesion displays the typical hyperechoic appearance of a haemangioma.

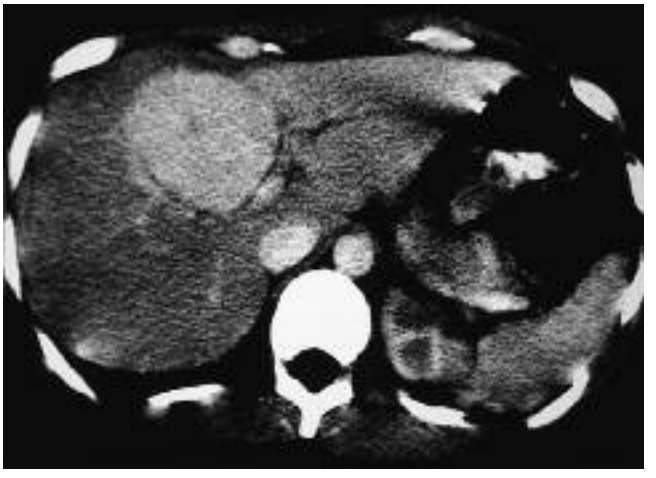

Figure 3. CT scan of a solid hepatic mass. The central 'scar' in this lesion suggests that it is focal nodular hyperplasia, which was confirmed on biopsy. Such a lesion could also represent an adenoma.

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fibrous septa (Figure 3). Its cause is uncertain but may be related to a vascular malformation. As with adenomas, these lesions may enlarge under the influence of female sex hormones.

On ultrasound, CT and MRI, focal nodular hyperplasia appears as a solid mass lesion in which the central scar may or may not be seen. As these lesions contain Kupffer cells (unlike adenomas) they may not be seen by radionuclide liver or spleen scanning. Angiography will reveal a vascular lesion; however, it may not be possible to differentiate focal nodular hyperplasia from an adenoma without resection. Histology of the lesion needs to be compared with that of an unaffected part of the liver as it may have an appearance consistent with cirrhosis. The finding of normal hepatic histology away from the lesion confirms the diagnosis of focal nodular hyperplasia.

Lesions resembling solid lesions

Focal fatty change

Focal areas of fatty change within the liver may simulate a space-occupying lesion on ultrasound, CT and/or MRI. On CT this change shows no mass effect and has a density similar to that of soft tissue. In contrast, metastases have a density similar to that of normal liver.

When to suspect malignancy

Solid or partially cystic mass lesions of the liver may be malignant. A mass lesion with irregular, ill-defined margins, with or without areas of necrosis, suggests malignancy. Metastatic disease should be suspected in patients with a liver lesion and a history of extrahepatic malignancy; however, a fine needle biopsy may be needed to confirm this diagnosis.

Ultrasound, CT and MRI have comparable sensitivities for the detection of hepatocellular carcinoma. Angiography or CT angiography can be diagnostically useful and is essential in planning surgical or intravascular therapy. Laparoscopy can be of value in assessing peritoneal spread and obtaining biopsy material.

Small, solitary hepatocellular carcinomas may be amenable to resection, and patients who are affected may be treated successfully with liver transplantation. These strategies may also be appropriate for a metastasis when the primary lesion has been treated adequately.

Conclusion

Solitary asymptomatic liver lesions should be investigated to exclude malignancy; in most cases they will be benign. Although none is ideal, imaging techniques can be used to identify most solitary liver lesions. Lesions that have a complex cystic or solid appearance may be malignant and require further investigation. Throughout the diagnostic work up, patients' needs and concerns must be considered. Many patients fear malignancy and this should be discussed openly. MT

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