Clinical Case Report

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Efficacy of infantile hepatic hemangioma with propranolol treatment

A case report

Mu-Chieh Tsai, MD[a], Hsi-Che Liu, MD[b,c], Chun-Yan Yeung, MD, PhD[a,c,d,*]

Abstract

Rationale: Hepatic hemangioma is rarely discovered during the infantile period. Although most of the cases are asymptomatic, some of them may suffer life-threatening situations. In this regard, early detection is mandatory for preventing the ominous consequences that might be culminated from the disease.

Patient concerns: A 2-month-14-day-old female infant was found incidentally to have multiple hepatic lesions during a newborn ultrasound screen. She was born smoothly at term after a non-eventful pregnancy course. Physical examination was completely normal and postnatal vital signs were stable.

Diagnosis: Infantile multiple hepatic hemangiomas.

Intervention: High-resolution ultrasound and abdominal computer tomogram were conducted to confirm the diagnosis. Propranolol was started at the age of 3 months and 7 days old with an initial dosage of 1.5 mg/kg per day and increased gradually to 2.5 mg/kg per day. No obvious adverse effects were noted during the treatment course. Rapid clinical improvement with decreasing size was observed by ultrasound 10 days after the treatment. Eventually, hepatic lesions totally disappeared 4.5 months later. Propranolol in dosage of 2.5 mg/kg per day was continued until 6 months after the initial prescription.

Outcomes: A period of 11-month follow-up revealed no evidence of recurrence of hemangiomas.

Lessons: Early diagnosis and intervention are mandatory for infantile hepatic hemangiomas to prevent possible ominous consequences. Though the propranolol therapy protocol for the disease is still under developing, the current report strengthens the recommendation to use propranolol as the first-line medication for treating infantile hepatic hemangiomas.

Abbreviation: IHs = infantile hepatic hemangiomas.

Keywords: hemangioma, infant, liver, propranolol

1. Introduction

Hepatic hemangioma is a rare disease in infant and early diagnosis is difficult since most of the cases are asymptomatic. However, with the advancement of high-resolution prenatal ultrasound technique and routine postnatal ultrasound check-up in some clinics, the incidence of infantile hepatic hemangiomas (IHs) increases in recent years.[1] Although the treatment protocol for the disease is still under developing, we report a successful treatment experience with propranolol in an infant with multiple hepatic hemangiomas.[2] We also review the most updated literature in the management of infantile hemangioma in this report.

2. Case report

A 2-month-14-day-old girl was referred to the outpatient department because of suspected hepatic hemangiomas disclosed by abdominal ultrasonography during newborn screening at a local clinic. The naturally conceived girl was delivered by a 36-year-old woman (gravida 2, para 1) after a non-eventful 40-week gestation, Apgar score - 9/9 with appropriate birth size. Prenatal examinations including array comparative genomic hybridization analysis of amniotic fluid and level II ultrasound performed at the fifth month of gestation were normal. Family history was non-contributory except that her great-grandfather died of hepatoma. On the visit, the vital signs and growth curve were normal and physical examination showed no abnormalities including any palpable masses, cutaneous lesions, signs of bleeding tendency, or heart failure. The results of complete blood count and biochemistry tests were unremarkable. There was no elevated alpha-fetoprotein level, impaired liver function, disseminated intravascular coagulation, or Kasabach–Merritt phenomenon. Abdominal ultrasound revealed more than 8 heterogeneous, hyperechoic, and hypervascular nodular to

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[a] Division of Gastroenterology and Hepatology, Department of Pediatrics, MacKay Children's Hospital, [b] Division of Hematology and Oncology, Department of Pediatrics, MacKay Children's Hospital, Taipei, [c] Department of Medicine, MacKay Medical College, New Taipei City, [d] Institute of Biotechnology and Department of Chemical Engineering, National Taipei University of Technology, Taipei, Taiwan.

[*] Correspondence: Chun-Yan Yeung, Division of Gastroenterology and Hepatology, Department of Pediatrics, MacKay Children's Hospital, MacKay Medical College, No. 92, Sec. 2, Zhongshan N. Rd., Taipei 10449, Taiwan (e-mail: cyyeung@mmh.org.tw).

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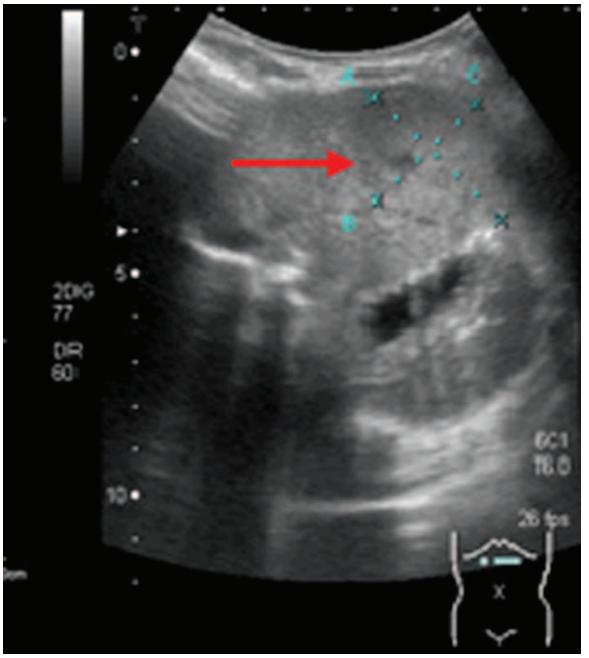

Figure 1. An abdominal ultrasound examination showed multiple hepatic heterogeneous mass lesions, with the largest one in size of 40.6*32.1 mm (arrow).

mass-like hepatic lesions with the largest one over left lobe (Fig. 1). Multifocal hepatic hemangiomas were highly suspected. Although without biopsy, a computed tomographic (CT) scan confirmed the diagnosis. Precontrast phase of CT scan showed 8 well demarcated and hypodense space-occupying hepatic lesions which were separated by normal intervening liver parenchyma. The largest one was 25*40 mm at left lobe of the liver (Fig. 2). After intravenous injection of contrast medium (arterial phase) (Fig. 3), the lesions were dominantly enhanced. All lesions showed progressively increased areas of contrast enhancement with a centripetal pattern in portal venous phase (Fig. 4). In delayed phase (Fig. 5), the majority of the lesions became homogeneous enhancement while the largest lesion demonstrated incomplete enhancement, probably related to necrosis or fibrosis.

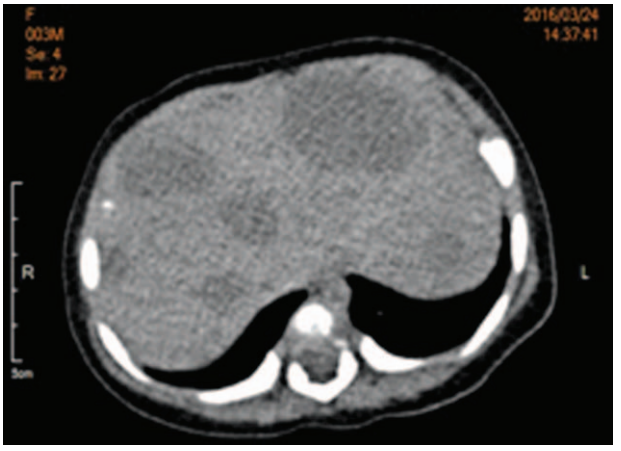

Figure 2. The precontrast CT scan illustrates nodules and masses of low attenuation in the liver, with the largest one in size of 25*40 mm at the left lobe. CT = computed tomographic.

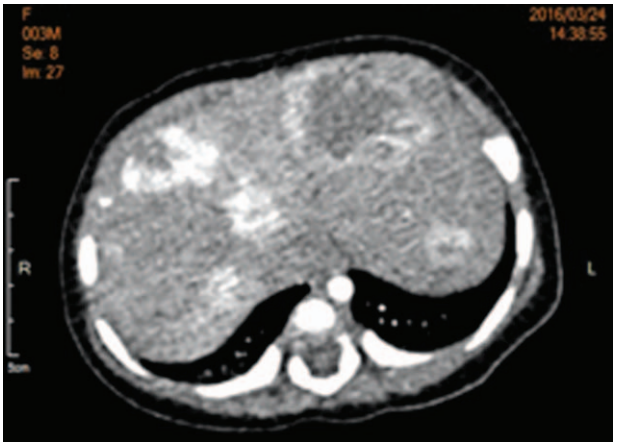

Figure 3. The arterial phase CT scan reveals enhancement of the lesions within the liver. CT = computed tomographic.

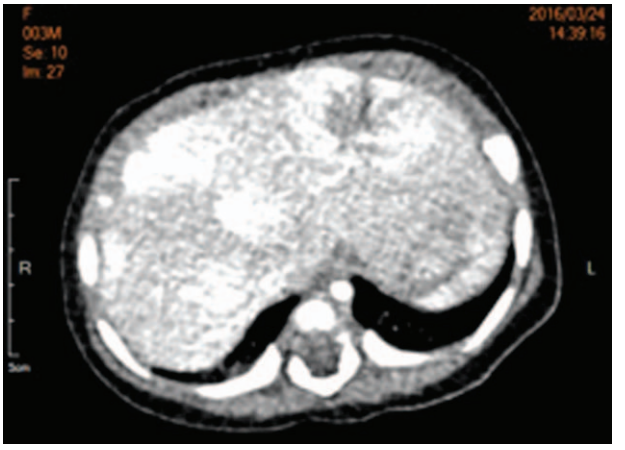

Figure 4. In portal venous phase of CT scan, all lesions showed progressively increased areas of contrast enhancement with centripetal pattern. CT = computed tomographic.

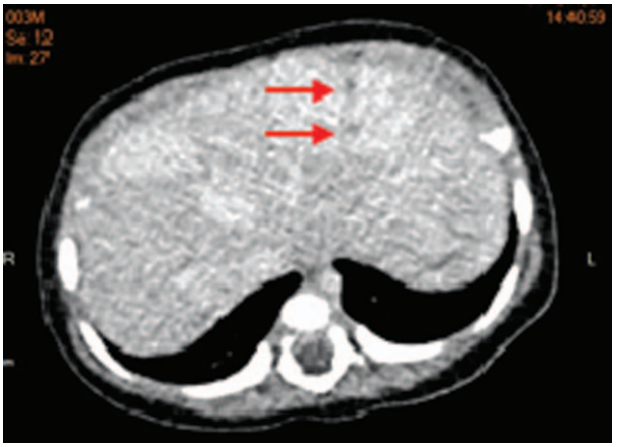

Figure 5. In delayed phase of CT scan, majority of the lesions became homogeneous enhancement while the largest lesion manifested incomplete enhancement, probably related to necrosis or fibrosis (arrows). CT = computed tomographic.

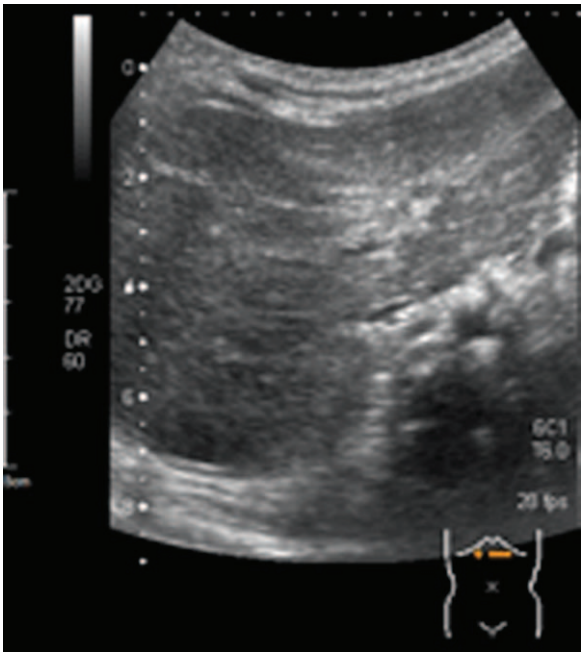

Figure 6. No lesions were detected under abdominal ultrasound after a 4.5-month treatment course of propranolol.

We started prescription of oral-form propranolol for the patient at the age of 3 months and 7 days at an initial dose of 1.5 mg/kg/day with subsequent dose increment by 0.5 mg/kg/day every week and finally 2.5 mg/kg/day. No obvious adverse effects were noted during the treatment course. Rapid clinical improvement with decreasing size was achieved and observed by ultrasound 10 days after the initiation of propranolol treatment. Hepatic lesions decreased in size gradually. After a total of 4.5-month treatment, no more hepatic lesions could be detected by abdominal ultrasound (Fig. 6).

Propranolol was continued for another 1.5 months after the total involution of the lesions. Under follow-up abdominal ultrasound for 11 months, no evidence of recurrence was noted and the child's developmental milestones were normal.

3. Discussion

Although most of the cases with IHs were asymptomatic, some of them may culminate in lethal clinical situations. It is thus important to have early diagnosis and intervention of the rare disorder. With the advancement of high-resolution prenatal ultrasound technique and routine postnatal ultrasound check-up in some clinics, the incidence of IHs increases in recent years. The incidence was higher in preterm infants, especially with low birth weight. Prenatal associations including older maternal age, placenta previa, and preeclampsia may all increase the risk of developing IHs.[3] The lesions characteristically undergo a proliferative phase for 1 year and then an involution phase lasting for a variable period of time.[4] The severity of hepatic hemangiomas ranges from asymptomatic to life-threatening, with clinical manifestations including anemia, thrombocytopenia, hepatomegaly with abdominal compartment syndrome, high-output congestive heart failure, respiratory distress, hepatic failure, jaundice, or hypothyroidism.[5,6] Hepatic hemangioma comprises 3 major categories: focal, multifocal, and diffuse. Multifocal hepatic hemangiomas commonly occur in the presence of multiple (≥5) skin hemangiomas and are probably asymptomatic. Some huge, with tumor size >60 mm, or diffuse hepatic hemangiomas are seen in neonates and infants are potentially fatal.[6] Early diagnosis with a screening abdominal ultrasound examination significantly reduced complication and mortality of IHs. It is thus recommended for patients younger than 6 months old with multiple (≥5) cutaneous hemangiomas and those who have hepatomegaly or congestive heart failure to receive abdominal ultrasound examination.[7] CT or magnetic resonance imaging scan may be helpful in characterizing the hepatic lesions and biopsy is only indicated for atypical lesions.[5]

To treat infantile hemangiomas, intervention may be required since the proliferative phase for complicated lesions may interfere with a vital structure or function. These include very large and rapidly growing cutaneous hemangiomas, lesions in the periorbital region, airway, liver, or gastrointestinal tract. Lesions associated with local complications (hemorrhage, ulceration, necrosis, increased risk of scarring, or disfigurement) are also indications of treatment.[8] Variable treatment options were mentioned for IHs included pharmacological therapy (steroidal hormones, interferon α-2a, vincristine, propranolol, or other beta blockers), surgical resection, embolization/ligation of the hepatic artery and liver transplantation.[6,9] Pharmacological therapy has been known as a primary therapy for infantile hemangiomas and propranolol is the first-line agent.[2] In a meta-analysis of 324 patients with infantile hemangiomas and 248 controls, propranolol was superior to other treatments in higher efficacy in tumor regression, lower risk of side effects and faster clinical improvement, sometimes as early as 24 hours, which may be evident in the majority of patients within the first week of treatment. In the subgroup analysis by site of tumor, propranolol therapy was also more effective when compared with other treatments. When the analyses were restricted to randomized controlled trials, propranolol therapy was more effective than steroid in treating infantile hemangiomas in subgroup analyses.[10] The issues of optimal dosage and treatment duration of propranolol for infantile hemangiomas remain open. Balancing considerations of safety, efficacy, and convenience, the expert council in Chicago in 2011 suggested to start treatment for infantile hemangiomas with oral propranolol at 1 mg/kg per day with divided doses, with the minimal interval of 6 hours. If tolerated, the dose may then be gradually increased over 1 to 2 weeks to the target dose of 1 to 3 mg/kg per day, with a median dose of 2 mg/kg per day, given with divided doses in the minimal interval of 6 hours. In the case of intercurrent illness, treatment should be temporarily held and then resumed.[2] Some experts continue therapy until the child reaches around 1 year of age, in which the spontaneous involution phase would normally begin.[11] Serious adverse effects of propranolol therapy including hypotension, bradycardia, hyperkalemia, bronchospasm, and hypoglycemia are infrequent. Restless sleep, constipation, diarrhea, or cold extremities are more commonly reported.[12] Due to the effect of oral propranolol peaks at 1 to 3 hours after administration, an expert consensus recommended to monitor the heart rate and blood pressure at 1 and 2 hours after the initial dose and after every dose increase of 0.5 mg/kg/day.[2]

In the current case, it was unique that multiple hepatic hemangiomas presented without multiple cutaneous lesions. Propranolol was effective for the lesions of our case under the strategy with the treatment course over the age of 6 months old and 1.5 months after the complete involution of the lesions. The patient has provided informed consent for publication of the case. Though the propranolol therapy protocol for IHs is still under

developing, the current report strengthens the recommendation to use propranolol as the first-line treatment agent for the disease entity.

Author contributions

Supervision: Chun-Yan Yeung, Hsi-Che Liu.
Writing – original draft: Mu-Chieh Tsai.
Writing – review and editing: Mu-Chieh Tsai.

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