Infantile hepatic hemangioendothelioma: an 8-month old infant successfully treated with a corticosteroid

Youssef Al-Tonbary. Ashraf Fouda
Mansoura University Children Hospital, Mansoura, Egypt
Correspondence: Youssef Al-Tonbary MD · Mansoura University Children Hospital, Mansoura, Egypt · ytonbary@gmail.com; ytonbary@mans.edu.eg

Infantile hemangioendothelioma is a rare benign vascular tumor of the liver. We report a case of hepatic hemangioendothelioma in an 8-month-old female infant who presented with hepatomegaly and respiratory distress, which was successfully treated with oral prednisolone for six months.

CASE
An 8-month-old female presented with abdominal enlargement that had been noticed by the mother for 3 months, and was associated with low-grade fever, loss of weight and mild respiratory distress. On examination, there was no jaundice, or pallor. Skin examination revealed a small purplish hemangioma over the anterior chest wall which was about 1.5×1 cm, firm, mobile and nontender. Cardiac and chest examinations were normal. The abdomen was diffusely enlarged. The span of liver right lobe was about 14 cm, and it was firm, nontender and with smooth surface. There was no splenomegaly nor ascites.

The alpha fetoprotein of 13.88 ng/mL was considered high compared with the adult reference value (up to 10.9 ng/mL), but was found to be normal when adjusted to the age of the patient (8.5±5.5 ng/mL for 8 months old) (Table 1). Abdominal ultrasonography revealed an enlarged liver with multifocal hypoechogenic well-defined lesions scattered all over the liver. Doppler examination showed a patent portal vein (5.7 mm) with no evidence of portal hypertension. CT of the abdomen revealed variable size hypodense nodules with enhancement arterial phase (Figure 1a, 1b) and with progressive centripetal filling in portal phase. A liver biopsy was not done for fear of hemorrhage.

After one month of follow up without therapy, there was progressive hepatomegaly and respiratory distress with enlargement of the previously described masses detected by serial ultrasonography. She was treated with oral prednisolone, according to regimen used in similar case report. It was started with a dose of 4 mg/kg/day in 2 divided doses for 2 weeks, then tapered to 4 mg/kg/day on alternate days for 2 weeks. It was further tapered to 2 mg/kg on alternate days for 6 weeks and 1 mg/kg on alternate days for 3 months. During the period of treatment, our patient had normal blood glucose and blood pressure with no side effects of steroids after 6 months follow up.

After treatment, there was a marked reduction in the abdominal enlargement, and the liver span was normal (about 7 cm). Post-contrast CT of the abdomen showed a marked reduction of the liver nodules (Figure 2). However, the skin hemangioma did not disappear and the patient was referred to plastic surgery.

DISCUSSION
IHE, the most common benign tumor of the liver in children, is seen almost exclusively (86%) in the first 6 months of life, with about one third of the cases presenting in the first month. It is rare in children over 3 years old. Girls are more frequently affected (1.7:1) and...
Case Report

Table 1. Results of laboratory tests.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Patient value</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>7.5</td>
<td>12.5-15 gm/dL</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>14.6</td>
<td>5-11×10^6/L</td>
</tr>
<tr>
<td>Platelet count</td>
<td>529</td>
<td>150-450×10^6/L</td>
</tr>
<tr>
<td>Serum Albumin</td>
<td>4.7</td>
<td>3.5-5.4 mg/dL</td>
</tr>
<tr>
<td>Serum Bilirubin</td>
<td>0.9</td>
<td>Up to 1 mg/dL</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>64</td>
<td>Up to 40 U/L</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>48</td>
<td>Up to 45 U/L</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>12.9</td>
<td>10-12 seconds</td>
</tr>
<tr>
<td>Activated partial thromboplastin time</td>
<td>52</td>
<td>25-38 seconds</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>1.1</td>
<td>0.9-1.2</td>
</tr>
<tr>
<td>Alpha fetoprotein</td>
<td>10.88</td>
<td>8.5±5.5 ng/ml</td>
</tr>
<tr>
<td>VMA/HVA</td>
<td>normal</td>
<td></td>
</tr>
</tbody>
</table>

VMA/HVA: Vanillyl mandelic acid/homovanilic acid

There is no racial predilection.⁴

Clinical presentation usually involves an enlarged abdomen noted by a parent, although about 10% to 15% of cases present with features of congestive heart failure, including high cardiac output, elevated right and left end-diastolic pressure, a small systolic pressure gradient across the pulmonary outflow tract, and mildly elevated artery pressure.⁵ Less frequently, symptoms include jaundice (20% of cases), failure to thrive, fever, and, rarely, liver failure or tumor rupture.⁴ Hemangiomas at other sites, including the skin, lung, lymph nodes, pancreas, retroperitoneum, and bone are seen in 10% to 15% of cases. The most frequently involved site is the skin, where single or multiple lesions may be present.⁴

IHE appears in solitary or (seldom) multiple form and may reach a size of some 15 cm. The unencapsulated tumor foci have blurred boundaries. They are sponge-like and reddish brown in color, but may become firm and grey in bigger tumors.⁴ Hemoglobin levels are decreased below 10 mg/dL in about 50% of cases, aspartate aminotransferase is elevated above 100 U/L in 32%, and bilirubin is increased in 20%.⁴ Alpha-fetoprotein is not elevated when adjusted for the age of the child. Normal levels of alpha-fetoprotein in neonates may be as high as 2500 ng/mL and the adult level of less than 25 ng/mL is not reached until 6 months of age.⁶

Plain x-ray may show hepatomegaly or an upper abdominal mass, which may have punctuate or speckled calcification of the lesion in 15% to 37% of cases.⁷,⁹ Cardiomegaly with or without prominent pulmonary vascular markings may be seen in infants with congestive heart failure.¹⁰ Ultrasonography may show solitary or multiple lesions, discrete or diffuse, with variable...
Echo-texture. A CT scan gives the exact size and spread of the lesion. In noncontrast scans, the lesions are solitary or multiple, homogenous or non-homogenous, with or without calcifications. Following contrast administration, there is early massive enhancement, which is either diffuse or peripheral.

IHE should be included in the differential diagnosis of other hepatic masses developing in infancy, such as cavernous hemangioma, hepatoblastoma, and mesenchymal hamartoma. Cavernous hemangioma rarely presents in infancy. It is the most common primary liver tumor in the older age group and is usually associated with other hemangiomas in the body. It rarely presents with congestive cardiac failure. Hepatoblastoma is the most common symptomatic malignant tumor presenting before the age of 5 years. It may be single or multiple and commonly involves the right lobe of the liver. The child commonly presents with an abdominal mass and is severely ill with weight loss, anorexia, pallor and weakness. The alpha-fetoprotein and human chorionic gonadotropin levels are usually elevated. Mesenchymal hamartoma is a developmental anomaly rather than a true neoplasm. Usually, the patient presents with abdominal distention, fever, vomiting and constipation. The alpha-fetoprotein levels are within normal limits. Plain films show a soft tissue mass. Ultrasonography, CT and magnetic resonance (MR) imaging show a predominantly cystic mass with multiple echogenic septae.

The management of IHE and hemangiomas is controversial. The severity of the presenting symptoms determines the approach to therapy. Most asymptomatic lesions can be managed expectantly, using serial ultrasound to visualize the anticipated spontaneous regression. In cases with a gradual onset of controllable symptoms, the use of digitalis and diuretics for congestive heart failure, and the administration of blood products to correct anemia and coagulopathy can occasionally be sufficient. This can be accompanied by steroid therapy in an attempt to suppress continued growth of the lesion or even encourage regression.

Relatively small solitary tumors are best treated by complete resection, which is often impossible and operation is risky. Therefore, various conservative treatments such as radiotherapy, hepatic artery ligation or embolization have been used. There have been several reports of orthotopic liver transplantation for massive, uncontrollable IHE. Apart from the young age of the patients and the urgency of the situation, there are major logistical problems, and the results in the few reported cases have not been good enough to propose orthotopic liver transplantation as a standard procedure in the treatment of large IHE. However, it was also reported to be successful after failed treatment with steroids and chemotherapy.

There has been widespread use of steroids to shrink the immature hemangiomatous tissues since Touloukian first reported success in an 8-month-old infant. Dosages of prednisolone used for treatment have been between 2 to 10 mg/kg/day. Successful improvement with steroid therapy was reported in many case reports. Steroid treatment results in dramatic shrinkage of the hemangioma in one third of cases, but a third may prove unresponsive to steroids and can be treated with interferon alfa-2a. However, investigators in many studies have argued that the side effects of high doses of steroids and their complications were serious, and also showed treatment failure with disappointing results.

Interferon-alpha therapy has also been used as a component of medical management. Successful treatment with cyclophosphamide after failure of steroid therapy was also reported. There is considerable optimism about the development of potent anti-angiogenic drugs. The angiogenesis inhibitor AGM-1470 was able to inhibit growth of hemangioendothelioma in a mouse model.

In summary, we report that high-dose prednisolone therapy has improved the symptoms of infantile hemangioendothelioma in a female infant and completely resolved the hepatic hemangioendothelioma on follow-up.
HEMANGIOENDOTHELIOMA

REFERENCES