

Multiple infantile hepatic hemangiomas leading to consumptive hypothyroidism successfully treated with propranolol: A case report

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ABSTRACT

Hepatic hemangioma is a commonly encountered benign vascular tumour of liver during infancy. Acquired hypothyroidism is one of the rare manifestation of this entity. We report a 4-month-old infant born to a diabetic mother who developed acquired hypothyroidism not responding to treatment due to multiple hepatic hemangiomas. The mechanism behind is increased type 3 deiodinase activity due to hemangiomas of liver, which catalyses conversion of T4 to rT3 and T3 to T2. Hemangiomas were successfully treated with propranolol which lead to its regression and ultimately resulted in euthyroidism. Hence, screening for hepatic hemangioma should be done in all cases of congenital hypothyroidism not responding to thyroxine treatment. We also propose early initiation of treatment of hemangiomas with propranolol as the first line therapy to prevent growth retardation and intellectual loss.

Keywords: Diabetic mother, hemangioma, hypothyroidism, management

Introduction

Hepatic Hemangiomas are commonly occurring tumor of infancy arising from mesenchymal liver tissue.^[1] They can be clinically silent to symptomatic; common presentation are hepatomegaly, abdominal mass, congestive cardiac failure and may be associated with cutaneous hemangiomas.^[2] Rarely splenomegaly, jaundice, ascites, gastrointestinal bleeding, anemia, feeding difficulties and consumptive hypothyroidism might be the manifestations.^[3-5]

In this study, we report a case of consumptive hypothyroidism due to multiple hemangiomas in an infant of diabetic mother successfully treated with propranolol and L- Thyroxine.

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Case

A 4-month-old female patient presented in out-patient department with history of constipation for last 2 months, not attaining milestones and increasing abdominal distention for last 1 month. She was diagnosed as a case of hypothyroidism 1 month back and was on treatment with L-Thyroxine at a dose of 25 mcg/day. She was born full term with birth weight of 2.5 kg to a non-consanguineous couple and had a healthy 2-year-old sibling. There is history of gestational diabetes in mother with no history of hypothyroidism. The patient's weight was 4.1 kg, length 61 cm, and head circumference 40 cm. Child was not recognizing mother and neck holding was not yet attained. Physical examination revealed massive abdominal distention, prominent superficial veins on the abdominal skin, and an enlarged liver palpable 8 cm below the right costal margin [Image 1]. Cutaneous hemangiomas were present on

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finger and posterior aspect of left thigh [Image 2]. The thyroid gland was not palpable.

Investigations showed normal complete blood count, liver function test, PTT/APTT. Initial thyroid levels were TSH 17.5 mIU/mL, T4 13.9 µg/dL, T3 98 ng/dl on which treatment was initiated. After 1 month TSH increased to 25 mIU/mL, T4 18.9 µg/dL (5.9-16.3), fT4 2.31 ng/dL (0.9-2.1), T3 106 ng/mL (50-275), and fT3 1.51 pg/mL (2-6.5). The mother's thyroid function tests were normal and thyroid autoantibodies were negative in mother as well as the infant. Thyroid ultrasonography was normal with right lobe measuring 0.7 × 1.1 × 2.6 and left lobe measuring 0.8 × 1 × 3.3 cm. Abdominal ultrasonography showed liver measuring 13 cm with altered echotexture and multiple hypoechoic lesions. USG doppler showed enlarged liver with multiple variable sized predominantly hypoechoic lesions scattered in both lobes largest being 2.6 × 4.8 cm. hepatic arteries showing low resistance wave forms (PSV = 40 cm/s) and portal veins not dilated. Abdominal CECT showed enlarged liver with multiple hypodense lesions in bilateral lobes. Lesions showed homogeneous contrast enhancement with non-enhancing hypodense central areas suggestive of multiple infantile hepatic hemangiomas [Image 3]. Mass effect over spleen and bilateral kidneys is seen. Abdominal aorta before the origin of celiac

trunk was 8 mm and distal to the origin was 5 mm. Celiac trunk appeared prominent measuring 6 mm. The alpha-fetoprotein level was high (161 IU/mL). Echocardiogram showed small muscular VSD with left to right shunt. Oral L- thyroxine was increased to 37.5 mcg and propranolol was started for hemangioma at a dose of 3 mg/kg/day.

After 3 months of treatment, abdominal distention subsided and hemangiomas regressed in size. Patient has become active and alert, gaining weight, started sitting without support and speaking monosyllables [Image 4]. On investigations, patient has attained euthyroid state on follow up. Consent was obtained from parents for publication of the case and ethical clearance was obtained from the institution.

Discussion

Thyroid hormones play an essential role in regulating normal growth and development during infancy. The regulation of thyroid hormone metabolism at tissue level is done by the widely expressed iodothyronine deiodinase enzymes, which activate and inactivate thyroid hormones. Whereas type 1 and



Image 1: Abdominal distension and visible superficial veins

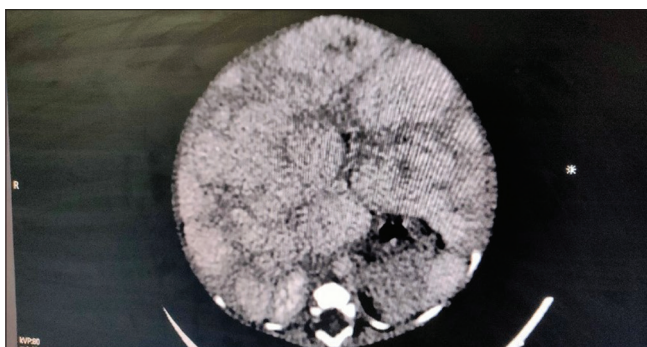


Image 3: CT images showing Enlarged liver with multiple infantile hemangiomas



Image 2: Cutaneous Hemangioma on posterior aspect of thigh



Image 4: Patient on follow up after 3 months of treatment

type 2 deiodinase (D1 and D2) convert thyroxine (T₄) into the active hormone triiodothyronine (T₃), type 3 deiodinase (D3) turns T₄ and T₃ into its inactive products reverse T₃ (rT₃) and diiodothyronine (T₂), respectively.^[6] Consumptive hypothyroidism occurs as a result of increased degradation of thyroxine due to paraneoplastic overexpression of type 3 deiodinase in hemangiomas and it cannot be compensated by upregulated hormone synthesis in the thyroid.^[4,7,8]

These lesions usually appear around 4th and 6th weeks of life but some may appear in neonatal period.^[8] Our patient had visible abdominal distension around 12 weeks of life.

The risk of congenital malformations in infants of diabetic mothers is known to be higher than those of non-diabetic mothers. Our patient was having acyanotic heart disease (VSD) in addition to hemangiomas. As per review of literature, only 1 case has been documented in infant of diabetic mother so far who had other vertebral abnormalities, central nervous system abnormalities, and multiple severe cardiac defects.^[4]

It is seen that AFP levels may be high in case of hemangiomas, but they are never as high as seen in hepatoblastoma.^[9] Similarly, our case has mildly raised AFP levels.

The treatment of hepatic hemangiomas remains controversial till date. Earlier, systemic corticosteroids used to be the mainstay in the treatment of hepatic hemangioendotheliomas, however side effects of high doses are of major concern in infants.^[10] Other invasive measures like hepatic artery ligation, embolization, or liver transplantation have been tried in cases in which medical therapy failed.^[9] Propranolol has recently been introduced as the first line treatment of hemangiomas and its use has now been proven in various published articles at doses of 2-3.5 mg/kg/day.^[11-13] Our patient was also treated with propranolol which resulted in resolution of hepatic hemangioma and ultimately corrected the thyroid dysfunction.

In many countries, screening for congenital hypothyroidism is a part of neonatal screening as it has serious consequences on growth and development of child. Early suspicion of hepatic hemangiomas by primary care physicians in patients with congenital hypothyroidism refractory to treatment lead to better outcome. This case report also highlights role of propranolol as first line therapy in the treatment of hepatic hemangiomas.

Conclusion

Diagnosis of consumptive hypothyroidism should be considered and investigated when hypothyroidism is not responding on even adequate doses of L-Thyroxine during infancy. Early detection and timely management by propranolol will prevent poor neurological outcome thereby reducing burden on family and community.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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