Hepatic Vascular Tumors in the Neonate: Angiosarcoma

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A 6-week-old infant girl presented to a local emergency department with blood-tinged emesis, lethargy, decreased oral intake, abdominal distension, and a pale appearance. Pregnancy was uncomplicated except for preterm labor with spontaneous vaginal delivery at 36 weeks' gestation. Initial laboratory values were significant for severe anemia (hemoglobin of 4.9 g/dL and hematocrit of 15.9%), thrombocytopenia (platelets of 61 000), and mild coagulopathy (prothrombin time of 17.8 seconds, international normalized ratio of 1.62, and partial thromboplastin time was 21.3); asparate aminotransferase level was 218 IU/L, alanine aminotransferase 19 IU/L, and glutamyl transferase 723 IU/L. Total bilirubin was 4.5 mg/dL with direct bilirubin of 1.1 mg/dL.

The patient was given a fluid bolus and packed red blood cells. An ultrasound (US) of the liver was obtained. Antibiotics and acyclovir were started for concerns of sepsis, and she was transferred to our tertiary care center.

On admission to the neonatal intensive care unit, the patient was noted to have pallor, tachypnea, retractions, tachycardia, dehydration, and significant abdominal distension with hepatomegaly. No rash or cutaneous lesions were present. She received numerous blood products for the underlying severe anemia, thrombocytopenia, and mild coagulopathy. US of the liver demonstrated 3 large hepatic masses nearly completely replacing all normal liver parenchyma (**Figure 1**, **Video 1** and **Video 2**; videos available at www.jpeds.com). Computed topography (CT) of the abdomen and pelvis was performed, which confirmed the 3 large liver masses, and multiple pulmonary nodules also were seen at the bases of the lungs (**Figure 2**). An echocardiogram revealed a patent foramen ovale and normal biventricular systolic function with inferior vena cava compression. Significant laboratory values included elevation of both beta-human chorionic gonadotropic (*β*-HCG) level of 385.6 mIU/mL (normal <5.0) and alpha fetoprotein (AFP) level of 547 ng/mL (normal <400 in a patient this age).[1] Thyroid studies were significant for a hyperthyroid state with thyroid-stimulating hormone of 0.071 μIU/mL (normal 1.7-9.1) and thyroxine of 14.89 μg/dL (normal 7.0-15.0). As a result of the diagnostic dilemma, clinical team consensus was to obtain tissue for histopathologic diagnosis. However, given the worsening respiratory distress of the patient, on hospital day 2 she was intubated and received propranolol and methylprednisolone per the guidelines on infantile hemangioma (IH) to halt growth of the liver masses if they were hemangiomas, with little anticipated adverse effect if they turned out to be malignant tumors.[2]

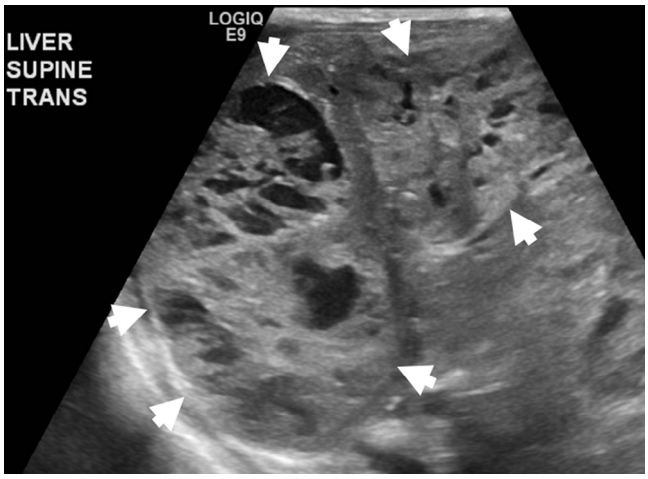

Figure 1. Grayscale US of the right upper abdomen in the transverse plane demonstrates 2 of the 3 hepatic masses (*white arrows*). Each mass is very heterogeneous in echogenicity with internal cystic spaces that are suspicious for necrosis.

On hospital day 4, the patient underwent surgical excisional biopsy of 2 pulmonary nodules from the left lower lobe (**Figure 3**; available at www.jpeds.com). The pulmonary nodules were sampled rather than the liver because of concerns for bleeding with the patient's coagulopathy and highly vascular and necrotic appearance of the liver tumors. The immediate fresh-frozen sample was inconclusive. Eight hours postoperatively, she developed severe anemia despite multiple transfusions, hypothermia, hypotension, and worsening abdominal distension with severe metabolic acidosis. The patient appeared to have abdominal compartment syndrome from presumed intra-abdominal hemorrhage. Surgical intervention was deferred by family, and she died on hospital day 5.

The biopsy and autopsy assessments showed an aggressive and poorly differentiated tumor involving the liver with lung

AFP	Alpha fetoprotein
B-HCG	Beta-human chorionic gonadotropic
CT	Computed tomography
IH	Infantile hemangioma
IHH	Infantile intrahepatic hemangioma
US	Ultrasound

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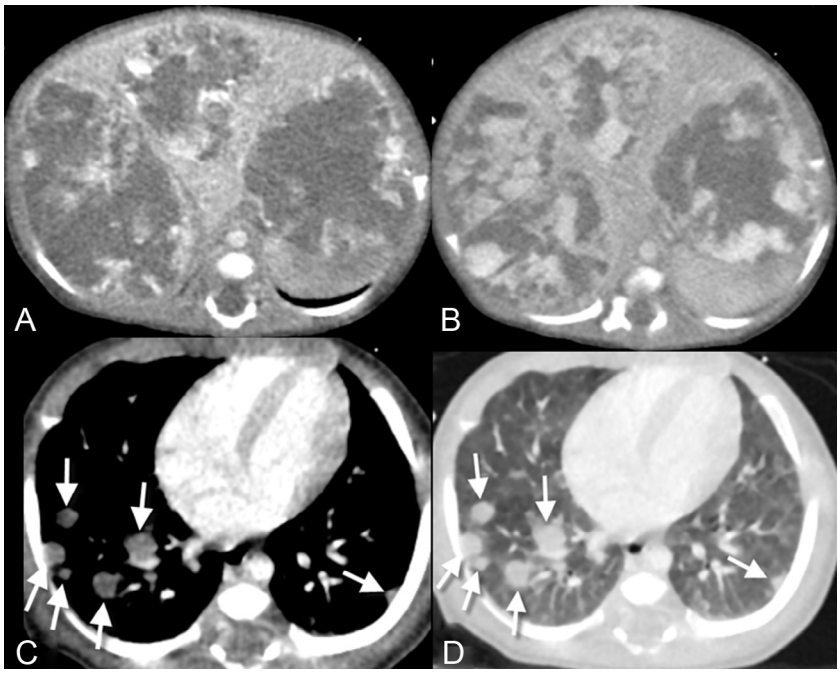

Figure 2. Axial contrast-enhanced CT of **A,** arterial and **B,** portal venous phases show 3 large hepatic masses with irregular heterogeneous early enhancement and some progressive heterogeneous enhancement (not centripetal) in portal venous phase. Axial chest CT of **C,** soft tissue and **D,** lung windows show multiple pulmonary nodules with similar attenuation (*arrows*).

metastases. There was massive hepatomegaly (liver weight = 498.5 g; normal = 133 g) with 3 large distinct hemorrhagic and friable masses that occupied the majority of the liver parenchyma (**Figure 3**).[3] One hepatic nodule protruding from the inferior and posterior aspect of the left lobe showed a 0.7-cm area of rupture, causing massive hemoperitoneum. The lungs showed multiple metastatic nodules associated with diffuse hemorrhage. Histologically, sections from the liver and lung tumor nodules revealed an extremely pleomorphic, atypical, and poorly differentiated tumor, forming vague and large vascular spaces, associated with extensive hemorrhage and necrosis. Focal expression of endothelial cell markers (CD31 and von Willebrand factor) was noted; an epithelioid pattern also was seen, highlighted by pan-keratin staining consistent with angiosarcoma (**Figure 3**).[3]

Discussion

In the fetal and neonatal period, hepatic tumors consist of 5% of neoplasms. The majority of infantile hepatic tumors include IH, mesenchymal hamartoma, and hepatoblastoma.[4] Hepatic tumors frequently are benign: IH, focal nodular hyperplasia, and mesenchymal hamartomas.[5,6] Malignant hepatic tumors described in infancy include hepatoblastoma, biliary tract rhabdomyosarcoma, angiosarcoma, rhabdoid tumor, undifferentiated embryonal sarcoma, or metastatic disease from neuroblastoma.[6,7] The first steps in identifying the type of hepatic tumor include laboratory work with AFP along with imaging: US, CT, and/or magnetic resonance imaging.

Many tumors have a cystic, solid, or vascular appearance. The focus of this case report will help discriminate between benign and malignant vascular hepatic tumors, which can be difficult without the availability of histology. The most common benign hepatic vascular tumors are rapidly involuting congenital hemangioma and the infantile intrahepatic hemangioma (IHH), either multifocal or diffuse types. Rapidly involuting congenital hemangioma is fully formed at birth, often can be noted on prenatal US, and is self-resolving usually by 15 months of age. The multifocal and diffuse types of IHHs are not seen at birth but rather develop in early infancy (first month of life), present as liver masses, and can proliferate extensively over the course of the first 5-9 months of life before gradual involution over months to years.[8,9]

IH is the most common pediatric tumor, affecting 4%-5% of infants.[10,11] It is a benign endothelial cell neoplasm that exhibits rapid postnatal growth followed by slow involution during childhood. In the presence of multiple cutaneous lesions (hemangiomatosis), visceral involvement can occur often in the liver. The visceral lesions share the same patterns of grown and regression as the cutaneous version. One retrospective study performed screening hepatic US on infants with either 6 or more or 1 large cutaneous hemangioma and found 23% of the patients had hepatic hemangioma(s).[12] The American Academy of Pediatrics section of Dermatology states US may be helpful to assess for hepatic lesions when 5 or more cutaneous IH lesions are present.[13]

The IHH initially proliferate extensively during the first year of life before gradual involution, often by 4 years of age.[8,9] Large tumors are associated with complicating physiologic changes

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