Mesenchymal hamartoma of the liver - a case report and literature review

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ABSTRACT

We report a case of a mesenchymal hamartoma of the liver in a two-year-old boy. He presented to the emergency room with abdominal distention and vomiting. Abdominal ultrasound and computed tomography were performed and revealed a large, intra-peritoneal lesion, with thick wall, multiple cysts of variable size and solid septa. The lesion was surgically resected. Pathological examination revealed a mesenchymal hamartoma of the liver. We are including a short literature review, highlighting the main features of mesenchymal hamartoma of the liver, and discussing its differential diagnosis.

CASE REPORT

CASE REPORT

A two-year-old boy with no relevant personal or family medical history was admitted at the emergency department with a two week history of vomiting and abdominal distention. On physical examination a large, painless abdominal mass was noted. It extended through the right hypochondrium, epigastrium and umbilical region, crossing the midline and causing abdominal distention. Laboratorial studies showed elevated serum levels of AST: 1200 U/L (normal range < 37U/l), ALT: 870 U/L (normal range < 41 U/L) and LDH: 1187 U/L (normal range 24-480 U/L), with normal complete blood count and normal renal function.

The abdominal plain radiography showed a soft tissue opacity occupying the right and middle quadrants of the abdomen and displacing the bowel loops peripherally (Fig 1).

An abdominal ultrasound (US) was performed and demonstrated a large heterogeneous mass, which measured about 16cm in major axis and had a mixed echotexture with a peripheral solid area and a central cystic component (Fig.2). The peripheral solid area measured about 30mm thick. It was heterogeneous and slightly hyperechoic relative to adjacent liver parenchyma. The central cystic component of the mass measured 13cm in the major axis and had a complex appearance, containing cysts of variable size and multiple septa. The lesion was well demarcated, with smooth borders, abutting the right lobe of the liver (Fig 3). Spleen, pancreas and kidneys were compressed by the mass.

For further characterization, a contrast-enhance computed tomography (CT) of the abdomen was performed, confirming the presence of a large intra-peritoneal mass, with 16x9x15cm (transversal x antero-posterior x longitudinal axis). It abutted the right lobe of the liver, extended to the retroperitoneum and to the anterior and lateral abdominal wall and displaced bowel loops to the periphery (Fig 4). The limits of the lesion were smooth and slightly lobulated. The mass had a peripheral heterogeneous area with nodular enhancement after contrast injection and a central area of water density (Fig. 5). The central cystic area had multiple septa that enhanced after contrast injection (Fig. 6).

Surgical resection of the mass was performed and the origin of the mass in the right lobe of the liver (segment V) was confirmed. The pathological examination found typical aspects of a mesenchymal hamartoma of the liver, establishing the final diagnosis (Fig. 7 and 8).

Follow-up has been based on US and blood analysis. One year after surgery, there are no signs of recurrence.

DISCUSSION

Benign liver tumors are rare in the pediatric age group, with a reported incidence of 0.7 per million population per year. Mesenchymal hamartoma account for 18% to 29% of these tumors [1]. Its etiology is not completely understood, but it seems to represent a congenital, localized, abnormality of the ductal plate development [2, 3]. Its origin is probably in the connective tissue along the portal tracts. Progressive enlargement is caused by areas of cystic degeneration with further fluid accumulation [4, 5].

Mesenchymal hamartoma occur almost exclusively in young children with an average age of 15 months. It is usually seen in children younger than 2 years old, with nearly all lesions (95%) discovered by age of 5 years [2, 4, 5]. There is a slightly male predominance with a 3:2 male:female ratio [4]. Association with polycystic kidney disease, congenital hepatic fibrosis and biliary hamartoma has been described. Children typically present with progressive abdominal enlargement and a palpable, asymptomatic mass in the right upper quadrant of the abdomen. Serum levels of AFP are usually normal [4, 5].

Imaging studies usually show a large, well-marginated, solitary mass measuring up to 30 cm. Most lesions contain cysts of varying sizes, ranging from a few millimeters to more than 15 cm. The mass arises in the right lobe of the liver in 75% of cases and it may be pedunculated [4]. Calcifications and hemorrhage are rare. At unenhanced CT, mesenchymal hamartoma has a heterogeneous appearance. The stromal elements appear hypoattenuating, whereas the cystic component is of water attenuation. After contrast administration the mesenchymal component enhances [2]. The appearance of the mass depends on whereas it is predominantly stromal (mesenchymal) or cystic, ranging from multiple small cysts in a solid mass (Swiss cheese appearance), to a multilocular cystic lesion with solid septa. The case described is an example of a cystic variant, which is far more common than the solid one. When the cystic component of the mass predominates, its hepatic origin may be difficult to identify, particularly in larger masses [6].

The MR imaging appearance of mesenchymal hamartoma of the liver is also variable. It depends on the cystic versus stromal composition of the mass, as well as on the protein content of the fluid [2]. Solid areas may appear hypointense to adjacent liver both on T1- and T2-weighted images owing to fibrosis. The cystic areas are generally close to water signal intensity on T2-weighted images and demonstrate variable signal intensity on T1-weighted images, depending on the protein content of the cyst fluid. After intravenous administration of gadolinium, enhancement is mild and limited to the septa and stromal components [4].

Treatment consists of surgical resection. Pathologically, the mesenchymal hamartoma of the liver is a large mass composed of loose edematous tissue, blood vessels, small groups of hepatocytes, abnormal bile ducts and immature mesenchyme in variable proportions. The cysts are areas of tissue degeneration with fluid accumulation, separated by thin strands of connective tissue [5, 6].

Differential diagnosis includes other causes of intraperitoneal cystic masses such as hydatid cysts, mesenteric cysts, gastrointestinal duplication cysts and cystic teratomas of the mesentery [7, 8].

Hydatid cysts are caused by a parasitic infection (E. Granulosus), which is endemic in the Mediterranean Basin. At US they range from purely cystic to solid-appearing lesions. Smooth borders and well-defined walls are typical. Cystic components may contain internal wavy bands of a delaminated endocyst or multiple daughter cysts surrounded by hyperecoic debris. At CT, calcifications are often seen with a peripheral distribution [7]. MR imaging can demonstrate the pericyst as a hypointense rim on both T1 and T2-weighted images, the matrix or hydatid sand which appears hypointense on T1-weighted images and markedly hyperintense on T2-weighted images, and the daughter cysts, hypointense relative to the matrix on both T1- and T2-weighted images.

Enteric duplication cysts are usually attached to normal bowel and result from duplication of the bowel wall (mucosa, muscular layers and nerve plexus). At US they appear as unilocular cysts with a thick double-layered wall resembling the intestinal wall. Intracystic hemorrhage may occur resulting in internal debris. CT and MR imaging reveal cystic masses with thick walls, which enhance after intra-venous contrast administration [8, 9].

Among mesenteric cysts, a lymphangioma could be suspected. Lymphangiomas are chylous or serous cysts with an endothelial lining. Sonographically they appear as large, thin walled, multilocular cystic masses. They may be anechoic or contain internal echoes and debris. At CT their attenuation values range from those of water (if serous) to those of fat (if chylous). An MR imaging, the cyst content intensity is similar to fluid on T1 and T2-weighted images. Mesothelial and enteric cysts are thin-walled unilocular cysts, and therefore, less suitable for the differential diagnosis [8, 10].

Cystic teratoma of mesentery is a rare benign tumor of the pediatric age group with a variable appearance. Teratomas contain multiple tissues, forming a well-defined mass with cystic and solid components. At US they have pure, well demarcated cystic areas and diffuse focal echogenicities with acoustic shadowing characteristic of calcifications. CT and MR imaging demonstrate the mixed content of these tumors, with areas of water and fat, as well as calcifications [8, 11].

Although the cystic component of the mesenchymal hamartoma usually predominates, appearance at imaging can be sometimes solid, and therefore, hepatoblastoma, infantile hemangioendothelioma, hepatocellular carcinoma fibrolamellar type and metastatic lesions should also be included in the differential diagnosis.

Hepatoblastoma is the most common primary hepatic tumour in children. It is a malignant neoplasm whose cells resemble embryonic liver. AFP is usually elevated. At US, the appearance depends on the histologic type. These tumours are most often hyperechoic relative to adjacent liver parenchyma.

CT demonstrates a well circumscribed mass that is slightly hypoattenuating to the adjacent liver. Calcifications and haemorrhage are common findings. The tumour enhances slightly, but less than normal liver parenchyma. At MR imaging, the tumour can be homogeneous or heterogeneous depending on its histologic type. It is slightly hypointense in T1-weighted images and hyperintense on T2-weighted images. Fibrotic septa may be present, with characteristic hypointensity on both T1 and T2-weighted images [12, 13].

Infantile hemangioendothelioma is a benign but aggressive liver tumor that usually manifests in children younger than 6 months old. It is composed of a network of connecting vascular channels, appearing as a solid, large solitary mass or as multifocal masses. At US hemangioendothelioma is generally hypoechoic or of mixed echogenicity relative to adjacent liver. Calcifications and areas of hemorrhage, necrosis or fibrosis are common in larger lesions. Color Doppler shows large hepatic arteries and veins and feeding and draining vessels. At unenhanced CT hemangioendothelioma usually appears as a well-defined hypoattenuating mass. After intra-venous administration of contrast material, the enhancement pattern is similar to that of haemangiomas [2]. On arterial phase images there is usually intense nodular peripheral enhancement. On portal venous and delayed phases there is progressive centripetal fill-in of enhancement of the tumor. MR imaging is the preferred modality for evaluating infantile hemagioendotheliomas, as they are markedly hyperintense on T2-weighted images, owing to their vascular nature. At dynamic gadolinium-enhancing imaging the enhancing pattern is similar to that seen on contrast-enhanced CT [4].

Hepatocellular carcinoma fibrolamellar type occurs in adolescents and young adults and it is typically not associated with underlying liver disease or elevated serum levels of AFP. The tumor has multiple fibrous septa, which coalesce to form a central fibrous scar. Calcifications of the central scar are common. At US these tumors appear as large, heterogeneous, hypoechoic or isoechoic masses. The central scar, if present, is hyperechoic, with or without calcifications. At CT the mass is hypoattenuating relative to the adjacent liver. After contrast enhancement, the tumor becomes hyperattenuating in the arterial phase, with variable contrast wash-out in portal and venous phases. The central scar is hypoattenuating relative to the rest of the tumor and it may have some degree of enhancement on delayed phase. MR imaging demonstrates a hypointense or isointense mass on T1-weighted images, which is hyperintense or isointense on T2-weighted images. If present, the fibrous central scar and septa appear hypointense on both T1 and T2-weighted images [13].

Metastatic lesions are the most common liver tumors in children. In this age group the most common primaries are neuroblastoma, Wilms' tumor, leukemia and lymphoma. Liver metastases generally appear as multiple solid lesions. Less often metastatic disease can cause diffuse infiltration of the liver. Atypical findings like cystic lesions or solitary solid masses can sometimes be seen [14].

Mesenchymal hamartoma is a developmental anomaly rather than a neoplasm. It appears as a large mass with cystic spaces of variable size [6]. Its hepatic origin is a main clue to the diagnosis, however it may be difficult to identify, particularly in the larger, predominantly cystic masses. US is frequently used for initial evaluation, but further characterization by CT or MR imaging is need. Total surgical resection is recommended. Some authors suggested the possibility of a malignant mesenchymoma arising from a mesenchymal hamartoma and emphasized the need for complete removal of the lesion and a long-term follow-up [15]. Other authors have showed spontaneous resolution of mesenchymal hamartoma and suggested the possibility of conservative management [16]. In most cases prognosis is excellent. To our knowledge, there are no reported cases of recurrence after surgical excision. Mortality is related to surgical complications [5].

TEACHING POINT

Hepatic mesenchymal hamartoma is a rare, benign hepatic tumor with a variable appearance in imaging studies, ranging from multiple small cysts in a solid mass, to a multilocular cystic mass with solid septa. Surgical excision is a curative treatment.

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FIGURES

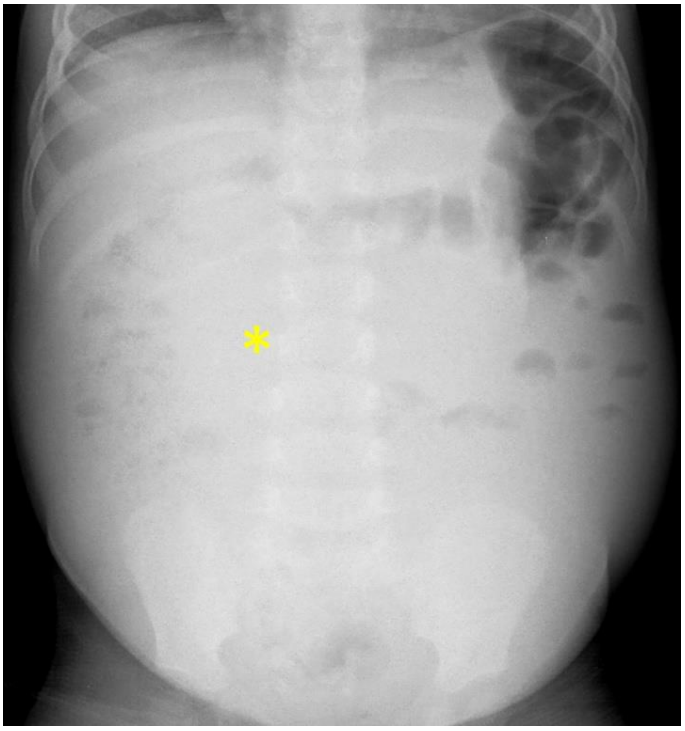

Figure 1: Two year old boy with mesenchymal hamartoma of the liver. Upright plain abdominal radiograph demonstrates a large, soft tissue density abdominal mass, extending through the right hypochondrium, epigastrium and umbilical region, crossing the midline and displacing bowel loops to the periphery of the abdominal cavity.

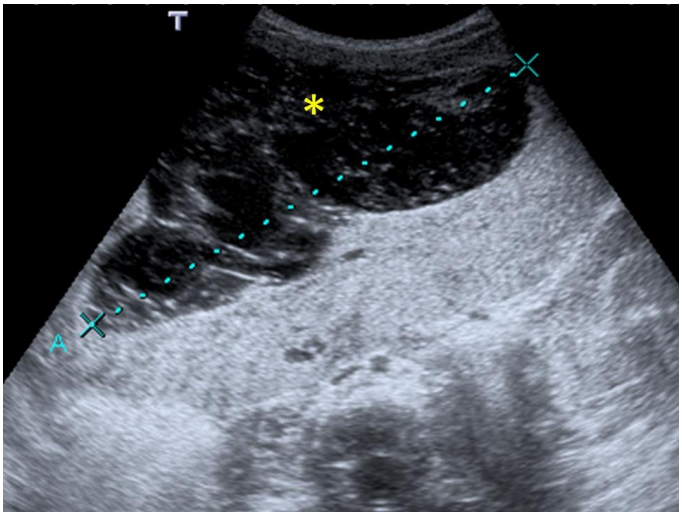

Figure 2: Two year old boy with mesenchymal hamartoma of the liver. Abdominal grayscale US scan performed with a convex array transducer (3-6MHz) in a Toshiba SSA-700A APLIO ®. Coronal scanning plane through the right hypochondrium demonstrates a large abdominal mixed cystic and solid mass, measuring about 16cm. The central cystic component of the mass (*) measures 13cm in the major axis and has a complex appearance, containing cysts of variable size and multiple septa. At the periphery of the lesion it is visible a hyperechoic and heterogeneous solid area.

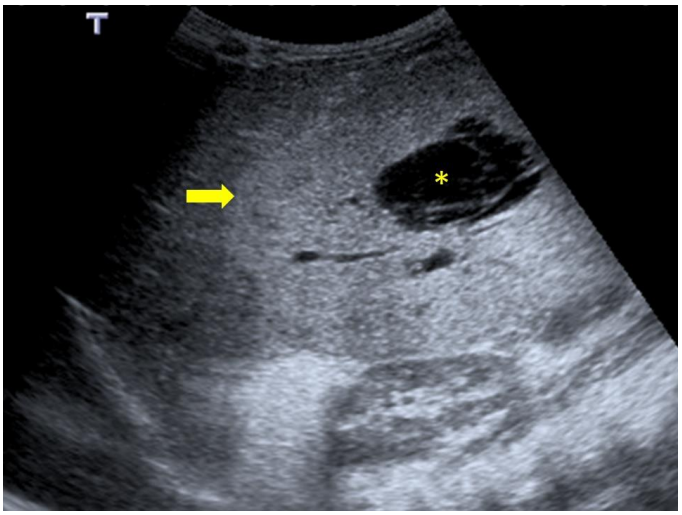

Figure 3 (left): Two year old boy with mesenchymal hamartoma of the liver. Abdominal grayscale US scan performed with a convex array transducer (3-6MHz) in a Toshiba SSA-700A APLIO®. Paramedian scanning plane demonstrates a large abdominal mass abutting the liver. The transition zone between the lesion and the normal liver parenchyma is well seen (arrow). The solid peripheral component of the mass measures about 30mm and is slightly hyperechoic relative to adjacent liver parenchyma. The central cystic component of the mass is also visible (*).

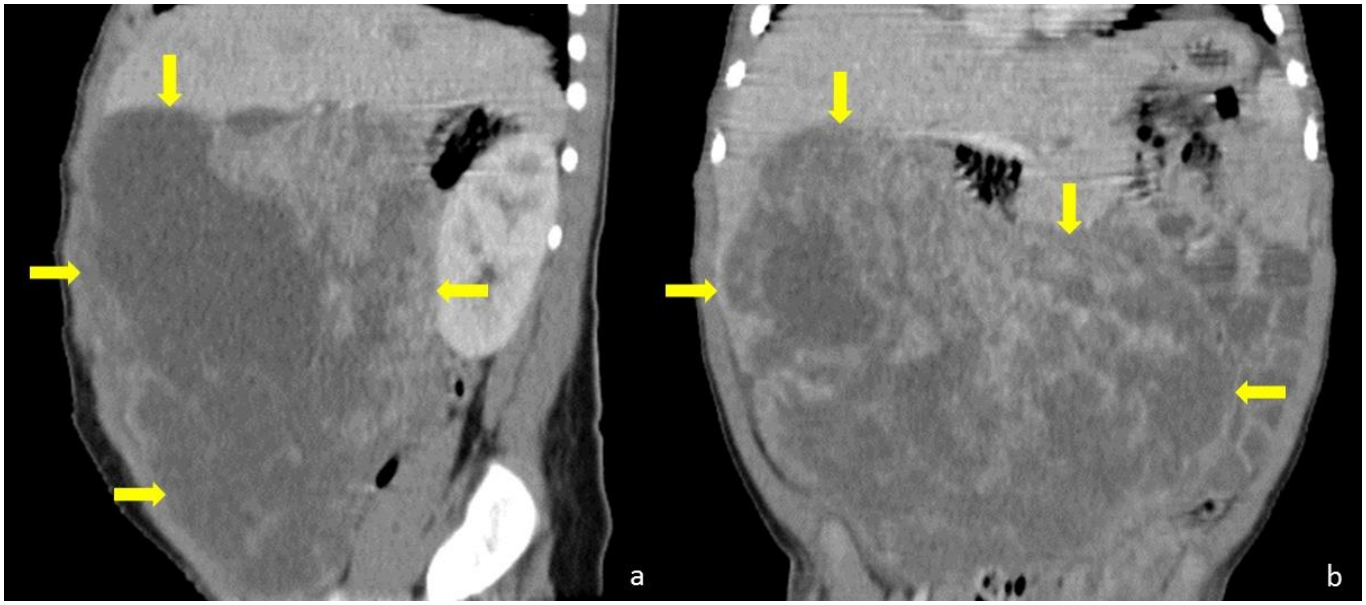

Figure 4: Two year old boy with mesenchymal hamartoma of the liver. Contrast enhanced low dose CT, performed with a GE Light Speed Plus (4 slice-CT). Injection of 28ml (2ml/Kg) of 300mg/ml iodine concentration non-ionic contrast agent. Sagittal (a) and coronal (b) reconstructions of 2,5mm thickness, demonstrate a large intra-peritoneal mass (arrows) measuring 16x9x15cm. It displaces the bowel loops to the periphery. The mass is heterogeneous, containing multiple areas of water density with no contrast-enhancement, corresponding to the cystic components of the lesion.

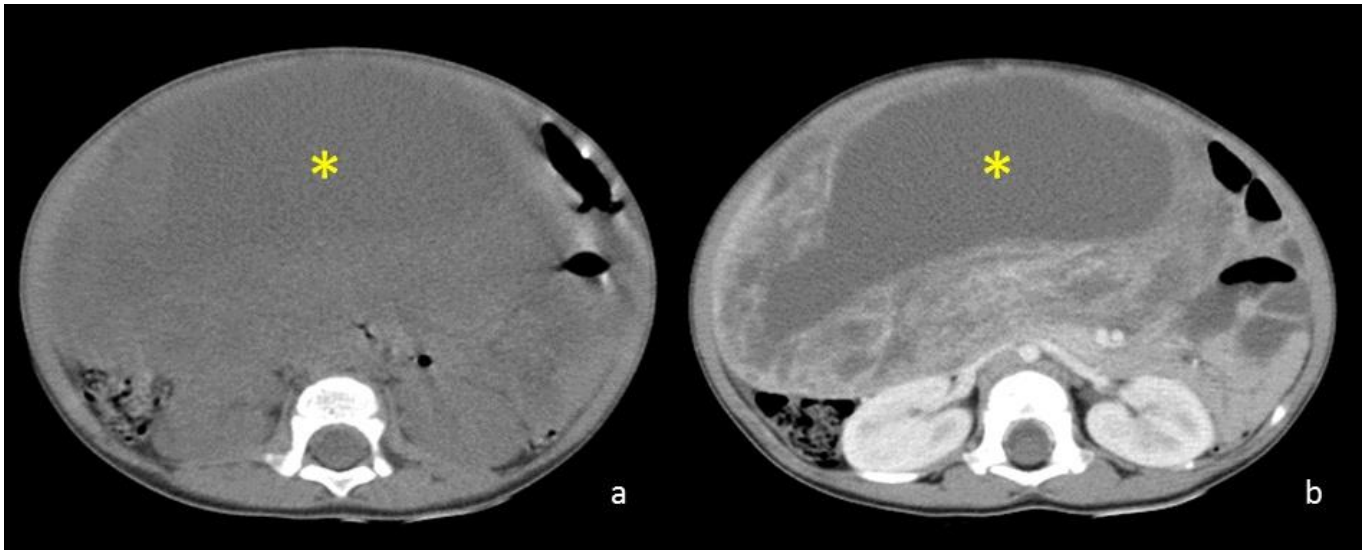

Figure 5: Two year old boy with mesenchymal hamartoma of the liver. Low dose CT, performed with a GE Light Speed Plus (4 slice-CT). Injection of 28ml (2ml/Kg) of 300mg/ml iodine concentration non-ionic contrast agent. Non-enhanced (a) and contrast-enhanced (b) 2,5mm thickness reconstruction images in similar axial planes demonstrate a large abdominal mass, contacting the anterior and lateral abdominal wall and displacing laterally and posteriorly the bowel loops. The mass is well demarcated and has mixed density, with a central non-enhancing area of water density (*) and a peripheral soft tissue density, heterogeneous, hyperenhancing area measuring about 30mm in thickness.

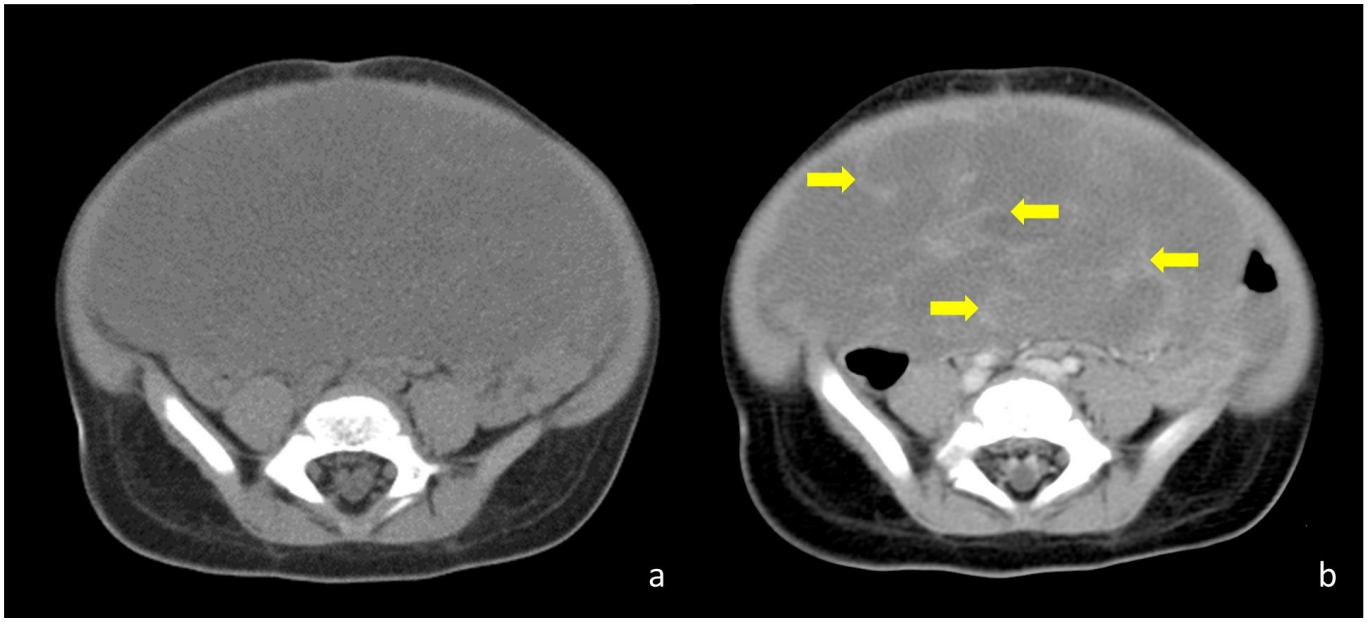

Figure 6: Two year old boy with mesenchymal hamartoma of the liver. Low dose CT, performed with a GE Light Speed Plus (4 slice-CT). Injection of 28ml (2ml/Kg) of 300mg/ml iodine concentration non-ionic contrast agent. Non-enhanced (a) and contrast-enhanced (b) 2,5mm thickness reconstruction images in similar axial planes demonstrate a large mass extending through the lower quadrants of the abdomen. In this plane, it is predominantly cystic, containing multiple enhancing septa (arrows).

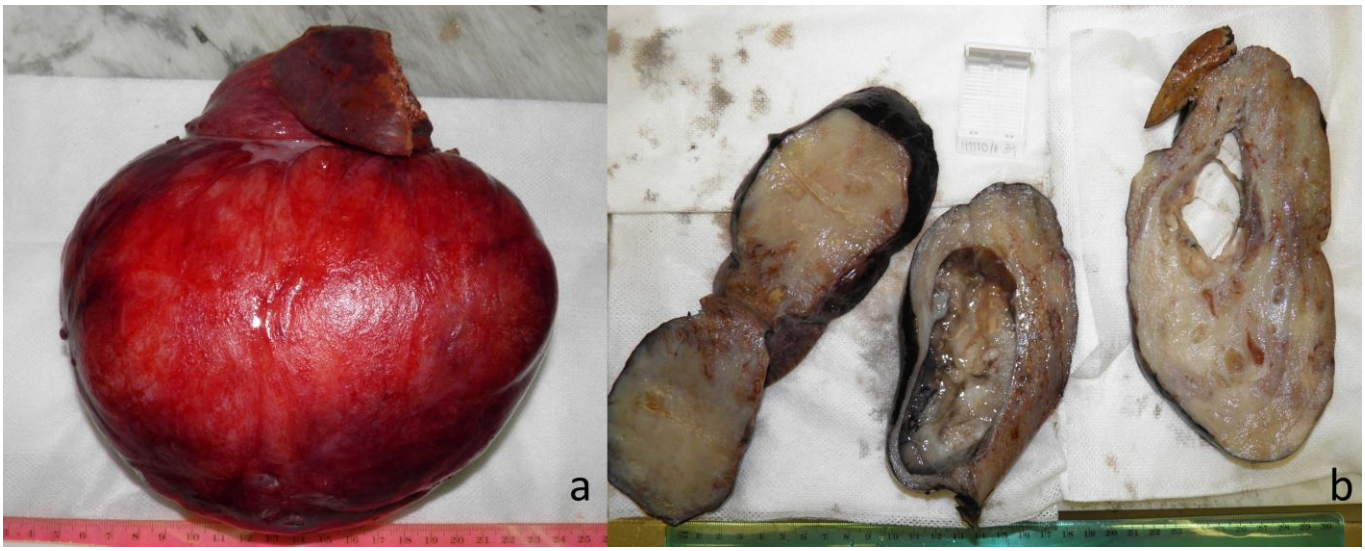

Figure 7: Two year old boy with mesenchymal hamartoma of the liver. Gross examination of the surgical specimen. Tumorectomy specimen (a), with 836g and 19x16x13cm, with well demarcated limits and involved by a thin capsule. The surface is brown and slightly bosselated. The specimen is in continuity with a hepatic segment of normal appearance, measuring 11cm in major axis. The cross section (b) is white and brown, with a heterogeneous appearance, containing solid components and multiple cystic areas of serous fluid. The major cystic area has 12cm and internal smooth walls.

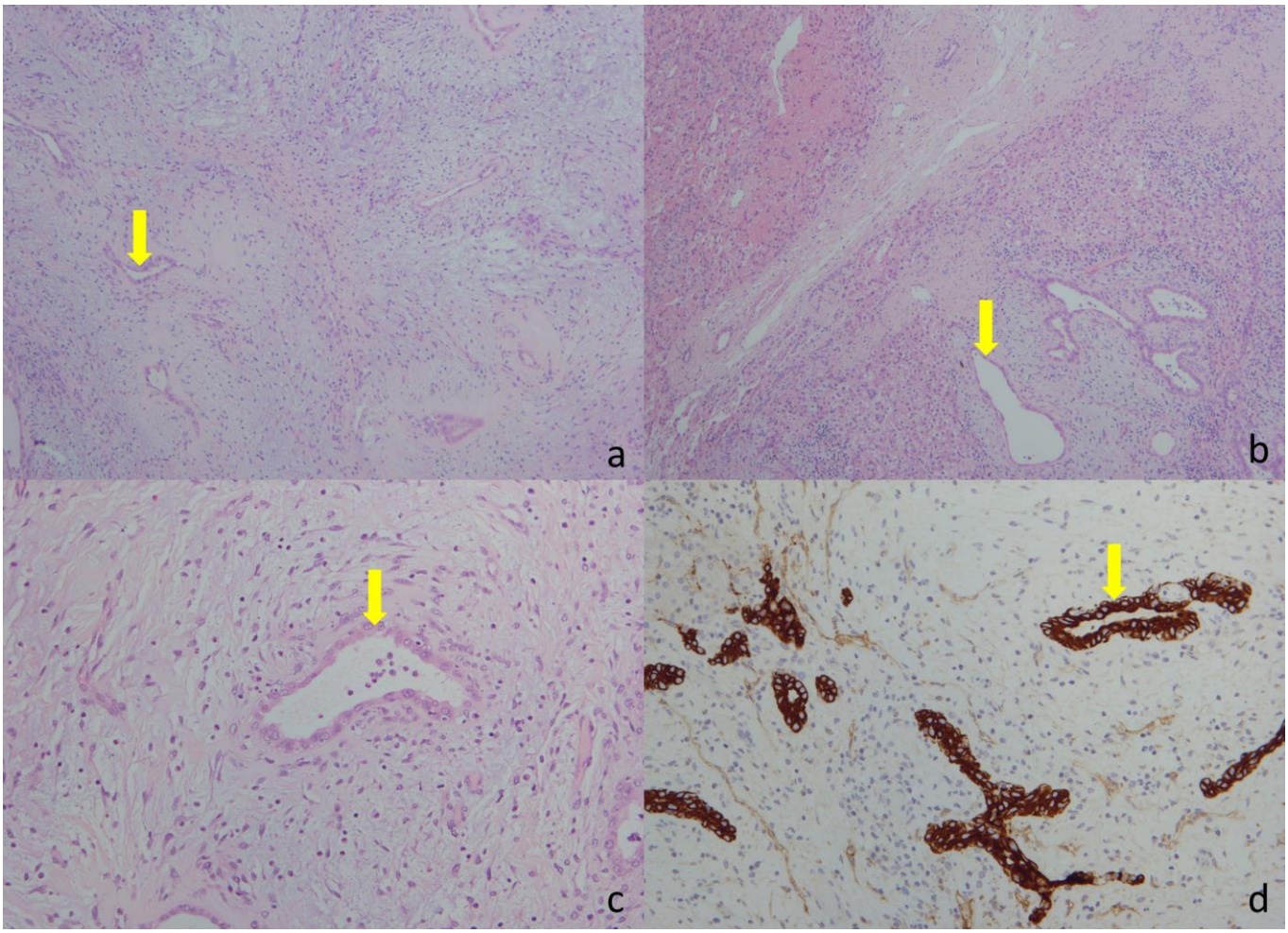

Figure 8: Two year old boy with mesenchymal hamartoma of the liver. Pathological study of the surgical specimen (a and b-Hematoxylin and eosin (HE) x 40, c-HE x 100, d-Cytokeratin7 (CK7) x 100) demonstrates immature mesenchyme containing blood vessels, small groups of hepatocytes and abnormal bile ducts (arrows). Figure 8d demonstrates that the specimen was positive for CK7, which confirms the presence of bile ducts.

	Ultrasonography	**Computed Tomography**	**MR imaging**
Mesenchymal Hamartoma of the Liver	Large, intra-peritoneal mass. Solid component and multiple cysts of variable sizes. Solid septa. Calcifications and hemorrhage are rare but may occur.	Heterogeneous appearance. Central water attenuation areas. Peripheral thick, heterogeneous area, which enhances after contrast injection. Calcifications and hemorrhage.	Solid areas are hypointense both on T1 and T2. Cystic areas have water signal intensity on T2 and variable signal on T1. Enhancement is mild and limited to the septa and stromal components.
Hydatid cyst of the liver	Variable findings according to the evolution phase: 1-Symple cysts. 2-Cysts with internal membranes. 3-Cysts with internal daughter cysts and debris 4-Densely calcified masses	Well-defined wall. Homogeneous water attenuation cystic components or heterogeneous cystic components with internal membranes or multiple daughter cysts. Peripheral calcifications.	The pericyst is seen as a hypointense rim on both T1 and T2. The hydatid matrix appears hypointense on T1 and markedly hyperintense on T2. Daughter cysts are hypointense on both T1 and T2.
Enteric duplication cyst	Unilocular cysts. Thick double-layered wall. Intracystic hemorrhage may occur.	Water attenuation masses with tick wall. Enhancement of the wall after contrast administration.	Water signal intensity on T2. Thick wall, which enhances after gadolinium administration.
Lymphangioma	Large cystic masses. Thin walled. Multilocular. Anechoic or containing internal echoes and debris.	Variable density. Water attenuation lesions (serous content) to fat attenuation lesions (chylous content).	Cyst content intensity similar to water on T1 and T2-weighted images.
Cystic Teratoma	Heterogeneous mass. Pure cystic components. Calcifications.	Heterogeneity, with areas of water and fat attenuation. Calcifications.	Signal intensity characteristics of fat (hyperintense on T1) and water (hypointense on T1 and hyperintense on T2).
Hepatoblastoma	Well circumscribed solid hyperechoic mass.	Slightly hypoattenuating. Calcifications and haemorrhage are common. Enhancement after contrast administration but less than normal liver.	Slightly hypointense on T1 and hyperintense on T2. Fibrotic septa are hypointense on both T1 and T2-weighted images.
Hemangio-endothelioma	Hypoechoic or of mixed echogenicity. Calcification, hemorrhage, necrosis and fibrosis in larger lesions. Color Doppler shows enlarged vessels.	Well-defined hypoattenuating mass. Calcification and haemorrhage. After contrast administration the enhancement pattern is similar to that of the haemangiomas.	Hyperintense on T2-weighted images. After gadolinium administration enhancing pattern is similar to that seen on CT.
Fibrolamellar HCC	Heterogeneous, hypoechoic or isoechoic. The central scar is hyperechoic, with or without calcifications.	Hypoattenuating mass. Contrast enhancement in arterial phase. Variable wash-out in portal and venous phases. The central scar is hypoattenuating and it may have some enhancement on delayed phase.	Typically hypointense on T1 and hyperintense on T2. Fibrous central scar and septa hypointense on both T1 and T2-weighted images.
Metastases	Multiple solid lesions or diffuse infiltration of the liver. Cystic lesions or solitary solid masses are rare.	Often hypoattenuating masses. Variable appearance and patterns of contrast enhancement.	Most metastases are hypo- to isointense on T1 and iso- to hyperintense on T2. Variable enhancement.

Table 1: Differential diagnosis table for mesenchymal hamartoma of the liver

Etiology	Not completely understood, probably an abnormality of the ductal plate development.
Incidence	Rare. Less than 0.2 cases per million population per year.
Gender Ratio	Male predominance with a 3:2 male:female ratio.
Age Predilection	Average age 15 months. 95% of the lesions occur in children younger than 5 years old.
Risk Factors	Polycystic kidney disease, congenital hepatic fibrosis and biliary hamartomas are associated anomalies.
Treatment	Surgical excision.
Prognosis	Excellent. Mortality is related to surgical complications.
Findings on Imaging	Large, solitary, cystic mass. Ranges from a solid mass with multiple small cysts, to a multilocular cystic mass with solid septa. After contrast administration the solid component enhances. Calcifications and hemorrhage are rare but may occur.
Findings on Pathology	Edematous tissue, blood vessels, small groups of hepatocytes, abnormal bile ducts and immature mesenchyme in variable proportions. Areas of degeneration and fluid accumulation.

Table 2: Summary table for mesenchymal hamartoma of the liver

ABBREVIATIONS

AFP: alpha-fetoprotein
ALT: Alanine transaminase
AST: aspartate aminotransferase
CK: citokeratin 7
CT: computed tomography
HCC: hepatocellular carcinoma
HE: hematoxylin-eosin
LDH: lactate dehydrogenase
MR: Magnetic resonance
US: ultrasound

KEYWORDS

Mesenchymal hamartoma; liver; abdominal cystic masses