Magnetic resonance imaging of infantile hemangioendothelioma

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Infantile hemangioendothelioma is the most common benign hepatic tumor during infancy and also follows a benign course. During the routine physical examination of a 10-month-old female patient, masses of the liver were incidentally found. Laboratory studies revealed elevated liver function tests but normal alpha-fetoprotein level. Following the ultrasound (US) examination that demonstrated multiple hypoechoic liver masses, we performed magnetic resonance imaging (MRI) for further characterization of these lesions. Imaging features of the lesions were thought to be consistent with infantile hemangioendotheliomas especially based on dynamic post-contrast images. Although the patient's clinical condition was stable and she did not have any serious symptoms indicating congestive heart failure or coagulopathy, in terms of having a definitive diagnosis and ruling out a malignancy, a tru-cut liver biopsy was performed and histopathological examination confirmed the diagnosis.

Key words: hemangioendothelioma, hepatic imaging, infants.

Hepatic tumors in children are relatively uncommon and account for about 2%-3% of all pediatric tumors[1,2].

Hemangioendothelioma is a rare vascular tumor of the liver. Two types of these tumors occur, one predominantly found in the pediatric population (infantile hemangioendothelioma) in infants less than one year of age, and another found in adults (epithelioid hemangioendothelioma).

Case Report

A 10-month-old female patient was admitted to the hospital for upper respiratory tract infection symptoms, namely cough and fever. During her physical examination, incidental abdominal masses were palpated by the pediatrician and the patient was referred to ultrasound (US) examination, which revealed multiple hypoechoic liver lesions coexisting with an enlarged liver. Physical examination was otherwise unremarkable. Laboratory investigations showed elevated liver function tests, but alpha-fetoprotein level was within normal limits. Following US, the patient was examined by magnetic resonance imaging (MRI) for further evaluation and characterization of these lesions.

We performed axial 3D FSPGR (fast spoiled gradient echo) T-1 and SSFSE (single shot fast spin echo) T-2 weighted images, and following intravenous gadolinium DTPA administration (0.1 mmol/kg), also obtained 3D FSPGR T-1 weighted dynamic post-contrast liver images using a 1.5 tesla superconducting magnet (GE, Signa, Milwaukee, Wisconsin, USA).

These images revealed multiple liver masses scattered throughout the liver parenchyma ranging between 1 and 4 cm in diameter which showed hypointense signal intensity on T-1 weighted images (Fig. 1) and very high signal intensity on T-2 weighted images in comparison to the liver (Fig. 2).

Following gadolinium administration, they demonstrated a contrast enhancement pattern which was identical to that of hemangiomas. On early dynamic images they showed peripheral nodular type enhancement, and with delayed images variable central filling of the lesions was observed (Figs. 3, 4).

The patient underwent a tru-cut biopsy to rule out a malignancy such as hepatoblastoma. Following histopathologic analysis, the patient was diagnosed as having infantile hemangioendotheliomas. She was scheduled

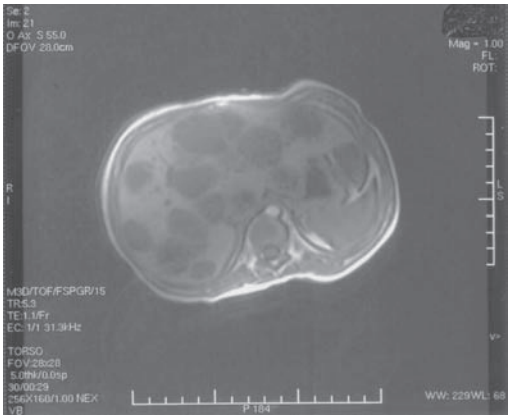

Fig. 1. Axial 3D FSPGR (fast spoiled gradient echo) T-1 weighted image: multiple hypointense signal intensity masses are seen throughout the liver.

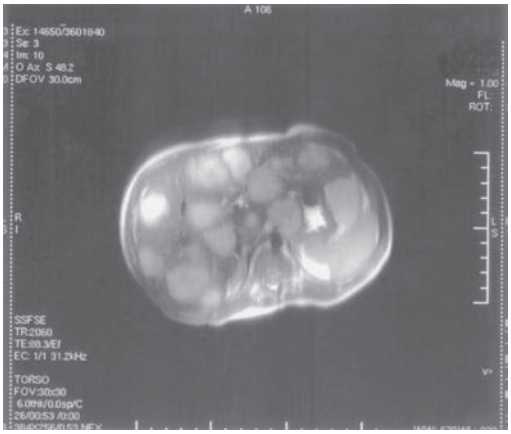

Fig. 2. Axial SSFSE (single shot fast spin echo) T-2 weighted image: these masses have very high signal intensity in comparison to liver parenchyma.

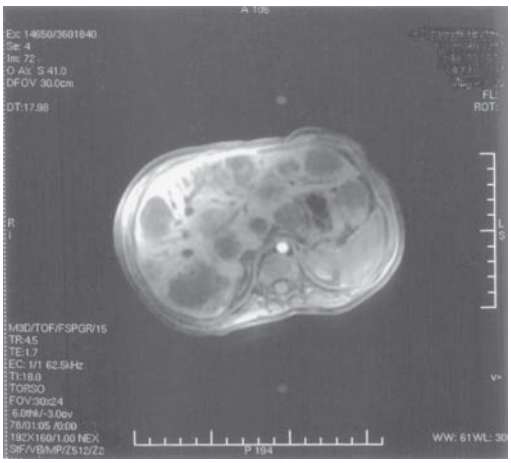

Fig. 3. Axial 3D FSPGR (fast spoiled gradient echo) T-1 weighted early post-contrast image: lesions show mostly peripheral enhancement.

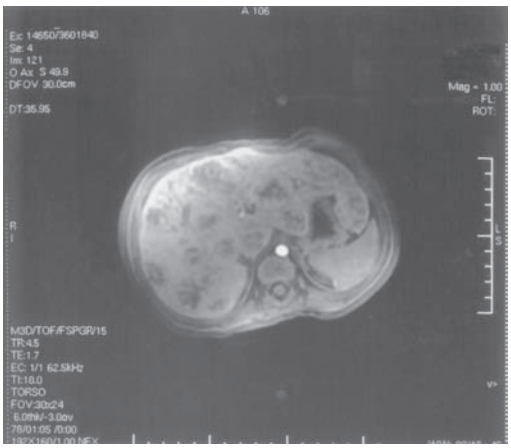

Fig. 4. Axial 3D FSPGR (fast spoiled gradient echo) T-1 weighted late post-contrast image: lesions demonstrate variable central contrast filling with delayed time.

for follow-up MRI examination three months later to determine whether or not these lesions would be subject to any regression. She is also being closely followed up clinically by her pediatricians in case she develops any serious condition like congestive heart failure or coagulopathy.

Discussion

Infantile hemangioendothelioma is the third most common hepatic tumor in children, the most common benign vascular tumor of the liver in infancy, and the most common symptomatic liver tumor during the first six months of life[3-5]. The tumor has a 2:1 female predilection[3,6,7]. The lesions may be single or multiple, and calcifications are seen at histopathologic analysis in 50% of cases[5].

Although infantile hemangioendotheliomas are usually benign, malignant sarcomas have been reported to arise in existing hemangioendotheli omas[3,4,8]. Most tumors continue to grow during the first year of life and then spontaneously regress, probably due to thrombosis and scar formation[3,5,7,8].

The clinical manifestation of hemangio-endothelioma is variable. The tumor, as in our case, may be asymptomatic and discovered incidentally. More often, the tumor is large and manifests as hepatomegaly, abdominal

distension, or a palpable upper abdominal mass. There may be extensive arteriovenous shunting within the lesion, resulting in decreased peripheral vascular resistance. Thus, increased blood volume and cardiac output are required to maintain vascular bed perfusion, which may lead to high cardiac output and congestive heart failure in up to 50% to 60% of patients[3,5,9]. Hematologic abnormalities may be seen, including anemia and especially thrombocytopenia caused by trapping of thrombocytes within the hemangioendothelioma with consumptive coagulopathy (Kasabach-Merritt syndrome)[3,5,6]. Other symptoms such as jaundice, elevated transaminase levels, failure to thrive, respiratory difficulty, intestinal obstruction, or, rarely, hemoperitoneum and shock secondary to tumor rupture[3,4,7] may also be present. Serum alpha-fetoprotein levels are usually normal or slightly increased[3-5].

Ultrasonography shows solitary or multiple lesions, discrete or diffuse, with variable echotexture ranging from hypoechogenic to isoechogenic or strongly echogenic patterns[10], depending on cellular content and presence of large sinusoids with areas of hemorrhage, fibrosis and calcification. Occasionally, the lesions may show streaky or even anechoic channels with calcification.

On Doppler examination, a variable Doppler pattern of blood flow is noted from the liver with increased velocity. There is a frequency shift of 3 KHz, which is higher than in hemangioma but lower than in hepatocellular carcinoma. The technique of color Doppler sonography is particularly valuable in these cases, since the often extremely high blood flow through the celiac trunk and hepatic artery into the lesion can be visualized and measured. In cases with severe arteriovenous shunting, an abrupt decrease in the width of the abdominal aorta directly caudal to the branching of the celiac trunk can be seen. Usually, these findings are typical for infantile hemangioendothelioma and may function as a basis for this diagnosis[11].

At unenhanced computerized tomography (CT), infantile hemangioendothelioma usually manifests as a well-defined mass that is hypoattenuating relative to the normal liver parenchyma[8].

At contrast-enhanced CT, the enhancement pattern may resemble that of an adult giant hemangioma[4,8], with "nodular" peripheral puddling of contrast material in the early phase, subsequent peripheral pooling, and central enhancement with variable delay[1,6,8]. In larger tumors, central enhancement is often lacking due to fibrosis, hemorrhage, or necrosis[4,9]. Conversely, small lesions, which tend to be multifocal, frequently enhance completely and typically do not demonstrate hemorrhage or necrosis[8].

At unenhanced MR imaging, the lesions have low signal intensity on T-1 weighted images and high signal intensity on T-2 weighted images[4,6,9]. Because of the simultaneous presence of hemorrhage, necrosis, and fibrosis, the mass often appears heterogeneous on both T-1 and T-2 weighted images[4]. After intravenous administration of gadopentetate dimeglumine, the lesions usually show an enhancement pattern similar to that described at CT[4,8].

The most important alternative diagnosis to infantile hemangioendothelioma in this age group is hepatoblastoma[5]. It is more commonly located in the right hepatic lobe (>60% of cases). The serum alpha-fetoprotein level is elevated in up to 90% of patients with hepatoblastoma[1,2,3,6]. The lesions are usually large and solitary but may also be multifocal.

Mesenchymal hamartoma[3-5] is another important differential diagnosis. Mesenchymal hamartomas characteristically have a cystic or multicystic appearance, which helps distinguish them from other hepatic masses[3,6,12]. If solid components predominate, differentiation between mesenchymal hamartoma, infantile hemangioendothelioma, and hepatoblastoma may be impossible[4,6,7].

Finally, metastatic neuroblastoma may contribute to the differential diagnosis spectrum. Lack of clinical evidence of further metastatic disease or elevated vanillylmandelic acid levels may argue against neuroblastoma, especially in children over one year old[1,4,5].

The differentiation of benign from malignant hepatic hemangiomas and neoplasms may not be possible by imaging modalities. Tru-cut biopsy of a vascular tumor under the best circumstances may be considered too risky in most cases. It may cause life-threatening bleeding due to disrupted hemostasis tests and increased hemorrhage risk in these patients. However, this procedure would be helpful in making a differential diagnosis in these

vascular lesions. If the tumor size is large and the patient's clinical condition does not permit, a diagnostic biopsy should not be performed. Since biopsy is not always possible, the treatment decision is therefore often made without histologic information.

Tumors that do not behave like typical hemangiomas - absence of associated cutaneous hemangiomas, initial manifestation after six months of age, atypical radiological findings, unresponsiveness to treatment - may represent a different type of neoplasm, and in these situations a biopsy should be performed[13].

The differentiation between an infantile hemangioendothelioma with only slightly enlarged cavernous spaces and a fetal hepatoblastoma or a benign hyperplastic regenerative node of the liver can be extremely difficult[14]. Therefore, before starting specific treatment, histology should be reviewed by an experienced pediatric pathologist. Usually, histology shows normal, still immature cords of hepatic cells divided by more-or-less vascular spaces lined by a single layer of plump, regular endothelial cells[15]. The dimensions of these vascular spaces determine whether they are categorized as capillary hemangioendothelioma or cavernous hemangioma[16]. Increased mitotic activity is usually not apparent in these tumors.

Patients with infantile hemangioendothelioma usually have an excellent prognosis, especially with spontaneous regression after the first year of life. Treatment is determined on the basis of the tumor size and the severity of symptoms. Intervention is necessary only if the lesion is symptomatic and cannot be managed conservatively while the expected involution occurs. Surgical resection is indicated if life-threatening symptoms are present or if the mass cannot be distinguished from a malignant tumor radiologically[3]. Medical therapy includes steroid and interferon therapy to accelerate the natural involution of the mass and radiation therapy or chemotherapy, as well as supportive care for congestive heart failure and coagulopathy[3,5,6,9].

In summary, primary liver tumors are very rare during the neonatal period and a precise diagnosis is sometimes problematic because of nonspecific clinical symptoms. In this age group, infantile hemangioendothelioma should be always considered in the differential diagnosis. Although it usually undergoes spontaneous regression, it sometimes may be life-threatening due to congestive heart failure and/or consumptive coagulopathy. In this situation, treatment with resection, embolization or arterial ligation may be necessary. Furthermore, it is necessary to differentiate infantile hepatic hemangioendothelioma from hepatic malignancies.

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