Hospital Topics

Focal liver lesions: a plan for management

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Abstract

A management plan for patients with suspected focal liver lesions which avoids early biopsy includes routine laboratory investigations, ultrasound scanning, and assessment for evidence of extrahepatic metastases and non-hepatic primary tumours. Angiography and computed tomography may also be indicated, and laparotomy or laparoscopy is undertaken to assess any potentially resectable focal liver lesions. The plan requires modification to suit individual circumstances.

Introduction

The patient with a focal lesion in the liver may present a difficult management problem. Upper abdominal symptoms may lead to the diagnosis but the wider application of ultrasound and more recently computed tomography has identified increasing numbers of patients with no symptoms related to their hepatic lesions. In some cases the cause for liver disease may become rapidly obvious but in many no easy diagnosis can be made and further investigation is required. There is no widely accepted protocol for assessing these lesions, although different algorithms have been suggested.[1,2] The variation in quality and availability of different investigations is partly responsible for this lack of uniformity; nevertheless, such shortcomings should not be the rationale for inadequate or inappropriate investigations. In this paper we describe a plan for the assessment of these lesions which aims both at avoiding unnecessary overinvestigation and also at selecting those patients who might benefit from high quality specialist studies. One of the major aims is the avoidance of early biopsy of these lesions as not only is this often unhelpful to the management of these patients but also carries the risk of serious complications and may jeopardise later surgical resection.

Investigation of a focal liver lesion

Patients at the hepatobiliary surgical unit at Hammersmith Hospital who present with a focal liver lesion have the following baseline investigations: full blood count with differential white cell count; determinations of blood concentrations of urea, and electrolytes, and serum creatinine; liver function tests including bilirubin, alkaline phosphatase, aspartate transaminase, and albumin; tests for α fetoprotein, carcinoembryonic antigen, and hepatitis B surface antigen; and chest *x* ray and plain abdominal *x* ray films. In appropriate cases blood samples are taken for hydatid serology and for estimations of plasma neurotensin and serum vitamin B_{12} binding capacity.

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The latter two may prove to be useful tumour markers should the lesion later be shown to be a fibrolamellar hepatoma.[3,4] The figure shows the plan for further investigation of these cases. It is not designed for patients with obstructive jaundice, whose investigation we have described,[5] although such patients may also have a focal hepatic tumour (metastatic deposit, local invasion from cholangiocarcinoma or carcinoma of the gall bladder, or primary hepatoma with tumour present in the biliary tract).

Ultrasound scanning permits early separation into cystic or solid lesions in almost all cases, and also excludes large bile duct obstruction. It may also identify multiple hepatic lesions. In many cases high resolution real time scanning further characterises these lesions, avoiding the need for computed tomography, although tomography may be necessary with cystic lesions and is recommended for a solitary, solid lesion. Technical difficulties with ultrasound scanning may arise in some patients—due, for example, to obesity or overlying bowel gas—and computed tomography is then necessary. Computed tomography also has an increased overall accuracy compared with ultrasound.[6,7] Rapid sequence computed tomography after intravenous contrast may show the characteristic appearances of a haemangioma, and we routinely use intravenous contrast enhancement.[7,8]

Neither computed tomography nor ultrasound is particularly reliable in determining the nature of solitary hepatic lesions apart from the characteristic haemangioma, hydatid cyst, or benign simple cyst. Small or involuting haemangiomas and some hydatid cysts have atypical computed tomographic and ultrasound appearances.[8,9] Cyst formation in a malignant lesion or malignant change in a previously benign hepatic cyst may also occur. For these reasons non-characteristic cysts are probably best managed as if they were unknown solid lesions. We assess patients routinely for evidence of extrahepatic secondary tumour by clinical findings, chest *x* ray film, and radionucleide bone scan. Upper and lower gastrointestinal endoscopy or barium studies and mammography when appropriate are also advisable to exclude the commoner primary tumours that present with a single secondary deposit in the liver. A solitary, solid lesion without any evidence of primary tumour elsewhere or secondary spread is our major indication for angiography provided the patient's general condition will allow hepatic resection. We do not use hepatic radionucleide scanning because of its low level of resolution, especially with central lesions.[10] The role of nuclear magnetic resonance in assessing liver tumours is not clear, but it appears that it may give better imaging than computed tomography of some hepatic tumours.[11]

Angiography may show multiple tumours not detected on ultrasound or computed tomography, the characteristic appearances of a haemangioma,[8] a tumour circulation localised to the site of the previously identified focal lesion, or an avascular mass with displacement of hepatic blood vessels suggesting an intrahepatic haematoma, an avascular tumour, or, alternatively, a misidentified cystic lesion. Haemorrhage into an hepatic tumour may also result in a misleading avascular appearance on angiography. Angiography also provides a vascular "road map" for later surgical resection, which is particularly useful, as anomalous hepatic arterial patterns are common.[5]

While in some cases computed tomography and ultrasound scanning may give suggestive evidence of major venous invasion with tumour, indirect splenoportography almost always gives good visualisation of the portal vein. This is important as portal vein branch invasion may be the sole contraindication to resection. In patients in whom the lesion appears close to the inferior vena cava we perform inferior vena cavography. Invasion of the cava is usually a contraindication to resection, but caval displacement without invasion does not preclude resection.

Apart from those with the characteristic appearances of a haemangioma on computed tomography or angiography, it is our policy to assess all potentially resectable focal solid liver lesions by direct visualisation at either laparoscopy or laparotomy, and to perform appropriate resectional surgery or biopsy as required. Laparoscopy is a lesser procedure and is preferred in

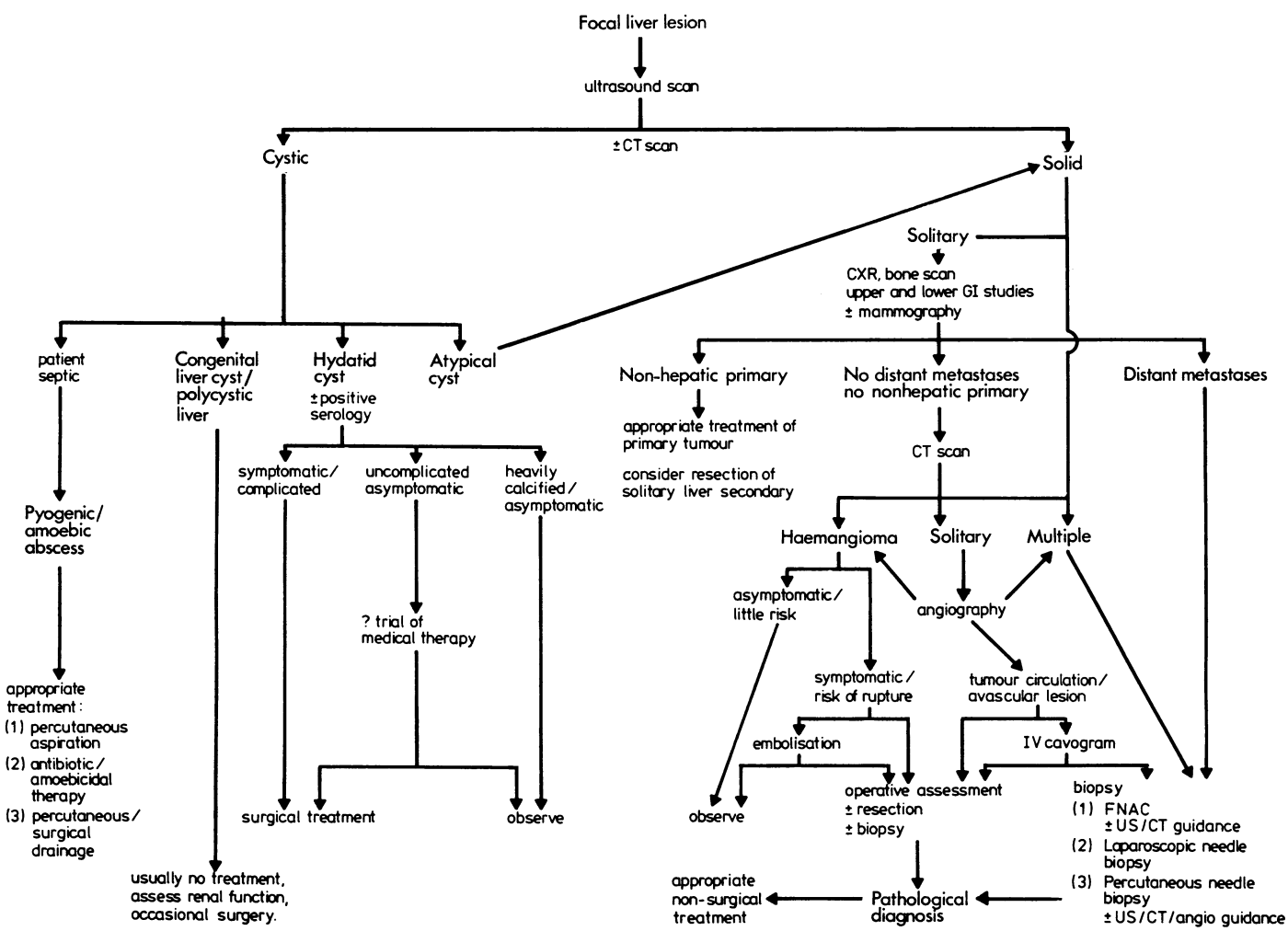
patients with lesions that on the basis of preoperative investigations are unlikely to come to resection. These include probable haemangiomas, areas of focal nodular hyperplasia, and malignant lesions when multiple tumour deposits or extrahepatic spread is suspected. Laparoscopy is also useful when biopsy of relatively vascular lesions is required, as haemorrhage may be controlled directly, and for assessment of the non-tumourous liver, especially in primary hepatoma. Nevertheless, it may not be satisfactory in patients who have intra-abdominal adhesions after previous surgery[12] or those with deeply or posteriorly situated hepatic lesions. Inadequate laparoscopy necessitates open operative assessment; this may require only a minilaparotomy but the surgeon should be prepared to proceed to hepatic resection if indicated.

When pathological confirmation is required in patients with a contraindication to resection we favour either the use of percutaneous fine needle aspiration cytology under ultrasonic or computed tomographic guidance (except where the tumour is readily palpable) or needle biopsy under direct laparoscopic control. Biopsy under direct vision permits accurate localisation of the biopsy into tumour tissue, preferably through a small amount of undiseased liver. We occasionally use percutaneous needle biopsy under ultrasonic, computed tomographic, or angiographic guidance for biopsy of deeply situated hepatic lesions or to biopsy non-diseased liver tissue where the possibility of cirrhosis exists as this would be a contraindication to major hepatic resection. Biopsy during angiography has the advantage that immediate embolisation is possible if haemmorrhage occurs.

Between April 1979 and December 1984 122 patients with suspected focal liver lesions were assessed in our unit. Thirty nine of these patients were thought to have a solitary secondary deposit from a previously resected non-hepatic primary tumour (33 colorectal, six other). Laparotomy was done in 77 patients with resection or other definitive surgical treatment in 61. Sixteen had surgical exploration only with or without biopsy, because of previously undetected multiple deposits (10) or local tumour irresectability (four), while two haemangiomas were left in situ. Laparoscopy and biopsy were used in seven cases. No surgery was done in 38 patients because of preoperative identification of multiple liver deposits (11), distant metastases (seven), or local tumour extent (five), four lesions were seen to be haemangiomas (on enhanced computed tomography or angiography); eight patients were considered unfit for resection or declined surgery; and three were treated non-surgically. The lesions found were 53 secondary tumours (34 colorectal, 11 unknown primary, two breast, two pancreatic endocrine, and four other), 32 hepatomas, 18 cystic lesions (11 hydatid, seven other), 14 benign hepatic tumours (eight haemangiomas, four focal nodular hyperplasias, two adenomas), two lymphomas, and three other lesions.

Discussion

The main objective of the management plan outlined is to avoid early biopsy of focal hepatic lesions until their nature and extent have been adequately defined, thus preventing both unnecessary complications and jeopardising subsequent potentially curative resection. That complications arise from percutaneous liver biopsy is well documented and a complication rate of roughly 6% has been reported recently.[13] Serious problems requiring surgery occur much less frequently, at least in experienced hands.[2] The incidence of complications does not appear to be higher in patients with focal lesions compared with those who have diffuse hepatic disease.[13] Biopsy is obviously contraindicated in those with an audible bruit, suspected hydatid cysts, or who appear to have highly vascular tumours on investigation. We have seen four patients in the past year who have required urgent surgical control of their haemorrhage after biopsy of vascular liver tumours at referring hospitals. Haemangiomas and occasionally hydatid cysts may have atypical appearances on initial investigation and percutaneous biopsy may result in life threatening haemorrhage, anaphylaxis, or hydatid dissemination.



An algorithm for the management of cystic and solid focal liver lesions. CT=computed tomography, US=ultrasound, FNAC=percutaneous fine needle aspiration cytology.

Though the incidence of early complications, particularly biliary leakage and significant haemorrhage, is known, the extent of tumour dissemination after needle biopsy is uncertain, although there is every reason to suppose that this occurs. Fine needle aspiration cytology appears to carry less risk than needle biopsy[14] and is being successfully used to confirm hepatic malignancy especially with ultrasound guidance, although false negative results occur in up to one third of cases[15] and an experienced cytologist is required. Even this procedure is not without complications and implantation of tumour in the needle tract has also been reported.[14]

The risks of biopsy must be balanced against the potential gains. Blind percutaneous biopsy may miss focal lesions, although biopsies guided by ultrasound or computed tomography are more often successful. Small and possibly unrepresentative or necrotic tissue specimens may be obtained by needle biopsy and lead to difficulties in histological or cytological interpretation. Benign tissue may be obtained from a tumour in which malignant change has occurred. Such inadequate or unrepresentative biopsy specimens may delay the recognition of early hepatic malignancies and thus prevent potentially curative resection or other appropriate specific treatment. The pathological report of preoperative biopsy specimens rarely influences the surgical approach to a potentially resectable focal lesion. Biopsy of a focal liver lesion may reveal definite evidence of a *secondary* tumour deposit despite the absence of any other evidence of a primary tumour; such a finding is uncommon in our practice, although this may be partly due to selection before referral. Nevertheless, even definite biopsy evidence of a metastatic tumour is not necessarily a contraindication to resection of a solitary secondary deposit.[16]

The major benefit of a percutaneous biopsy of a solitary liver lesion would be the avoidance of any subsequent surgery. This benefit might be thought to be particularly relevant to benign tumours, which consist largely of haemangiomas, focal nodular hyperplasia, and liver cell adenomas. Haemangiomas will usually have a characteristic appearance on computed tomography or angiography, but this is not always the case and subsequent visual inspection is sometimes necessary to confirm the diagnosis and percutaneous biopsy is obviously contraindicated. Focal nodular hyperplasia is often difficult to confirm histologically with needle biopsy but may be diagnosed on open incision biopsy after visual inspection at operation; excision is not usually necessary.[16] Liver cell adenomas, which are closely associated with use of the oral contraceptive pill,[17] may be biopsied and their progress followed after cessation of all hormone treatment.[18] Nevertheless, as these adenomas may bleed, suffer necrosis, or occasionally undergo malignant change resection is desirable in most cases.[16] Thus direct inspection of benign tumours is often indicated and resection not infrequently required.

It seems prudent to carry out percutaneous biopsy of a solid hepatic tumour only when there is evidence of primary tumour at another site, secondary spread from the hepatic primary tumour, tumour irresectability (see below), cirrhosis, or other concomitant disease which precludes hepatic resection. Even in such cases biopsy is indicated only when pathological confirmation of tumour is required. There is a risk that multiple haemangiomas may occasionally be mistaken for secondary tumour deposits, and this possibility should be considered before percutaneous biopsy. Computed tomography or angiography will usually resolve this difficulty. Solitary hepatic tumours presumed to arise from resected colonic carcinomas should be assessed in a similar way to primary liver lesions since hepatic resection is worthwhile in these patients.[16] Multiple colonic secondary deposits or multifocal primary malignancies confined to one hepatic lobe may occasionally be resected, but are usually considered a contraindication to surgery. Though some agree with this cautious approach to solitary hepatic lesions,[16] others have advocated percutaneous biopsy at an earlier stage.[1 2 19]

The criteria for irresectability of hepatic tumours require careful definition. Evidence of deposits in both lobes of the liver, invasion of the portal venous supply to the proposed liver remnant, or venographic evidence of inferior vena caval invasion is normally considered a definite contraindication to resection. Computed tomography may give a misleading impression of extrahepatic spread into adjacent tissues and organs. Large tumours arising from extrahepatic structures may occasionally mimic liver masses.[20] Size alone is seldom a contraindication to attempted resection of a primary solitary hepatic lesion, and we have excised several extensive primary hepatomas in young patients who had previously been regarded as inoperable purely on the basis of the extent of primary tumour on computed tomography.

The plan described here has proved a useful guide to our management of focal liver lesions. It is not comprehensive and requires appropriate modification to individual circumstances, but we hope that it will prove helpful to others faced with similar problems.

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Is there any evidence that multiple sclerosis is caused by a virus transmitted by household pets, especially dogs?

No agent has so far been convincingly linked to multiple sclerosis. Viral particles have not been consistently found in multiple sclerosis tissues. Lymphocytic reactivity does not occur, and viral antibodies have not been isolated from the cerebrospinal fluid. Nevertheless, significantly raised antibody titres for measles virus and canine distemper virus have been found in serum. A cross reactivity exists between measles and distemper antibody; thus the canine distemper virus neutralising component in serum may be absorbed on cells infected with measles virus. Previous exposure to either virus can modify the antibody titres to both viruses. Recent epidemiological papers do not support any possible relation between the keeping of household dogs or cats and multiple sclerosis. No other canine virus is associated with multiple sclerosis. Nevertheless, there is renewed support for a possible relation between measles infection at a later age than normal and the subsequent development of multiple sclerosis.—E M R CRITCHLEY, consultant neurologist, Preston.

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