ABC of diseases of liver, pancreas, and biliary system
Liver tumours

I J Beckingham, J E J Krige

Tumours of the liver may be cystic or solid, benign or malignant. Most are asymptomatic, with patients having normal liver function, and they are increasingly discovered incidentally during ultrasonography or computed tomography. Although most tumours are benign and require no treatment, it is important for non-specialists to be able to identify lesions that require further investigation and thus avoid unnecessary biopsy. Modern imaging combined with recent technical advances in liver surgery can now offer many patients safe and potentially curative resections for malignant, as well as benign, conditions affecting the liver.

Cystic liver lesions

Cystic lesions of the liver are easily identified by ultrasonography. Over 95% are simple cysts. Asymptomatic cysts are regarded as congenital malformations and require no further investigation or treatment as complications are rare. Aspiration and injection of sclerosants should be avoided as it may cause bleeding and infection and does not resolve the cyst. Rarely, simple cysts can grow very large and produce compressive symptoms. These are managed by limited surgical excision of the cyst wall (cyst fenestration), which can usually be done laparoscopically.

About half of patients with simple cysts have two or more cysts. True polycystic liver disease is seen as part of adult polycystic kidney disease, an uncommon autosomal dominant disease that progresses to renal failure. Patients nearly always have multiple renal cysts, which usually precede development of liver cysts. Liver function is normal, and most patients have no symptoms. Occasionally the cysts cause pain because of distension of the liver capsule, and such patients may require cyst fenestration or partial liver resection.

Thick walled cysts and those containing septa, nodules, or echogenic fluid may be cystic tumours (cystadenoma, cystadenocarcinoma) or infective cysts (hydatid cysts and abscesses; see later article in this series), and patients should be referred for specialist surgical opinion. Cystic dilatations of the bile ducts (Caroli's disease) are important as they may produce cholangitis and are premalignant with the potential to develop into cholangiocarcinoma.

Benign tumours

Benign liver tumours are common and are usually asymptomatic. Although most need no treatment, it is important to be able to differentiate them from malignant lesions.
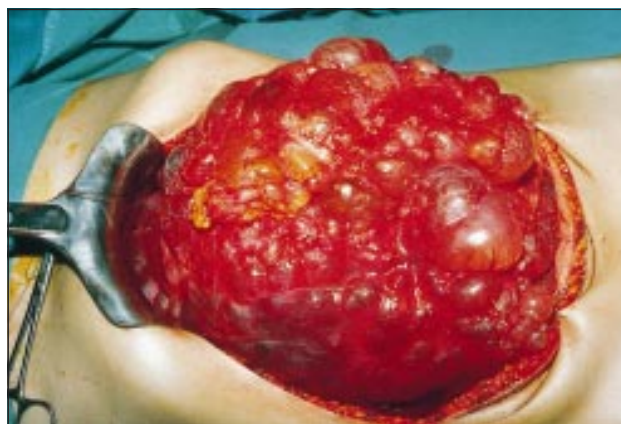
Haemangiomas
Haemangiomas are the commonest benign solid tumours of the liver, with an incidence in the general population of around 3%. Those over 10 cm in diameter occasionally produce non-specific symptoms of abdominal discomfort and fullness and, rarely, fever, thrombocytopenia, and hypofibrogenaemia due to thrombosis in the cavernous cavities. Malignant transformation and spontaneous rupture are rare. Contrast enhanced computed tomography is usually sufficient to

Liver biopsy of a tumour mass should be reserved for patients with suspected malignancy who are not suitable for surgery and in whom the diagnosis may have clinical impact—for example, ovarian or neuroendocrine tumours, carcinoid, or lymphoma

Characteristics of simple cysts
- Thin walled
- Contain clear fluid
- Contain no septa or debris
- Surrounded by normal liver tissue
- Usually asymptomatic
- Present in 1% of population

Polycystic liver disease
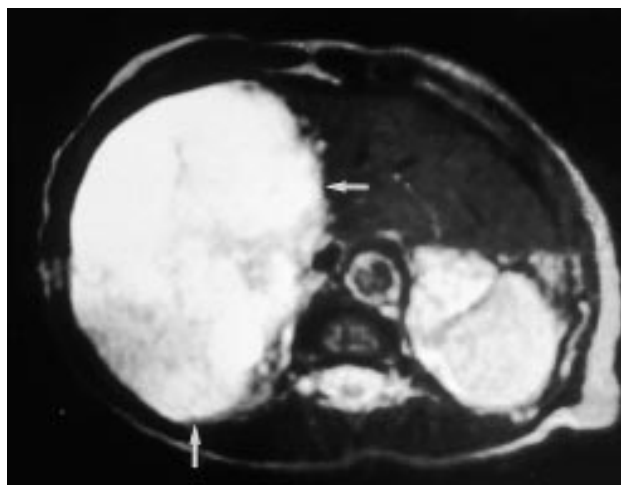
T2 weighted magnetic resonance image of large benign haemangioma showing light bulb sign

diagnose most haemangiomas, and in equivocal cases magnetic resonance imaging or technetium-99 labelled red blood cell scintigraphy will confirm the diagnosis. Angiography and biopsy are seldom required. Resection is indicated only for large symptomatic tumours.

Liver cell adenoma and focal nodular hyperplasia

These uncommon tumours occur predominantly in women of childbearing age. Liver cell adenoma became more prevalent with the widespread use of oral contraceptives in the 1960s, but the reduced oestrogen content of modern contraceptives has made it less common. Most patients present with pain due to rapid tumour growth, intratumour haemorrhage, or the sensation of a mass. The risk of rupture is 10%, and malignant transformation is found in 10% of resected specimens. Patients should have liver resection to prevent these events.

Focal nodular hyperplasia is not related to use of oral contraceptives, is usually asymptomatic, and is not premalignant. Mass lesions usually contain a central stellate scar on computed tomography and magnetic resonance imaging. It does not require treatment unless symptomatic.

In a small proportion of patients a firm radiological diagnosis cannot be reached and the distinction from a malignant liver tumour is uncertain. Histological distinction between focal nodular hyperplasia and cirrhosis and between liver cell adenoma and well differentiated hepatocellular carcinoma can be difficult with tru-cut biopsy or fine needle aspiration samples, and biopsy has the added risk of bleeding and tumour seeding. The histology should therefore be determined by surgical resection, which in specialist centres has a mortality of < 1%.

Malignant tumours
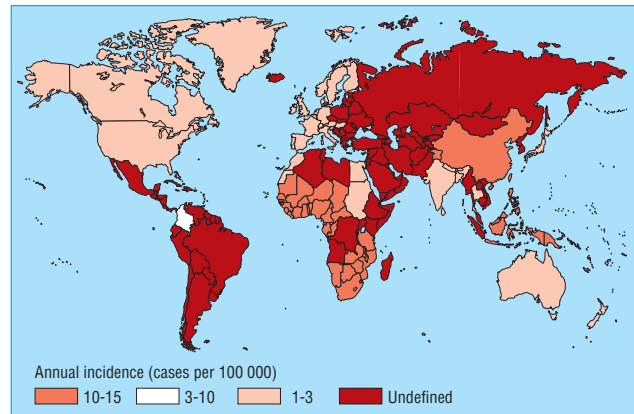
Hepatocellular carcinoma

Hepatocellular carcinoma is uncommon in the United Kingdom and accounts for only 2% of all cancers. Worldwide there are over one million new cases a year, with an annual incidence of 100 per 100 000 men in parts of South Africa and South East Asia. The incidence of hepatocellular carcinoma is increased in areas with high carrier rates of hepatitis B and C and in patients with haemochromatosis. More than 80% of hepatocellular carcinomas occur in patients with cirrhotic livers. Once viral infection is established it takes about 10 years for patients to develop chronic hepatitis, 20 years to develop cirrhosis, and 30 years to develop carcinoma. In African and Asian countries aflatoxin, produced as a result of contamination of imperfectly stored staple crops by *Aspergillus flavus,* seems to be an independent risk factor for the development of hepatocellular carcinoma, probably through mutation of the p53 suppressor gene. Seasonal variation in incidence is seen in these countries.

In patients with cirrhosis, the diagnosis should be suspected when there is deterioration in liver function, an acute complication (ascites, encephalopathy, variceal bleed, jaundice), or development of upper abdominal pain and fever. Ultrasonography will identify most tumours, and the presence of a discrete mass within a cirrhotic liver, together with an α fetoprotein concentration above 500 ng/ml is diagnostic. Biopsy is unnecessary and should be avoided to reduce the risk of tumour seeding. Surgical resection is the only treatment that can offer cure. However, owing to local spread of tumour and severity of pre-existing cirrhosis, such treatment is feasible in less than 20% of patients. Average operative mortality is 12% in cirrhotic patients, and five year survival is around 15%.
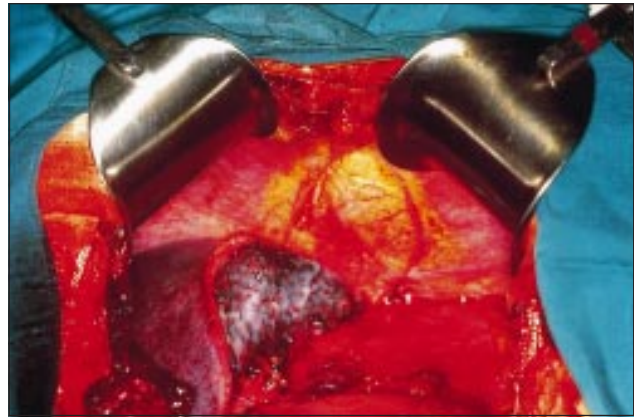
Intraoperative view after left hepatectomy—raw surfaces of liver are coated with fibrin glue after resection to aid haemostasis and prevent small bile leaks

Hepatocellular carcinoma is the commonest malignant tumour worldwide

Annual incidence (cases per 100 000)
10-15　　3-10　　1-3　　Undefined

Distribution of hepatocellular carcinoma

Computed tomogram of large hepatocellular carcinoma

Patients with cirrhosis and small (<5 cm) tumours should have liver transplantation. Injection of alcohol or radiofrequency ablation can improve survival in patients with small tumours who are unsuitable for transplantation. For larger tumours, transarterial embolisation with lipiodol and cytotoxic drugs (cisplatin or doxorubicin) may induce tumour necrosis in some patients.

In patients without cirrhosis, hepatocellular carcinomas usually present late with an abdominal mass and abnormal liver function. Computed tomography has a greater sensitivity and specificity than ultrasonography, particularly for tumours smaller than 1 cm. α Fetoprotein concentrations are raised in 80% of patients but may also be raised in patients with testicular or germ cell tumours.

Fibrolamellar carcinoma is an important subtype of hepatocellular carcinoma. It occurs in patients without cirrhosis or previous hepatitis infection. It accounts for 15% of hepatocellular carcinoma in the Western hemisphere. The prognosis is better than for other hepatocellular carcinomas, with a five year survival of 40-50% after resection.

Metastatic tumours

Liver metastases are common and are found in 40% of all patients dying from cancer. They are most frequently associated with carcinomas of the gastrointestinal tract (colorectal, pancreas, and stomach) but are nearly as common in carcinomas of the bronchus, breast, ovary, and lymphoma. With the exception of liver metastases of colorectal cancer, tumour deposits are almost always multiple and seldom amenable to resection.

Colorectal liver metastases

Around 8-10 % of patients undergoing curative resection of colorectal tumours have isolated liver metastases suitable for liver resection, equivalent to around 1000 patients in the United Kingdom a year. Half will have metastases at the time of diagnosis of the primary tumour (synchronous metastases) and most of the rest will develop metastases within the next three years (metachronous metastases).

Without surgical resection the five year survival rate for all patients with liver metastases is zero, compared with an overall five year survival after resection of 30%. Patients most suited for resection are those with fewer than three or four metastases in one lobe of the liver, but tumours need not be confined to one lobe. The principle of complete tumour removal, however, remains a prerequisite, and one limitation is the need to leave enough liver to function. This depends both on the extent and distribution of the tumour burden and the general fitness of the patient and his or her liver. The liver has an enormous capacity for regeneration. A fit patient with a healthy liver will regenerate a 75% resection within three months. Age is only a relative contraindication, and several series have reported low mortality in septuagenarians.

Liver resection

Liver resection has advanced rapidly over the past two decades because of several important developments. The segmental anatomy of the liver, with each of the eight segments supplied by its own branch of the hepatic artery, portal vein, and bile duct, was first described by Couinaud in 1957. It is now possible to remove each of these segments individually when required, reducing the amount of normal liver unnecessarily removed.
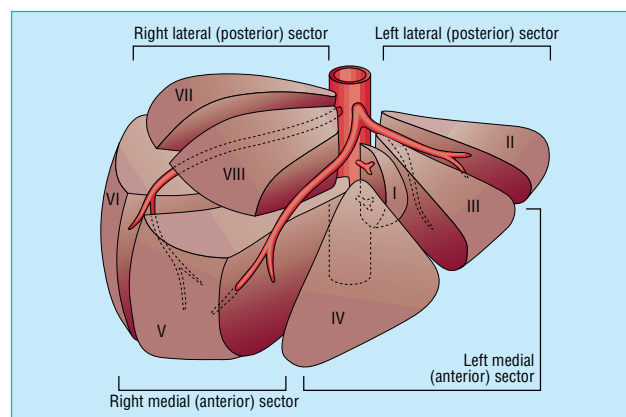
Subsequently surgical techniques have been developed to divide the liver parenchyma, either by crushing with a clamp or by ultrasonic dissection, allowing the vascular and biliary radicals

Inoperable extensive liver metastases

Solitary metastasis in segment IV of liver

Couinaud's segmental anatomy of liver

to be individually ligated. Blood loss has been reduced by occlusion of the vascular inflow (Pringle manoeuvre) and where possible the appropriate hepatic vein, together with lowering of the central venous pressure during resection, and blood transfusion is now unnecessary in 60% of major liver resections.

Improvements have also occurred in anaesthetic and postoperative care, including epidural anaesthesia to reduce postoperative pain and chest complications and the ability to manage postoperative fluid or bile collections by radiological or endoscopic drainage. These developments mean that the median hospital stay for patients having liver resection is now 7-10 days and mortality is around 5%. Liver resection has evolved from a hazardous bloody procedure into a routine operation.

J E J Krige is associate professor of surgery, Groote Schuur Hospital and University of Cape Town, South Africa

Summary points

- Simple liver cysts are common, benign, and require no treatment
- Patients with solitary liver masses should be referred to a hepatobiliary surgeon and liver biopsy avoided
- Liver resection is a safe procedure in non-cirrhotic patients, with a mortality around 5%
- 10% of patients with colorectal cancer develop potentially curable liver metastases and should have six monthly liver ultrasonography or computed tomography
- Five year survival after resection of colorectal metastases is >30%

Further reading

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- Neeleman N, Andersson R. Repeated liver resection for recurrent liver cancer. *Br J Surg* 1996;83:885-92

Lesson of the week
Splenic trauma complicating cardiopulmonary resuscitation

A Fitchet, R Neal, P Bannister

Unexplained hypotension after cardiopulmonary resuscitation might be due to intra-abdominal trauma and concealed haemorrhage

Manchester Heart Centre, Manchester Royal Infirmary, Manchester M13 9WL
A Fitchet
specialist registrar in cardiology

Blackburn Royal Infirmary, Bolton Road, Blackburn BB2 3LR
R Neal
specialist registrar in elderly medicine

Department of Medicine, Manchester Royal Infirmary
P Bannister
consultant physician

Correspondence to:
A Fitchet
Alan.Fitchet@mhc.cmht.nwest.nhs.uk

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Cardiopulmonary resuscitation can result in trauma to abdominal organs. We report two cases of splenic rupture causing life threatening haemorrhage.

Case reports

Case 1—A 64 year old woman who had undergone coronary artery bypass grafting 10 years previously had a cardiorespiratory arrest at a railway station late one night. Cardiopulmonary resuscitation was started immediately by bystanders and continued for 20 minutes until paramedics arrived. Ventricular fibrillation was confirmed, and she was externally defibrillated. On arrival at hospital she was alert and breathing spontaneously but hypotensive with a blood pressure of 80/40 mm Hg and a sinus tachycardia of 100 beats/min. Clinical examination suggested hypovolaemia with lowered central venous pulse pressure, normal heart sounds, and clear breath sounds. Electrocardiography confirmed an acute inferior myocardial infarction. Thrombolysis was not given because of prolonged resuscitation. She clinically improved on challenge with intravenous fluid. The central venous pulse became visible and her blood pressure rose to 120/70 mm Hg. Over the next hour progressive hypotension recurred, once again with clinical evidence of hypovolaemia. Blood pressure was restored with further intravenous fluid. An echocardiogram excluded major pericardial effusion, showing a non-dilated left ventricle with inferior wall akinesia and overall moderate function. At this stage the patient complained of left sided abdominal pain, with tenderness elicited over the left hypochondrium. Chest *x* ray

films taken in the erect position showed no evidence of rib fractures or subdiaphragmatic gas. Ultrasonography showed free fluid in the abdominal cavity, and aspiration of this fluid confirmed blood. Computed tomography of the abdomen showed a tear in the upper pole of the spleen (figure). At emergency laparotomy 2 litres of free blood were found, and the ruptured but histologically normal spleen was removed. She made a full recovery after a prolonged postoperative course, and she was discharged from hospital six weeks later.

Case 2—A 50 year old man attended the casualty department with general malaise. Examination revealed lower limb cellulitis. He had a fever at 37.9°C, and his blood pressure was 114/70 mm Hg and heart rate 120 beats/min. Initial investigations showed a haemoglobin concentration of 36 g/l (normal range 130-180) (mean corpuscular volume 96 fl (80-97)), white cell count of 2×10^9/l (4-11), and platelet count of l34 $\times 10^9$/l (150-400); a bone marrow aspirate later confirmed megaloblastic anaemia. Intravenous piperacillin and gentamicin were started. Soon after this he developed bradycardia followed by a cardiorespiratory arrest requiring two brief episodes of cardiopulmonary resuscitation and insertion of a temporary pacing wire. He was transferred to the intensive care unit and was transfused 12 units of blood over the next 48 hours. He was given folate and vitamin B-12 supplementation. Blood cultures taken before insertion of the pacing wire confirmed *Staphylococcus aureus* septicaemia. Haemoglobin concentration increased to 90 g/l with transfusion over 48 hours and then decreased to 66 g/l over the next 24 hours. Ultrasonography and