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Case Report

Giant hepatic mesenchymal hamartoma in a preterm newborn: a case report and literature review

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Abstract: Mesenchymal hamartoma of the liver (MHL) often presents as a painless right upper abdominal mass in young children. However, MHL is rarely reported in the neonatal period. We presented the case of a preterm newborn with a huge MHL. The boy was delivered at 30 weeks weighing 1750 g. Abdominal distention was the initial presentation. Ultrasound and computed tomography showed a highly vascularized mass originating from the left lobe. Liver hemangioma was initially suspected and oral propranolol was administered. However, the tumor was rapidly enlarging, resulting in compromised respiratory status and severe anemia. Surgical resection and neonatal management were successful. The patient required cardiopulmonary resuscitation in the operating room and received packed red blood cells. The histopathological result was mesenchymal hamartoma. The baby recovered well after one-year follow-up. We also reviewed the clinical courses and treatment strategies of preterm MHL cases in published English literature from 1990 to 2021.

Keywords: Mesenchymal hamartoma, hemangioma, liver, preterm newborn, operation, case report, literature review

Introduction

Mesenchymal hamartoma of the liver (MHL) is a type of benign liver tumor in children which is characterized by a multi-cystic mass with fibrous septae. MHL has the second highest occurrence among pediatric benign liver tumors [1]. MHL often presents in children younger than two years, with a slight male predominance. The imaging appearance of MHL shows single or multiple smooth cystic tumors with different amounts of solid tissue. The diagnosis is challenging, especially in fetuses and neonates, and needs to be differentiated from other liver tumors [2]. Complete surgical resection is curative. This report describes the clinical and radiological features as well as treatment of a premature infant with a large MHL. In addition, we reviewed and discussed the clinical findings and outcomes of 16 cases of preterm MHL reported in English literature.

Case description

Ethical approval was obtained from the Ethics Board of Shanghai Children's Hospital. Written informed consent was obtained from the patient's parents for the publication of this case. A 12-day-old preterm boy was referred to Shanghai Children's Hospital due to abdominal distention after achieving full enteral feeding. The male infant was delivered via vaginal delivery due to premature rupture of membranes. Gestational age was 30 weeks and birth weight was 1750 g. The mother was 35-year-old and gravida 5 and para 2. No medication was administrated during her pregnancy. Fetal abnormalities or hepatic lesions were not detected prenatally. However, no fetal magnetic resonance imaging (MRI) was performed. Physical examination revealed a large palpable mass in the left upper abdomen. A small cutaneous hemangioma with a diameter of 0.5 cm was observed on the back of the patient. The infant was admitted to the neonatal intensive care unit. Abdominal ultrasound showed a large mass in the left hepatic lobe, with clear boundary, irregular shape, uneven internal echo, and 7.2 × 6.2 × 5.8 cm in size. Then, computed tomography (CT) confirmed the mass with highly vascularized peripheral area (**Figure 1**). Blood hemoglobin was 102 g/L. Other laboratory in-

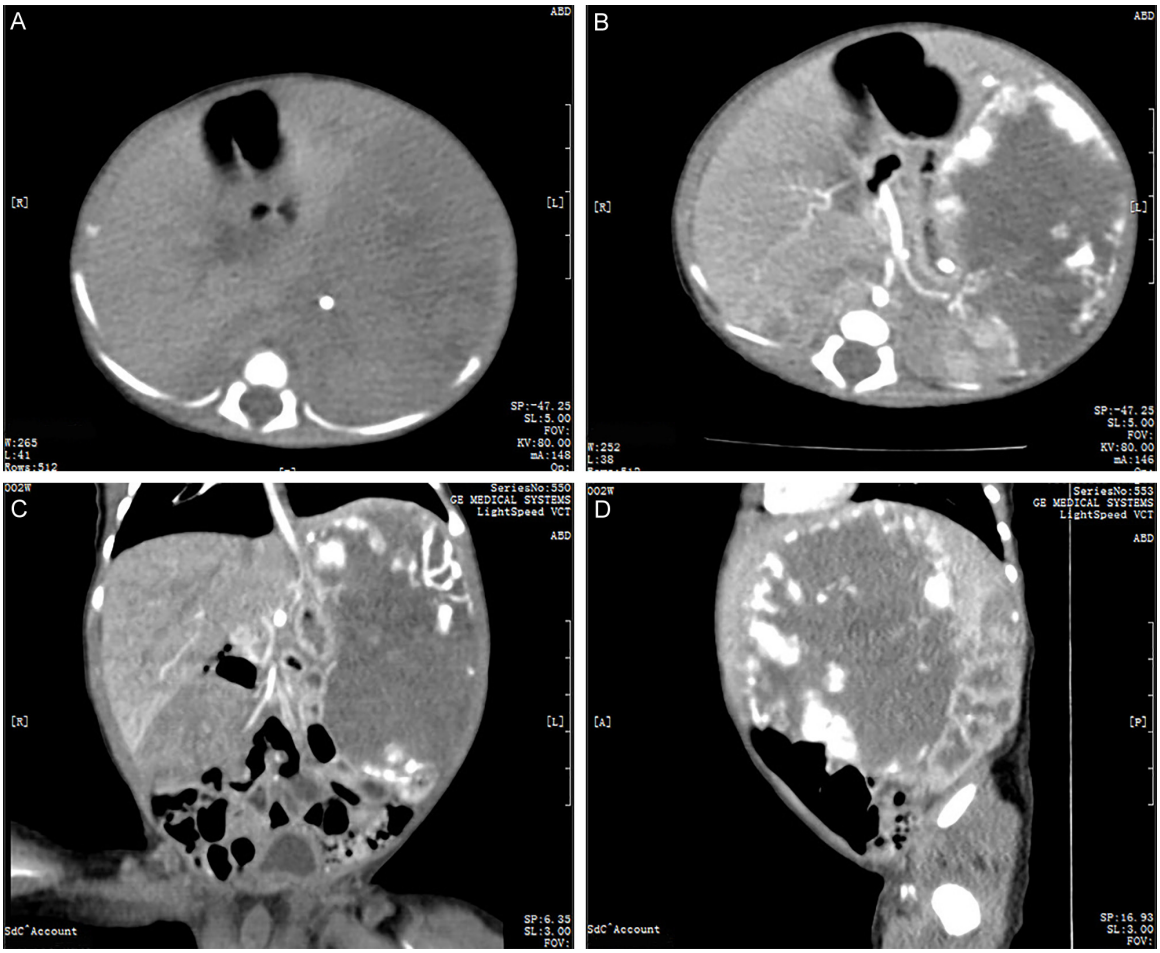

Figure 1. CT scan showing a highly vascularized tumor from the left lobe of the liver. Axial view (A) and intravenous contrast-enhanced axial (B), coronal (C) and sagittal (D) views.

vestigations including platelets, liver enzymes, bilirubin, albumin, electrolytes, blood gas analysis, prothrombin time, and thyroid function were normal. Hepatitis B virus and cytomegalovirus infection were not detected. Notably, the serum alpha-fetoprotein (AFP) value was 54000 ng/ml, but declined continuously on serial evaluation.

Based on the above findings, focal liver hemangioma was initially suspected. Oral propranolol was administrated according to the consensus in China, and cardiovascular monitoring was ascertained during therapy and dosage escalation. After three weeks of propranolol treatment, the tumor had progressively enlarged to 13 × 12 × 9 cm. The infant's abdomen showed marked distention, and engorged veins were visible over the anterior abdominal wall (**Figure 2A**). His respiratory status worsened due to the rapidly expanding tumor. Hemoglobin decreased to 78 g/L, requiring packed red blood cells transfusion. To improve the clinical status of the critically ill infant, laparotomy was performed on the 58th day of life. A firm, solid-cystic mass was found in segments 2 and 3 (**Figure 2B**). Multiple obviously tortuous vessels were also noted. No enlarged lymph nodes were noted. The tumor was first isolated from surrounding tissues. Hepatic ligamentum teres, falciform ligament, left triangle ligament and left coronary ligament were divided. The liver resection line was marked, 1 cm from the tumor margin. Then, the tumor was completely resected, weighing 650 g. A drainage tube was placed under the left diaphragm. The patient required cardiopulmonary resuscitation in the operating room and received 150 ml packed red blood cells. The tumor was composed of both solid and cystic components, and had abundant

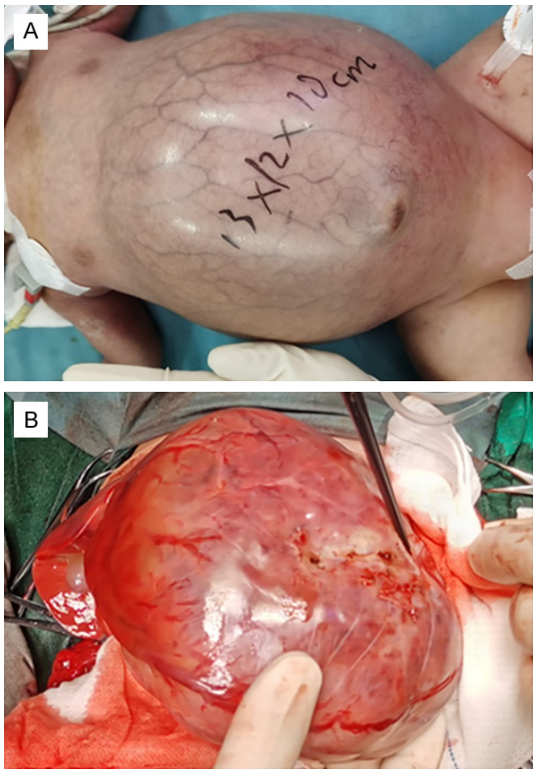

Figure 2. Clinical photography of the preterm newborn showing marked abdominal distension (A), and intraoperative view of the hepatic mesenchymal hamartoma (B).

blood vessels. There was necrosis and hemorrhage within the tumor. The histopathology showed different proportions of mesenchymal and epithelial components, and confirmed the diagnosis of mesenchymal hamartoma, with negative surgical margin (**Figure 3**). Immunohistochemical results revealed vimentin (+), smooth muscle actin (+), desmin (+), CD34 (+), cytokeratin 7 (+), cytokeratin 19 (+), GLUT1 (-). The proliferation-associated Ki-67 index was 20%. The infant recovered uneventfully after the operation and was thriving at the one-year follow-up.

Discussion

MHL is extremely rare in preterm newborns. To date, 17 cases of preterm MHL have been reported in English literature from 1990 to 2021, including our patient [3-17] (**Table 1**). There were 5 males and 12 females, with an average birth weight of 2256 ± 1023 g (range, 960 to 4500 g). The median gestational age was 34 weeks (range, 27 weeks 4 days to 36 weeks). The mass was detected by antenatal ultrasonography in 13 cases or by postnatal physical examination in 4 cases. The reported rate of cesarean delivery was 66.7%. The location of origin was the left lobe in 7 cases, right lobe in 5 cases, and both lobes in 4 cases. Most tumors were cystic (82%, 14/17). The most common clinical presentations were abdominal distention and hepatomegaly. Significant compression symptoms such as respiratory distress caused by tumor enlargement were presented in the majority of preterm newborns. In this series, there were 4 cases associated with placental mesenchymal dysplasia, of which two died. Surgical resection was the main therapy in 15 cases, involving complete resection (n=10), partial resection (n=3), aspiration (n=1), and deroofing (n=1). However, watchful waiting was performed in an extremely low birth weight premature infant, who was not eligible for surgery [16]. The overall survival for preterm MHL was 66.7% (10/15). Three patients were alive with residual tumor.

MHL was first described by Dr. Edmondson in 1956, and is the second most common hepatic benign tumor after hepatic hemangioma in children. The cause of MHL is un-clear, but some cases have been reported to be related to chromosomal 19q13.4 abnormalities, DICER1 syndrome, Beckwith-Wiedemann syndrome, and placental mesenchymal dysplasia [6, 10, 18-20].

MHL can present as abdominal distention, or abdominal mass. Other symptoms include anorexia, vomiting, high-output cardiac failure, renal compromise, and other compression symptoms caused by tumor enlargement. Mild to severe respiratory distress may occur in newborns [1]. Ultrasonography and CT/MRI scan show single or multiple smooth cystic tumors, usually with septum, but some may have different amounts of solid tissue. Most MHL lesions appear hypovascular on imaging. After injection of iodized intravenous contrast agent, the solid composition and septum are enhanced. Occasionally, the tumor has highly vascularized peripheral and central areas, leading to misdiagnosis of hemangioma, which was consistent with our patient. Calcification and hemorrhage are atypical in mesenchymal hamartoma. In some cases, MHL can be detected by ultrasound or fetal MRI in late pregnancy [4, 5]. The serum AFP is usually normal or mildly

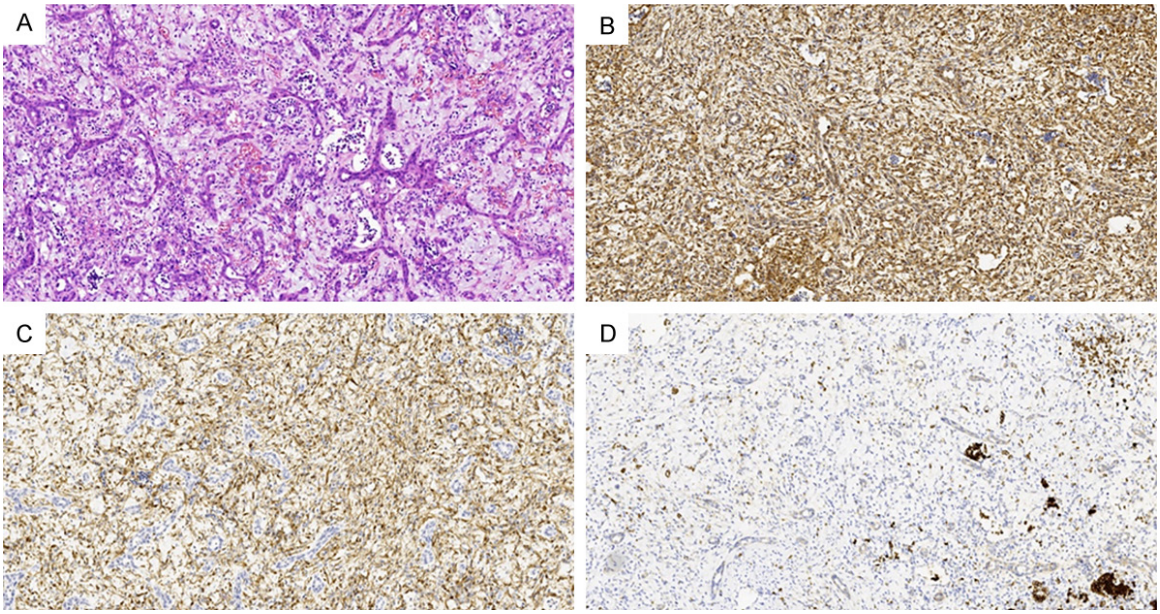

Figure 3. Hematoxylin-eosin staining showing that the tumor was composed of mesenchymal and epithelial components (A, original magnification × 100). Immunohistochemical staining demonstrating positive to vimentin (B) and smooth muscle actin (C), but negative to GLUT1 (D). (Original magnification × 100).

increased. The preoperative accurate diagnosis is always difficult and should be differentiated from hepatoblastoma and hepatic hemangioma, which often relies on the histological evaluation after tumor resection. On histopathology examination, the tumor shows malformed bile ducts, liver cell cysts and loose mesenchymal tissues.

Complete resection by open or laparoscopic approach is the first choice in most symptomatic cases, although simple observation may be useful in some cases. Surgical resection in preterm newborn is a tough challenge for surgeons. If possible, the operation should be deferred beyond the neonatal period. The overall prognosis of MHL is satisfactory, though there is risk of recurrence and malignant transformation into undifferentiated embryonal sarcoma of the liver. The preterm MHL cases reported to date had varying treatment strategies and outcomes (**Table 1**). Death due to perioperative complications, including on-table hypovolemic arrest, persistent coagulopathy, cardiac failure and multi-organ failure, has rarely been reported [8, 10, 13].

The current case was unusual from several aspects. First, the child was a very preterm infant with low body weight, and the tumor was huge and enlarged rapidly after conservative treatment. Moreover, the blood supply of the tumor was very abundant which significantly increased the difficulty of preoperative accurate diagnosis and the risk of operation. Intraoperative challenges included significant bleeding and cardiac arrest. The excised tumor accounted for about one-fifth of the body weight. In addition, the tumor was located in the left hepatic lobe, while the majority of reported MHL lesions occurred in the right lobe of the liver. The compromised clinical status of the infant improved after tumor resection.

In conclusion, although MHL is very rare, clinicians need to pay attention, particularly for treating benign liver tumors in children. If the lesion increases instead of decreasing after the use of propranolol in suspected hepatic hemangioma, other diagnoses should be considered. Because the clinical and imaging manifestations are atypical, the diagnosis of MHL is more difficult in preterm newborns. Their clinical course is always aggressive and surgical treatment is significantly challenging. In order to ensure a good prognosis, timely and complete resection is necessary.

Disclosure of conflict of interest

None.

Table 1. Reported cases of MHL in preterm newborn

Author, year, reference	Clinical findings	Associated anomalies	Postnatal management	Outcome
Bessho, 1996 [3]	Abdominal distension, generalized skin edema	None	No surgery	Dead
Bejvan, 1997 [4]	Abdominal distention, palpable mass	None	Percutaneous aspiration, complete resection	Alive
Tovbin, 1997 [5]	Abdominal distention	None	Partial resection	Alive
Kitano, 2000 [6]	Palpable mass, abdominal distension, respiratory compromise	Placental mesenchymal dysplasia	Open biopsy, Extended left hepatic trisegmentectomy	Alive
Mittermayer, 2002 [7]	Respiratory insufficiency	None	Complete resection	Alive
Tsao, 2002 [8]	Mild respiratory distress and prune belly appearance	None	Laparoscopic resection	Alive
Tsao, 2002 [8]	Abdominal distension	Bilateral cystic encephalomalacia	Complete resection	Dead
Kamata, 2003 [9]	Abdominal distension	None	Complete resection	Recurrent, alive
Francis, 2007 [10]	Abdominal distension, severe respiratory distress	Placental mesenchymal dysplasia, necrotizing enterocolitis	Percutaneous aspiration, deroof, primary intestinal anastomosis	Dead
Heyer, 2007 [11]	Vomit	None	Complete resection	Alive
Cornette, 2009 [12]	Abdominal distension, progressive respiratory insufficiency	None	Complete resection with microscopic positive margins	Alive
Wan, 2009 [13]	Abdominal distension, hepatomegaly, severe respiratory distress, petechiae	None	Steroids, right hepatic artery embolization, right hepatectomy	Dead
Mack, 2011 [14]	Abdominal distension, acute respiratory and renal failure	Placental mesenchymal dysplasia	Enucleation, second partial resection, chemotherapy, third operation without resection	Recurrent, dead
Ruhland, 2011 [15]	Abdominal distension	Placental mesenchymal dysplasia	Repeat punctures	Alive
Salihoglu, 2013 [16]	Abdominal distension, respiratory distress	None	No surgery	Alive
Berte, 2018 [17]	Abdominal distension, hepatomegaly, severe respiratory distress, bowel obstruction	Hepatic hemangioma	Partial resection, corticoids, propranolol, 2nd and 3rd hepatectomy	Alive
Current study	Abdominal distension, respiratory distress	Infantile hemangioma	Propranolol, complete resection	Alive

MHL, Mesenchymal Hamartoma of the Liver.

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References

[1] Stringer MD and Alizai NK. Mesenchymal hamartoma of the liver: a systematic review. J Pediatr Surg 2005; 40: 1681-1690.

[2] Fuchs J, Warmann SW, Urla C, Schafer JF and Schmidt A. Management of benign liver tumors. Semin Pediatr Surg 2020; 29: 150941.

[3] Bessho T, Kubota K, Komori S, Ohtsuka Y, Uneo Y, Uematsu K and Koyama K. Prenatally detected hepatic hamartoma: another cause of non-immune hydrops. Prenat Diagn 1996; 16: 337-341.

[4] Bejvan SM, Winter TC, Shields LE, Brock BV, Nghiem HV, Schmiedl UP and Waldhausen JH. Prenatal evaluation of mesenchymal hamartoma of the liver: gray scale and power Doppler sonographic imaging. J Ultrasound Med 1997; 16: 227-229.

[5] Tovbin J, Segal M, Tavori I, Lotan G and Maymon R. Hepatic mesenchymal hamartoma: a pediatric tumor that may be diagnosed prenatally. Ultrasound Obstet Gynecol 1997; 10: 63-65.

[6] Kitano Y, Ruchelli E, Weiner S and Adzick NS. Hepatic mesenchymal hamartoma associated with mesenchymal stem villous hyperplasia of the placenta. Fetal Diagn Ther 2000; 15: 134-138.

[7] Mittermayer C, Bettelheim D, Horcher E, Fakhari M, Deutinger J and Bernaschek G. Prenatal sonographic detection of a giant multiseptate hepatic cyst in the third trimester. Ultrasound Obstet Gynecol 2002; 20: 97-98.

[8] Tsao K, Hirose S, Sydorak R, Goldstein RB, Machin GA, Albanese CT and Farmer DL. Fetal therapy for giant hepatic cysts. J Pediatr Surg 2002; 37: E31.

[9] Kamata S, Nose K, Sawai T, Hasegawa T, Kuroda S, Sasaki T, Okada A and Tawara M. Fetal mesenchymal hamartoma of the liver: report of a case. J Pediatr Surg 2003; 38: 639-641.

[10] Francis B, Hallam L, Kecskes Z, Ellwood D, Croaker D and Kent A. Placental mesenchymal dysplasia associated with hepatic mesenchy-

mal hamartoma in the newborn. Pediatr Dev Pathol 2007; 10: 50-54.
[11] Heyer C, Weitkaemper A, Teig N, Mueller A, Rieger C and Nicolas V. Hepatic mesenchymal hamartoma in a preterm newborn: demonstration by low-dose multidetector CT. Acta Paediatr 2007; 96: 1538-1542.
[12] Cornette J, Festen S, van den Hoonaard TL and Steegers EA. Mesenchymal hamartoma of the liver: a benign tumor with deceptive prognosis in the perinatal period. Case report and review of the literature. Fetal Diagn Ther 2009; 25: 196-202.
[13] Wan P, Susman J, Kandel J, Jan D, Jerome EH and Parravicini E. Neonatal hepatic mesenchymal hamartoma causing cardiac failure and disseminated intravascular coagulopathy. Am J Perinatol 2009; 26: 601-604.
[14] Mack-Detlefsen B, Boemers TM, Groneck P and Bald R. Multiple hepatic mesenchymal hamartomas in a premature associated with placental mesenchymal dysplasia. J Pediatr Surg 2011; 46: e23-25.
[15] Ruhland B, Schroer A, Gembruch U, Noack F and Weichert J. Prenatal imaging and postnatal pathologic work-up in a case of fetal hepatic hamartoma and placental mesenchymal dysplasia. Ultrasound Obstet Gynecol 2011; 38: 360-362.
[16] Salihoğlu O, Can E, Can S and Hatipoğlu S. 'Watchful waiting' may be an appropriate treatment for ELBW infant with hepatic mesenchymal hamartoma. Iran J Pediatr 2013; 23: 366-368.
[17] Berte N, Filfilan A, Mainard L, Mansuy L and Lemelle JL. Co-existing infantile hepatic hemangioma and mesenchymal hamartoma in a neonate. J Surg Case Rep 2018; 2018: rjx260.
[18] Apellaniz-Ruiz M, Segni M, Kettwig M, Gluer S, Pelletier D, Nguyen VH, Wagener R, Lopez C, Muchantef K, Bouron-Dal Soglio D, Sabbaghian N, Wu MK, Zannella S, Fabian MR, Siebert R, Menke J, Priest JR and Foulkes WD. Mesenchymal hamartoma of the liver and DICER1 syndrome. N Engl J Med 2019; 380: 1834-1842.
[19] Cajaiba MM, Sarita-Reyes C, Zambrano E and Reyes-Múgica M. Mesenchymal hamartoma of the liver associated with features of beckwith-wiedemann syndrome and high serum alpha-fetoprotein levels. Pediatr Dev Pathol 2007; 10: 233-238.
[20] Rakheja D, Margraf LR, Tomlinson GE and Schneider NR. Hepatic mesenchymal hamartoma with translocation involving chromosome band 19q13.4: a recurrent abnormality. Cancer Genet Cytogenet 2004; 153: 60-63.