Infantile hepatic hemangioendothelioma successfully treated by low dose of propranolol

Hémangioendothéliome hépatique traité efficacement par des faibles doses de propranolol

Introduction
Infantile hepatic hemangioendothelioma (IHH) is a benign vascular tumor that presents most commonly in infants under 6 months of age [1]. It may undergo spontaneous regression but can sometimes be life-threatening due to liver dysfunction, congestive cardiac failure and/or consumptive thrombocytopenia and coagulopathy. The treatment strategy for IHH has not yet been established. The efficacy of propranolol, a beta-blocker, has been emphasized in recent publications. We report a five-month-old girl that presented with abdominal distension and hepatomegaly caused by multiple hepatic hemangiomas (hepatic hemangioendothelioma) that have been well controlled with propranolol as monotherapy.

Case presentation
A five-month-old girl was referred for hepatomegaly, which was incidentally found. Physical examination revealed cutaneous hemangiomata, present over the nape of the neck and hepatomegaly; the liver was enlarged at 5 cm below the right costal margin. Physical examination was otherwise unremarkable. Laboratory investigation showed normal liver function tests. Her hematological profile was unremarkable. Thyroid-function tests were normal. Alpha fetoprotein (AFP) serum level was elevated (184.2 ng/ml). The ultrasound examination revealed multiple hypoechogenic liver lesions coexisting with an enlarged liver. Abdominal computed tomography showed features suggestive of hemangioendothelioma of the liver (figure 1). The patient was examined by magnetic resonance imaging (MRI) for further evaluation and characterization of hepatic lesions. MRI revealed multiples liver masses scattered throughout the liver parenchyma which showed hypointense signal intensity on T1 weighted images and very high signal intensity on T-2 weighted images in comparison to the liver (figure 2). The echocardiography was normal. The patient was diagnosed as having infantile hepatic hemangioendothelioma. She was treated by propranolol. The starter dose was 0.5 mg/kg per day orally with further increase to 1.5 mg/kg per day. This dose was maintained for 12 months and tapered progressively. After a follow-up of 12 months, the hepatomegaly regressed totally. A repeat CT scan scheduled at the end of treatment showed a clear regression of the previously described masses (figure 3). The patient's growth and psychomotor development were normal.

Discussion
Hepatic hemangioendothelioma is the third most common hepatic tumor in children (12% of all childhood hepatic tumors) [1], the most common benign vascular tumor of the liver in infancy, and the most common symptomatic liver tumor during the first 6 months of life [1,2]. Most tumors continue to grow during the 1st year of life and then spontaneously regress, probably due to thrombosis and scar formation [2]. In most of the cases, IHH remains asymptomatic and detected in ultrasound of abdomen by chance. Some hemangiomas are discovered on routine prenatal imaging [3]. But, sometimes, it can cause severe symptoms such as abdominal distension, gross hepatomegaly as was seen in our case, severe arteriovenous shunting with congestive cardiac failure [2,4], fulminating hepatic failure, anemia, thrombocytopenia (Kasabach-Merritt syndrome), consumptive coagulopathy and intra-abdominal hemorrhage. Other symptoms rarely, biliary obstruction with jaundice, vomiting, and gastric outlet obstruction has been reported [5].

Radiological evaluation is useful for patient diagnosis, with Doppler sonography often being the initial diagnostic modality. Sonography shows solitary or multiple lesions, discrete or diffuse, with variable texture ranging from hypoechogenic to isoechogenic or strongly echogenic pattern [6]. Occasionally, the lesions may show streaky or even anechoic channels with calcification. At unenhanced MR imaging, the lesions have low signal intensity on T1 weighted images and high signal intensity on T2 weighted images [6]. Serum AFP should be done in all cases, AFP levels may be high in case of IHH but they are never as high as seen in hepatoblastoma [2].

The treatment of IHH remains controversial. Although children with asymptomatic lesions may experience spontaneous regression within a year, symptomatic lesions require aggressive management to avoid fatal complications. A variety of therapeutic options, including medical, surgical resection and interventional modalities, have been suggested. Systemic corticosteroids have become the mainstay in the treatment of hepatic hemangioendotheliomas. Daily doses of 2–3 mg/kg of prednisolone are usually given and some
investigations have recommended higher doses like 5 mg/kg/day [2]. Of patients treated with steroids alone, 30% will achieve resolution of the lesion [2]. Moreover, side effects of high doses of corticosteroids often limit their use in infants. Once medical therapy has failed, invasive measures like hepatic artery ligation, embolization or liver transplantation may be tried with rapid onset of severe symptoms [1,7].

Propranolol is a nonselective beta-blocker, which has recently been introduced as a novel modality for the treatment of...
proliferating hemangiomas. The use of propranolol for the treatment of severe cutaneous hemangiomas was initially described by Léauté-Labréze et al. in 2008 [8]. The use of propranolol for the treatment of IHH has recently been validated in several series and case reports [9,10]; in all these published cases, propranolol was effective and very well tolerated, the adequate dose varied from 2 to 3.5 mg/kg/day [10].

Conclusion
Our experience with this case emphasizes that propranolol may be tried in treating patients with IHH as a first line treatment.

Consent
Written informed consent was obtained from the parents of the child for publication of this case report and any accompanying images

Disclosure of interest: the authors declare that they have no competing interest.

Acknowledgements: none.

References

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Received 7 October 2016
Accepted 24 January 2017
Available online:
http://dx.doi.org/10.1016/j.lpm.2017.01.010
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