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Hepatobiliary rhabdomyosarcoma in children: diagnostic radiology

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Abstract Rhabdomyosarcoma (RMS) occurs infrequently in the liver and biliary tree. Although the radiological diagnosis may be simple when the tumour involves the extrahepatic bile ducts, no specific imaging features are known for hepatic RMS. We present four cases and discuss the role of diagnostic radiology in the management of this tumour.

Introduction

Although rhabdomyosarcoma (RMS) is the most common tumour of the biliary tree in childhood [1, 2], it is a rare lesion, accounting for about 1 % of all RMS (or about 0.04 % of all cancer) in children [3, 4]. When a large tumour arises in the liver in children, a biliary origin is difficult to prove [5], as intraductal growth can not always be demonstrated.

Histological classification of RMS has traditionally been different in the United States [6] and Europe [7], but the new International Classification of Rhabdomyosarcoma [8] may now become universal. Hepatobiliary RMS in childhood is of the embryonal or botryoid types [3]. The radiological findings of hepatobiliary RMS have been described in small series [1, 5, 9–13] and case reports [14–20]. We present four new cases and discuss the imaging features, the differential diagnosis and the role of radiology in the assessment of operability, the search for metastatic disease, the evaluation of response to therapy and surveillance following surgery.

Case reports

Case 1

A 28-month-old Latino boy presented with a 2-week history of jaundice and fever and 1 week of pruritus, nausea and diarrhoea. On examination, he was icteric, with firm hepatomegaly. US, CT, MRI and percutaneous transhepatic cholangiography (PTC) were performed (Fig. 1), and these showed a mass in the intra- and extrahepatic bile ducts consistent with RMS. He was treated by pylorus-sparing pancreaticoduodenectomy with resection of the common bile duct. Histopathological examination confirmed embryonal RMS. Lymph node biopsies showed no tumour, but there was microscopic disease at the proximal resection margin of the bile duct. Postoperatively he was given vincristine, actinomycin D and doxorubicin, and he remains in continuous complete remission 6 years later.

Case 2

A 36-month-old Latino boy presented with a 1-week history of jaundice, abdominal distension and diarrhoea. US showed a mass at the porta hepatis with intrahepatic duct dilatation. This was confirmed by CT (Fig. 2a), which also revealed extension into the duodenum (Fig. 2b) and enlarged para-aortic lymph nodes in the inferior mediastinum. An open liver biopsy confirmed the diagnosis of embryonal RMS. PTC and external biliary drainage were performed (Fig. 2c), and this was converted to bilobar internal-external drainage 4 days later. There was progression of disease

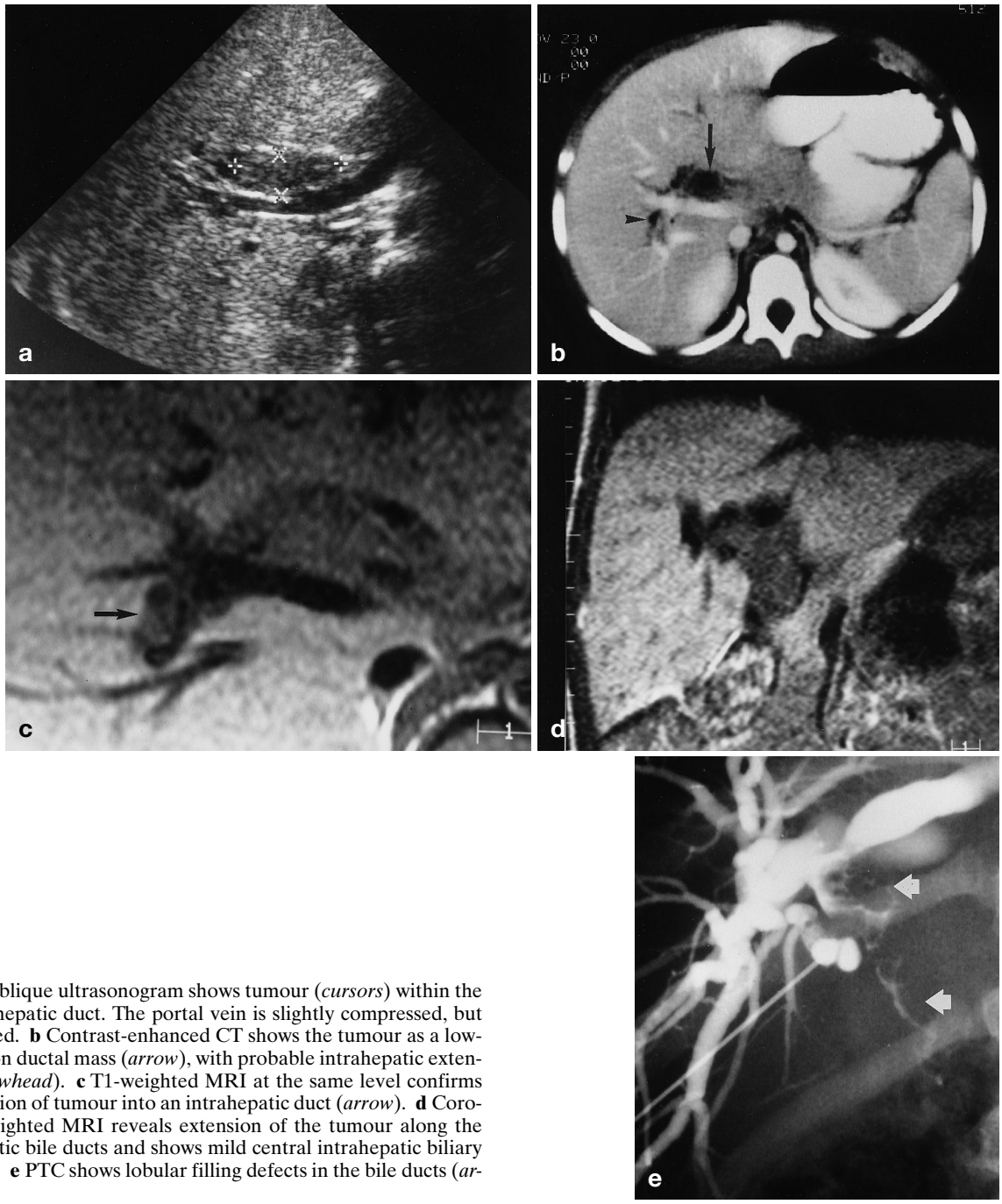


Fig. 1 **a** Oblique ultrasonogram shows tumour (*cursors*) within the common hepatic duct. The portal vein is slightly compressed, but not invaded. **b** Contrast-enhanced CT shows the tumour as a low-attenuation ductal mass (*arrow*), with probable intrahepatic extension (*arrowhead*). **c** T1-weighted MRI at the same level confirms the extension of tumour into an intrahepatic duct (*arrow*). **d** Coronal T1-weighted MRI reveals extension of the tumour along the extrahepatic bile ducts and shows mild central intrahepatic biliary dilatation. **e** PTC shows lobular filling defects in the bile ducts (*arrows*)

despite systemic chemotherapy, and the patient died a few months after presentation.

Case 3

A 12-year-old Chinese girl presented with a 3-week history of jaundice and loss of appetite. On examination, there was a huge abdominal mass. Liver enzymes and total bilirubin were elevated. US (Fig. 3a), CT (Fig. 3b) and MRI (Fig. 3c–e) were performed in an attempt to characterise the liver mass. The pattern of contrast enhancement on CT and MR was considered compatible with a vascular lesion, but this was excluded by a technetium-99m labelled red blood cell scan (Fig. 3f) which showed a photopenic mass. Open liver biopsy revealed embryonal RMS. She was treated with vincristine, actinomycin D, ifosfamide and cyclophosphamide, but died of disease progression 9 weeks after presentation.

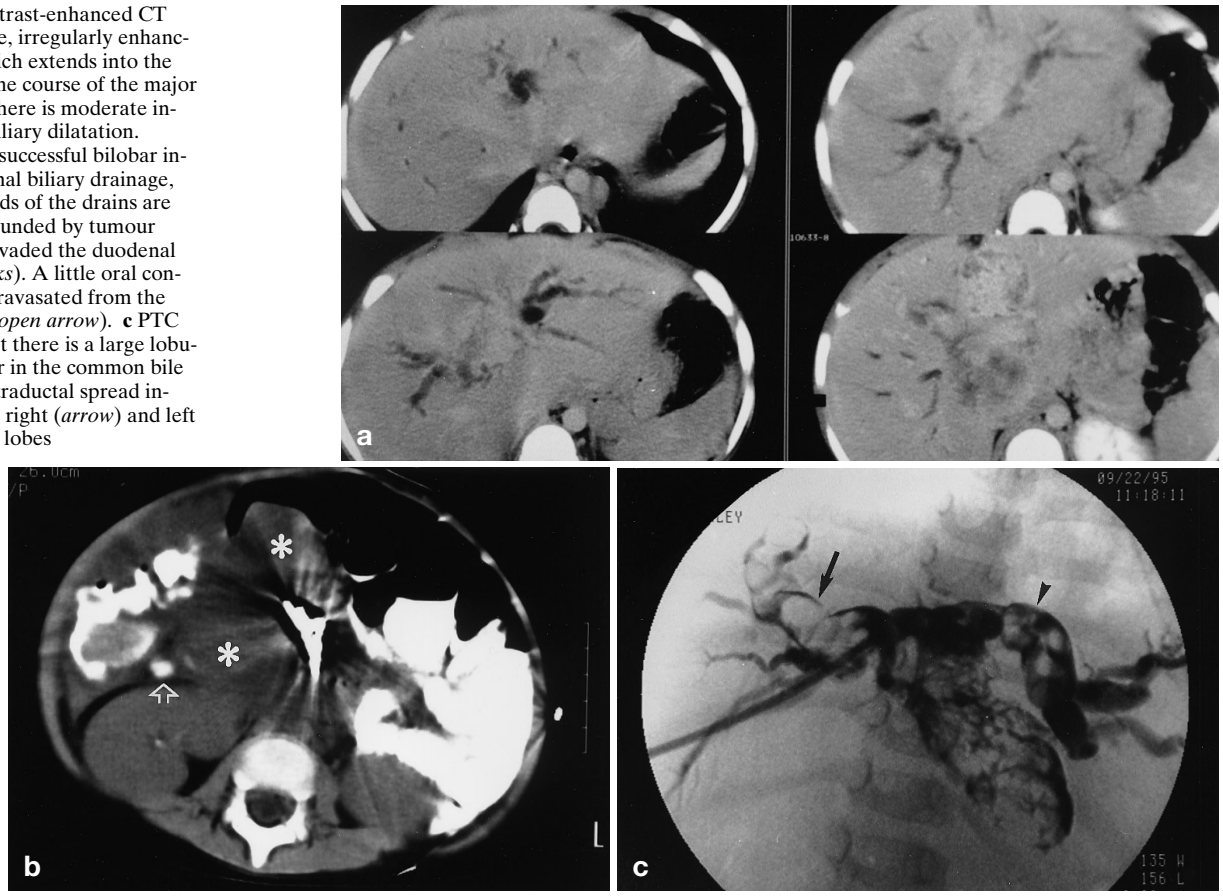


Fig. 2 **a** Contrast-enhanced CT shows a large, irregularly enhancing mass which extends into the liver along the course of the major bile ducts. There is moderate intrahepatic biliary dilatation. **b** Following successful bilobar internal-external biliary drainage, the lower ends of the drains are almost surrounded by tumour which has invaded the duodenal wall (*asterisks*). A little oral contrast has extravasated from the duodenum (*open arrow*). **c** PTC confirms that there is a large lobulated tumour in the common bile duct with intraductal spread involving both right (*arrow*) and left (*arrowhead*) lobes

Case 4

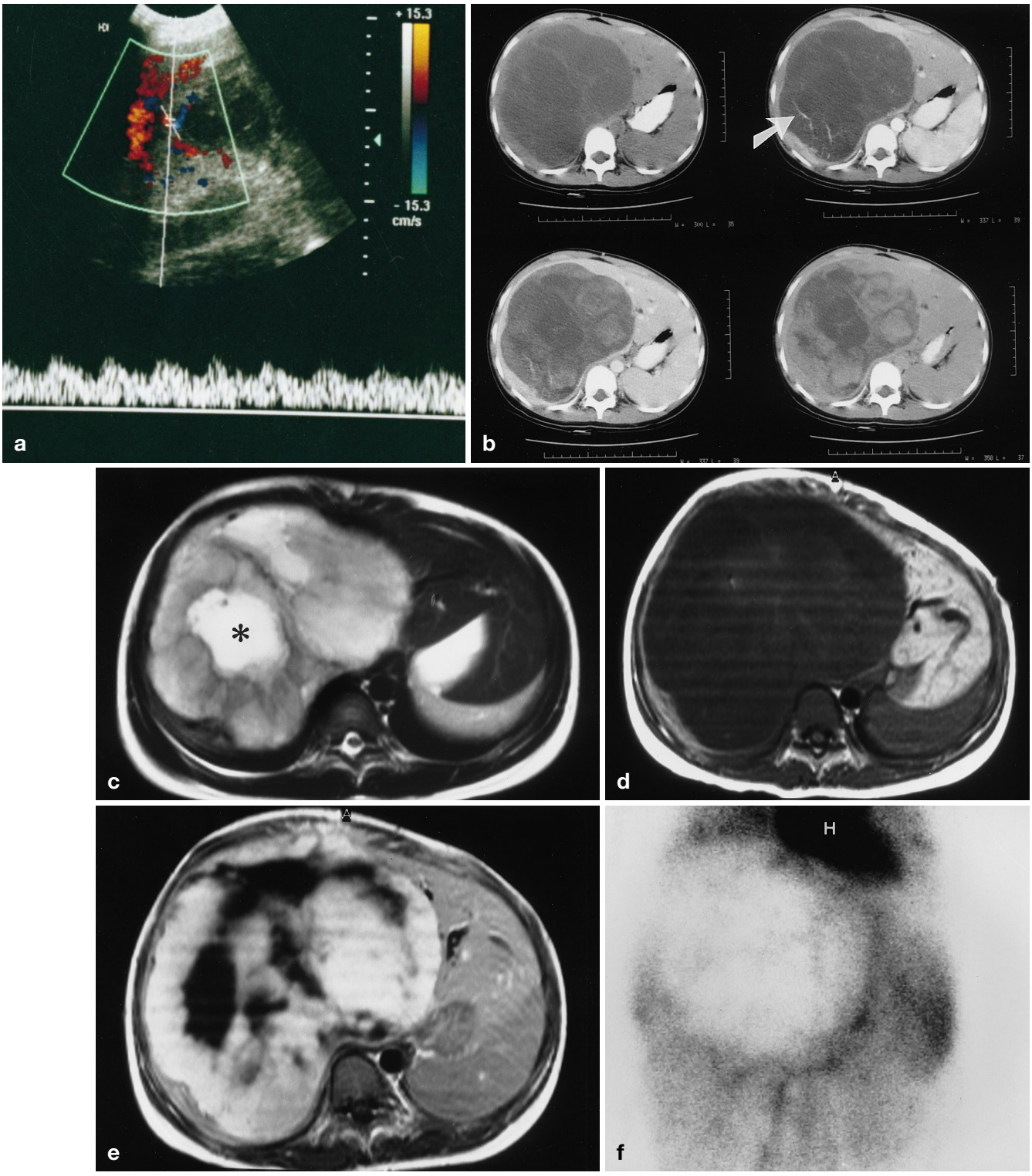
A 6-year-old Chinese boy presented with a 4-week history of jaundice and abdominal distension. CT (Fig. 4 a,b) revealed a 6-cm mass centred on the common bile duct, with mild left lobe intrahepatic biliary dilatation. Percutaneous core needle biopsy showed embryonal RMS. External biliary drainage was performed. An MRI study, undertaken after the biliary drainage (Fig. 4c–f), confirmed the location of the mass and showed extension into the left hepatic duct. He has been treated with chemotherapy (initially vincristine, actinomycin D, cyclophosphamide, etoposide and ifosfamide, and later cisplatin and doxorubicin) and external beam radiotherapy, with moderate reduction in tumour size. He is currently being reassessed for surgery, 1 year after diagnosis.

Discussion

Hepatobiliary embryonal or botryoid RMS is a disease of young children, occurring at a median age of about 3 years [3, 21]. It is rare after the first decade [3]. There may be a slight preponderance of male patients [3, 10, 12, 21]. The tumour may arise in the liver or intrahepatic ducts [9, 22] (Fig. 3), an intrahepatic cyst [12], the gallbladder [14], the cystic duct [21], the extrahepatic bile ducts [21] (Figs. 1, 2, 4), the ampulla [16, 23] or a choledochal cyst [15]. Extension into the duodenum (Fig. 2 b) is not uncommon [3]. Median diameter at diagnosis is about 8 cm [3]. The most common clinical features are jaundice and abdominal distension [3, 12]. Pain, nausea, vomiting and fever are less frequent [3, 12, 21].

Differential diagnosis

When a tumour of the bile ducts is discovered in a child, the diagnosis of RMS is very likely [1, 2]; other possible lesions, such as inflammatory pseudotumour [24] and cholangiocarcinoma arising in a choledochal cyst [25, 26], are extremely rare. The diagnosis is more difficult if a hepatic lesion shows no intraductal growth pattern. In the first year of life RMS is much less common than haemangioendothelioma, hepatoblastoma and mesenchymal hamartoma [2]. Of these conditions, haemangioendothelioma has typical clinical and radiological features [27] and mesenchymal hamartoma usually has a distinctive multicystic appearance on cross-sectional imaging [28]. Later in childhood, hepatoblastoma, hepatocellular carcinoma (HCC) and undifferentiated (embryonal) sarcoma must also be considered [2, 13]. The



age of the child, the presence of conditions which are associated with HCC, and the serum alpha-fetoprotein (AFP) level may be helpful, since there are no pathognomonic imaging features of hepatic RMS [5]. AFP is elevated in almost all patients with hepatoblastoma and in most with HCC [29], but not in those with RMS.

Resectability

Although biliary RMS typically grows along the bile ducts into both lobes of the liver (Figs. 1, 2), aggressive resection with biliary reconstruction may still be possible [11, 12, 16], and involvement of both left and right hepatic ducts need not be a contraindication to surgery. This is because the tumour may remain localised to the bile ducts, and also because complete excision may not be a prerequisite for long-term survival [3, 11, 30]. In Intergroup Rhabdomyosarcoma Studies I and II, five of the ten patients with hepatobiliary RMS had macroscopic residual tumour following surgery (clinical group III). Of these, four were alive at the time of reporting, having survived 28–351 weeks after diagnosis [3]. (It should be noted that hepatobiliary RMS has recurred as late as 9 years after therapy [10].)

Operability is therefore a different concept for biliary RMS than for malignant liver tumours [11, 12], in which complete excision is probably essential. The main purposes of preoperative radiology are to provide the surgeon with a map of the extent of the ductal tumour [12] and to allow assessment of response to therapy. It is not clear which imaging modality is best for this and what degree of accuracy can be achieved.

Imaging modalities

US typically reveals biliary dilatation [5, 10, 14, 16–18] and an intraductal mass [5, 10, 14, 17, 18] (Fig. 1a). Although the portal vein may be displaced by a large tumour, portal vein thrombosis has not been described [10]. Larger masses may have fluid ("cystic") areas within them [13, 16], possibly reflecting tumour necrosis. When the tumour arises in the liver, there may be no distinguishing US features. Colour Doppler imaging in one of our patients showed numerous abnormal tumour arteries with low resistive index (Fig. 3a).

CT may also show an intraductal mass (Fig. 1b) with or without biliary dilatation (Fig. 2a). Hypodense and heterogeneous attenuation patterns (Figs. 1b, 3b, 4a) have been described [10]. Several reports mention the presence of low attenuation areas within the tumour [9, 13, 15, 16] (Fig. 3b). Enhancement with intravenous contrast medium [9] and the administration of cholangiographic contrast medium [17] have been used to show the lesion more clearly. There is no consistent pattern of contrast enhancement. The tumours in our patients showed four different patterns: strong heterogeneous (Fig. 2a), incomplete globular (Fig. 3b), mild (Fig. 4b) and none (Fig. 1b).

MRI (Figs. 1c,d, 3c–e, 4c–e) offers several advantages in the evaluation of hepatobiliary tumours [31]. These include excellent contrast, multiplanar imaging and accurate assessment of the number and extent of lesions and, in particular, their relationship to the hepatic vasculature. In our cases the tumours showed predominantly low signal intensity on T1-weighted images with intense but inhomogeneous contrast enhancement (Figs. 3d,e, 4d). On T2-weighted images the tumours were moderately or markedly hyperintense (Figs. 3c, 4e). MR cholangiography (MRC) is a promising tool for evaluation of the major bile ducts in children [32]. Bile duct dilatation and irregularity are well demonstrated (Fig. 4f).

The typical finding at PTC is the presence of extensive, often bizarre, filling defects corresponding to ductal tumour [9, 18] (Figs. 1e, 2c), with or without obstruction of the extrahepatic bile ducts. Despite claims to the contrary [12], PTC can be performed in cases of RMS without biliary dilatation, either by blind fine-needle puncture of an intrahepatic bile duct [33, 34], or by ultrasound-guided transhepatic puncture of the gallbladder [17, 33]. Endoscopic retrograde cholangiography can be performed in infants and small children [35, 36]. It offers certain advantages over PTC, particularly if there is a coagulopathy, but is unlikely to be better than PTC at defining the degree of intraductal extension. If there is obstructive jaundice, PTC is likely to be better because adequate biliary drainage can be achieved whether or not the obstruction can be crossed with a catheter. This is extremely important if neoadjuvant chemotherapy is to be used, since the regimen may include drugs which depend largely on a hepatobiliary mechanism of excretion, such as vincristine and perhaps doxorubicin [37]. PTC also allows other interventional procedures to be performed after access

◀ **Fig. 3** **a** Colour Doppler imaging shows a huge liver mass of mixed echogenicity with numerous pathological vessels which show low-resistance flow. **b** Sequential images from a dynamic contrast-enhanced CT study show a mass of predominantly low attenuation with progressive but incomplete globular enhancement. No specific features suggest RMS. Numerous small arteries are shown within the tumour (*arrow*). **c** On the transverse T2-weighted MRI, the peripheral parts of the mass show much higher signal intensity than normal liver and there are central areas of very high signal (*asterisk*) which may reflect necrosis. **d,e** Transverse T1-weighted MRI before **d** and after **e** intravenous contrast show a similar enhancement pattern to the CT. Non-enhancing areas correspond to the regions of very high signal on T2-weighted images. **f** Technetium-99m-labeled red cell scan (anterior view) shows a huge photopenic mass. (*H* = heart)

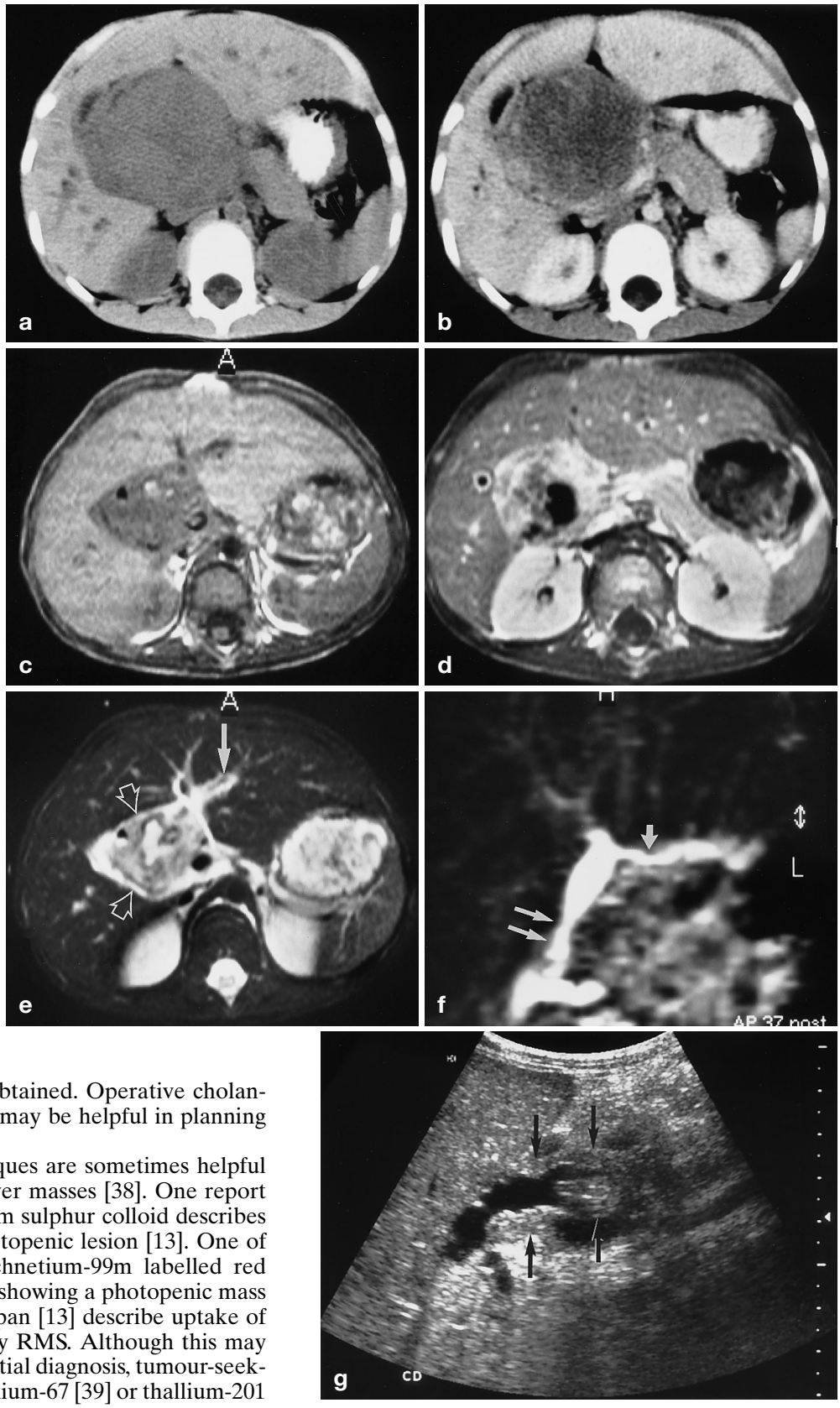


Fig. 4 **a** Non-contrast CT shows a low attenuation mass, apparently arising from the extrahepatic bile ducts. **b** There is only mild enhancement with intravenous contrast. **c** Transverse T1-weighted MRI shows areas of high intensity within the tumour. These could represent small foci of haemorrhage or proteinaceous fluid. **d** Following intravenous contrast medium, an image at a slightly more caudal level shows marked heterogeneous enhancement. **e** Fat-suppressed T2-weighted MRI shows an external biliary drain in the mildly dilated left hepatic duct (*arrow*). The tumour (*open arrows*) surrounds the dilated lumen of the common hepatic duct. **f** MR cholangiogram shows dilated left hepatic, common hepatic and common bile ducts. The right hepatic duct is not well shown because it is of approximately normal calibre. The irregularity of the common bile duct (*long arrows*) indicates the presence of tumour. The irregular contour of the left hepatic duct (*short arrow*) could also be related to the presence of the external biliary drain. **g** Oblique US image taken after 10 months of therapy shows dilatation of the common hepatic duct and a decrease in the size of the tumour (*arrows*). Contrast-enhanced CT also showed the interval change in tumour size well

to the bile ducts has been obtained. Operative cholangiography [1, 11, 14, 16, 20] may be helpful in planning the surgical approach.

Nuclear medicine techniques are sometimes helpful in the characterisation of liver masses [38]. One report of the use of technetium-99m sulphur colloid describes hepatobiliary RMS as a photopenic lesion [13]. One of our patients underwent technetium-99m labelled red blood cell scintigraphy, also showing a photopenic mass (Fig. 3f). Miller and Greenspan [13] describe uptake of gallium-67 in a hepatobiliary RMS. Although this may not be helpful in the differential diagnosis, tumour-seeking radionuclides such as gallium-67 [39] or thallium-201

[40] can be used in the assessment of metastatic disease and for surveillance following therapy.

Extrahepatic disease

The most frequent site of metastatic disease is the liver [3, 21]. The presence of extrahepatic metastatic disease indicates a poor prognosis [3], and may lead to a change of therapeutic plan. CT of the chest should be performed at diagnosis, since lung metastases are not uncommon [3, 21]. Metastases are also found with some frequency on peritoneal surfaces, including the omentum, mesentery and diaphragm, and in lymph nodes and bone [3, 21]. It is reasonable to perform bone scintigraphy at diagnosis.

Imaging strategy at diagnosis

At least one cross-sectional imaging technique will be required. The best single modality is CT, which can cover the chest, abdomen and pelvis in one examination. If availability and financial considerations permit, MRI with MRC may be helpful (Fig. 1 c), although there is no evidence that this is cost-effective. Gallium or thallium scintigraphy (with or without bone scintigraphy) could also be performed to assess for metastatic disease and to allow follow-up of gallium- or thallium-avid tumours.

Response to neoadjuvant chemotherapy

Unlike hepatoblastoma and HCC, there are no practical markers for RMS in the blood, and therapeutic response must be judged on the basis of imaging findings. Since the aim of preoperative chemotherapy is to maximise the probability of successful surgery, regular follow-up imaging is desirable to assess change in size of the tumour. US is useful for this purpose (Fig. 4 g) and may be repeated frequently [10]. Cholangiography is conveniently performed if there is an external or internal-external biliary drain. Detailed imaging, including a reassessment of ductal extension and evaluation for metastatic disease, will be required immediately before surgery.

Surveillance imaging following surgery

The aim of follow-up imaging is to monitor any residual disease and to detect recurrence and metastasis. It is not clear that this is an effective policy, but it is customary in most centres. The issue of which imaging modality to use has been specifically addressed by Geoffray et al. [10], who concluded that the presence of bowel gas at the porta hepatis or a hepatectomy defect made CT superior to US following surgery. All eight of their patients suffered a recurrence; two of these presented as septated fluid collections. The use of MRI in follow-up imaging has not been reported. Surveillance imaging may be appropriate for many years after treatment in view of the possibility of late recurrence [10].

Conclusion

Diagnostic imaging in hepatobiliary RMS is directed at the assessment of the extent of the tumour within the liver (and especially along the intrahepatic bile ducts), regional spread and distant metastases. Conventional definitions of resectability are not appropriate in hepatobiliary RMS, since aggressive surgery with biliary reconstruction may be possible and incomplete resection is compatible with long-term survival. A careful search for extrahepatic disease is required since distant metastases imply a poor prognosis. The best single cross-sectional imaging modality at diagnosis is CT, but MRI provides multiplanar images and MRC is feasible. PTC and biliary drainage may be required when there is obstructive jaundice.

US may be the best technique to assess response to preoperative chemotherapy. Repeat cholangiography is simple if there is an external biliary drain. CT may be the best technique for surveillance following surgery. Gallium or thallium scintigraphy may also be useful.

References

1. Davis GL, Kissane JM, Ishak KG (1969) Embryonal rhabdomyosarcoma (sarcoma botryoides) of the biliary tree. Cancer 24: 333–342
2. Chandra RS, Stocker JT (1992) The liver, gallbladder, and biliary tract. In: Stocker JT, Dehner LP (eds) Pediatric pathology, vol 2. Lippincott, Philadelphia, pp 703–789
3. Ruymann FB, Raney RB, Crist WM, et al for the Intergroup Rhabdomyosarcoma Study of CCSG and POG (1985) Rhabdomyosarcoma of the biliary tree in childhood: a report from the Intergroup Rhabdomyosarcoma Study. Cancer 56: 575–581
4. Newton WA Jr, Soule EH, Hamoudi AB, et al (1988) Histopathology of childhood sarcomas, Intergroup Rhabdomyosarcoma Studies I and II: clinicopathologic correlation. J Clin Oncol 6: 67–75
5. Cohen MD (1992) Imaging of children with cancer. Mosby Year Book, St Louis, pp 320–321

6. Horn RC, Enterline HT (1958) Rhabdomyosarcoma: a clinicopathological study and classification of 39 cases. Cancer 11: 181–199
7. Caillaud JM, Gérard-Marchant R, Marsden HB, et al (1989) Histopathological classification of childhood rhabdomyosarcoma: a report from the International Society of Pediatric Oncology pathology panel. Med Pediatr Oncol 17: 391–400
8. Newton WA Jr, Gehan EA, Webber BL, et al (1995) Classification of rhabdomyosarcomas and related sarcomas. Cancer 76: 1073–1085
9. Linstedt-Hilden M, Brambs HJ (1994) Two different manifestations of botryoid sarcoma (embryonal rhabdomyosarcoma) of the biliary tree. Bildgebung 61: 40–43
10. Geoffray A, Couanet D, Montagne JP, et al (1987) Ultrasonography and computed tomography for diagnosis and follow-up of biliary tract rhabdomyosarcomas in children. Pediatr Radiol 17: 127–131
11. Martinez-F LA, Haase GM, Koep LJ, Akers DR (1982) Rhabdomyosarcoma of the biliary tree: the case for aggressive surgery. J Pediatr Surg 17: 508–511
12. Schweizer P, Schweizer M, Wehrmann M (1994) Major resection for embryonal rhabdomyosarcoma of the biliary tree. Pediatr Surg Int 9: 268–273
13. Miller JH, Greenspan BS (1985) Integrated imaging of hepatic tumors in childhood. Part I: malignant lesions (primary and metastatic). Radiology 154: 83–90
14. Mihara S, Matsumoto H, Tokunaga F, et al (1982) Botryoid rhabdomyosarcoma of the gallbladder in a child. Cancer 49: 812–818
15. Patil KK, Omojola MF, Khurana P, Iyengar JK (1992) Embryonal rhabdomyosarcoma within a choledochal cyst. Can Assoc Radiol J 43: 145–148
16. Caty MG, Oldham KT, Prochownik EV (1990) Embryonal rhabdomyosarcoma of the ampulla of Vater with long-term survival following pancreaticoduodenectomy. J Pediatr Surg 25: 1256–1258
17. Arnaud O, Boscq M, Asquier E, Michel J (1987) Embryonal rhabdomyosarcoma of the biliary tree in children: a case report. Pediatr Radiol 17: 250–251
18. Friedburg H, Kauffman GW, Böhm N, et al (1984) Sonographic and computed tomographic features of embryonal rhabdomyosarcoma of the biliary tract. Pediatr Radiol 14: 436–438
19. Cannon PM, Legge DA, O'Donnell B (1979) The use of percutaneous transhepatic cholangiography in a case of embryonal rhabdomyosarcoma. Br J Radiol 52: 326–327
20. Nagaraj HS, Kmetz DR, Leitner C (1977) Rhabdomyosarcoma of the bile ducts. J Pediatr Surg 12: 1071–1074
21. Lack EE, Perez-Atayde AR, Schuster SR (1981) Botryoid rhabdomyosarcoma of the biliary tract: report of five cases with ultrastructural observations and literature review. Am J Surg Pathol 5: 643–652
22. Horowitz ME, Etcubanas E, Webber BL, et al (1987) Hepatic undifferentiated (embryonal) sarcoma and rhabdomyosarcoma in children: results of therapy. Cancer 59: 396–402
23. Isaacson C (1978) Embryonal rhabdomyosarcoma of the ampulla of Vater. Cancer 41: 365–368
24. Haith EE, Kepes JJ, Holder TM (1964) Inflammatory pseudotumor involving the common bile duct of a six-year-old boy: successful pancreaticoduodenectomy. Surgery 56: 436–441
25. Iwai N, Deguchi E, Yanagihara J, et al (1990) Cancer arising in a choledochal cyst in a 12-year-old girl. J Pediatr Surg 25: 1261–1263
26. Todani T, Tabuchi K, Watanabe Y, Kobayashi T (1979) Carcinoma arising in the wall of congenital bile duct cysts. Cancer 44: 1134–1141
27. Keslar PJ, Buck JL, Selby DM (1993) Infantile hemangioendothelioma of the liver revisited. Radiographics 13: 657–670
28. Stanley P, Hall TR, Woolley MM, et al (1986) Mesenchymal hamartomas of the liver in childhood: sonographic and CT findings. AJR 147: 1035–1039
29. Howard ER, Ruers TJ (1994) Hepatobiliary malignancy in childhood. In: Terblanche J (ed) Hepatobiliary malignancy: its multidisciplinary management. Edward Arnold, London, pp 252–270
30. Akers DR, Needham ME (1971) Sarcoma botryoides (rhabdomyosarcoma) of the bile ducts with survival. J Pediatr Surg 4: 474–479
31. Schnall M (1995) Magnetic resonance imaging of focal liver lesions. Semin Roentgenol 30: 347–361
32. Hirohashi S, Hirohashi R, Uchida H, et al (1997) Pancreatitis: evaluation with MR cholangiopancreatography in children. Radiology 203: 411–415
33. Chait PG (1996) Interventional gastrointestinal radiology. In: Walker WA, Durie PR, Hamilton JR, Walker-Smith JA, Watkins JB (eds) Pediatric gastrointestinal disease: pathophysiology, diagnosis, management, vol 2, 2nd edn. Mosby, St Louis, pp 1775–1799
34. Teplick SK, Flick P, Brandon JC (1991) Transhepatic cholangiography in patients with suspected biliary disease and nondilated intrahepatic bile ducts. Gastrointest Radiol 16: 193–197
35. Allendorph M, Werlin SL, Geenen JE, et al (1987) Endoscopic retrograde cholangiopancreatography in children. J Pediatr 110: 206–211
36. Guelrud M, Jaen D, Torres P, et al (1987) Endoscopic cholangiopancreatography in the infant: evaluation of a new prototype pediatric duodenoscope. Gastrointest Endosc 33: 4–8
37. Velez-Yanguas MC, Warrier RP (1996) The evolution of chemotherapeutic agents for the treatment of pediatric musculoskeletal malignancies. Orthop Clin North Am 27: 545–549
38. Kinnard MF, Alavi A, Rubin RA, Lichtenstein GR (1995) Nuclear imaging of solid hepatic masses. Semin Roentgenol 30: 375–395
39. Bitran JD, Bekerman C, Golomb HM, Simon MA (1978) Scintigraphic evaluation of sarcomata in children and adults by Ga67 citrate. Cancer 42: 1760–1765
40. Nadel HR (1993) Thallium-201 for oncological imaging in children. Semin Nucl Med 23: 243–254