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Special review

Mesenchymal hamartoma of the liver: a systematic review

Mark D. Stringer*, **Naved K. Alizai**

Children's Liver & GI Unit, St. James's University Hospital, Leeds LS9 7TF, UK

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Abstract Mesenchymal hamartoma of the liver is the second commonest benign liver tumor in children, yet its biology and pathogenesis are poorly understood. Cytogenetic studies have suggested that the tumor may be a neoplasm rather than a hamartoma. Typically, it presents as a large benign multicystic liver mass in a child younger than 3 years amenable to complete resection. However, its imaging characteristics are variable, ranging from a few large cysts to a solid mass occupying one or both lobes of the liver. In addition, the tumor occasionally contains angiomatous elements or is multifocal. Most tumors gradually increase in size, some reaching enormous proportions, which can make surgery challenging. Paradoxically, a few undergo incomplete spontaneous regression and, on rare occasions, others have shown malignant transformation to undifferentiated (embryonal) sarcoma. These unusual pathological and biological features must be taken into account when considering the management of affected individuals.

After hemangiomas, mesenchymal hamartoma is the second commonest benign hepatic tumor in childhood. However, its origin and biology are poorly understood and its management controversial. This systematic review is based on a detailed literature search of electronic databases and older publications and personal experience with this tumor in a referral center dealing with complex pediatric hepatobiliary disorders. The article aims to summarize our current knowledge about mesenchymal hamartoma of the liver (MHL) and review the evidence base for current clinical management.

The first definitive description of MHL, a tumor previously been known by various diverse terms, was by Edmondson [1] in 1956. In a review of more than 1200 pediatric liver tumors, Weinberg and Finegold [2] found that MHL accounted for 6% of all specimens. Nevertheless, these tumors are relatively rare, and large children's hospitals are unlikely to see more than 1 new case every 2 years [3-6]. Most MHLs are large benign multicystic masses that present in the first 2 years of life [5,7]. An analysis of 134 cases reported from 14 institutions shows that approximately 85% of affected children present before the age of 3 years and that the tumor is slightly more common in boys [2-6,8-16].

1. Presentation

Mesenchymal hamartoma of the liver may be found incidentally on physical examination or imaging, but typically it presents with abdominal distension and/or an upper abdominal mass. Abdominal pain, anorexia, vomiting, and poor weight gain have also be reported, but pain is seldom a dominant feature. Typically, examination reveals a large, nontender, firm, and smooth liver tumor.

* Corresponding reviewer. Children's Liver and GI Unit, Gledhow Wing, St James's University Hospital, LS9 7TF Leeds, UK. Tel.: +44 0113 206 6689; fax: +44 0113 206 6691.
E-mail address: mdstringer@dial.pipex.com (M.D. Stringer).

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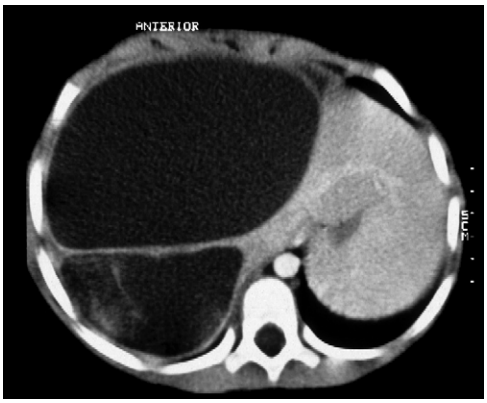

Fig. 1 Abdominal CT scan of a 7 year-old girl with an MHL consisting predominantly of 2 large cysts.

There may be visibly engorged veins over the anterior abdominal wall and, rarely, lower limb edema from inferior vena cava compression.

Other presentations are age related and include:

- Prenatal. Mesenchymal hamartoma of the liver has been detected by prenatal ultrasound (US), most often in the last trimester of pregnancy [17-27]. Maternal serum α-fetoprotein (αFP) and/or β human chorionic gonadotrophin may be elevated [17,24,28], and there may be polyhydramnios.
- Newborn. The tumor can cause respiratory distress [3,8,15,28] or apnea [29]. High-output cardiac failure has been reported in several infants, including 2 with relatively small and localized tumors [10,30-32]. There are isolated case reports of MHL causing pulmonary hypertension, vascular steal and thrombocytopenia [33], perinatal tumor rupture with ascites [34], obstructive jaundice [10], and fatal bleeding into the tumor after birth trauma [35]. In the newborn, the tumor may expand rapidly to cause life-threatening abdominal distension [36].
- Older children. Rarer presentations include obstructive jaundice [37], disseminated intravascular coagulation [38], constipation [39], and spontaneous abscess formation [40]. Fewer than 5% of MHL present after the age of 5 years.
- Adults. Mesenchymal hamartomas of the liver are rare in adults in whom they may cause abdominal pain and distension. In a review of the literature, Papastratis et al [41] identified 15 patients older than 18 years with MHL, and Cook et al [42] subsequently added 3 additional cases. The oldest reported patient was 69 years old and she had a tumor that weighed 3600 g [43]. Mesenchymal hamartomas of the liver in adults tend to contain more hyalinized fibrous tissue, fewer ductal structures, and are frequently more vascular than their pediatric counterpart. Cystic or solid components may predominate [42,44].

Typically, MHLs are not associated with other congenital anomalies. However, the following associations have been described: congenital heart disease [5,6], endocardial fibroelastosis [11], intestinal malrotation (the cystic liver tumor was considered to have prevented normal gut rotation) [45], esophageal atresia with or without an annular pancreas [4,46], biliary atresia [9,12], exomphalos [47], myelomeningocele [48], and Beckwith-Wiedemann syndrome [25]. Adrenal cytomegaly and pancreatic islet cell hyperplasia were noted at autopsy in 2 infants that died at or soon after birth, but the possibility of Beckwith-Wiedemann syndrome in these cases was not discussed [11].

2. Investigations

Biochemical liver function tests are usually normal, but may be mildly deranged. In some patients the serum αFP concentration is moderately elevated [49,50]; levels decrease to normal after complete tumor resection [8,12,50-52], but this may take up to a year because of ongoing liver regeneration [49]. The source of αFP is the hepatocytes and bile duct epithelium within the loose myxoid stroma of the tumor [51]. The possibility of a moderately raised αFP in a child with MHL is important because some patients have received inappropriate chemotherapy for presumed hepatoblastoma before the tumor was biopsied [49,50].

Plain radiography may show calcification within the hepatic tumor but this is uncommon [53]. Ultrasound, computed tomography (CT), and magnetic resonance imaging demonstrate a multiloculated cystic tumor with a variable amount of solid tissue. Cysts are frequently septated, but

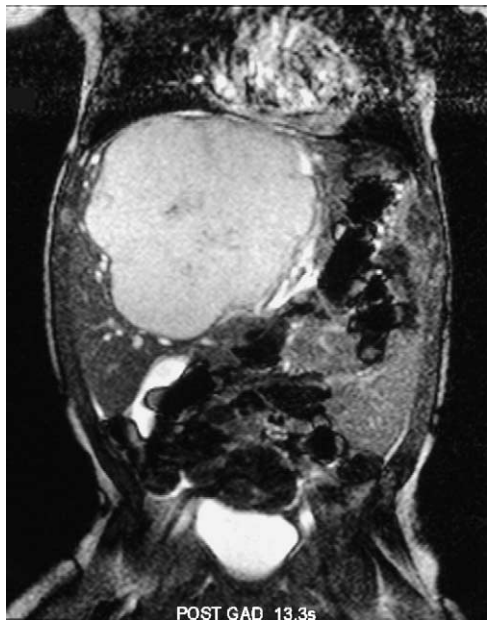

Fig. 2 Magnetic resonance scan of a 2-month-old baby with a large, dominantly solid MHL (after gadolinium contrast).