Clinics in Diagnostic Imaging (89)

W H Ng, A S C Ching, K F Chan, W T Fung

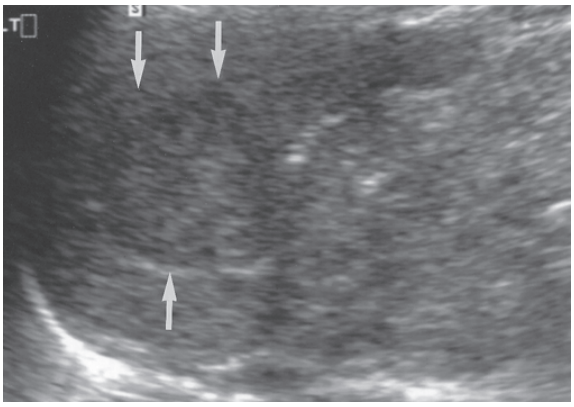

Fig. 1a Longitudinal US scan of the spleen.

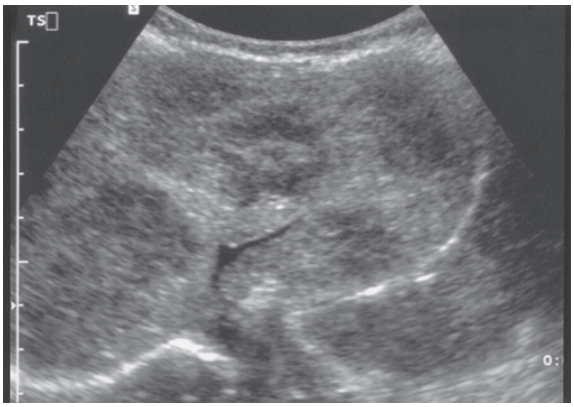

Fig. 1b Transverse US scan of the liver.

CASE PRESENTATION

A six-month-old female infant was transferred to our institution from a peripheral hospital for investigation of hepatosplenomegaly. The infant was born at 40 weeks of gestation with normal vaginal delivery. Clinical examination at birth revealed no abnormality. The infant also presented with cough and vomiting for two weeks, and was diagnosed to have acute bronchiolitis due to respiratory syncytial viral infection. On admission, the baby girl was alert and active. Her body weight was 7.6 kg (75^{th} - 90^{th} percentile) and length was 67 cm (75^{th} - 90^{th} percentile). Heart rate was 100 beats per minute, blood pressure was 96/62 mmHg, and respiratory rate was 26 breaths per minute. The lungs showed fair air entry, but there were diffuse rhonchi and basal crepitations. The heart was normal. Abdominal distension was noted on physical examination. The liver was enlarged, extending 5 cm below the right costal margin. The tip of the spleen was also palpable. There was no abdominal bruit on auscultation. No cutaneous abnormality or lymphadenopathy was noted.

Initial laboratory evaluation at the peripheral hospital had been remarkable for elevated platelet count of 437 x 10^9/L (normal: 152-358) and serum alpha-fetoprotein level of 40.4 ng/ml (normal: <9.0). Biochemical analysis revealed normal haematological profile, liver function parameters and clotting test. Serological viral tests, including those for hepatitis, cytomegalovirus, Ebstein-Barr virus and human immunodeficiency virus, were negative. The urine vanillylmandelic acid, adrenaline, noradrenaline and dopamine were also negative. Ultrasonography (US) of the abdomen was performed (Figs. 1a-b). What does this show? What is the diagnosis and what further investigation will be useful for confirming the diagnosis?

Department of Diagnostic Radiology and Organ Imaging
Prince of Wales Hospital
Hong Kong SAR China

W H Ng, FRCR
Medical Officer

Department of Radiology
North District Hospital

A S C Ching, FRCR
Senior Medical Officer

W T Fung, FRCR
Senior Medical Officer

Department of Anatomical and Cellular Pathology
Chinese University of Hong Kong
Hong Kong SAR China

K F Chan, FRCPA
Medical Officer

Correspondence to:
Dr Ng Wing Hong
Tel: (852) 2632 2892
Fax: (852) 2645 1520
Email: ngwhalex@yahoo.com

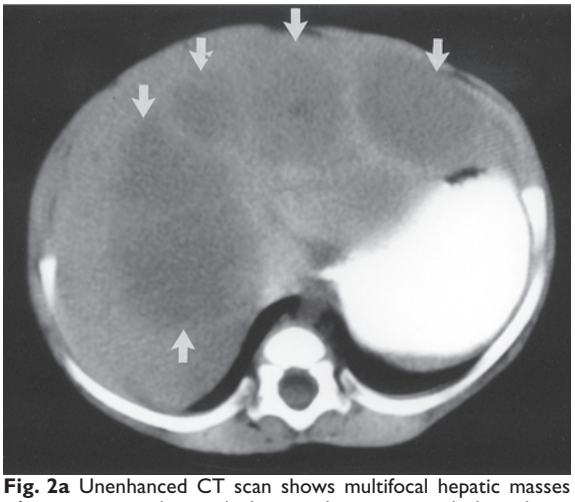

Fig. 2a Unenhanced CT scan shows multifocal hepatic masses of varying sizes (arrows) that are homogeneously hypodense in attenuation.

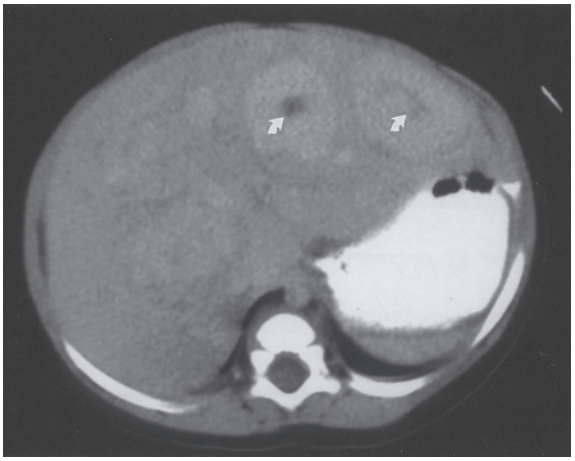

Fig. 2b Enhanced CT scan shows that the lesions have marked rim enhancement with well-defined lobulated contours. Some of them have central cleft-like hypodense areas (curved arrows) indicating tumoral necrosis.

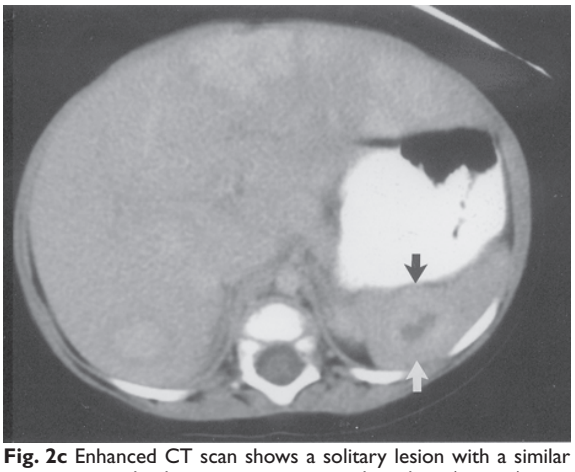

Fig. 2c Enhanced CT scan shows a solitary lesion with a similar appearance and enhancement pattern in the spleen (arrows).

IMAGE INTERPRETATION

US showed multifocal lesions in the liver and a solitary lesion in the spleen. The splenic lesion had an isoechoic centre with a well-defined hypoechoic rim (arrows) (Fig. 1a). There was no ultrasonographical feature to suggest intralesional calcification or septation. The multiple hepatic masses were more heterogeneously-echoic compared to the splenic lesion. Some of them exhibited an irregular ill-defined, thick hypoechoic rim. Mild vascular signals were identified on Doppler US imaging. The portal veins were compressed but not invaded (Fig. 1b). There was no intraluminal thrombus. The kidneys, suprarenal regions and retroperitoneum were normal.

Computed tomography (CT) confirmed multifocal hepatic masses of varying sizes (Fig. 2a). These masses were homogeneously hypodense on unenhanced images and showed marked rim enhancement after intravenous contrast agent administration. They had well-defined, lobulated contours. Some of them showed central cleft-like hypodense areas (Fig. 2b). Hepatic and portal veins were compressed and displaced. A solitary lesion with a similar appearance and enhancement pattern was found in the spleen (Fig. 2c).

DIAGNOSIS

Infantile hepatosplenic haemangioendotheliomas.

CLINICAL COURSE

US-guided core biopsy of a right lobe hepatic lesion was performed. Histological examination revealed small thin-walled capillary-sized vascular channels. These were lined by plump endothelial cells with mild nuclear pleomorphism, separated by thin fibrous tissue stroma. Immunohistochemical staining was positive for endothelial markers (Fig. 3). Because of the similar appearance and enhancement pattern of the splenic lesion on CT, the diagnosis was infantile haemangioendothelioma with hepatosplenic involvement.

The infant recovered completely from bronchiolitis. In view of the imaging and histopathological findings, a conservative approach to management was adopted. The patient had no clinical evidence of congestive heart failure or consumption coagulopathy. Repeat US nine months after the initial presentation showed size reduction of the hepatosplenic lesions, consistent with gradual spontaneous involution (Fig. 4).

DISCUSSION

Most hepatosplenic masses in infancy are either neoplastic or infectious, and are usually detected on US. Haemangioendotheliomas are rare mesenchymal tumours of childhood accounting for less than 0.03% of all paediatric neoplasia that cause lesions, mainly in the liver, salivary glands and skin[1]. This benign neoplasm is the most common hepatic tumour in infancy but seldom affects the spleen. Other rare manifestations, including the trachea, lung, gastrointestinal tract,

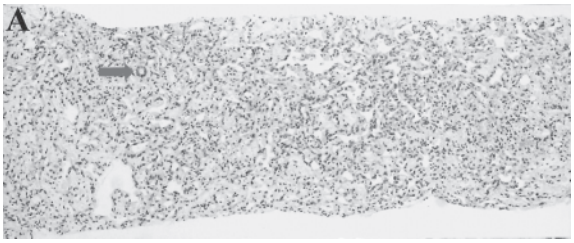

Fig. 3a Low magnification photomicrograph of the infantile haemangioendothelioma is characterised by proliferation of multiple small and thin-walled vascular channels supported in a loosely myxoid stroma. A small residue bile duct is indicated by a small arrow. (Haematoxylin and eosin stain, x10 magnification.)

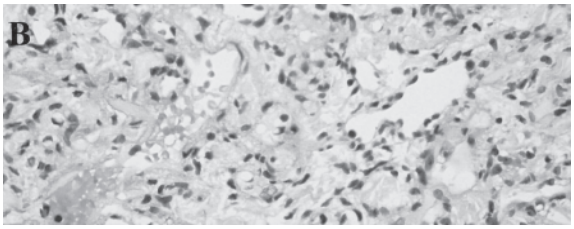

Fig. 3b High magnification photomicrograph shows that the neoplastic vessels are lined by cytologically-bland endothelial cells, characteristic of infantile haemangioendothelioma. (Haematoxylin and eosin stain x40 magnification.)

thymus, pancreas and even the meninges, have been reported[2]. This lesion may be difficult to diagnose without histopathology due to its highly variable morphological and imaging appearances. The tumour is characterised histologically by multiple small ill-defined vascular spaces lined by immature endothelial cells that exhibit low mitotic activity and only moderate cellular atypia interposing in variable amounts of fibrous stroma and bile ductules[3,4]. Areas of haemorrhagic necrosis, dystrophic calcification, thrombosis or fibrosis are frequently present. Synonyms found in the literature such as cavernous haemangioma, haemangiomatosis, arteriovenous malformation, and angioma, probably reflect previous ambiguity about the pathological classification of the tumour[1].

The incidence of infantile haemangioendothelioma is higher in girls (female to male ratios ranging from 1.3:1 to 2:1), and 85% of cases present in the first six months of life[5]. There is no racial predilection. The majority of reported cases present with an abdominal mass that is noted by the parents or discovered at routine physical examination. Associated symptoms (47.7%) include high-output congestive cardiac failure (8% - 68%), consumption coagulopathy with thrombocytopaenia (Kassabach-Merritt syndrome) (11.6%), disseminated intravascular coagulopathy, anaemia, encroachment on surrounding organs and rarely, spontaneous rupture and malignant transformation into angiosarcoma[1]. Hydrops foetalis, hydramnios and chorioangioma are reported manifestations of haemangioendothelioma *in utero*[6]. There is an association with other clinical abnormalities such as renal agenesis, atrial septal defect, absent common bile duct, heterotopic liver with diaphragmatic hernia, hemihypertrophy, chromosome 6q deletion, trisomy 21, and Cornelia de Lange syndrome[4,6].

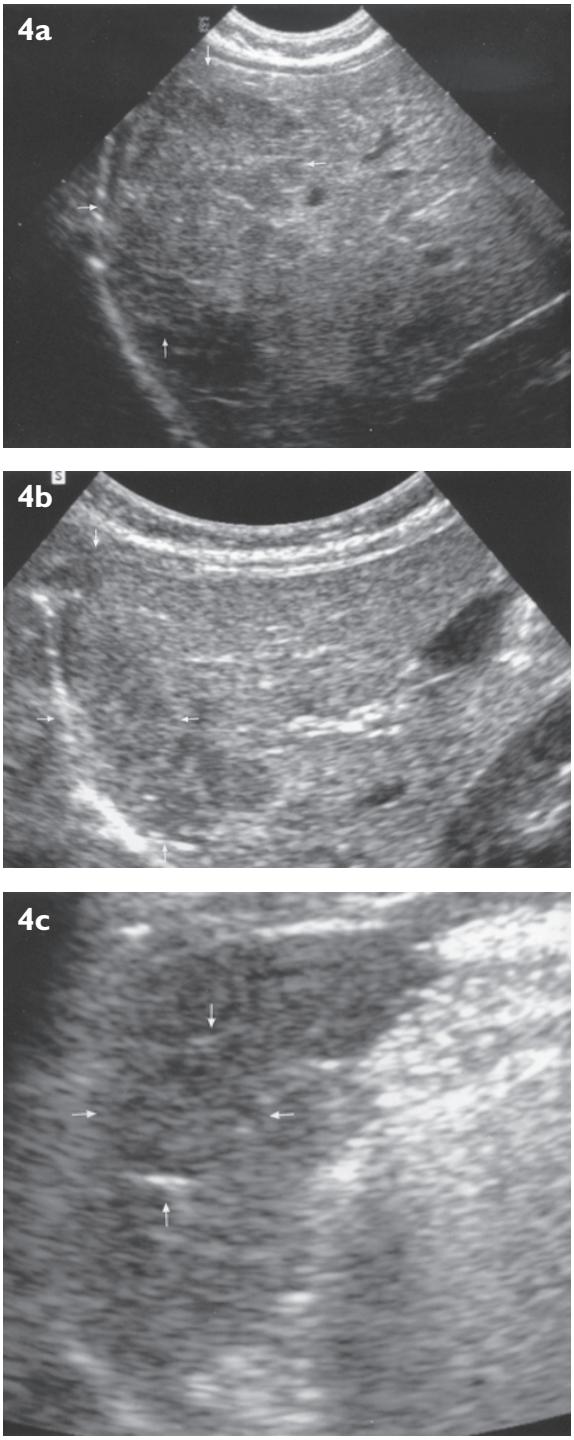

Fig. 4 US scans show reduction in size of haemangioendotheliomas in the liver and spleen. (a) Initial US scan of the liver shows one of the haemangioendotheliomas in segment 6 (arrows) at presentation. (b) Follow-up US scan done 9 months later shows that the corresponding haemangioendothelioma has spontaneously reduced in size (arrows). (c) Follow-up US scan taken at 9 months shows that the lesion in the spleen has also reduced in size (arrows), compared to the earlier US scan (Fig. 1a).

Radiographs are not sensitive but may sometimes demonstrate hepatomegaly and the fine speckle or fibrillar type of calcifications within the haemangioendothelioma[2].

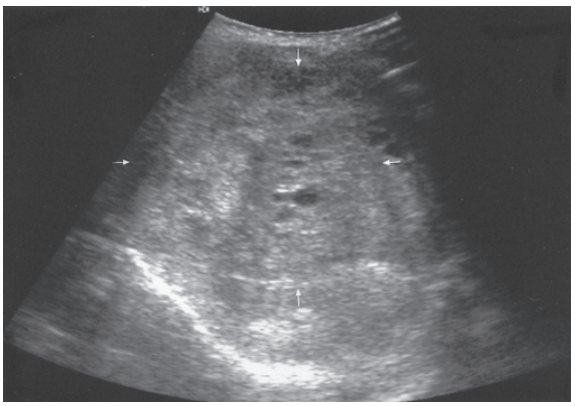

Fig. 5 Hepatoblastoma in a 5-month-old male infant. Longitudinal US scan shows a well-defined heterogeneously-echogenic mass (arrows) within the right lobe of liver. Small cystic components are evident inside the tumour mass. Hepatoblastoma was confirmed histologically.

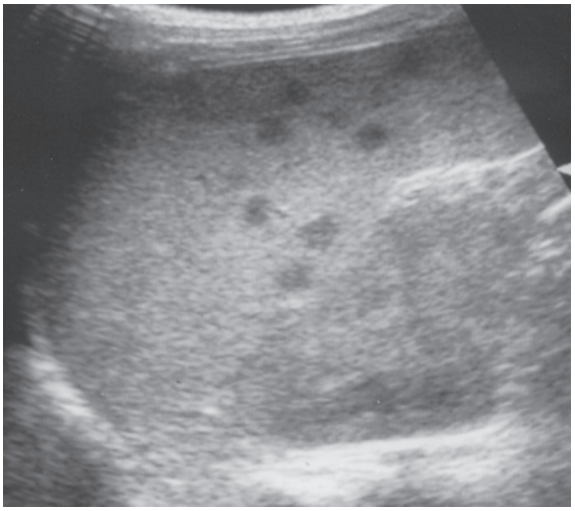

Fig. 6 Splenic abscesses in a 11-year-old boy with a history of aplastic anaemia. Longitudinal US scan shows multiple well-defined homogeneously-hypoechoic nodules of varying sizes within the spleen. Histology showed necrotising granulomatous inflammation with fungal spores.

Table I

Causes of Hepatosplenic Lesions In Infants	
A. Neoplasms	
Primary	*Benign*
	- Haemangioendothelioma/haemangioma
	- Mesenchymal hamartoma
	- Lymphangiomatosis
	- Teratoma
	Malignant
	- Hepatoblastoma (with splenic metastasis)
	- Malignant angiosarcoma
Metastatic disease	- Wilm's tumour
	- Neuroblastoma
	- Embryonal rhabdomyosarcoma
Infiltrative lesions	- Lymphoma/leukaemia
B. Non-neoplastic	
Infective	- Abscesses (e.g. Staphylococcus aureus, Amoebiasis, Candida albicans)
	- Fungal disease (in immunosuppression)
	- Tuberculosis

Haemangioendotheliomas have the typical US findings of well-marginated hypoechoic lesions consisting predominantly of anechoic components. Doppler US scans may reveal venous flow in anechoic spaces of the lesion, corresponding to intratumoral tortuous vascular cavities. The tumours however may be hypoechoic or heterogeneously-echoic. In our case, the splenic lesion was seen as a well-marginated isoechoic mass with a hypoechoic rim. This is not the typical appearance of splenic haemangioendothelioma that has been previously reported[3]. Furthermore, the splenic lesion had a very different appearance compared to the liver lesion on the same ultrasonographical scan, where the liver lesions were heterogeneous with irregular and thicker hypoechoic rims. To the best of our knowledge, this US pattern of hepatosplenic haemangioendotheliomas has not been previously described.

The differential diagnosis of the hepatosplenic manifestation of infantile haemangioendothelioma is not straightforward and it includes hamartoma, hepatoblastoma, metastatic lesions, lymphoma and abscesses (Table I). Hamartomas occur most commonly in the paediatric age group. They are characterised by an admixture of normal tissues arranged in an anomalous fashion. The US appearances depend upon the combination of sinusoidal and stromal components. The majority of cases are macrocystic and may produce a predominantly hypoechoic appearance. Hepatoblastomas are embryonic malignant tumours and often appear as a single palpable mass. They are seldom associated with splenic metastasis. The US appearance of hepatoblastoma varies according to the different histological types. They are usually well-defined, multilobulated and septated. They can vary in appearance from homogeneously-hypoechoic masses to heterogeneously-echogenic lesions (Fig. 5). Clinical, biochemical and histopathological criteria are used to differentiate hepatoblastoma from haemangioendothelioma.

In addition to these rather rare diseases, the most difficult differential diagnosis include metastases and infiltrative disorders such as lymphoma or leukaemia, all of which have highly variable US appearances. Differentials such as metastatic neuroblastoma, embryonal rhabdomyosarcoma and even Wilm's tumour may appear in the first year of life as abdominal masses. Infiltrative haematological disorders in infancy are also less common but should be considered. They may produce hypoechoic or rarely hyperechoic masses, and are usually associated with characteristic lymphadenopathy or bone marrow changes. If clinically septic, abscesses should also need to be considered in the differential diagnosis (Fig. 6).

Compared with US, CT offers advantages of more precise anatomical localisation, tissue enhancement and characterisation. Our case showed similar CT appearances as described in the literature, being iso- to hypodense on unenhanced images, and becoming seen as well-defined hyperattenuated masses with cleft-like centres after contrast administration[3,7]. Intense enhancement is a common finding in infantile haemangioendothelioma. With the arterial phase, the tumour shows early peripheral enhancement with variable delayed central enhancement. On magnetic resonance (MR) imaging, infantile hepatic haemangioendothelioma has been described to be heterogeneous on both T1- and T2-weighted images[8]. Dynamic gadolinium-enhanced MR imaging shows an early, prominent and nodular peripheral enhancement, followed by delayed central enhancement[6]. MR imaging features of splenic haemangioendothelioma have not been previously reported.

Radionuclide sulphur colloid and Technetium-99m labelled red blood cell scans can be diagnostic of haemangioendothelioma, showing increased flow to the viable portions of the lesion during the angiographical phase. This finding is different from the appearance of adult haemangioma which is typically photopenic on flow images. During the delayed phase, the lesions are seen as photopenic defects on sulphur colloid scans and as increased areas of activity on red cell scans[9]. However, it may be difficult to establish the definite diagnosis based solely on imaging findings. Histological confirmation is usually required. Treatment of infantile haemangioendothelioma is determined by the severity of symptoms and the size of the tumour. Infantile haemangioendothelioma, as in our case, tends to grow over the first year of life, then spontaneously regresses without treatment[10].

ABSTRACT

The ultrasonographical and computed tomography findings of a six-month-old female infant with haemangioendotheliomas of the liver and spleen are described. The splenic lesion had an unusual ultrasonographical appearance of a well-defined isoechoic mass with a hypoechoic rim. Diagnosis was confirmed by histological examination of the hepatic biopsy specimen. Hepatosplenic lesions in the first year of life may be due to a variety of pathological processes. It is important to include haemangioendotheliomas in the differential diagnosis of hepatosplenic masses in an infant.

Keywords: infantile haemangioendothelioma, hepatosplenic lesions, ultrasonography, computed tomography

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REFERENCES

1. Wong DC, Masel JP. Infantile hepatic haemangioendothelioma. Australas Radiol 1995; 39:140-4.
2. Keslar PJ, Buck JL, Selby DM. Infantile hemangioendothelioma of the liver revisited. Radiographics 1993; 13:657-70.
3. Ferrozzi F, Bova D, De Chiara F. Hemangioendothelioma of the spleen: imaging findings at color Doppler, US, and CT. Clin Imaging 1999; 23:111-4.
4. Zenge JP, Fenton L, Lovell MA, Grover TR. Case report: infantile hemangioendothelioma. Curr Opin Pediatr 2002; 14:99-102.
5. Selby DM, Stocker JT, Waclawiw MA, Hitchcock CL, Ishak KG. Infantile hemangioendothelioma of the liver. Hepatology 1994; 20:39-45.
6. Mortele KJ, Vanzieleghem B, Mortele B, Benoit Y, Ros PR. Solitary hepatic infantile hemangioendothelioma: dynamic gadolinium-enhanced MR imaging findings. Eur Radiol 2002; 12:862-5.
7. Stanley P, Geer GD, Miller JH, Gilsanz V. Landing BH. Boechat IM. Infantile hepatic hemangiomas. Clinical features, radiologic investigations, and treatment of 20 patients. Cancer 1989; 64:936-49.
8. Powers C, Ros PR, Stoupis C, Johnson WK, Segel KH. Primary liver neoplasms: MR imaging with pathologic correlation. Radiographics 1994; 14:459-82.
9. Moinuddin M, Allison JR, Montgomery JH, Rockett JF, McMurray JM. Scintigraphic diagnosis of hepatic hemangioma: its role in the management of hepatic mass lesions. Am J Roentgenol 1985; 145:223-8.
10. Jackson C, Greene HL, O Neill J, Kirchner S. Hepatic hemangioendothelioma. Angiographic appearance and apparent prednisone responsiveness. Am J Dis Child 1977; 131:74-7.