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Case Report

CASE REPORT

Diffuse infantile hepatic haemangioma—how to manage an incidental but potentially lethal finding

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Abstract

Infantile hepatic haemangioma (IHH) is a rare vascular tumour that is potentially lethal due to its associated complications, including heart failure, hepatic failure, hypothyroidism and abdominal compartment syndrome. The authors report a case of an asymptomatic diffuse IHH in a newborn male, which was presented as an incidental finding at the time that the patient was diagnosed with pyloric stenosis. The patient was treated with increasing doses of propranolol that were well tolerated. With the regression of the IHH by the time that the patient reached one year of age, there was a significant imagiologic improvement. Because there is no consensus on the optimal approach for the treatment of liver tumours in newborns, it is important to adopt a systematic approach. After the diagnosis of diffuse IHH has been established, the decision to initiate treatment and the therapeutic of choice is often controversial. Regular follow-up is recommended to monitor possible complications.

INTRODUCTION

The incidental finding of a liver tumour in a newborn requires careful investigation and the exclusion of malignancy. Amongst other diagnoses, infantile hepatic haemangioma (IHH) should be included as a possible differential diagnosis. IHH is a rare vascular tumour, which despite its benign histology, can be aggressive and potentially lethal [1]. IHH can be classified by the following three types of lesions: focal, diffuse and multifocal [1]. Each lesion type has distinct characteristics that refer to their prognosis, radiologic features, clinical presentation and physiologic behaviour [1].

IHH can be asymptomatic, presenting as an incidental imaging finding, or it can manifest as a complication (e.g. heart failure, hepatic failure, hypothyroidism or abdominal compartment syndrome) [1–3]. While the treatment options for IHH are controversial, they can include surgery, propranolol chemotherapy, corticosteroids and other immunomodulators. The authors of the current report discuss a case where a diffuse IHH was incidentally found in a newborn male. The case's therapeutic approach and follow-up management strategy are also reviewed.

CASE REPORT

On the 24th day of his life, a term newborn male was presented to the emergency department with non-bilious projectile vomiting

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for 48 h. He was born full term via vaginal delivery following a non-complicated pregnancy and normal prenatal sonograms. The newborn's birth weight, birth length and head circumference were 3050 g, 47 cm and 35.5 cm, respectively. Physical examination of the newborn proved to be unremarkable, with no indications of skin lesions or palpable visceral enlargement.

The diagnosis of pyloric stenosis (PS) was established with an abdominal ultrasound that revealed pyloric muscle thickness (4 mm) and pyloric canal length (25 mm) that were above the normal limits. In addition to the PS, the ultrasound revealed hepatomegaly with a heterogeneous structure due to multiple hypoechoic nodules that presented in both liver lobes (Fig. 1a and b). The differential diagnosis included diffuse IHH, hepatoblastoma and an unknown metastasized primary tumour. Blood tests were within the normal range, excluding complications or malignant aetiology. These included blood count, electrolytes, alpha fetoprotein, vanillylmandelic acid, neuron specific enolase and liver and thyroid function tests. The imagological study was complemented by abdominal magnetic resonance. The craniocaudal dimension of the liver was 78.5 mm, and the abdominal magnetic resonance confirmed countless nodules in both hepatic lobes. Characteristic of diffuse IHH, these findings included hyperintense lesions with prominent flow void on T2 imaging and hypointense lesions on T1 imaging (Fig. 2a and b). An echocardiogram that was performed to exclude complications revealed no alterations.

The PS was treated with pyloromyotomy, which proved to be uneventful. After stabilization, the patient's treatment for IHH was initiated with propranolol. Doses of propranolol started at 1 mg/kg/day and increased to 3 mg/kg/day. Treatment was well tolerated, and the patient was discharged on the ninth day of treatment. No adverse effects were registered upon initiation or during the course of treatment. After 3 weeks of treatment, an abdominal ultrasound showed numeric and volumetric regression of the hepatic nodules and reduced heterogeneous hepatic structure. In addition, a Doppler ultrasound showed decreased blood flow. During the initial ultrasound, the largest nodules measured in at 14 mm. At the third and eighth weeks, the largest nodules measured in at 10 and 6 mm, respectively. When the patient reached 15 months of age, a follow-up ultrasound revealed a single hepatic nodule that measured in at 6 mm. At this time, the patient was still being treated with propranolol (1.8 mg/kg/day).

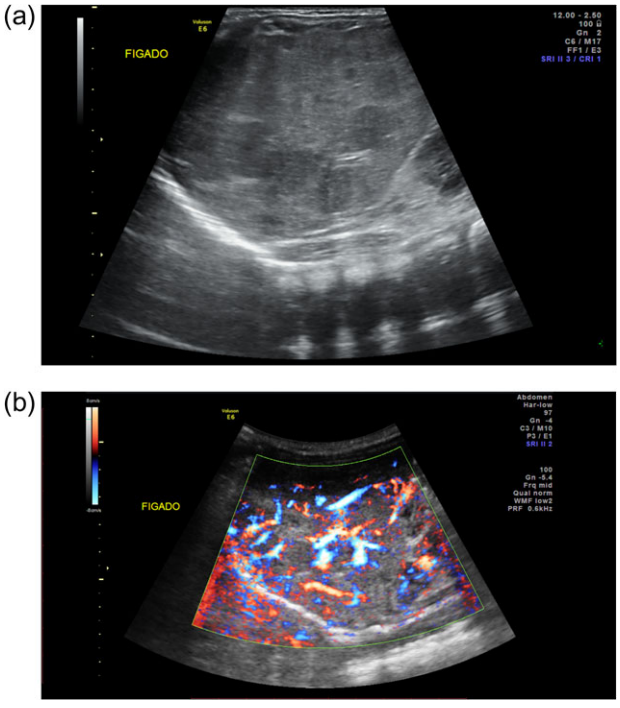

Figure 1: Abdominal ultrasound revealing heterogeneous hepatic structure due to countless hypoechoic nodules (**a**) with diffuse hypervascularization areas in Doppler ultrasound (**b**)

DISCUSSION

Currently, there is controversy about how IHH should be managed. There have been a few small case series and some isolated case reports about IHH but no consensual published guidelines. Treatment approaches must be decided according to each individual, considering each patient's condition and the number, location and dimensions of their lesions [1, 4]. Christison-Lagay *et al.* proposed a treatment algorithm that considers a conservative approach in patients with asymptomatic focal or multifocal lesions through regular follow-up and ultrasonography. With this algorithm, a complete regression typically occurs within 2 years of age [1, 4–7]. Since the progression of these lesions can lead to fatal complications shortly after the onset of symptoms, pharmacologic or surgical treatment is recommended for diffuse or symptomatic IHH [1]. Complications of IHH include hepatic failure, massive hepatomegaly that causes abdominal compartment syndrome, congestive heart failure

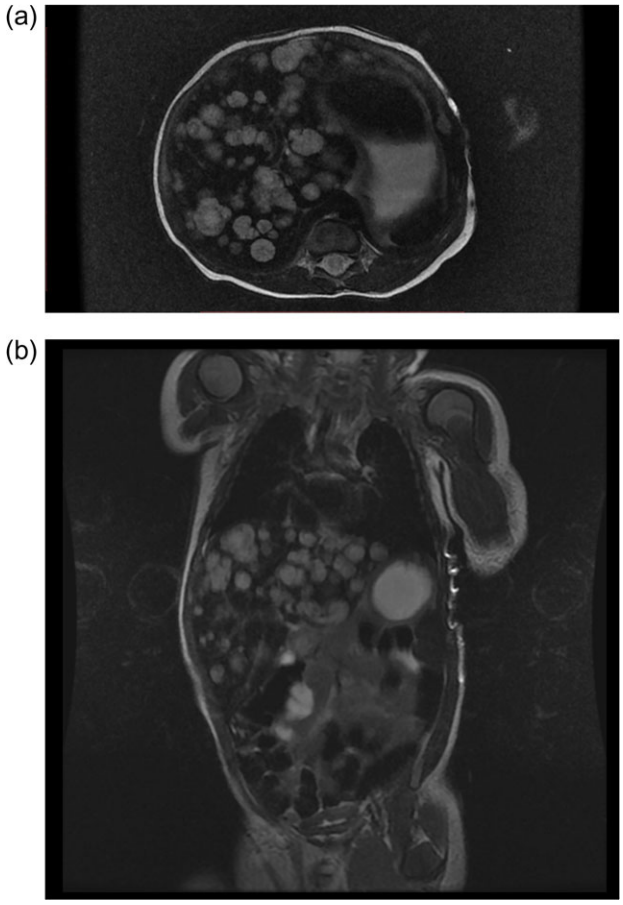

Figure 2: Abdominal magnetic resonance revealing countless nodules in all hepatic lobes, hyperintense on T2 imaging (**a**—axial plane; **b**—coronal plane)

due to shunting and/or severe hypothyroidism and hypothyroidism caused by the overproduction of type III iodothyronine deiodinase [1–3]. Diffuse IHH patients are at a high risk for mortality and complications [2, 8]. Kulungowski *et al.* [2] reported a higher prevalence of heart failure and hypothyroidism in patients with diffuse IHH than in patients with focal and multifocal IHH .

Traditionally, steroids, chemotherapy, radiotherapy and alpha interferon have been used to pharmacologically treat IHH [1, 4, 5]. These treatment options have presented serious and well-known side effects and variable rates of success. Refractory cases may require surgical management or even a combined approach of medical and surgical therapy [1, 10]. Due to the higher risk of complications and death, diffuse IHH patients may also require hepatic transplantation [1].

Propranolol is a beta blocker that has commonly been used to treat paediatric patients with cardiac disease, and since 2008, cutaneous infantile haemangiomas [7]. The safety, efficacy and success rate of propranolol in cutaneous infantile haemangiomas has made it the first line of treatment for this condition [11]. In more recent publications, propranolol has been reported to be successful in the treatment of non-cutaneous haemangiomas, producing no significant adverse effects under the prescribed doses [9, 12]. While propranolol's mechanism of action is partially unknown, its benefits can include vasoconstriction, apoptosis of the capillary endothelial cells and decreased expression of the vascular endothelial growth factor and fibroblast growth factor [9, 12]. Since treatment with steroids can increase the activity of propranolol, some authors have also suggested an association between propranolol and prednisone during therapy for diffuse IHH [13, 14].

The approach to this case included a multidisciplinary discussion with the participation of radiologists, neonatologists and paediatric surgeons. Upon consideration of the diffuse nature of IHH, with countless lesions, extensive hepatic involvement and the associated high risk for complications in this setting, it was decided that the patient should be treated with propranolol. The propranolol was well tolerated. Doses started at 1 mg/kg/day and were titrated to a target dose of 3 mg/kg/day [9, 11]. Ultrasound re-evaluations at 1, 2, 4, 6 and 12 months of age sufficiently documented the regression of the hepatic lesions. In summary, the authors found this strategy to be safe and successful.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

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ETHICAL APPROVAL

No approval is required.

CONSENT

As Corresponding Author, I certify that patient permission was obtained for the use of potentially identifiable photograph(s) or other health information contained in my submission and that the patient is aware of the context of such use. I understand that it is my responsibility to have secured this permission and maintain the security of such personal health information.

GUARANTOR

Alexandra Rodrigues.

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