Case Report

Classical Findings of Infantile Hepatic Hemangiomas

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Abstract

Introduction
Hemangiomas are benign vascular tumors that are common during infancy. They are most commonly noted as superficial bright red lesions on the skin but can also be found deeper as subcutaneous lesions. Patients with multifocal cutaneous hemangiomas are at risk of visceral involvement with the liver being most commonly affected. Most hemangiomas can be monitored clinically as they are self-limiting. Despite this, hepatic hemangiomas can have serious complications including large arteriovenous shunts leading to cardiac compromise as well as severe hepatomegaly which can cause abdominal compartment syndrome, impaired ventilation and renal vein compression.

Clinical Findings
A six-month-old female, born full term and previously healthy, presented due to worsening abdominal distention and hepatomegaly. On examination, abdominal distention, hepatomegaly and three superficial hemangiomas on her torso and scalp were appreciated.

Outcome
The patient had an extensive workup which showed an elevated AFP and TSH. An abdominal ultrasound revealed numerous rounded regions of hypoechogenicity throughout the hepatic parenchyma. These findings were consistent with diffuse infantile hemangiomas; however, metastasis could not be ruled out with ultrasound alone. An MRI of the abdomen was obtained which confirmed infantile hemangiomas. The patient's MRI and lab findings are the classical findings of infantile hepatic hemangiomas. She had elevated blood pressures during the hospital course and was subsequently evaluated by cardiology for concern of cardiac compromise. Treatment with propranolol was initiated and continued upon discharge. A six month follow-up ultrasound showed significant decrease in size of the hemangiomas.

Conclusion
Hepatic hemangiomas should be monitored closely for serious complications. Although rare, it is important to identify which patients with multifocal cutaneous hemangiomas should be worked up for hepatic hemangiomas and their complications. It is recommended that infants younger than 6 months of age with 5 or more cutaneous hemangiomas undergo early evaluation with abdominal ultrasound.

Keywords
hemangioma; hepatic; infant; liver neoplasms; propranolol

Background
Hemangiomas are benign vascular tumors that are common during infancy. Approximately 5 to 10% of one-year-olds have a superficial hemangioma, with females being more commonly affected than males at a ratio of 3:1. Hemangiomas are also more common in white, non-Hispanic infants and preterm infants. They are characterized as clusters of proliferating endothelial cells that demonstrate rapid proliferation and growth for up to 14 months, followed by a slow regression. This involution phase can take 3 to 10 years to complete. Hemangiomas in early infancy occasionally appear as superficial pale white macules with telangiectasia that progress to bright red, elevated lesions on the skin. Subcutaneous lesions appear as a mass with a bluish hue or discoloration to the skin.

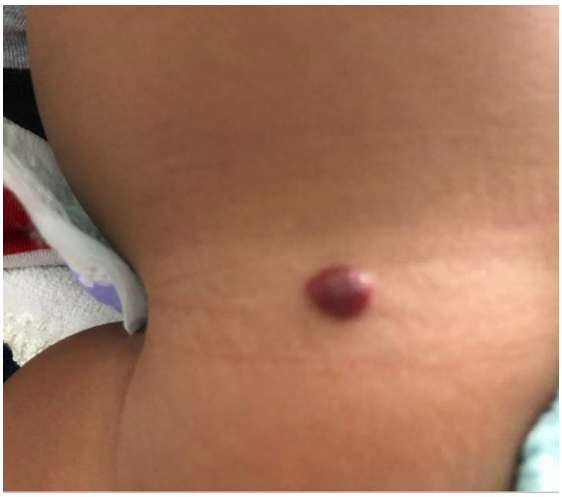

Figure 1. Superficial hemangioma measuring 10 mm on posterior left hip.

Most hemangiomas are monitored clinically as they are self-limiting; however, there are certain presentations that require further workup and management. Patients with multifocal cutaneous hemangiomas are at risk of visceral involvement with the liver being most commonly affected. Hepatic hemangiomas can have serious complications including large arteriovenous shunts leading to cardiac compromise, as well as severe hepatomegaly, which can cause abdominal compartment syndrome, impaired ventilation and renal vein compression.

Case Presentation

A previously healthy six-month-old biracial full-term female presented to the emergency department due to abdominal distention and hepatomegaly discovered during a routine well-child check. The patient had a previous history of abdominal distention, which was attributed to constipation and gas. This distention had been unresponsive to formula changes, over the counter oral simethicone and altered feeding strategies. The child had no other associated symptoms and demonstrated appropriate weight and developmental milestone progression. Review of systems was negative for preceding illness, fever, lethargy, poor appetite, decreased urine output, bloody stools, hematuria, rashes and easy bruising.

On arrival to the emergency room, the patient's vital signs comprised of temperature 36.3ºC, pulse 110 bpm, blood pressure 115/69 mmHg, respiratory rate 32, SpO2 97%, weight 7.145 kg and height 61.5 cm. Her weight and height were in the 27th and 3rd percentile for age, respectively. It was noted that the patient was fussy and crying while vitals were taken. On physical examination she was playful, well developed and in no distress. She had a regular heart rate and rhythm with no murmurs and equal pulses in all four extremities. Her abdomen was distended but soft. Hepatomegaly was noted, as well as an easily reduced umbilical hernia. She had a 2 mm bright red macule on the right frontal scalp, a 2 mm bright red macule on the left chin and a 10 mm bright red papule on the posterior left hip. **(Figure 1)** The remainder of her exam was unremarkable.

The patient had an extensive workup in the emergency department including complete blood count, comprehensive metabolic panel, alpha fetoprotein, human chorionic gonadotropin, lactate dehydrogenase, uric acid and lactate. Her platelets were slightly elevated at 468,000 per microliter. Alpha fetoprotein was elevated at 34.9 ng/ml. Comprehensive metabolic panel results showed elevated alanine transaminase at 43 IU/L. All other labs were within normal limits. Her chest x-ray, looking for possible metastasis and/or mediastinal masses, was normal. An abdominal ultrasound revealed numerous rounded regions of hypoechogenicity throughout the hepatic parenchyma, the largest measuring 4.63 x 2.98 cm. **(Figure 2)** These findings were consistent with diffuse infantile hemangiomas; however, metastasis could not be ruled out with ultrasound alone. The patient was admitted to the pediatric hematology/oncology service for further management.

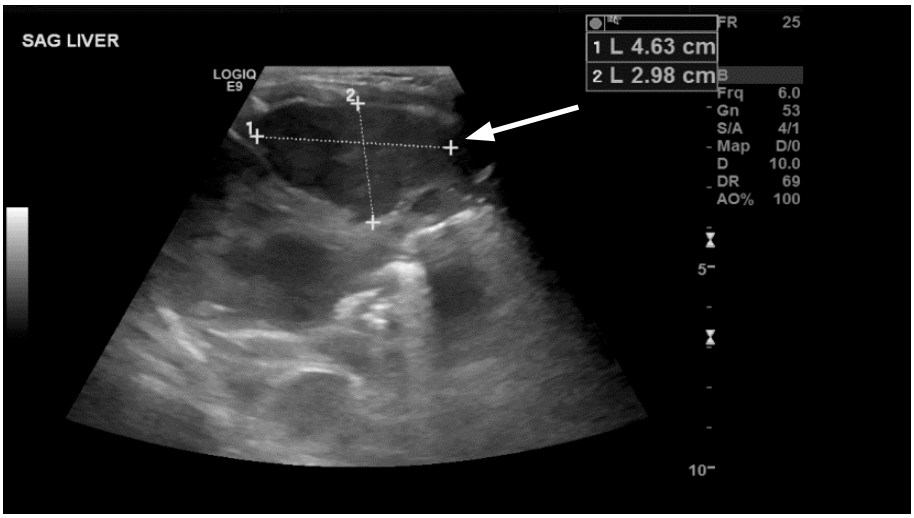

Figure 2. Hepatic ultrasound, sagittal view, obtained at admission with a hemangioma measuring 4.63 x 2.98 cm (arrow).

During the hospital course, an abdominal magnetic resonance imaging (MRI) with and without contrast was obtained, illustrating lesions throughout the hepatic parenchyma consistent with diffuse infantile hemangiomas **(Figure 3, Figure 4)**, the largest being 1.6 x 3 x 4.4 cm. At this time thyroid stimulating hormone and free thyroxine were collected as hypothyroidism occasionally occurs with hepatic hemangiomas. Thyroid stimulating hormone was elevated at 9.39 uIU/ml, as normal range for age is 0.58 to 5.56 uIU/ml. Free thyroxine was within normal limits. The constellation of the patient's history, imaging and laboratory findings was consistent with infantile hepatic hemangiomas.

The hospital course was complicated by elevated blood pressures. The highest blood pressure recorded was 134/79 mmHg, which is in the 99th percentile for age for systolic and diastolic blood pressures. Manual blood pressures averaged approximately 100s/70s, which is in the 97th percentile for age for systolic blood pressure and the 99th percentile for age for diastolic blood pressure. Pediatric cardiology was consulted over concerns for cardiac dysfunction. Echocardiography demonstrated normal anatomy and wall motion, with incidental normal variant trace tricuspid regurgitation and pulmonary insufficiency. Cardiology recommended starting treatment with close monitoring of blood pressures and blood glucose.

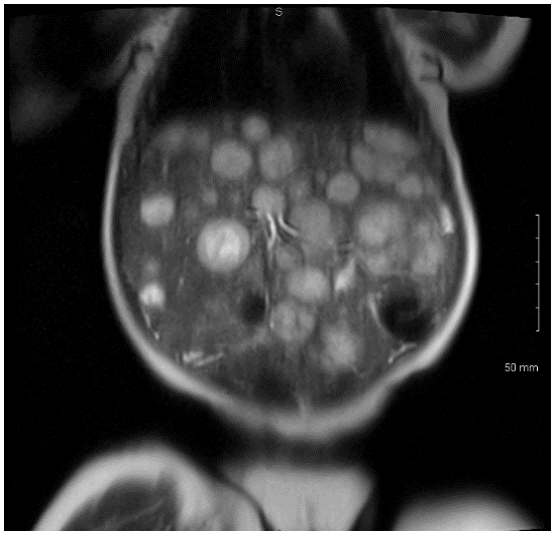

Figure 3. MRI abdomen showing hepatomegaly secondary to innumerable hepatic hemangiomas.

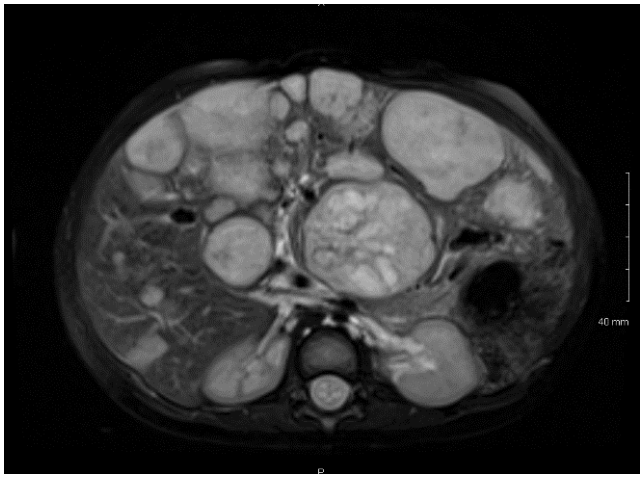

Figure 4. MRI abdomen showing possible renal compression secondary to hepatomegaly.

Treatment for the infantile hemangiomas included propranolol 0.5 mg/kg/dose twice daily. She was monitored for hypoglycemia and hypotension, which she did not encounter. Her elevated thyroid stimulating hormone and normal thyroxine were interpreted as compensated hypothyroidism. The patient was discharged and her parents were instructed to complete an increasing propranolol dosing regimen with a target of 1 mg/kg/dose twice daily.

At the patient's six month follow-up, her abdominal ultrasound showed a significant decrease in hepatic hemangiomas, with the largest being 2.42 cm. **(Figure 5)** However, her superficial hemangiomas had not changed significantly in size. The patient continues to follow-up with cardiology and her follow-up echocardiograms are unchanged and show no signs of cardiac compromise.

Discussion

Infantile hemangiomas are the most common benign tumors of childhood. Most hemangiomas are self-limiting and can be monitored without intervention. Rarely, hemangiomas can be life threatening, so it is imperative for physicians to know the indications requiring further investigation. Clinical guidelines recommend that patients younger than six months of age with five or more cutaneous hemangiomas be worked up for hepatic hemangiomas, as the liver is the most commonly effected visceral organ.[1,2] Usually, an abdominal ultrasound is sufficient for diagnosis.[1,2] Diagnostic criteria for hepatic hemangiomas via ultrasound are the following: (1) ultrasound showing well demarcated, homogeneous hyperechoic masses, (2) lesions less than 3 cm and (3) no past history of cirrhosis or extrahepatic malignancy. In this

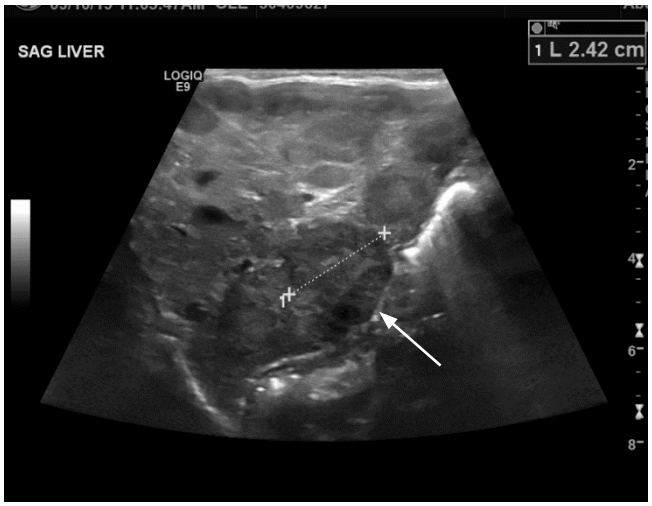

Figure 5. Hepatic ultrasound, sagittal view, with a hemangioma measuring 2.42 cm (arrow), obtained 6 months after treatment.

case, the ultrasound noted hypoechoic masses. Hypoechogenicity is secondary to the surrounding parenchyma, giving a bright signal. An MRI with contrast was recommended because the ultrasound diagnostic criteria was not met. An MRI with contrast has a 90% sensitivity and specificity for the diagnosis of intrabdominal infantile hepatic hemangiomas.[3]

Once hepatic hemangiomas are diagnosed it is recommended to screen the infant for hypothyroidism.[1,4] Hepatic hemangiomas can cause consumptive hypothyroidism, which was seen in this case. This is secondary to a thyroid deactivating enzyme, type 3 iodothyronine deiodinase, which is produced in excess during the proliferative phase of hepatic hemangiomas. This usually does not require treatment.[4,5]

Pharmacologic treatment is recommended for hepatic hemangiomas based on clinical concern for possible complications. Complications include large arteriovenous shunts leading to cardiac compromise as well as severe hepatomegaly leading to abdominal compartment syndrome, impaired ventilation and renal vein compression.[1,5] This patient's age and rapidly progressing abdominal distention were indications for initiating treatment. Infantile hepatic hemangioma treatment coincides with treatment of other high-risk hemangiomas. The first line therapy is propranolol, a nonselective beta-blocker that vaso-constricts blood vessels. This process decreases the expression of vascular endothelial growth factor leading to apoptosis. In theory, propranolol inhibits the proliferation of hemangiomas and prompts the regression phase.[6] Contraindications of propranolol use are premature infants with corrected age less than five weeks, history of bronchospasms or wheezing, conditions affecting blood glucose and cardiac compromise. Cardiac compromise includes heart failure, chronic bradycardia, second/third degree heart block and cardiogenic shock.[7] If any of the above are noted other treatments should be sought out or propranolol should be initiated under the guidance of a cardiologist. The initial propranolol dose is often 0.5 mg/kg/dose twice daily and advanced by 0.5 mg/kg weekly, as tolerated, to a goal of 2 mg/kg/dose twice daily. Patients are kept on this dosage for six months and reevaluated. If hemangiomas reoccur or further regression is desired, a second course is repeated at an adjusted dose for the patient's weight. For this patient, the six month follow-up ultrasound showed improvement in the total number and size of the hemangiomas. This patient was continued on propranolol for an additional six months by the pediatric cardiology team.

Conclusion

Infantile hepatic hemangiomas are fairly benign but should be monitored closely as their rapid proliferation can lead to significant complications. Clinical guidelines recommend that patients younger than six months of age with five or more cutaneous hemangiomas be evaluated for hepatic hemangiomas. A diagnosis is usually made by abdominal ultrasound. Once confirmed, patients should be screened for hypothyroidism and treated accordingly. Most hepatic hemangiomas can be closely monitored without intervention. Treatment is indicated based on clinical concern for possible complications, including cardiac compromise and abdominal compartment syndrome. The first line therapy is propranolol 2 mg/kg/dose twice daily for six months. This case features excellent imaging and lab results that are consistent with infantile hepatic hemangiomas as well as significant improvement with appropriate management.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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