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CASE REPORT

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Infantile hepatic hemangioendothelioma associated with pulmonary arterial hypertension and cardiac insufficiency successfully treated with oral propranolol—a rare case report

Debashree Priyadarshini*, Goolla Akhila, Rachita Sarangi and Anuspandana Mahapatra

Abstract

Background Infantile hepatic hemangioendothelioma (IHHE) is a benign liver tumor associated with a varied spectrum of presentations ranging from asymptomatic hepatomegaly and cutaneous hemangiomas to some life-threatening complications like cardiac failure, consumptive hypothyroidism, pulmonary arterial hypertension, gastrointestinal bleeding, and coagulopathy. Hypothyroidism results from increased activity of type 3 iodothyronine deiodinase in the liver. Clinico-radiological correlation is essential for a definite diagnosis. Although children with asymptomatic lesions may experience spontaneous regression within a year, those with symptomatic lesions require aggressive management due to the risk of mortality once the symptoms commence. Treatment modalities can be either pharmacologic or interventional depending on the clinical presentation, with propranolol being considered the first-line agent.

Case presentation Here, we describe a 2-month-old female infant with progressive abdominal distension, signs of congestive cardiac failure, and pulmonary arterial hypertension, confirmed as IHHE by abdominal ultrasonography and contrast-enhanced MRI. It was complicated by consumptive hypothyroidism and coagulopathy. The child was successfully treated with oral propranolol, levothyroxine, and supportive measures.

Conclusion Early aggressive treatment in a symptomatic patient is linked to successful outcomes. Hypothyroidism should be focused on and managed earlier to prevent intellectual and growth retardation.

Keywords Infantile, Hepatic, Hemangioendothelioma, Consumptive hypothyroidism, Pulmonary arterial hypertension, Propranolol

*Correspondence:
Debashree Priyadarshini
drdebashreedas@gmail.com
Full list of author information is available at the end of the article

Background

Infantile hepatic hemangioendothelioma (IHHE) is the most common type of benign hepatic vascular tumor accounting for about 1 in 20,000 live births [1]. The ratio of male to female is 1:1.3 to 2 with female predominance [2]. Hemangioendotheliomas have various presentations, from asymptomatic hepatomegaly to some life-threatening complications. Although the majority of clinicians concur that treatment is not indicated for several minor hepatic hemangiomas in asymptomatic individuals, there are currently no established methods for treating IHHE. Very few cases of IHHE have been reported so far; hence, very little is known about the treatment of life-threatening complications. Here, we report a case of an infant girl who presented with heart failure, pulmonary arterial hypertension, consumptive hypothyroidism, and coagulopathy with a good response to oral propranolol therapy.

Case presentation

A 2-month-old girl born out of nonconsanguineous marriage with an uneventful neonatal period presented with progressive abdominal distension for 10 days and breathing difficulty for 3 days. There was no vomiting, jaundice, pale-colored stool, or any bleeding manifestation. On examination, there were coarse facies, wide-open anterior fontanelle, pallor, bilateral pitting pedal edema, a hugely distended abdomen with engorged veins, and severe respiratory distress (Fig. 1a). Her respiratory rate was 78 per minute, and heart rate was 156 beats per minute, with an oxygen saturation of 88% at room air. Systemic examination revealed a systolic murmur of grade 3/6 and massive hepatomegaly measuring 8 cm below the right costal margin with a span of 12 cm. Investigations revealed hemoglobin of 7.7 g/dl, a total leucocyte count of 6860/cumm, and a platelet count of 1.98 lakhs. Total/direct bilirubin was 5.74/3 mg/dl, serum albumin was 2.4 g/dl, SGOT/SGPT/ALP was 106/28/179 IU/L, PT/INR was 21 s/1.89, and APTT was 53 s. Renal function test, serum electrolytes, blood sugar, fasting lipid profile, LDH, CPK, serum uric acid, and AFP were normal. Serum TSH was > 100 mIU/l (normal: 0.58–5.57mIU/l). Ultrasound of the abdomen with Doppler showed a grossly enlarged liver, diffusely coarse parenchymal echotexture with near complete replacement of hepatic parenchyma by multiple islands of hypoechoic nodules separated by echogenic septations with increased lesional vascularity, and congested hepatic vasculature along with hypertrophic hepatic artery and celiac trunk suggestive of infantile hepatic hemangioendothelioma (Fig. 1b). Chest x-ray showed cardiomegaly and pulmonary venous

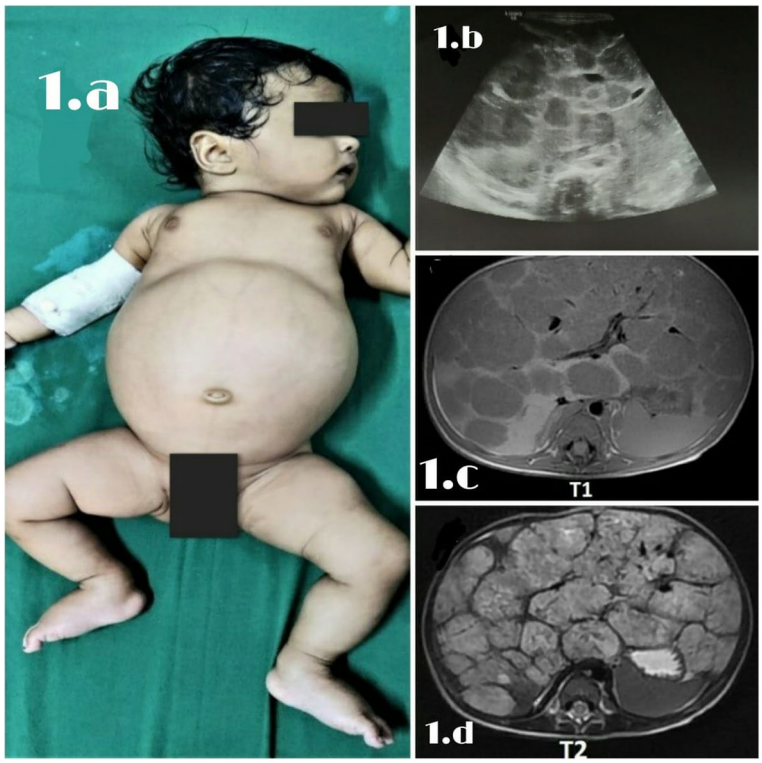

Fig. 1 **a** Clinical image of the index case before treatment. **b** Ultrasound abdomen image of index case before treatment. **c** T1W CE MRI image showing nodular hepatic lesions. **d** T2W CE MRI image showing hyperintense nodular hepatic lesions

congestion. Echocardiography suggested moderate pulmonary arterial hypertension (PAH) with a gradient of 44 mmHg, mild mitral regurgitation, and moderate tricuspid regurgitation with mildly dilated four chambers and normal LV function. Contrast-enhanced MRI of the abdomen confirmed our diagnosis showing multiple well-marginated variable size T2W hyperintense lesion studded in both lobes with progressive centripetal enhancement on the triphasic study, the largest discrete lesion measuring 37 × 31 mm in segment VIII (Fig. 1c, d). Ophthalmic examination and USG neck were normal.

Based on the above findings, the patient was diagnosed with IHHE complicated with PAH, heart failure, consumptive hypothyroidism, anemia, and coagulopathy. The child was started on 10 mcg/kg/day of L-thyroxine and 1 mg/kg/day of propranolol, with subsequent titration of the doses depending on the level of TSH. Doses were titrated as high as 20 mcg/kg/day of L-thyroxine as TSH was persistently more than 100 mIU/l and 1.5 mg/kg/day of propranolol due to slower regression in the size of hepatic lesions. High-output cardiac failure was managed with fluid restriction, oxygen support, diuretics, and packed red blood cell transfusion.

The baby survived the crisis phase. After 8 months of regular follow-up, there has been a significant improvement in her growth, development, clinical and cardiac status, and laboratory profile. Serum TSH has come down to 4.96 mIU/mL. Ultrasound of the abdomen also showed significant improvement with a reduction in the size of the liver as well as the parenchymal lesions, the largest lesion measuring 1.7 × 1.2 cm along with a reduction in the caliber of the hepatic artery (Fig. 2a). The child is currently taking 10 mcg/kg/day of L-thyroxine and 1 mg/kg/day of propranolol.

Discussion

IHHE is the most common vascular tumor of the liver in children accounting for 12% of all childhood hepatic tumors [3] and 1–4% of all pediatric solid tumors [4]. IHHE affects 85% of babies in the first 6 months of life [2]. IHHE is classified into diffuse, focal, and multifocal [4]. It is often associated with vascular malformations at various other sites like the brain, skin, lungs, bone, kidney, and digestive tract. The most common presenting complaints include asymptomatic hepatomegaly and abdominal mass (50%), cutaneous hemangioma (10–40%), hemolytic anemia, thrombocytopenia, and peritoneal bleeding [5]. Conditions like disseminated intravascular coagulation and Kasabach-Merritt phenomenon can result from consumptive thrombocytopenia. They can also present with a severe and uncommon form of hypothyroidism, i.e., consumptive hypothyroidism due to increased activity of type 3 iodothyronine deiodinase enzyme [6]. Complications like high output heart failure and pulmonary arterial hypertension are seen in 50–60% of cases [4] which can result from rapid arteriovenous shunting within the lesions and dilatation of hepatic arteries with recirculation of blood back to the right heart. Sonography, CT, and MRI are the common diagnostic modalities for this condition [2]. The factors like symptomatic mass, congestive cardiac failure, multiple tumor nodules, and absence of cavernous differentiation are associated with a bad

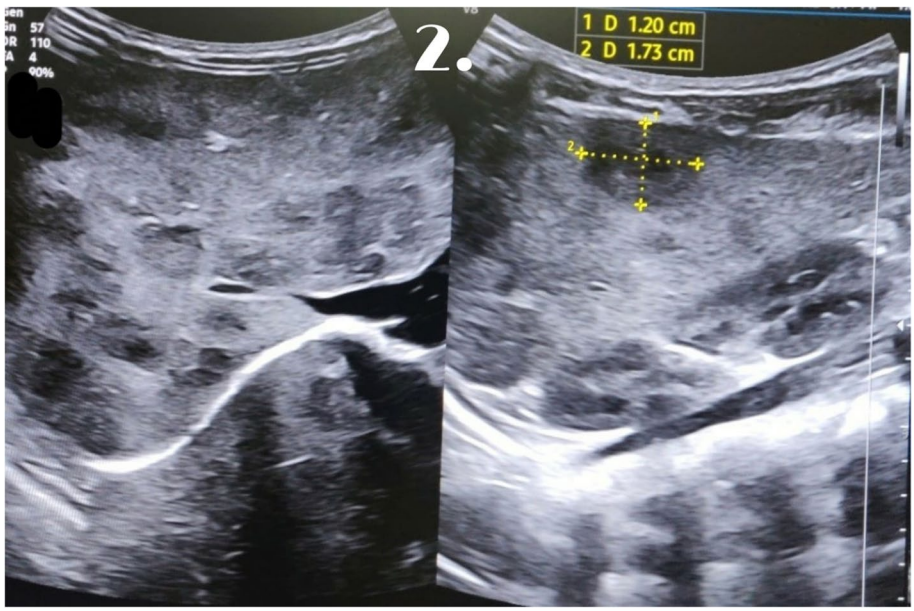

Fig. 2 Ultrasound abdomen image of index case after treatment

prognosis. IHHE grows during the first year of life and then regresses spontaneously with scar formation. Indications of treatment are cardiorespiratory compromise, coagulopathy, abdominal compartment syndrome, and worsening liver function.

Modalities of treatment can be either pharmacologic (propranolol, sirolimus, corticosteroids, interferon-alpha, vincristine) to accelerate the natural regression of lesions or interventional (hepatic artery ligation, embolization, resectional surgery, or liver transplantation). Propranolol is considered the first-line pharmacological agent. According to Tsai et al., propranolol outperformed other treatments in terms of safety, tumor regression efficacy, and clinical improvement [4]. R. Tian et al. found that oral propranolol provided satisfactory results in 85% of cases with the longest treatment lasting 22 months and the shortest only 4 months. The initial treatment for IHHE, according to Maalouland colleagues, was low-dose propranolol at 0.5 mg/kg/day, subsequently increased to 1.5 mg/kg/day and maintained for 12 months. Propranolol's ability to promote cardiac health is likely a result of reduced hepatic blood flow, which is caused by a reduction in the diameter of the arteries. Hypothyroidism may resolve as a result of tumor regression and type 3 iodothyronine deiodinase suppression [7]. Transarterial embolization is an effective treatment for critically sick children when IHHE is complicated with AV malformations and high-output congestive heart failure, especially when there is a failure of first-line treatment. It helps by reducing the shunting of hemangiomas. However, it is associated with hazardous complications in a sick infant and needs a lot of technical expertise [8]. Surgical resection is recommended for huge masses with a low propensity for spontaneous regression.

Our patient presented with high-output cardiac failure and PAH with anemia, coagulopathy, and hypothyroidism. The child was managed with thyroxine supplementation, oral propranolol, and supportive measures for heart failure and coagulopathy. Though an early aggressive treatment in symptomatic IHHE is pivotal and propranolol and/or transcatheter arterial embolization seems promising, especially in cases of IHHE with life-threatening complications, we observed a tremendous improvement with oral propranolol therapy. Serial follow-up of the clinical condition, USG abdomen, and 2D ECHO was done which showed significant improvement in symptoms and cardiac status as well as regression of hepatic lesions.

Conclusion

IHHE is usually asymptomatic and associated with spontaneous regression. However, some cases can present with fatal complications. The leading cause of death is cardiac insufficiency and consumptive coagulopathy. Early aggressive treatment in a symptomatic patient is associated with a favorable outcome. Early diagnosis during pregnancy is particularly crucial, and immediate postpartum care produces excellent results.

Abbreviations

SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic-pyruvic transaminase
ALP	Alkaline phosphatase
PT/INR	Prothrombin time/international normalized ratio
APTT	Activated partial thromboplastin clotting time
AFP	Alpha-fetoprotein
LDH	Lactate dehydrogenase
CPK	Creatine phosphokinase
MRI	Magnetic resonance imaging
TSH	Thyroid stimulating hormone
FT3	Free triiodothyronine
FT4	Free thyroxine

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Authors' contributions
The conceptualization and design of the study were done by RS and AM. Literature search, material preparation, data collection, and analysis were performed by DP and GA. The final draft of the manuscript was written by GA and DP. Critical review and final approval were done by RS and AM. All authors have approved the final version of the manuscript.

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Availability of data and materials
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Declarations

Ethics approval and consent to participate
Not applicable as confirmed by our institute.

Consent for publication
Written informed consent has been taken from the legal guardian of the index case for publication of anonymized patient details.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Paediatrics, IMS & Sum Hospital, Bhubaneswar, Odisha, India.

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