Benign conditions of the liver

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Abstract
Benign conditions of the liver are relatively common and can pose diagnostic problems due to the difficulty in differentiating them from malignant hepatic lesions. They are usually asymptomatic and are discovered incidentally during investigations. They occasionally produce chronic non-specific symptoms and seldom present as an emergency.

Liver function tests are usually within the normal range and diagnosis is established by abdominal ultrasound, CT, MRI or PET. Further diagnostic tests include hepatic angiography, diagnostic laparoscopy and intraoperative ultrasonography. Biopsy or aspiration in the diagnosis of benign disease of the liver is controversial, but is clearly contraindicated in certain scenarios. Management strategies may vary from simple observation to complex hepatic resections.

Awareness of the natural history, clinical presentation and management strategies ensures appropriate initial treatment and prompt referral to specialist Hepatobiliary Units.

Keywords benign liver lesions; haemangioma; adenoma; focal nodular hyperplasia; benign hepatic tumours; liver cysts; liver abscess

Benign lesions of the liver are relatively common and are occasionally discovered during investigations for unrelated intra-abdominal disease. Most are asymptomatic, but chronic non-specific symptoms are occasionally encountered; acute presentations are rare.

In general, liver biochemistry is normal and does not provide definite diagnostic clues, but prompts towards benign disease. Diagnosis is established by ultrasonography, CT, MRI and PET or angiography alone or in combination. Occasionally, these are complemented by diagnostic laparoscopy and laparoscopic ultrasound. Tissue biopsy or aspiration cytology is at best controversial for most benign lesions, and is clearly contraindicated for some lesions (e.g. haemangiomas, echinococcal cysts). Biopsy should be undertaken only in those patients who will not have surgery; the risk of tumour seeding in malignant lesions is too high.

The management of benign conditions of the liver varies from simple observation to complex liver resections. Familiarity with the natural history, clinical significance and treatment concepts are crucial, to ensure adequate initial management and prompt referral of appropriate patients to specialist Hepatobiliary Units.

Classification
A detailed classification of the benign conditions of the liver is shown in Table 1. Most of these lesions are rare and most of those encountered in practice comprise haemangioma, benign liver cysts, liver cell adenoma, focal nodular hyperplasia and bile duct adenoma.

Solid benign lesions of the liver

Haemangiomas
Incidence: haemangiomas are the commonest benign lesion of the liver, with an estimated prevalence of 0.7–7.3% in the general population. They:

- peak in incidence between the third and fifth decade
- are more common in women
- are randomly distributed in the liver.

A relationship with hormonal activity has been suggested, explaining the increase in size and the higher risk of complications associated with pregnancy or oestrogen administration.

The aetiology is unclear, but they are considered to be benign congenital hamartomas that grow by progressive ectasia. They have a honeycomb appearance and are encapsulated by a rim of fibrous tissue, with a clear dissection plane between the lesion and normal liver parenchyma.

Presentation: most are clinically silent but large haemangiomas (>10 cm) can cause pain and other non-specific symptoms due to compression of surrounding organs. Pain is the main indication for surgery, but up to 42% of patients have associated disease (duodenal ulcer, gallstones, (see page 16), hiatus hernia) which may explain the persistence of symptoms even after haemangiomas have been removed. Rarely, haemangiomas can present acutely with spontaneous rupture into the abdominal cavity or with haemobilia or jaundice. Laboratory investigations are usually normal, but anaemia or a consumption coagulopathy can be noted.

Imaging: haemangiomas appear hyperechoic on abdominal ultrasonography, with a posterior acoustic shadow, and may be difficult to differentiate from primary or secondary tumours of the liver. Contrast-enhanced dynamic CT (Figure 1a) shows a ‘cotton wool’ appearance in the arterial phase; these findings are diagnostic and imaging using hepatic angiography has diminished considerably. MRI (Figure 1b) is sensitive (90%) and specific (93%), T2 images showing a characteristic ‘light bulb sign’. Laparoscopy (+ laparoscopic ultrasound) is useful for superficially placed lesions; needle biopsy is contraindicated.

Management: small lesions (<4 cm) do not require removal and patients should be reassured once the exact nature of the nodule has been ascertained. For all other patients, the risks of surgery
should be balanced against the natural history of untreated lesions, particularly because there is a minimal risk of rupture even in patients with large asymptomatic haemangiomas. Enucleation or resection is indicated for symptomatic patients with lesions >6 cm or if the nature of the lesion is uncertain despite thorough investigation. Arterial embolization/ligation can temporarily control haemorrhage; orthotopic liver transplantation (see page 42) has been used to treat giant unresectable haemangiomas.

Liver cell adenoma

Hepatocellular adenomas are benign lesions of epithelial origin, arising as a round, occasionally encapsulated masses within normal liver tissue. They are commonest in women between the third and fifth decade and have been associated with oral contraceptives. Despite their benign nature, these lesions have been associated with an increased risk of hepatocellular carcinoma.

Presentation: liver adenomas are quiescent, but occasionally patients present with a mass and pain or haemorrhagic shock due to intraperitoneal rupture/bleeding. Diagnosis is by ultrasound, CT and MRI. CT shows a hypodense lesion before contrast infusion, and a wide range of densities after administration. MRI shows a well-demarcated fat-containing or haemorrhagic lesion. Biopsy can be misleading and should not delay referral to a specialist centre.

Management: liver cell adenoma can harbour tumour foci and may be a premalignant lesion, so resection is indicated even for asymptomatic patients. For liver adenomas presenting as emergencies, temporary control of bleeding by packing or hepatic artery embolization can facilitate the transfer to a specialist centre; hepatic resection is the definitive treatment.

Focal nodular hyperplasia

Focal nodular hyperplasia is a non-neoplastic, tumour-like condition of the liver that may be difficult to differentiate from a liver adenoma. The appearance is that of a lobulated lesion localized in normal liver parenchyma. The incidence appears to be increasing, but is most probably due to increased detection due to improvements in imaging.

Presentation: vague abdominal discomfort is present in fewer than 10% of patients; most are asymptomatic. The diagnosis is established by ultrasonography or CT (Figure 2). The
pathognomonic finding is of a central scar (although this finding may not be consistently seen). Arteriography shows a zystypical ‘spoke wheel’ pattern, but has been replaced by MRI (98% specificity and 70% sensitivity).\textsuperscript{11} Contrast enhancement with gadolinium or superparamagnetic iron oxide particles may further improve the sensitivity and specificity of MRI.

Management: further treatment is not required if the diagnosis of focal nodular hyperplasia is beyond doubt and the patient is asymptomatic. Enucleation or resection is indicated in symptomatic cases or if the diagnosis is uncertain.

Nodular regenerative hyperplasia
Nodular regenerative hyperplasia is a benign proliferative process that occurs in older patients; it is associated with lymphoproliferative disorders, rheumatological diseases and organ transplantation. The hepatic architecture is replaced by regenerative nodules of hepatocytes in which liver cell dysplasia is occasionally seen. Patients are usually asymptomatic but can present with hepatomegaly and portal hypertension (see page 28). It should be suspected in patients with symptoms of portal hypertension but no cirrhosis on liver biopsy. Further treatment is not required in most cases, but liver transplantation may be indicated if patients develop hepatic failure.

Bile duct adenoma (bile duct hamartoma)
Bile duct adenomas can easily be mistaken for liver metastases at laparoscopy or laparotomy due to their macroscopic appearance as raised grey-white lesions on the liver surface. They are usually <1 cm in diameter and are asymptomatic. When encountered, excisional biopsy should be done to confirm the diagnosis. Histology confirms a mass of mature bile ducts surrounded by a fibrous stroma.

Miscellaneous benign tumours
The remainder of the solid tumours listed in Table 1 are rarely encountered in routine surgical practice.

Liver abscess
Pyogenic liver abscess
The incidence of pyogenic liver abscess has remained constant despite advances in antibiotic treatment. Choledocholithiasis or malignant biliary obstruction and associated sepsis (see Kumar; Hargunani, CROSS REFERENCES) are the primary causes for pyogenic abscesses.\textsuperscript{12} Sepsis in the portal system territory due to diverticulitis, pancreatitis or appendicitis is another major source; haematogenous spread from
non-gastrointestinal sources accounts for 10–20% of abscesses and may result from:

- bacterial endocarditis
- urinary sepsis
- osteomyelitis
- pneumonia
- intravenous drug abuse.

Direct extension after gallbladder, colonic, gastric or duodenal perforation may also occur. The cause is unknown in 15–35% of cases.

**Presentation** commonly includes pain in the right upper quadrant, fever, anorexia and weight loss. Laboratory investigations show leukocytosis, raised concentrations of acute-phase proteins (e.g. C-reactive protein), hypoalbuminaemia and anaemia. Ultrasonography shows a fluid-filled cavity; CT may show the primary source of infection and the extent of extrahepatic disease. Magnetic resonance cholangiopancreatography is particularly helpful in patients with symptoms and signs of biliary obstruction.

**Management:** successful treatment involves:

- drainage of the abscess
- appropriate antibiotic treatment (determined by microbiological culture)
- drainage of the biliary system (if obstructed).

Enteric organisms predominate and polymicrobial infections are often encountered, requiring broad-spectrum antibiotic therapy. Treatment should be continued for 3–6 weeks after successful drainage to ensure complete eradication of the infection. Percutaneous drainage is the first-line treatment and has a success rate of almost 100%.

Surgical drainage is indicated if percutaneous drainage fails and for patients who require treatment of the underlying disease. Drainage of the biliary tree is particularly important if the bile duct is obstructed, and can be done by endoscopic retrograde cholangiopancreatography, percutaneous transhepatic biliary drainage or a combination of the two methods.

**Amoebic abscess**

A liver abscess is the commonest extra-intestinal presentation of infection with *Entamoeba histolytica*. Between 75% and 90% of abscesses are localized in the right hemiliver and presentation is similar to that of a pyogenic abscess.

Ultrasonography and CT shows an abscess with a poorly defined boundary (unlike the pyogenic abscess). Diagnosis is by detecting serum antiamoeba antibodies using an indirect haemaglutination test or by enzyme-linked immunosorbent assay.

Metronidazole is the first-line treatment and lack of response indicates incorrect diagnosis or secondary bacterial infection. Percutaneous drainage produces a sterile fluid with an ‘anchovy paste’ appearance, but should be reserved for patients who fail medical treatment; open drainage is for complicated cases.

**Hydatid cyst**

Hydatid cysts are the result of infection with *Echinococcus granulosus* or *Echinococcus multilocularis*. They are usually unilocular and have a characteristic appearance: an external laminated membrane (ectocyst layer) and an internal germinal layer (endocyst layer) that produces the hydatid fluid, the brood capsules and daughter cysts.

**Presentation:** clinical symptoms are often insidious, but history-taking should identify previous contact with dogs or sheep. Pain in the right upper quadrant may be the only symptom. Jaundice is rare, but may be caused by extrinsic biliary compression or cyst rupture into the biliary tree.

**Investigations** reveal abnormal liver function tests and eosinophilia. Diagnosis is helped by positive serology and a typical appearance on ultrasound or CT of a cyst containing daughter cysts or ‘hydatid sand’ (brood capsules).

**Management:** percutaneous aspiration/drainage is contraindicated due to the risk of anaphylaxis and dissemination. Surgery is indicated for most patients, due to the natural history of the disease i.e. progressive enlargement of the cysts and risk of rupture into the peritoneal or thoracic cavity. The principles of surgery are to:

- eradicate the parasite by aspiration of the hydatid fluid and remove the endocyst and its contents
- prevent spillage of cyst contents by packing the operative field
- obliterate the residual cavity by marsupialization, plication or omental packing.

Hepatic resection may be considered for small, peripheral lesions and anthelmintic agents (p.o.) can be used perioperatively.

**Simple cysts of the liver**

Non-parasitic liver cysts result from a congenital malformation of the intrahepatic bile ducts and can be single, multiple or diffuse (polycystic). They:

- are lined by a single layer of cuboidal or columnar epithelial cells
- contain clear fluid
- do not communicate with the biliary tree.

There is a higher prevalence in females; huge cysts (>10 cm in diameter) are almost exclusively present in women aged >50 years.

**Presentation:** most simple cysts are asymptomatic, but symptoms may include abdominal pain or symptoms due to compression of surrounding viscera. Complications (e.g. rupture, intracystic haemorrhage, infection, torsion, jaundice, portal hypertension) are rare.

**Imaging:** ultrasonography is diagnostic and shows a well-defined, anechoic area in the liver, with no obvious cyst wall and no acoustic shadow. CT provides more accurate characterization and can differentiate cysts with intracystic haemorrhage from hydatid cysts.

**Management:** asymptomatic cysts do not require treatment. Symptomatic or complicated cysts require intervention and several treatment strategies have been advocated. Laparoscopic...
deroofing is the preferred treatment, but an open approach may be required depending on the location of the cyst.17 Percutaneous aspiration and sclerotherapy reduces the rate of symptomatic and radiological recurrence, but has a risk of introducing infection and is rarely indicated.18 A more radical hepatic resection is indicated for centrally located cysts, which tend to recur after deroofing.

**Polycystic liver disease**

Polycystic liver disease is part of an autosomal dominant disorder and is associated with adult polycystic kidney disease (see Callaghan, CROSS REFERENCES). Histologically, the cysts are identical to simple cysts, but they are distributed throughout the liver and can replace most of the parenchyma. The overall prognosis of the disease is dictated by the renal involvement because of the significant risk of renal failure.

**Presentation:** most patients are asymptomatic. Abdominal distension, a palpable mass or respiratory compromise may be present due to a significantly enlarged liver. Ultrasound and CT confirm multiple cysts replacing most of the liver parenchyma.

**Management:** asymptomatic patients do not require intervention. Extensive deroofing has been advocated for symptomatic relief in patients complaining of significant abdominal discomfort.19 A more aggressive approach combining liver resection with deroofing of residual cysts allows decompression of the liver parenchyma and produces better long-term results.20 Liver transplantation is indicated in selected cases with hepatic failure or persistent discomfort or if other surgical treatments have failed.

**Cystadenoma**

Cystadenoma is a solitary, multiloculated lesion that tends to recur and has malignant potential. Patients present with vague abdominal symptoms. Histology shows a single layer of cuboidal/columnar cells that forms occasional intracystic papillary projections.

Diagnosis is by ultrasound and CT, which show a typical appearance of an irregular anechoic, fluid-filled mass, with irregular margins and internal echoes due to septae or papillary projections from the cystic wall. Malignant transformation may be suspected radiologically due to septal calcifications and large projections into the cyst lobules.21 If diagnosed, a cystadenoma should be excised, even if asymptomatic.

**Summary**

Practice points are shown in Table 2.

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**REFERENCES**


**CROSS REFERENCES**


FURTHER READING

Practice points
- Benign lesions of the liver are often encountered in surgical practice
- The natural history and presentation of benign hepatic lesions is important because successful management requires an accurate diagnosis
- Inappropriate investigations may give rise to morbidity and could delay and compromise definitive treatment
- Most benign lesions of the liver are asymptomatic and do not require surgical intervention
- Liver resection can be done with minimal morbidity and mortality in selected cases in specialist Hepatobiliary Units
- Symptomatic lesions, or lesions that may grow or undergo malignant transformation, require surgical treatment

Table 2