

Imaging focal liver lesions in children

RAD Magazine, 39, 453, 29-30

by Dr H Woodley
Consultant paediatric radiologist,
Leeds Teaching Hospitals Trust

email: helen.woodley@leedsth.nhs.uk

There is a wide differential diagnosis of focal liver lesions in children including inflammatory lesions, cystic lesions and benign and malignant neoplasms. Imaging confirms the presence of a focal liver lesion, assesses the extent of disease and characterises the lesion. Initial ultrasound findings will determine if other imaging modalities are required, which include nuclear medicine (NM), computed tomography (CT) and magnetic resonance imaging (MRI). Imaging may also guide biopsy and be used in therapeutic intervention. Clinical findings and laboratory tests are important considerations in evaluation.

This article aims to provide a practical approach to the assessment of the focal liver lesion in a child and review in more detail pathologies unique to the paediatric age group.

Clinical findings

The age of the child, clinical presentation and findings, laboratory tests and underlying syndromes or diseases are crucial in narrowing the differential diagnosis.

The most common liver masses in children under three years are hepatoblastoma and infantile haemangioendothelioma (IHE), while in older children hepatocellular carcinoma is the most common malignant liver tumour (table 1).

<3 years	>3 years
Hepatoblastoma	Hepatocellular carcinoma (HCC)
Metastases	Embryonal sarcoma
Haemangioendothelioma	Metastases
Cystic mesenchymal hamartoma	Fibronodular hyperplasia
	Adenoma
	Fibrolamellar HCC

TABLE 1
Differential diagnosis of liver masses by age.

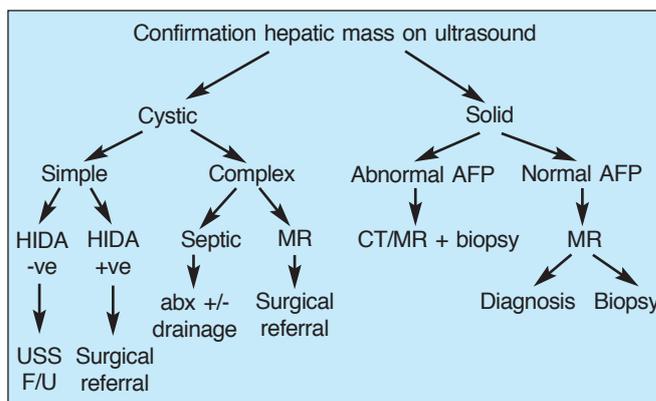
Most children present with an abdominal mass, although presentation may be with non-specific abdominal pain or an incidental finding. However, in the context of sepsis underlying liver abscess is the major differential, while an infant presenting with congestive cardiac failure (CCF) or consumptive coagulopathy suggests IHE.

Several syndromes or underlying diseases predispose to liver tumours (table 2).

Alpha fetoprotein (AFP) is raised in 90% of children with hepatoblastoma and 70% of children with hepatocellular carcinoma, and thus of key importance. Elevated gonadotrophins may be seen with hepatoblastoma and metastatic choriocarcinoma and cause precocious puberty.

Hepatoblastoma	Beckwith wiedemann Hemihypertrophy Fetal alcohol syndrome Familial polyposis Gardners syndrome VLBW
Hepatocellular carcinoma	Viral hepatitis B & C Glycogen storage disease Tyrosinaemia Alpha 1 antitrypsin deficiency Haemochromatosis Portocaval shunts
Adenoma	Glycogen storage disease Diabetes type MODY3 OCP

TABLE 2
Predisposing factors for focal liver lesions.



Imaging algorithm.

Aims of imaging

Ultrasound is the first imaging modality of choice due to its accessibility, lack of ionising radiation and no requirement for GA or sedation. Examination includes a full survey of the abdomen and pelvis with curvilinear and high frequency linear probes including colour Doppler examination of any masses and the hepatic vasculature. Assessment should confirm intrahepatic location, presence of solitary or multiple lesions¹ and extrahepatic disease, eg adrenal mass with multiple liver lesions suggests metastatic neuroblastoma. Signs of pre-existing chronic liver disease should be sought. Characterisation includes assessment of cystic or solid nature, calcification, vascularity, involvement of hepatic vessels (thrombosis of vessels is most likely related to malignant lesions) and biliary dilatation (duct dilatation may be secondary to compression by central masses but raises the possibility of rhabdomyosarcoma or cholangiocarcinoma).

Further cross-sectional imaging with CT or MRI provides characterisation of solid or complex lesions and maps the exact extent of disease. MRI is the preferred imaging modality of choice due to the lack of ionising radiation and potential use of liver-specific contrast agents but in most children under six years requires GA. CT has the disadvantage of ionising radiation but may avoid the need for sedation or GA and enables full staging in cases of malignant disease.

Differential diagnoses

Inflammatory lesions

Inflammatory lesions should be considered in the context of: pyrexia of unknown origin; known abdominal sepsis, eg

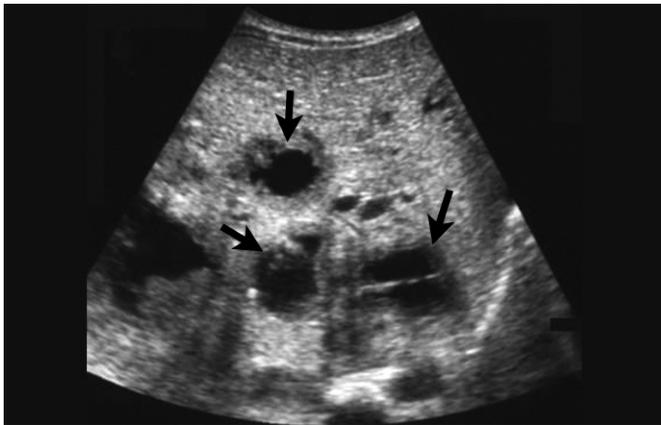


FIGURE 1
 Ultrasound demonstrates multiple focal liver abscesses in a child presenting with sepsis and jaundice secondary to an obstructed type 1 choledochal cyst.

Simple liver cyst
Cystic mesenchymal hamartoma
Choledochal cyst
Foregut cyst
Syndromic, eg polycystic renal disease
Inflammatory, eg echinococcal, amoebic
Extrahepatic, eg omental, mesenteric

TABLE 3
 Differential diagnosis of cystic liver lesions in the child.

appendicitis; immunocompromise, eg neutropenic sepsis; or immunodeficiency. In the neonate abscesses may be secondary to umbilical vein catheterisation. On ultrasound lesions are often multiple but may be solitary, the lesions are variable in appearance, usually illdefined and either heterogenous or predominately hypoechoic (**figure 1**). Aspiration and drainage can be performed under ultrasound guidance if there is failure to respond to antibiotic treatment or diagnostic uncertainty.

Cystic lesions

The differential diagnosis for cystic liver lesions is shown in **table 3**. If the cyst is small and simple follow-up ultrasound may be adequate. Hepatobiliary scintigraphy using Tc 99m iminodiacetic acid derivatives (HIDA) can confirm connection with the biliary tract therefore suggesting a choledochal abnormality. Further cross-sectional imaging by CT or MRI should be performed in large or complex lesions where surgery is considered.

Benign hepatic masses

One third of primary liver tumours in children are benign.² The differential includes lesions unique to children and more common in adults³ (**table 4**). IHE is the most common benign hepatic tumour in infancy with cystic mesenchymal hamartoma the second. Specific imaging features may enable a diagnosis to be reached, although biopsy will be required if there remains diagnostic uncertainty.

It is beyond the scope of this article to describe the imaging features of all paediatric liver tumours but certain lesions specific to paediatrics are described.

Infantile haemangioendothelioma (IHE) is a benign vascular tumour. The natural history is rapid proliferation followed by involution. Ninety per cent of lesions present in the first six months of life, one-third within the first month. Clinical presentation may be with a liver mass or CCF secondary to large arteriovenous shunts or consumptive coagulopathy (Kassabach-Merritt syndrome). Laboratory tests can show anaemia and mild hyperbilirubinaemia but AFP is not raised.

Benign	Malignant
Infantile haemangioendotheliomata	Metastases
Cystic mesenchymal hamartoma	Hepatoblastoma
Cavernous haemangioma	Hepatocellular carcinoma
Focal nodular hyperplasia	Fibrolamellar carcinoma
Hepatic adenoma	Rhabdomyosarcoma
Focal fat	Embryonal sarcoma
Nodular regenerative hyperplasia	

TABLE 4
 Liver neoplasms in children.

On ultrasound multifocal lesions are small, well delineated homogenous and usually hypoechoic, while solitary lesions tend to be large and heterogenous with central haemorrhage, necrosis, fibrosis and calcification. High flow is seen within the lesions with enlargement of the hepatic arteries and veins.

On CT precontrast lesions are hypoattenuating with speckled calcification in 50%. Dynamic post contrast imaging is diagnostic with intense peripheral nodular enhancement on arterial phase followed by progressive centripetal infilling on portal venous and delayed imaging. In large lesions with central fibrosis and necrosis, complete central enhancement may not occur.

On MRI lesions on T1w pre-contrast sequences are low signal, hyperintense on T2w sequences with heterogeneity in larger unifocal lesions. On dynamic post gadolinium imaging there is intense peripheral nodular enhancement with centripetal infilling on portal venous and delayed filling (**figure 1**).

No treatment is required in asymptomatic lesions while symptomatic lesions may be treated by steroids, vincristine, interferon, embolisation, surgery or transplantation.

Mesenchymal hamartoma (MH) present with abdominal distension, abdominal pain or incidentally on antenatal scans. Liver function tests and AFP are normal. MH are a developmental anomaly. The predominance of the mesenchymal or cystic component determines the imaging findings, varying from a few large cysts to a solid mass. MH are usually solitary although occasionally multifocal, with case reports of malignant transformation.⁴

On ultrasound cystic lesions contain low level echoes with echogenic septae and echogenic solid components (**figure 2**). Calcification is rare. At CT appearances are of a complex cystic mass with enhancement of the septa and solid components. MRI appearances will again depend on the cystic versus mesenchymal components and protein content of the fluid. Solid portions are hypointense on T1 sequences but variable on T2 sequences due to fibrosis, while cystic components are hyperintense on T2 sequences and variable on T1 sequences depending on the protein content. Enhancement is limited to septa and solid components. MH is best treated by complete excision.

Malignant hepatic masses

Metastatic disease is the most common neoplasm involving the liver – most commonly neuroblastoma, Wilms tumour or lymphoma.⁵ However, one third of primary liver tumours are malignant although account for just 1-2% of all childhood cancers.⁶ Hepatoblastoma is the most common primary malignant tumour in children under five years with hepatocellular carcinoma the most common in older children.⁷ Other malignant tumours in order of frequency are fibrolamellar carcinoma (adolescents without raised AFP), undifferentiated embryonal sarcoma (presents in young children as a cystic and mucoid tumour), angiosarcoma and embryonal rhabdomyosarcoma (**table 4**).

Hepatoblastoma (HBL) can be associated with underlying syndromes but usually presents with abdominal enlargement and non-specific symptoms. Metastatic disease

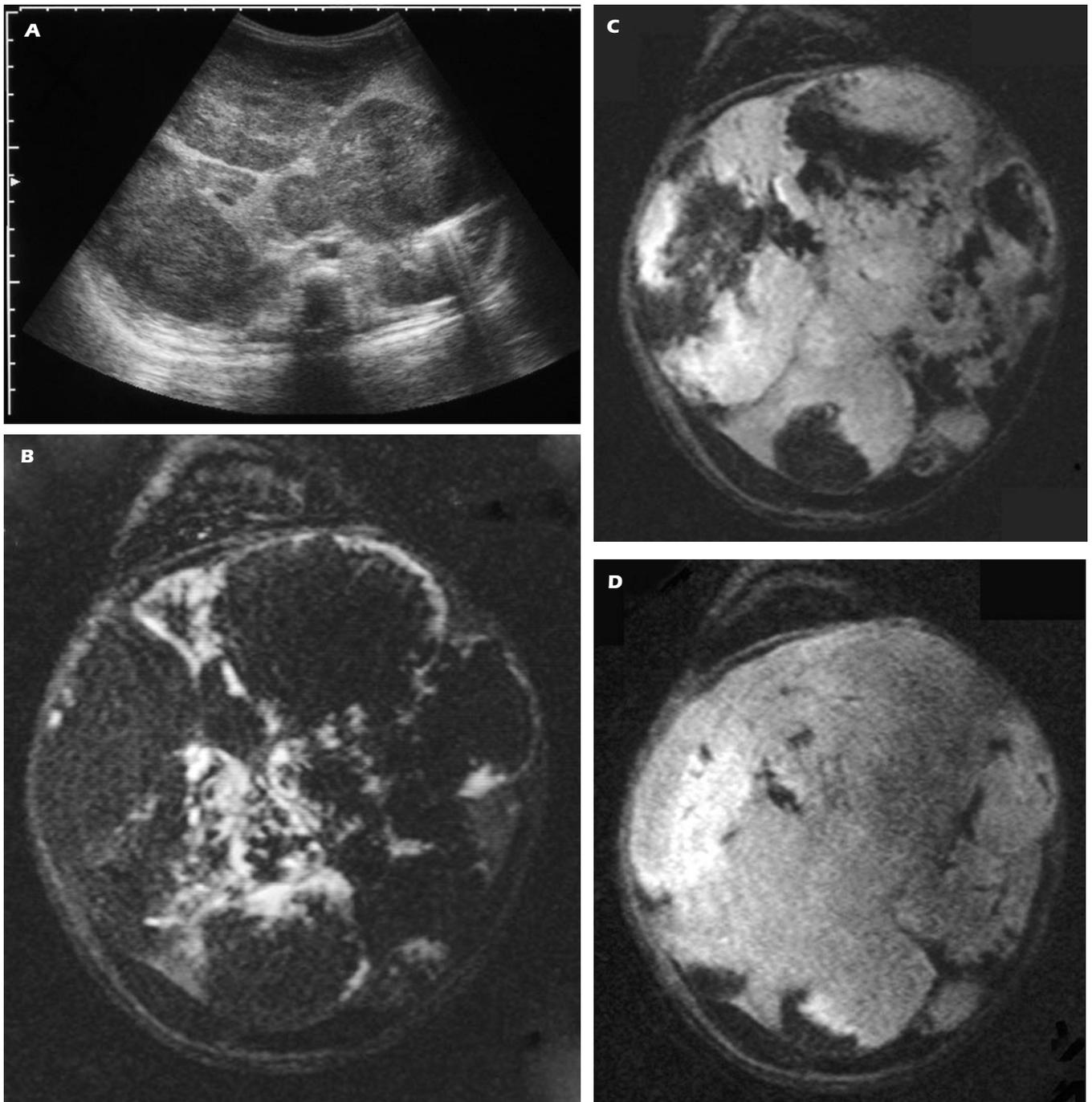


FIGURE 2

Multiple infantile haemangioendotheliomata in a six-week-old baby girl presenting with CCF. (A) Ultrasound demonstrates multiple hypoechoic focal liver lesions. Dynamic post gadolinium coronal oblique images in (B) arterial, (C) portal venous and (D) delayed phases show characteristic enhancement pattern.

most commonly involves the lungs (10-20%). Ninety per cent of patients have raised AFP. Levels are used to monitor response to treatment and detect recurrence. Occasionally HBL may secrete human chorionic gonadotrophin.

HBL derives from embryonic and fetal hepatocytes and usually presents as a large, well circumscribed mass, although multifocal or diffuse disease and hepatic vasculature invasion may occur.

At ultrasound HBL are usually hyperechoic or heterogeneous with foci of calcification and haemorrhage. CT usually demonstrates a well demarcated hypointense mass with speckled or amorphous calcification in 50% which enhances mildly. MR appearances range from a hypointense T1, hyperintense T2 mass to a more heterogeneous lesion due to haemorrhagic and fibrotic components (**figure 4**). CT and MRI provide accurate staging prior to preoperative chemotherapy and surgery.⁸

Hepatocellular carcinoma (HCC). In Western countries pre-existing liver disease is found in 50% of children.

HCC may be detected during screening or with an abdominal mass with or without abdominal pain, weight loss and anorexia. Metastatic disease is present in up to 50% at time of diagnosis. AFP is elevated in 70%.

HCC is a malignant tumour of hepatocytes with histological and gross features similar to adult types. Lesions may be solitary, multifocal or diffuse and vascular invasion is common.

Imaging features are similar to those in adults although small lesions are less common. On ultrasound small lesions are homogenous and usually hypoechoic, larger lesions are heterogeneous due to fat, haemorrhage and necrosis. At CT masses are hypodense precontrast and hypervascular on arterial phase imaging, with variable washout on portal venous imaging. On MR lesions are slightly hyperintense on T2 and variable on T1 often heterogeneous in larger lesions. Lesions are hypervascular on arterial imaging and may show washout on portal venous phase. CT and MRI provide accurate staging prior to treatment with complete

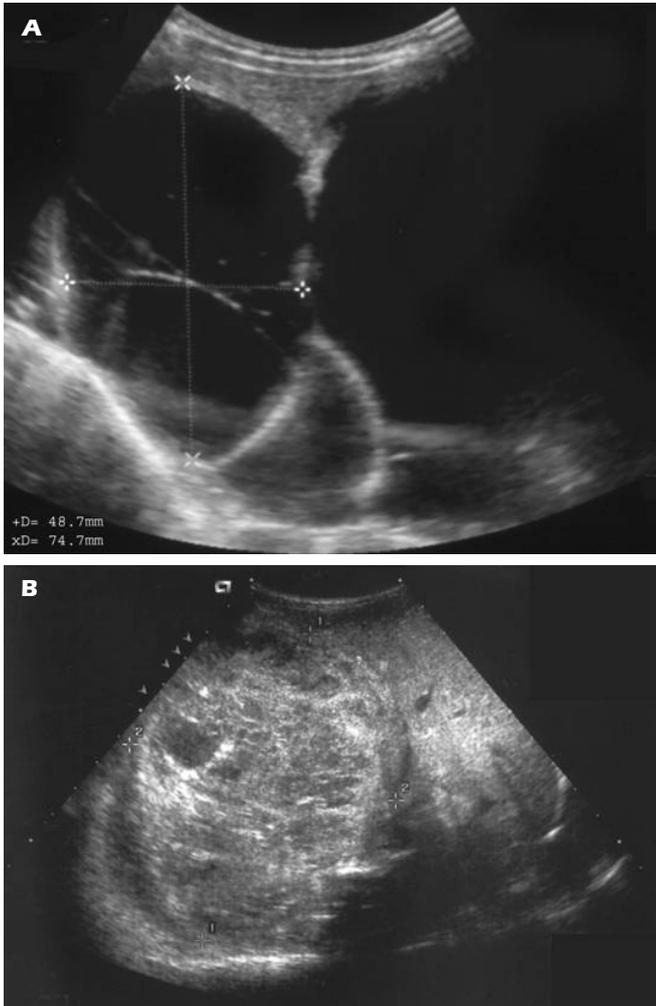


FIGURE 3
 Ultrasound demonstration of variable appearances of mesenchymal hamartoma. (A) Multicystic lesion with septae in three-month-old girl presenting with antenatally diagnosed intrahepatic cysts. (B) Complex solid and cystic lesion presenting in neonate with gross abdominal distension.

tumour resection the best option for long-term survival. Only one third of cases in children have resectable disease due to multifocal or massive involvement of the liver, major vascular involvement or metastatic disease.

Conclusion

There is a wide and varied differential diagnosis for focal liver lesions in children. Clinical findings and laboratory tests play a crucial role in narrowing the differential diagnosis. Ultrasound is the first imaging modality of choice but complex cysts or solid mass lesions are likely to require further evaluation by CT or MRI. A specific diagnosis may be possible on the basis of clinical findings, laboratory tests and imaging findings but biopsy will be required if a diagnosis is not possible or alpha feto protein is raised in keeping with a malignant mass lesion.

References

- 1, Duigenan S, Anupindi S A, Nimkin K. Imaging of multifocal hepatic lesions in pediatric patients. *Ped Rad* 2012;42:1155-1168.
- 2, Helmberger T K, Ros P R. Pediatric liver neoplasms: a radiologic-pathologic correlation. *EUR Rad* 1999;9:1339-47.
- 3, Chung E M, Cube R et al. Pediatric liver masses: Radiologic-pathologic correlation part 1. Benign tumours. *Radiographics* 2010;30:801-8264.
- 4, Stringer M D, Alizai N K. Mesenchymal hamartoma of the liver: A systematic review. *Journal Ped Surg* 2005;40:181-1690.
- 5, Stocker J T. Hepatic tumors in children. *Clin Liver Dis* 2001;5:259-281.
- 6, Pobel R S, Bisset G S. Pictorial essay: Imaging of liver tumours in the infant and child. *Ped Rad* 1995;25:495-5067.
- 7, Chung W M, Lattin G E et al. Pediatric liver masses: Radiologic-pathologic correlation part 2. Malignant tumours. *Radiographics* 2011;31:483-507
- 8, Roebuck D J, Aronson D, Clapuyt P et al. PRETEXT: A revised staging system for primary malignant liver tumours of childhood developed by the SIOPEL group. *Pediatr Radiol* 2007;37(2):123-132.

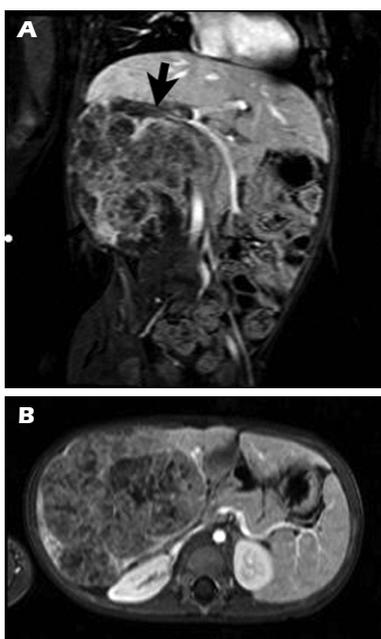


FIGURE 4
 Hepatoblastoma in an 18-month-old child. Coronal oblique (A) and axial (B) dynamic post contrast images demonstrates large heterogeneous exophytic tumour with tumour thrombus within right portal vein (arrow).