Mesenchymal hamartoma of the liver – case report and short literature overview

Marcin Orłowski¹, Danuta Bręborowicz²

¹Department of Pathomorphology, Regional Hospital, Poznań
²Department of Tumour Pathology, Greater Poland Cancer Centre, Poznań

Mesenchymal hamartoma (MH) is an uncommon benign hepatic tumour that presents mostly before the age of 2 years. Its biology and pathogenesis are poorly understood.

We present the case of a 1-year-old male patient with a huge tumour of the right lobe of the liver which showed rapid enlargement. Imaging procedures revealed a central solid lesion, 18 cm in diameter in the right lobe of the liver, with cystic degeneration.

After surgical resection a diagnosis of mesenchymal hamartoma was established by pathological examination of the surgical specimen.

Postoperative recovery of the patient was uneventful.

Key words: mesenchymal hamartoma, liver tumour.

Case report

A 13-month-old boy was admitted to the haematology-oncology unit of the University Hospital with a hugely bulging abdomen. On presentation, he was anicteric, lacked ecchymoses or evidence of bleeding diathesis. Physical examination revealed a large painless mass in the right abdomen. A computed tomography scan disclosed a solid, partially cystic tumour mass extending from the right lobe of the liver, filling the right portion of the abdominal cavity and displacing the coeliac trunk. No intra-abdominal lymphadenopathy was identified. Laboratory studies revealed normal levels of liver enzymes and bilirubin. AFP, β-HCG and CEA were also normal. Because of aspiration of food during feeding and further problems with breathing, the patient was transferred to the intensive care unit. Despite the implementation of chemotherapy to reduce the tumour, the patient’s condition did not improve, and he soon developed signs of heart failure.

To save the patient’s life, laparotomy was performed and the tumour was totally resected.

The gross specimen measured 18 × 15 × 10 cm. The tumor was well circumscribed, but not encapsulated.

The cut surfaces of the mass were composed of solid areas, grey-pink in colour and numerous cysts ranging up to 3.2 cm. Cystic spaces were filled with yellow gelatinous material (Fig. 1).

On microscopic examination the tumour was composed of branching bile ducts without atypia surrounded by myxomatous connective tissue with myofibroblast-like cells (Fig. 2) and multiple cysts without epithelial lining (Fig. 3). Scattered inflammatory cells were also present in loose stroma.

Fig. 1. The cut surface of the tumour mass removed from the right lobe of the liver
Between the bile ducts and mesenchymal stroma large groups of hepatocytes were present (Fig. 4).

In immunohistochemical staining, the bile duct epithelial cells were positive for CK7 and Cam5.2 but negative for CK20. Stromal cells were strongly positive for vimentin and focally positive for desmin. HepPar-1 immunoreactivity was strong in groups of hepatocytes. Ki67 antigen was positive in both tubular epithelium and the stroma (Fig. 5).

Discussion

Epidemiology

Mesenchymal hamartoma (MH) is an uncommon hamartomatous growth of mesenchymal tissue, bile ducts, hepatic cords and blood vessels in the liver [1]. MH represents 5-8% of paediatric hepatic tumours and is the second most common benign hepatic tumour in childhood [2, 3]. Eighty percent are diagnosed before the second year of life and the remainder are detected by 5 years of age [4]. Only 15 cases of hamartomas in adults have been reported in the English language literature worldwide [5].

Clinical presentation

Symptoms of MH depend on the patient’s age, tumour size and growth rate.

Due to its rapid increase in size, it is often misdiagnosed clinically as a malignant tumour or as a hepatic cyst because of its cystic appearance [6]. MH may be observed prenatally in ultrasonography as a hypoechoic mass in the liver coexisting with placental abnormalities such as thickening, multicystic enlargement of the placenta or mesenchymal stem villous hyperplasia [7-9].

Rapidly growing cystic tumours may result in fluid loss to the cysts and with decreased fetal albumin production. It can increase the risk of hydrops. Intestinal tract obstruction may lead to polyhydramnion and elevation of the diaphragm increases the risk of pulmonary hypoplasia. By the displacement of internal organs and compression of the inferior vena cava and umbilical vein, the large tumour mass may lead to premature birth, poor start or congestive heart failure and intrauterine death [7, 9, 10].

In older children and adults the only symptom might be a non-tender abdominal mass. Ascites, jaundice or congestive heart failure may appear when the tumour mass compresses surrounding structures [5].

Laboratory studies reveal normal or elevated liver enzyme levels as well as AFP and β-HCG [3].

Gross pathology

Most tumours arise in the right lobe of the liver. Both lobes are rarely involved. Typically MH is

Fig. 2. Branching bile ducts embedded in loose connective tissue stroma. HE, magnification 200×

Fig. 3. Multilocular cyst without epithelial lining, surrounded by fibrous tissue blood vessels and hepatocytes. HE, magnification 100×

Fig. 4. Groups of hepatocytes between connective tissue and bile ducts. HE, magnification 100×
pedunculated or bulges from the surface of the liver, a solitary nodule, often greater than 1 kg in mass and well demarcated from the adjacent liver tissue [11, 12]. MH may have a predominantly solid or multicystic appearance or might be a mixture of both types [13]. Solid areas are grey or pink in colour and cystic spaces might be filled with clear to yellow fluid or gelatinous material. Tumours may vary in size from a few centimetres up to 30 cm [3].

**Microscopic pathology**

Microscopically MH consists of branching bile ducts without atypia, often cystically dilated, lying in a loose, myxoid stroma with myofibroblast-like...
cells. For this reason, the microscopic appearance under low magnification of MH may resemble breast fibroadenoma [14]. Numerous thin-walled dilated blood vessels and lymphatics are also visible in the stroma. Between mesenchymal tissue and proliferating bile ducts hepatocytes in single cords or in large groups are present [15]. There are no atypical mitoses or invasion of adjacent liver parenchyma. The tumour is well circumscribed but not encapsulated [3].

In fine-needle aspiration cytology, benign-appearing spindle cells are visible singly or in clusters. Background in smears is myxoid and proteinaceous [16].

Pathogenesis and molecular characteristics

The pathogenesis of MH is not fully understood and is still debated. There are many theories about pathogenesis of MH. Some theories point to developmental abnormalities, regional ischaemia or biliary obstruction as a possible cause [3, 17, 18].

Aberrations involving the chromosomal region 19q13.4 are probably very important in pathogenesis and have been described in many reported cases with cytogenetic analyses [1]. Translocations t(11;19)(q13;q13.4), t(11;19)(q13.3), t(15;19)(q13;q13.4) have been reported, as well as interstitial deletion del(19)(q13.1q13.4) and complex rearrangements involving 11q2, 17p11, 19q13.3 [19-23].

Despite the benign character of this tumour in the literature there are described undifferentiated embryonal sarcomas (UES) arising within MH [2, 24, 25]. Karyotype analyses of UES revealed chromosomal rearrangement involving 19q13.4, similar to those in MH. For this reason it has been postulated that MH might be a precursor lesion to UES [23].

Diagnosis

Diagnosis of MH is generally based on clinical and imaging studies. More precise preoperative diagnosis, provides important information for pre- and postoperative management and surgical treatment can be based on fine needle aspiration (FNA) cytology [16].

FNA cytology can also provide the necessary information for differential diagnoses which include hepatoblastoma, hepatocellular carcinoma infantile haemangioendothelioma, undifferentiated sarcoma, smooth muscle tumours and inflammatory pseudotumour.

The presence of a spindle-cell lesion without atypia argues against hepatoblastoma and hepatocellular carcinoma. In hepatoblastoma neoplastic hepatocytes and small round cells are visible. For hepatocellular carcinoma clusters of hepatocytes of various sizes are typically surrounded by an outer layer of endothelial cells [16].

Infantile haemangioendothelioma has not been well defined in cytology and a diagnosis of this lesion should be based on histology and immunohistochemistry in which plump endothelial cells are positive for factor VIII-related antigen, CD31 and CD34.

Distinguishing from embryonal sarcoma in FNA is based on hypercellular smears with pleomorphic stellate cells and multinucleated giant cells lying in the background of haemorrhage and necrosis. Hyaline globules are also a typical finding in UES [24].

Leiomyomas and leiomyosarcomas of the liver may arise in patients with HIV infection [26]. In such cases diagnosis is based on immunohistoexpression of muscle actin and the presence of the human immunodeficiency virus.

Inflammatory pseudotumour is a rare lesion showing an admixture of fibroblasts, myofibroblasts and inflammatory cells such as neutrophils, eosinophils, lymphocytes, plasma cells and macrophages [27].

Immunohistochemically, the spindle cells in the stroma are strongly positive for vimentin, focally positive for desmin and negative for S100, CD31 and CD34. Bile ducts stain positively for CK7 and negative for CK20 [23].

Treatment and clinical outcomes

MH is a benign tumour and many authors recommend complete resection of the tumour as sufficient therapy [28]. After incomplete resection recurrent lesions are also benign [11, 29]. However, complications after resection such as haemorrhage, cardiac arrest and pulmonary problems including acute respiratory distress syndrome (ARDS) have been described in the literature with the mortality rate up to 17% [28].

The mortality rate is 35% when the tumour is diagnosed in the perinatal period. In such cases an appropriate mode of delivery should be chosen. With smaller lesions vaginal delivery is possible. Caesarean section is the preferred method for delivery when the tumour is large and there is a high risk of dystocia. Traumatic cyst rupture with fatal outcome after assisted delivery has also been reported [30].

Conclusions

Mesenchymal hamartoma is a benign tumour of childhood with a good prognosis after surgical resection. However, occurrence in the perinatal period is associated with higher mortality, due to its rapidly increasing size. Diagnosis is based on clinical and imaging studies as well as fine-needle aspiration cytology. MH must be suspected in any infant who presents with a multicystic liver mass. The treatment of choice is surgical resection. In our case the patient...
underwent an uneventful recovery and after two weeks on the surgical ward the patient was discharged in good condition.

References


Address for correspondence

Marcin Orłowski, MD
Department of Tumour Pathology
Greater Poland Cancer Centre
ul. Garbary 15, 61-866 Poznań
tel. +48 61 885 06 71
e-mail: orlowski.marcin@plusnet.pl