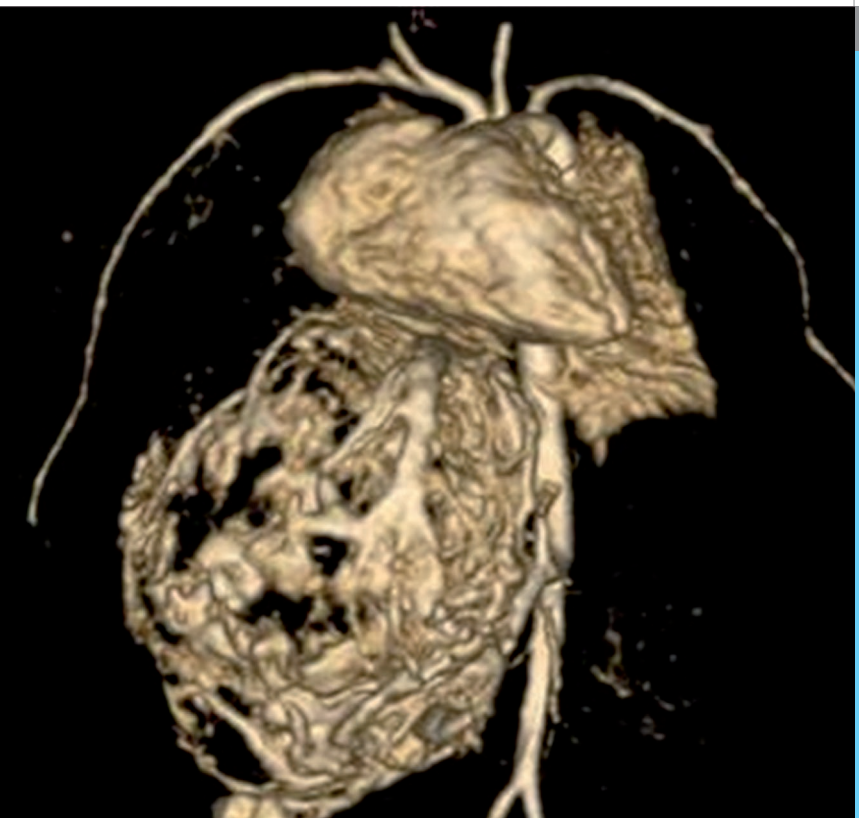
SWISS SOCIETY OF NEONATOLOGY

Fatal hepatic congenital hemangioma



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We describe a female infant born by Caesarean section to a healthy 24-year-old G1/P1 at 39 3/7 weeks of gestation. The course of the pregnancy had been uneventful up to the day of birth when fetal ultrasound examination revealed a nonspecific abdominal mass (Fig. 1). In addition, cardiomegaly with right ventricular hypertrophy and tricuspid insufficiency were seen. These findings, along with pathologic Doppler indices of the umbilical arteries and a suspicious CTG tracing, contributed to the decision to perform a Caesarean section.

Apgar scores were 8, 9, and 9 at 1, 5 and 10 minutes, respectively. Arterial umbilical cord pH was 7.26. Due to low preductal oxygen saturations supplemental oxygen was administered via facemask (maximum FiO2 0.4) for 7 minutes. The girl's birth weight was 2700 g (P3-5), her length was 46.5 cm and her head circumference was 32.0 cm (both below P3). Physical examination revealed a tense protruding abdomen (Fig. 2) with a mass being palpable in the right hemiabdomen. Within the first hour of life, the newborn developed respiratory distress. Laboratory analyses revealed mild respiratory and metabolic acidosis, normal electrolyte values, hypoglycemia of 0.4 mmol/L and hyperbilirubinemia of 124 µmol/L. An infusion with glucose 10% was started. Following initial stabilization the patient was transferred to the Intensive Care Unit of the University Children's Hospital of Zurich for further diagnostic evaluation.

Upon arrival, abdominal ultrasound showed an extensive inhomogeneous, intrahepatic vascular tumor (measuring 9 x 9 x 7 cm) displacing the hepatic parenchyma as well as the hepatic vessels (Fig. 3). Within the first few hours of life the patient developed hepatic failure (ALT 125 U/L [normal: < 31 U/L]; AST 507 U/L [normal: < 125 U/L] in third hour of life) leading to hyperbilirubinemia (total bilirubin 138 µmol/L [normal: < 68 µmol/L] with a conjugated bilirubin of 44 µmol/L [normal: < 30 µmol/L]) requiring phototherapy and exchange transfusion. Significant coagulopathy (INR 1.7 [normal: < 1.4]; fibrinogen 0.5 g/L [normal: 1.5-4.5 g/L]; PTT 73 sec [normal: < 55 sec]; α-fetoprotein not elevated) was treated with repetitive substitution of coagulation factors and platelets.

Abdominal MRI performed on the third day of life revealed a large inhomogeneous high-flow vascular tumor (diameter of 9 cm) within the right hepatic lobe and a small lesion in one segment of the left hepatic lobe, with central necrosis and hemorrhage (Fig. 4) and multiple intralesional arteriovenous shunts.

The suspected diagnoses were rapid involuting congenital hemangioma (RICH) and kaposiform hemangioendothelioma (KHE). Methylprednisolone and sirolimus, an immunosuppressive agent frequently used after renal transplantation, were started as initial therapy. Despite maximal conservative therapy the patient developed high-output cardiac failure, pulmonary hyper-

tension (caused by volume overload of the venous capacitance), and acute renal failure. Following multidisciplinary discussions, the interventional cardiology team performed endovascular coil embolization of the intralesional arteriovenous shunts on day five of life.

The coiling succeeded (Fig. 5), but at the end of the procedure, copious bleeding from the femoral puncture site was noted, which subsequently produced a massive retroperitoneal hematoma, intraabdominal bleeding and ultimately hemorrhagic shock. Cardiopulmonary resuscitation was performed. Extravasation of contrast agent was consistent with the diagnosis of a long segment dissection of the external iliac artery. The pediatric surgery team performed an emergent laparotomy and was able to tamponade the bleeding site, leading to transient stabilization. Severe pulmonary hypertension refractory to inhaled nitric oxide led to persistent hypoxemia and subsequent multi-organ failure. The patient died a few hours later.

Autopsy revealed a solitary, cystic and spongy mass measuring 9 x 6 x 5 cm, and a satellite focus of 1.5 cm (Fig. 6). Histology displayed large thin walled vessels congested with fresh blood. The endothelial cells were mitotically inactive and expressed CD34, while immunohistochemistry was negative for GLUT-1 (Fig. 7).

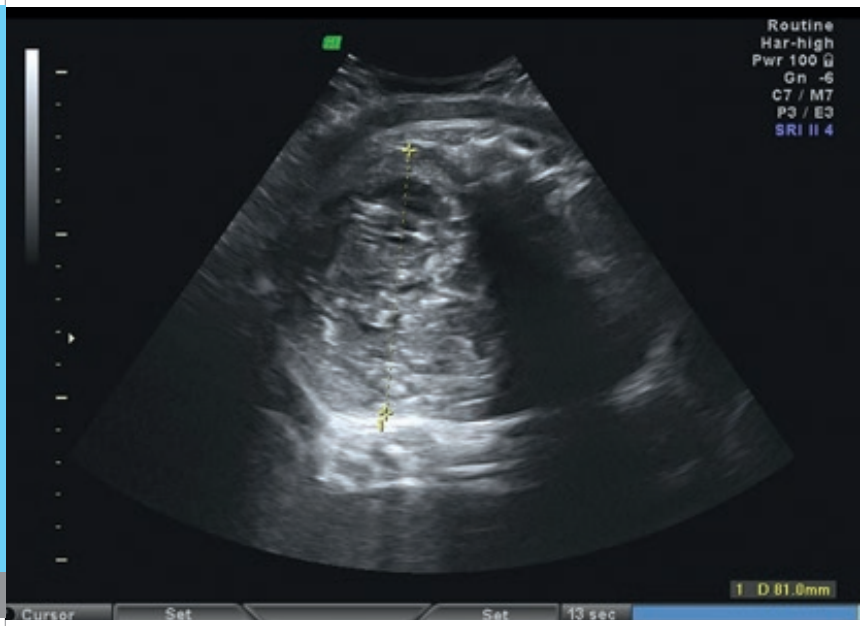

Fig. 1

Prenatal ultrasound: large intrahepatic tumor.

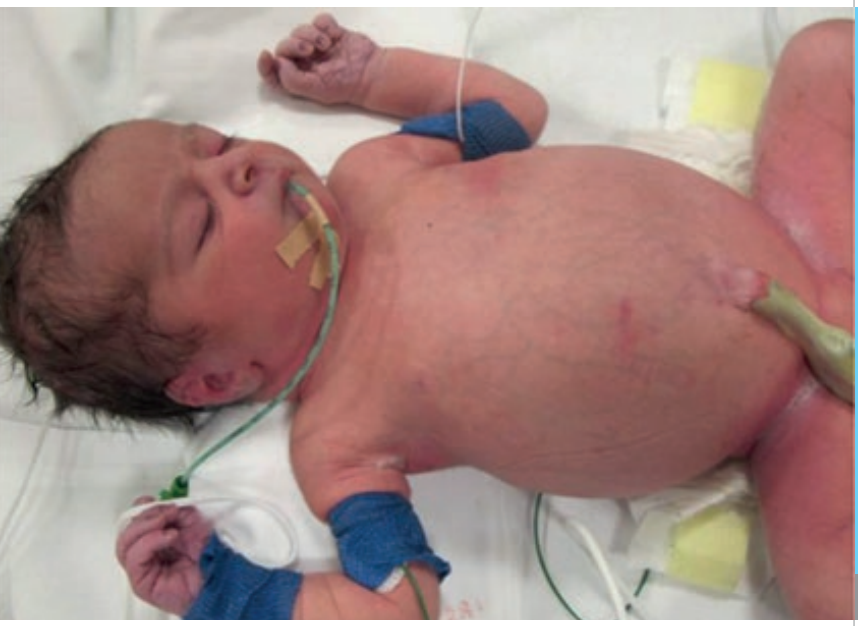

Fig. 2

Infant at birth: protruding abdomen with superficial vein enhancement.

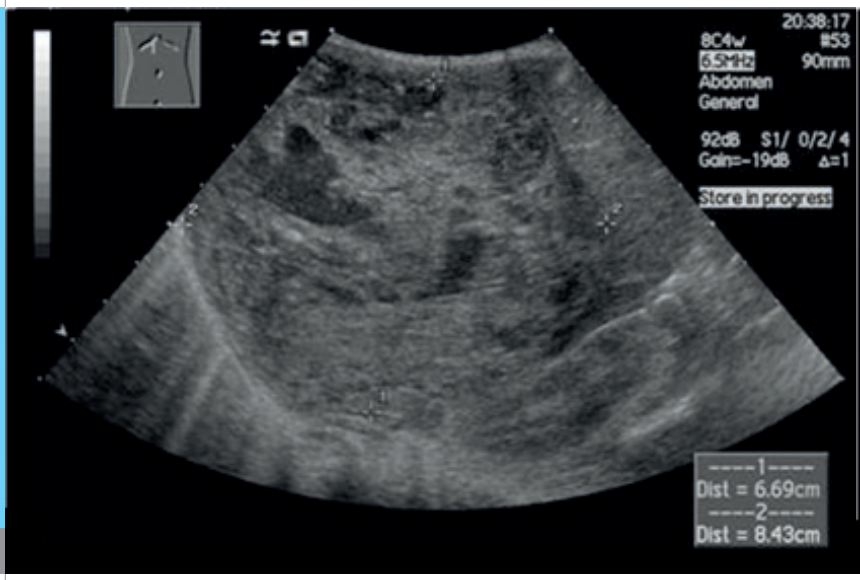

Fig. 3

Abdominal ultrasound scan (DOL 1): large, inhomogeneous intrahepatic vascular tumor (9 x 9 x 7cm) displacing the hepatic parenchyma and the hepatic vessels.

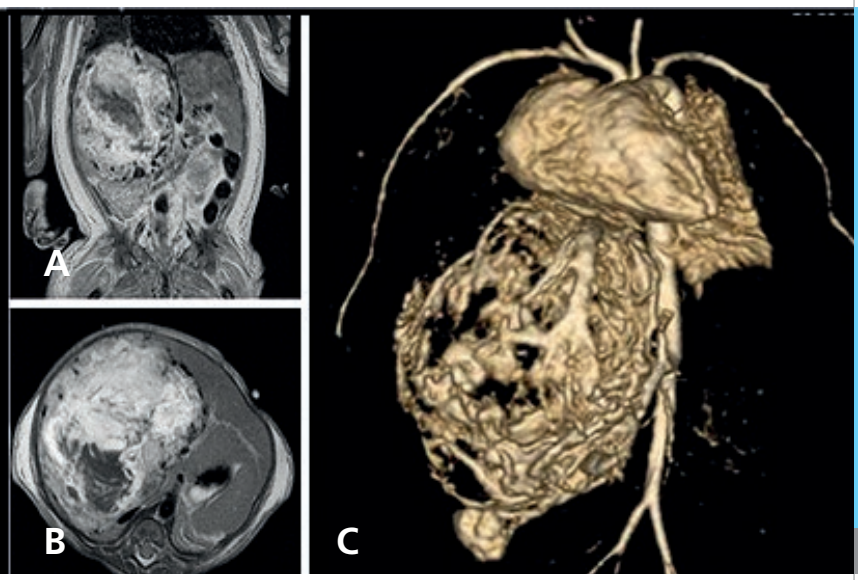

Fig. 4

Abdominal MRI (DOL 3): large vascular lesion within the right hepatic lobe and within one segment of the left hepatic lobe, both showing central necrosis and hemorrhage (A: coronal view, B: transverse view, C: MR angiography).

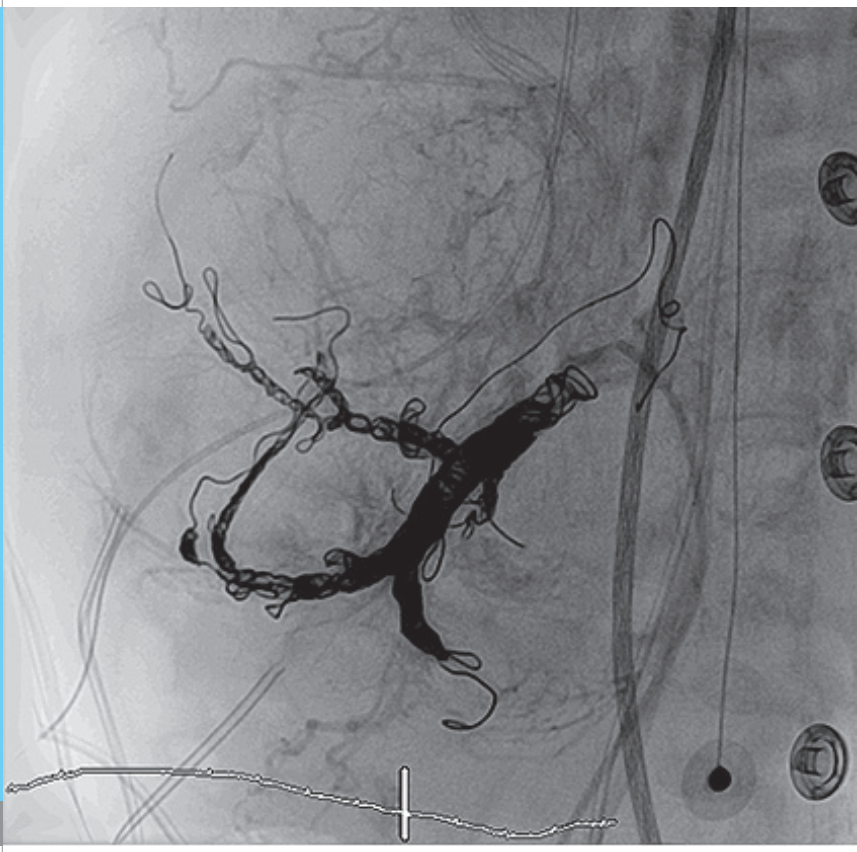

Fig. 5

Coil embolization (DOL 5): right hepatic artery with its branches and 25 coils.

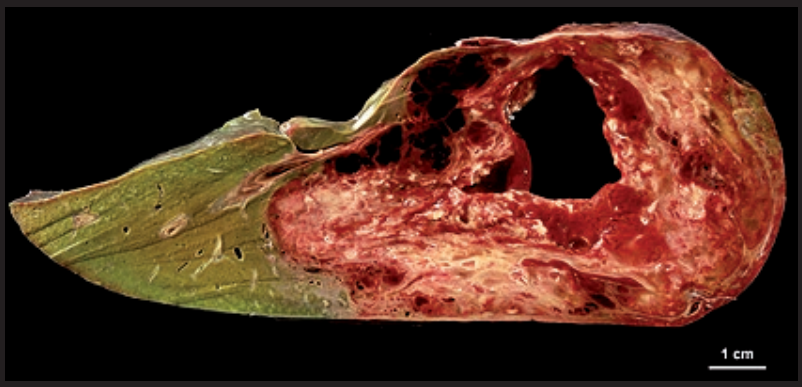

Fig. 6

Autopsy: cross section of the liver tumor.

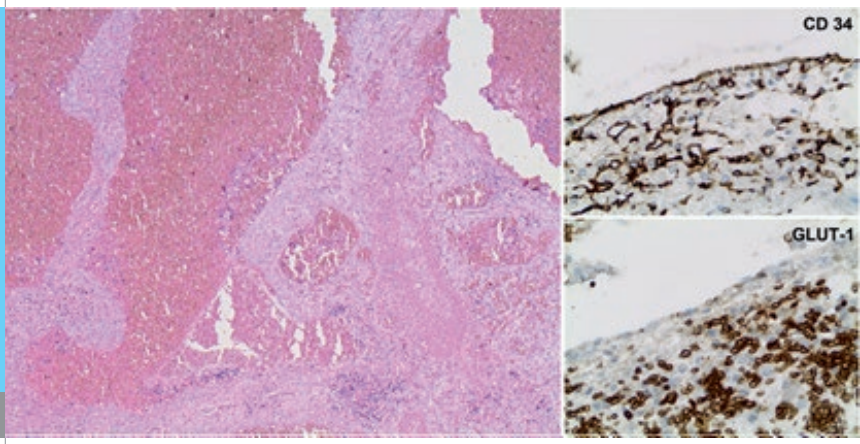

Fig. 7

Histopathology (H&E, left): vascular tumor with endothelial cells positive for CD34 (top right) and negative for GLUT-1 (bottom right).

Neonatal hepatic lesions share a broad differential diagnosis. The three main groups include vascular lesions (e.g., arteriovenous malformations and arterioportal fistulas), benign tumors (e.g., various forms of hemangiomas or mesenchymal hamartomas), and malignancies (e.g., hepatoblastomas, angiosarcomas, metastatic neuroblastomas or teratomas) (1).

The current classification of neonatal hepatic hemangiomas includes three categories: focal/solitary, multifocal and diffuse hemangiomas (2). Classic infantile hemangiomas (IH) of the liver occur in association with multiple cutaneous IH and usually present as multifocal or diffuse liver hemangiomatosis (3). Solitary or focal liver hemangiomas are known to represent RICH.

Classic IH are characterized by a unique growth pattern: at birth, they are very small or undetectable; then, they proliferate for several months, and, finally, begin to involute thereafter (1). In contrast, congenital hemangiomas (CH) present with maximal size already at birth, usually with high blood flow arteriovenous shunting. CH that shrink rapidly during the first months of life are referred to as RICH. CH that persist without evidence of shrinking within the first 1-3 years of life are defined as non-involuting congenital hemangiomas (NICH) (3).

Hepatic RICH are often clinically silent. Many are only detected coincidentally on images performed for un-

related reasons. Occasionally hepatic RICH may lead to high-output cardiac failure due to arteriovenous shunting within the tumor, as was the case in our patient. Thrombocytopenia, anemia and coagulopathy may be present (comparable to the Kasabach-Merritt phenomenon KMP); however, in RICH coagulopathy is usually not as severe and importantly self-limiting within a few weeks after birth. Classic KMP is known to occur in children with large kaposiform hemangioendotheliomas or tufted angiomas, which prompted our initial differential diagnosis. However, kaposiform hemangioendotheliomas are very unlikely to develop in the liver.

Another rare complication of hepatic RICH is hepatic failure. Of note, most RICH usually do not appear within the liver but elsewhere on the body, within the skin and soft tissue. Whereas high-output cardiac failure may occur in any RICH, coagulopathy seems to be specific for hepatic localization.

The diagnosis of hepatic RICH in a child or a newborn is not easy to establish. Clinical presentation may be strikingly similar to other forms of hepatic lesions. However, the following findings are highly characteristic for hepatic RICH: ultrasound imaging showing a solitary vascularized mass with minimal internal vascularity and few prominent peripheral vessels (2); MRI studies revealing a heterogeneous lesion with calcifications, central necrosis or hemorrhage and centripe-

tal enhancement on gadolinium sequences. A tumor biopsy for histopathology is not mandatory for the diagnosis and may be risky. If performed, histopathology of RICH is characterized by vascular endothelial cells positive for CD31 or CD34, enabling the identification of the vascular nature of the lesion. Unlike in IH, GLUT-1 staining is negative in CH (5).

The vast majority of patients diagnosed with RICH do not require any treatment, as they remain asymptomatic. Thus, observation is considered the gold standard (4). If the lesion does not shrink within one month, Roebuck et al. have recommended to perform a percutaneous needle biopsy in order to rule out a malignancy and to guide further management (6). When cardiac failure, thrombocytopenia, anemia, coagulopathy or hyperbilirubinemia occur, symptomatic conservative therapy should be initiated. Embolization, as performed in our patient, is the measure of last resort. Typical angiographic features of RICH are large and irregular feeding arteries, variable sized aneurysms, direct arteriovenous shunts and intravascular thrombi (7).

Although the prognosis of hepatic RICH is overall favourable, a proportion of patients may develop severe associated complications including coagulopathy and organ failure. If these complications occur, poor outcome (including death) correlates with the severity of cardiac failure and coagulopathy.

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