

## Infantile hemangioendothelioma of the liver: A case report and review literature

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*Herein is reported a case of infantile hepatic hemangioendothelioma (IHE) in a 2-week-old boy presented with an asymptomatic abdominal mass he had since birth and treated by hepatic lobectomy. IHE is a rare, benign vascular tumor of the liver that usually presents in infants <6 months old. The usual clinical manifestation is the characteristic triad of congestive heart failure, hepatomegaly and cutaneous hemangioma. Management has been varied including conservative treatment, systemic steroids, surgical resection, hepatic artery ligation, embolization and radiation depending on clinical experience. We review the diagnostic and therapeutic approaches.*

**Key words :** *Hemangioendothelioma, Vascular tumor, Liver, Infant, Neoplasm.*

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รายงานผู้ป่วยที่เป็นเนื้องอกตับชนิด *Infantile hemangioendothelioma* ในเด็กชายไทยอายุ 2 สัปดาห์ตรวจพบก้อนในช่องท้องตั้งแต่เกิดซึ่งได้รับการรักษาด้วยวิธีผ่าตัดเอาเนื้องอกออก เนื้องอกของตับชนิดนี้เป็นเนื้องอกชนิดไม่ร้ายแรงของหลอดเลือดซึ่งมักพบในเด็กที่มีอายุน้อยกว่า 6 เดือน โดยมีอาการแสดงสำคัญที่ตรวจพบได้ 3 อย่างคือ หัวใจล้มเหลว ตับโตและปานแดง การรักษาเนื้องอกชนิดนี้มีหลายอย่างเช่น การรักษาตามอาการ ยาสเตียรอยด์ การผ่าตัดก้อนเนื้องอก การผ่าตัดผูกหลอดเลือด *hepatic artery* และฉายรังสี เป็นต้น พวกเราได้รวบรวมวิธีวินิจฉัยและวิธีการรักษาต่าง ๆ ของเนื้องอกชนิดนี้

Infantile hepatic hemangioendothelioma (IHE) has been recognized for over 70 years. The first review was published by Foote in 1919. It is the most common benign vascular hepatic tumor occurring in infancy, but it is still uncommon and only about 100 cases are reported in the world's literature.<sup>(1-10)</sup> The usual clinical manifestation is the characteristic triad of cardiac failure, hepatomegaly and cutaneous hemangioma.<sup>(2-4,11-13)</sup>

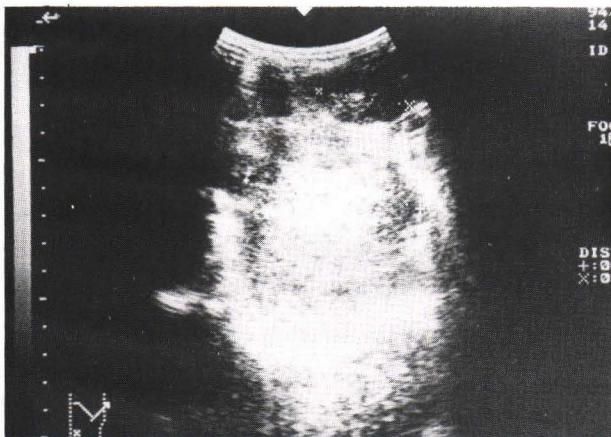
We had a chance to manage a case of IHE in a 2-week-old male infant who was presented with an asymptomatic abdominal mass at birth. We also review the literature of the management of this tumor.

#### A case report

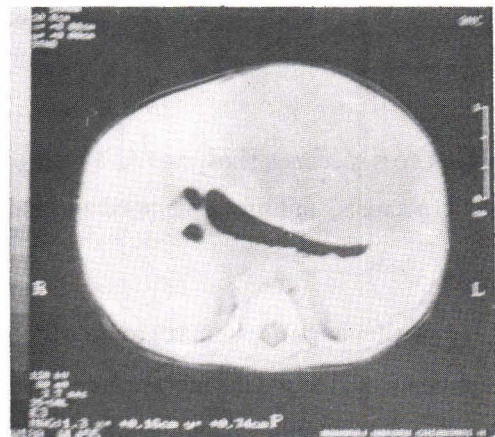
A 2-week-old term, male baby, body weight 3700 g. was presented to Maharaj Nakhon Chiangmai Hospital with an abdominal mass he had since born. The mass was 5x6 cm., firm, not tender, well demarcated on palpation and confined in the left upper abdomen.

Laboratory studies were normal except alpha-fetoprotein >548.9 IU/ml (0-42 IU/ml). Sonographic examination showed a well defined, homogeneous mass in the left lobe of the liver (Figure 1). Computed tomography revealed a well demarcated 5x6x7 cm. homogenous mass more dense than the surrounding liver. The periphery of the liver was significantly enhanced with an irregular inner border occupying the left lobe (Figure 2). The child underwent a left lobectomy with the impression of hepatoblastoma. The tumor readily bled and was adhered to the greater omentum (Figure 3).

The resected specimen was a well circumscribed solid mass confined in the left lobe. It measured 5x6x7 cm. On section, the mass was well demarcated, but not encapsulated, with pale gray to pink color. There were areas of central geographic necrosis with yellowish discoloration, multifocal hemorrhages and several thrombi within the mass (Figure 4). The consistency was resilient and spongy. The final pathologic examination was "Infantile hepatic hemangioendothelioma type I".



**Figure 1.** A sonography of the liver showing a well defined, sized 3.4x6.5 cm., homogenous mass confined in the left lobe of liver.



**Figure 2.** A computed tomography scan showing a huge well defined homogeneous hypodense mass with enhanced and irregular inner border confined in the left lobe of the liver.





**Figure 3.** Operative finding showing hepatic tumor that adhesive to the greater omentum.



A



B

**Figure 4.** Gross specimen showing (A) a well-circumscribed solid tumor and (B) cut surface has a central necrosis, multifocal hemorrhage and several thrombi within the mass.

### Discussion

Infantile hepatic hemangioendothelioma (IHE) is uncommon, but it is the most common vascular hepatic tumor of infancy.<sup>(2, 4)</sup> The exact incidence is difficult to determine because it has often been either misdiagnosed or mislabeled as “cavernous hemangioma” in the literature. Cavernous hemangioma is the primary hepatic tumor in older groups but it rarely occurs in

infants.<sup>(3-4, 13)</sup> Most of IHE (87%) presents before 6 months of life and predominates in females.<sup>(2, 8-9, 11)</sup> They may be either solitary or multicentric lesions, the latter being more frequent. Association with one or more cutaneous hemangiomas were present in about 45% of cases.<sup>(2)</sup>

The most common clinical presentation is hepatomegaly or abdominal mass, and the mass is often detected as an incidental finding during physical examination.<sup>(2, 8-9, 12-14)</sup> It is a histologically benign tumor, but it usual associated with potential life-threatening complications. High output cardiac failure is one of the complications that result from the large intrahepatic

arteriovenous shunting, which presents marked vascular bruit over the liver on examination.<sup>(6, 10)</sup> The incidence of this complication varies from 8-65% in the literature,<sup>(2-3, 5, 8-9, 12-14)</sup> and may have a mortality rate as high as 80% in severe cases which go untreated.<sup>(4)</sup> The solitary lesions have a better prognosis because of the smaller degree of cardiac failure. Other problems include massive intraabdominal hemorrhage due to

rupture,<sup>(5,9-10)</sup> thrombocytopenia,<sup>(7)</sup> anemia,<sup>(8-9,15)</sup> transient obstructive jaundice<sup>(2, 8, 13)</sup> and portal hypertension.<sup>(14)</sup>

The association of hemangiomas with thrombocytopenia and afibrinogenemia is known as "Kasabach-Merritt syndrome".<sup>(10)</sup> Laboratory findings are usually normal, although marked anemia may occur due to microangiopathic hemolysis.<sup>(2,9)</sup> Platelet trapping in the tumor leads to thrombocytopenia. Hyperbilirubinemia may be caused from the compression of the extrahepatic bile ducts, although it may be coincidental with physiologic jaundice. Serum alpha-fetoproteins may be mildly elevated, but markedly and persistently elevated in the hepatoblastoma.<sup>(8-9,11,13)</sup>

Histologic patterns of IHE are divided into two types. Type I is more mature, characterized by both irregularly dilated and small compressed vascular spaces lined by a single layer, or less often, several layers of pump endothelial cells with a bland cytologic appearance. Type II has a more aggressive appearance, characterized by large hyperchromatic pleomorphic endothelial cells arranged in irregular budding and branching structures.<sup>(2,13)</sup>

The initial radiographic evaluation of an infant with an abdominal mass should be plain film of the chest and abdomen, and abdominal sonography.<sup>(13, 16)</sup> The patients two associated with congestive heart failure will show cardiomegaly with or without prominent pulmonary vascular marking. Plain abdomen films may show an enlarged liver that may contain strippled calcification (16%).<sup>(13)</sup> An abdominal sonography should be performed to confirm the origin of the abdominal masses. However, there is a lack of specificity for hepatic mass in infants and children. A complex liver mass with large draining hepatic veins and a dilated proximal aorta indicates arterio-venous shunting is strongly suggested.<sup>(6)</sup>

These days, computerized tomographic scans with contrast injection is assuming a specific role in the diagnosis of IHE that characterize solitary or multiple, homogenous, hypodense lesions with early edge enhancement.<sup>(9,13,16)</sup> Radionuclide studies may be a useful adjunct to ultrasound and CT, as persistent radionuclide activity may be seen throughout the lesion on the dynamic scans and focal defects on the static images.<sup>(17)</sup>

Angiography has been replaced by CT in the investigation of IHE, but it should be reserved for patients with equivocal CT findings or when either surgery or therapeutic tumor embolization is being considered.<sup>(5, 9, 16)</sup> This can be performed through the umbilical artery in the new born or through the femoral artery in the older child.<sup>(9)</sup> It shows a decreased caliber of the aorta distal to the origin of the hepatic artery, enlarged tortuous feeding vessels which do not taper normally, and multiple diffuse angiomatous lesions throughout the liver with rapid filling of the large draining hepatic veins which indicate arteriovenous shunting within the hepatic mass.<sup>(9, 16, 18)</sup>

The natural history of most cutaneous capillary hemangiomas is one of spontaneous regression after a period of rapid growth, and similar regression may occur in IHE.<sup>(2-3,15)</sup> Therapy should be directed toward assisting this regression which usually starts within 6 - 8 months and relieves potentially life-threatening complications.<sup>(9, 15)</sup> Corticosteroids, therapeutic embolization, hepatic artery ligation, radiation, chemotherapy, and surgical excision have all been used either singly or in various combination.

Systemic corticosteroids - Prednisolone 2-5 mg/kg/day for 2-4 weeks - have been used but the mechanism of action in IHE is unclear.<sup>(8-9,12,19-20)</sup> It is likely that the

steroids cause vasoconstriction of rapidly proliferating endothelial cells lining the vascular channels.<sup>(20)</sup> There have been no controlled studies to show that it has been of any value for IHE, and it is difficult to be certain that this effect is a result of the treatment or the result of spontaneous regression.<sup>(8, 15)</sup>

Radiation therapy has been employed to destroy the rapidly proliferating and immature vasculature with relative sparing of the more radioresistant, normal parenchymal cells<sup>(9, 18)</sup> but there is always concern for radiation hepatitis, long term second neoplasms e.g. leukemia and angiosarcoma. Its use has declined recently because of fear of these effects.<sup>(8, 14-15)</sup>

Cyclophosphamide (10 mg/kg/day for 3-4 days) has been shown to be effective by damaging the endothelial cells of the tumor and decreasing the production of capillaries.<sup>(8-9, 18)</sup>

Hepatic artery ligation was first successfully performed by de Lorimeir in a giant hemangioma with heart failure due to arteriovenous shunt.<sup>(22-23)</sup> After successful ligation, the liver shrinks within minutes with dramatic improvements in congestive heart failure rates.<sup>(5-6, 8-9, 14)</sup> Surgical ligation has been replaced with selective hepatic embolization, with either polyvinyl alcohol particles, silicone balloons, gelforms, or wire coils. Selective embolization is a fairly new technique requiring great skill<sup>(10)</sup> and may fail despite successful occlusion of the hepatic artery because of the dominant portal venous supply to the hemangioma.<sup>(8)</sup>

Surgical excision is preferred for solitary lesions or if the lesion is confined to one lobe. It may be performed on an urgent basis in a child with heart failure or in whom the tumor ruptured.<sup>(8-9, 12, 15-16, 24)</sup> In IHE with necessary emergency resections, extensive intraoperative bleeding often occurs.<sup>(1)</sup> To assist

resection, hypothermic circulatory arrest has been used.<sup>(25)</sup> It is also recommended in localized tumors that are distinguishable from those that are malignant.<sup>(15)</sup>

Because this tumor is uncommon, treatment of infantile hepatic hemangioendothelioma remains controversial and varies in each institutional experience. If a tumor is discovered as an asymptomatic mass, no therapy is required to provide spontaneous regression to be monitored by serial ultrasound. In an infant in whom an abdominal mass is a predominate feature with no or minimal cardiac failure, systemic corticosteroids are given first, and given with digitalis and diuretics for control of the symptoms. Other therapeutic methods may be added for infants resistant to the medication, or who have either hepatic artery embolization or hepatic artery ligation, but after careful angiography to produce a preoperative road map in order to ensure appropriate vessels are ligated. If embolization is not applicable, surgical excision can be performed if there is a solitary lesion in a suitable location.

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