CASE REPORT

Spontaneous Regression of Infantile Hepatic Hemangioendothelioma

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Many primary hepatic tumors such as the rare pediatric neoplasms can be evaluated by sonography. Infantile hepatic hemangioendothelioma (IHH), the most common hepatic benign vascular tumor in infancy, has an excellent prognosis and spontaneous involution within 6-8 months in most cases. A 25-day-old baby girl was admitted to the hospital due to nonbilious vomiting for 2 days. Sonography showed multiple hypoechoic masses in the liver, and abdominal computed tomography demonstrated multifocal hypervascular lesions that were characteristic of IHH. The patient was then treated with supportive care and discharged in a stable condition without medication. Serial follow-up sonographic examinations showed that the size of the masses decreased gradually. At the age of 11 months, a follow-up sonogram confirmed complete resolution of IHH. Sonography is a useful and convenient method for diagnosis and follow-up of IHH. Long-term follow-up is necessary for IHH, even if the lesions are in regression, to watch for rare but possible malignant transformation.

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Introduction

Primary hepatic tumors are rare in children and account for about 0.2-5% of pediatric neoplasms [1]. Sonography is a useful imaging modality to evaluate neonatal liver tumors.

Infantile hepatic hemangioendothelioma (IHH), the most common hepatic benign vascular tumor in infancy, has an excellent prognosis and, in most cases, spontaneous involution within 6-8 months [2,3]. In the past, open liver biopsy and angiography were used most frequently to make the diagnosis. However, the sonographic feature of this condition has been described as multiple well-defined hypoechoic masses, and computed tomography (CT) demonstrated intense enhancement in these homogeneously hypodense masses after intravenous contrast agent administration. We present a case of IHH in which the
diagnosis was established with the use of noninvasive imaging techniques. Serial follow-up sonographic examinations were performed, and tumor regression without any medication was observed at the age of 11 months.

Case report

A 25-day-old baby girl presented with nonbilious vomiting for 2 days was transferred to our hospital. The infant was born at 37 weeks of gestation by normal vaginal delivery. Neither polyhydramnios nor abdominal mass was mentioned on prenatal sonographic examination, and there were no specific findings on the clinical examination at birth. On admission, her weight was 3.8 kg (25th and 50th percentiles) and length 57 cm (50th percentile). The heart rate was 130 beats per minute without murmur, and respiratory rate was 40 breaths per minute. On physical examination, abdominal distention and hepatomegaly were found 2 cm below the right costal margin, but there was no abdominal bruit on auscultation. No lymphadenopathy, splenomegaly, or cutaneous lesion was noted.

Initial laboratory evaluation showed that hemoglobin, hematocrit, platelet count, white blood cell count, and electrolytes were within normal limits. Plain films of the chest and abdomen revealed no specific findings. Abdominal sonography showed multiple hypoechoic tumors (the largest one was 3.8 cm in size) in the liver (Fig. 1A). On Doppler evaluation, blood flow without obvious shunting was noted within the tumors (Fig. 1B). Non-contrast-enhanced CT scan of the abdomen revealed diffuse, multifocal, homogeneous hypodense lesions of varying sizes in the liver (Fig. 2A); these lesions showed marked enhancement after the injection of contrast medium on arterial phase and remained mildly hyperdense in venous phase (Fig. 2B). Laboratory investigations of liver function later revealed that serum total bilirubin was 4.4 mg/dL (normal: <1.1 mg/dL), alanine aminotransferase 20 IU/L (normal: 5–40 IU/L), aspartate aminotransferase 33 IU/L (normal: 5–34 IU/L), and alpha-fetoprotein (AFP) 2946 ng/mL (normal: 30–5800 ng/mL). The multifocal tumors of vascular origin allowed the diagnosis of IHH to be made without the use of more invasive diagnostic procedures such as liver biopsy or angiography, which was considered unsafe due to a high risk of bleeding. Cardiac echogram showed no high-output congestive heart failure.

The patient was treated with supportive care and discharged in a stable condition without oral medication. The follow-up AFP level was 234 ng/mL (normal: 27–788 ng/mL) at the age of 3 months and 23 ng/mL (normal: 6–59 ng/mL) at the age of 11 months. A series of sonographic follow-up examinations (performed 1 month and 3 months, 6 months, and 9 months later) showed a gradual decrease in the size of the tumor and complete resolution at the age of 11 months (Fig. 3). The patient was completely clinically asymptomatic during follow-up.

Discussion

IHH, accounting for 2–3% of all pediatric neoplasms, is the most common vascular hepatic tumor in children [1]. Eight-five percent of patients are diagnosed within the first 6 months of life, and female-to-male ratio varies from 1.3:1 to 2:1 [1–3]. Previous literature reported that the most common clinical presentations are asymptomatic hepatomegaly and abdominal mass (38–83%), followed by cutaneous hemangioma (11–66%) [1–3]. Congestive heart failure with a high cardiac output was observed in up to 50–60% of patients; however, this feature seems relatively rare (0–30%) in recent studies, especially in oriental children [3–6]. Our patient had a history of 2 days of vomiting prior to admission, which was considered due to overfeeding, excessive air swallowing, or viral acute gastritis and presumed not related to the hepatic tumor. The exact presentation of IHH in our patient was abdominal mass, which was found by a detailed physical examination after admission.

The initial investigation for diagnosis of IHH is sonography, which often shows a single or, more commonly, multiple iso- or hypoechoic masses in the liver. Although the lesion is often homogeneous, it may sometimes be
heterogeneous, making it difficult to differentiate from hepatoblastoma, mesenchymal hamartoma, or metastatic neuroblastoma [7]. However, the AFP level is usually markedly elevated in patients with hepatoblastoma. In IHH, enlarged hepatic artery and proximal aorta with tapering of the diameter of distal aorta below the orifice of the celiac artery, low-resistance flow in the hepatic artery with arteriovenous shunting, and enlarged hepatic vein due to marked blood flow through lesions may be detectable on color Doppler examination; these features cannot be observed in mesenchymal hamartoma [7,8]. Antenatal diagnosis of IHH by sonography during routine pregnancy examination has been reported; however, the prenatal sonography in our patient failed to detect the hepatic tumors, possibly due to their small size. For follow-up examinations, sonography is the first choice because it is simple to perform, is inexpensive, and involves no radiation exposure. CT is a more accurate technique for diagnosing IHH; it demonstrates well-defined solitary or multifocal masses with varying size, which are homogeneously hypodense on nonenhanced image but show intense enhancement after contrast medium injection [8,9]. Some lesions have central cleft-like hypodense areas, indicating tumoral necrosis [10]. In addition, it can definitely exclude the possibility of metastasis from an intra-abdominal neuroblastoma. On magnetic resonance imaging (MRI), IHH lesions are heterogeneously hypointense on T1-weighted image and hyperintense on T2-weighted image, compared to the normal liver parenchyma [11]. Dynamic gadolinium-enhanced MRI shows an early, prominent, and nodular peripheral enhancement, followed by a delayed central enhancement [12]. Angiography should be reserved for patients with equivocal CT findings, or when either surgery or therapeutic tumor embolization is being considered [12].

There is no specific laboratory test for the diagnosis of IHH, but elevated aminotransferase levels were reported in 30–50% of IHH cases [3–6]. AFP, which is usually considered to be an important tumor marker for hepatoblastoma,

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**Fig. 2** (A) Nonenhanced computed tomography (CT) scan shows multifocal homogenous hypodense hepatic masses (black arrows) with varying size. (B) Enhanced CT scan shows marked enhancement of the lesions (black arrows).

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**Fig. 3** Sonography shows a reduction in the size of hemangioendothelioma in the liver. (A) Follow-up sonography performed at 6 months showed that the corresponding hemangioendothelioma has reduced in size spontaneously. (B) Follow-up sonography taken at 9 months showed that the lesion had reduced in size compared to the earlier sonography.
hepatocellular carcinoma, and germ cell tumors, is rarely elevated in IHH [5]. However, an increased AFP level of as high as 80% was reported in the study of Zhang et al [4]. Other hematologic abnormalities, including anemia, thrombocytopenia, thrombocytosis, hyperbilirubinemia, and leukocytosis, may also be present [4,5]. The laboratory evaluation in our patient showed no specific findings except mild elevation of serum bilirubin, which may be due to breast feeding.

The gold standard for diagnosis of IHH is histopathological examination, which reveals small vessels lined by a single layer of plump endothelial cells contained in a myxomatous stroma that includes small bile ducts [2,4]. However, liver biopsies are usually unnecessary to confirm the diagnosis and may result in significant uncontrollable internal bleeding [2–4]. Reviewing the literature, most of the diagnoses of IHH were made by imaging findings, and the tumors were examined histopathologically only when the diagnosis could not be established radiologically [5,6]. In our patient, the diagnosis of IHH was made by clinical magnifications and imaging studies such as sonography and CT.

Treatment of IHH is not needed in asymptomatic cases; they can be followed up clinically and sonographically, without any medication. However, for patients with symptoms such as congestive heart failure, anemia, thrombocytopenia, coagulopathy, and deterioration of hepatic function tests [3,4], treatment with oral corticosteroids, interferon-alpha, or vincristine is recommended as a first-line therapy. Surgical resection is recommended for a solitary huge mass with a low potential for spontaneous regression [3–5]. Embolization has been recently accomplished in many studies of multiple unresectable tumors and used in feeding artery. The use of therapeutic radiation and cyclophosphamide still remains controversial; however, the possibility of long-term sequelae of hepatic irradiation makes radiotherapy an undesirable form of treatment for children [13].

The prognosis of IHH is excellent, except in patients with thrombocytopenia, hemolytic anemia, intravascular consumption coagulopathy, and congestive heart failure, which contribute to the mortality substantially [4]. Pediatricians should be more alert and pay close attention to these complications, and choose the best treatment strategy. Although IHH is a benign tumor, the literature reported that two patients with IHH in infancy developed angiosarcoma 4 years and 5 years later [13]. In addition, a malignant liver tumor occurring several years after diagnosis of IHH with good response to medical treatment has been reported [14]. Therefore, long-term clinical and sonographic follow-ups should be scheduled in patients with IHH, irrespective of whether they are asymptomatic patients or tumor resolution cases. Our patient was asymptomatic; on serial sonographic follow-up, the number of lesions did not increase and regression of the largest lesion was visible after 2 months, with continued shrinkage up to 9 months. Follow-up sonography at the age of 11 months confirmed our clinical impression of resolution of the disease without complication. The patient is now 1.5 years old and still scheduled for long-term sonographic follow-up every 6 months.

IHH is the most common hepatic vascular tumor in infancy. Sonography is a useful and convenient method for diagnosis of IHH, which appears as a hypoechogenic liver mass. Asymptomatic patients can be followed up by serial sonography to visualize the anticipated spontaneous regression. Long-term follow-up is necessary, even if the lesions are in regression, to watch for rare but possible malignant transformation.

References