

CASE REPORT

Consumptive hypothyroidism in a two months old infant secondary to hepatic haemangiomas

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ABSTRACT

The case described in this report is of a two-month-old boy who presented with severe hypothyroidism. The infant also had multiple hepatic haemangiomas. The cause of hypothyroidism was found to be due to consumption of the hormone by the tumour. The patient was put on high dose of thyroxin and medical treatment for the haemangiomas. He was followed for three years, cured from the haemangiomas, was no more suffering from hypothyroidism, and all treatments were stopped. More details about this case and similar other cases have been discussed.

KEYWORDS:

Consumptive hypothyroidism; Hepatic haemangioma; 3-iodothyronine deiodinase.

INTRODUCTION

Hepatic haemangioma is a benign tumour of the liver composed of hepatic endothelial cells. It is the most common liver tumour, and is usually asymptomatic and diagnosed incidentally on radiological imaging. Liver haemangiomas are thought to be congenital in origin [1]. Several subtypes exist, including the giant hepatic haemangioma, which can cause significant complications [2].

This report describes an infant with massive hepatic haemangioma that is associated with severe hypothyroidism, which necessitated high doses of thyroid hormone to restore euthyroid status and normal thyroid stimulating hormone level. This complication occurs when the tumour releases in the blood circulation the enzyme 3-iodothyronine deiodinase, which disintegrates thyroid hormones leading to consumptive hypothyroidism [3,4].

CASE REPORT

A two-month-old baby boy was admitted to the paediatric wards of King Abdul-Aziz Medical City in Jeddah, Saudi Arabia for investigations. He was a product of full-term, spontaneous vaginal delivery. Umbilical cord blood thyroid-stimulating hormone (TSH) level was 7.23 mIU/L. He received phototherapy in the second day of delivery for indirect hyperbilirubinemia. His jaundice was secondary to rhesus incompatibility. He was discharged after three days in good condition. At the age of two weeks, the parents of the child noticed an increased abdominal distention, constipation and pallor. For these symptoms, they looked for a medical advice in a nearby hospital. The investigations done for him included full blood count, peripheral blood smear,

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Figure 1 - Abdominal ultrasound showing huge hepatomegaly with multiple diffuse nodules.

Coombs test, haemoglobin electrophoresis and liver function tests. All results were normal except for haemoglobin of 6 g/dL. He was transfused with packed cells.

The baby was on mixed breast feeding and formula feeding. He received polio and hepatitis B vaccines at birth. The parents did not have any concern about his growth and development. No significant information was revealed from the family and social history.

Examination of the child at the time of presentation revealed weight of 5.2 kg at 25th percentile (-0.46 standard deviation (SD)); length of 53 cm at 0.4 percentile (-2.61 SD) and head circumference of 37 cm at 4.2 percentile (-1.73 (SD)). The temperature, pulse and respiratory rate of the child were normal. The child was very pale, but not jaundice or dysmorphic. The respiratory system examination was normal. Cardiovascular examination revealed normal heart sounds and grade 2 systolic murmur heard at the left sternal border. Abdomen was distended with visible dilated veins. The liver was enlarged and palpable to the right iliac fossa. The spleen was palpable 5 cm below the left costal margin. There was also left inguinal hernia.

Investigations showed white cell count of 7.5×10^3 with normal differential. Haemoglobin was 10.6 g/dL and the Erythrocyte sedimentation rate (ESR) was 8 mm/hour. The liver function tests were normal apart from increase in Guanosine triphosphatase (GTP),

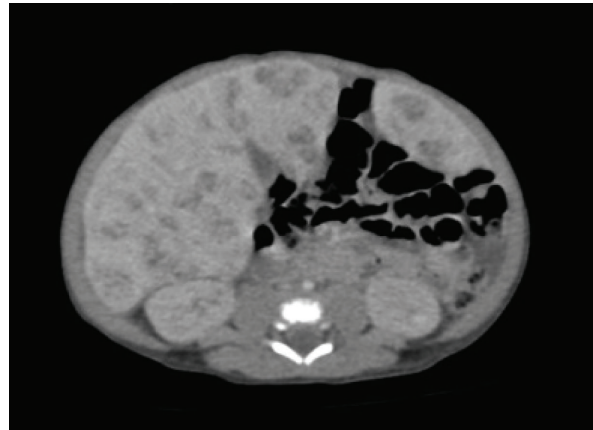


Figure 2 - Non-enhanced CT scan showing multiple hypo attenuating lesions in the liver.

which was 865. Urea, creatinine and electrolytes were normal. Both serum calcium and phosphate are normal. Coagulation profile showed prothrombin time 11 seconds, activated partial thromboplastin time 36 seconds, and international normalise ratio (INR) 0.9. Sickling test and haemoglobin electrophoresis were normal. Screening for viral hepatitis was negative. Alpha-fetoproteins level was high at 11,307 IU/mL. Due to clinical findings in abdominal examination, ultrasound abdomen was requested. The abdominal ultrasound showed huge hepatomegaly with multiple diffuse nodules (Figure 1).

Based on the results of the ultrasound scan, a computed tomography (CT) scan of the liver was done (Figure 2). The CT scan with contrast revealed multiple variable sized hypodense lesions with peripheral enhancement in the arterial phase. Findings were suggestive of diffuse hepatic haemangioendothelioma (multinodular hepatic haemangiomatosis).

Because of the history of chronic constipation and family history of thyroid disease, thyroid function tests were requested and the results were as follows:

Thyroid stimulating hormone: 281 (0.5–4.70 μ IU/mL), free T4 (FT4) 10.4 pmol/L (10–26 pmol/L), free T3 (FT3) < 1.5 (1.5–15.2 pmol/L).

These results suggest severe hypothyroidism. A radioisotope thyroid scan was then ordered. It showed (Figure 3) moderately enlarged gland

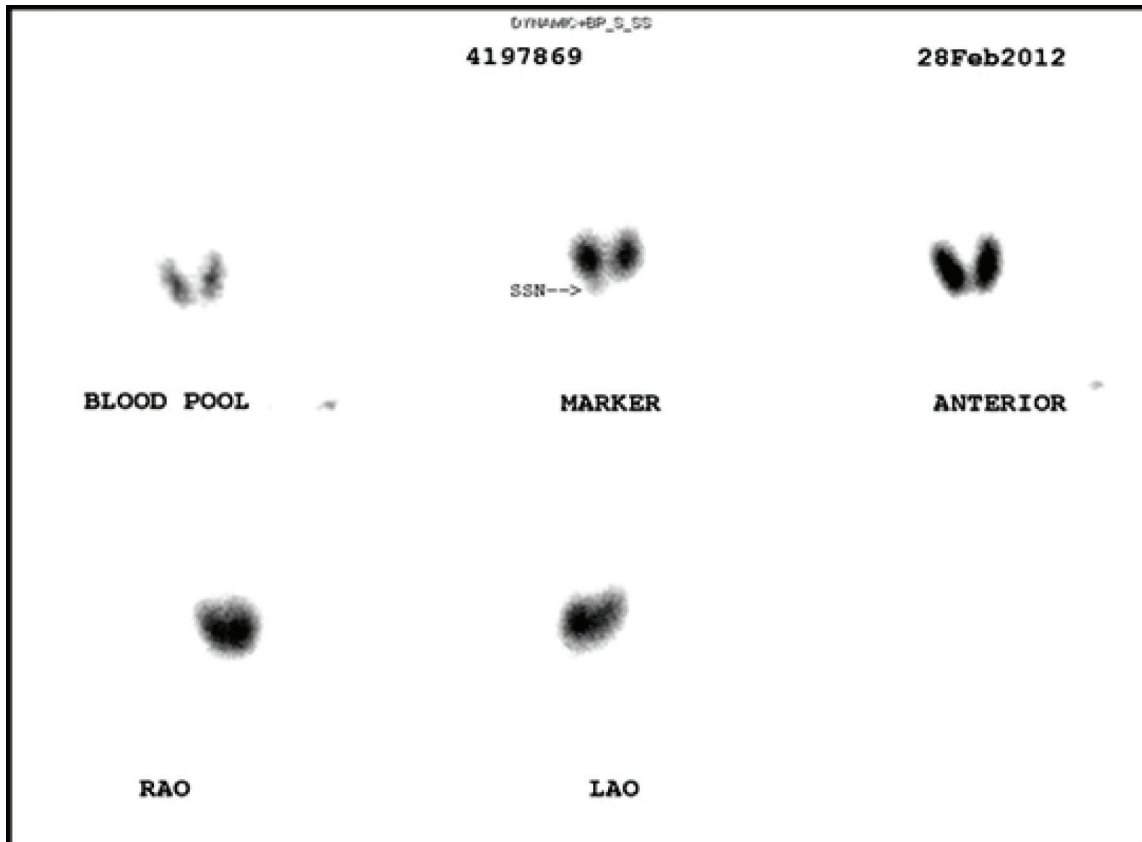


Figure 3 - Radioisotope thyroid scan showed moderately enlarged gland (left lobe 3.8 cm, right lobe 3.7 cm) with normal location, shape and blood flow.

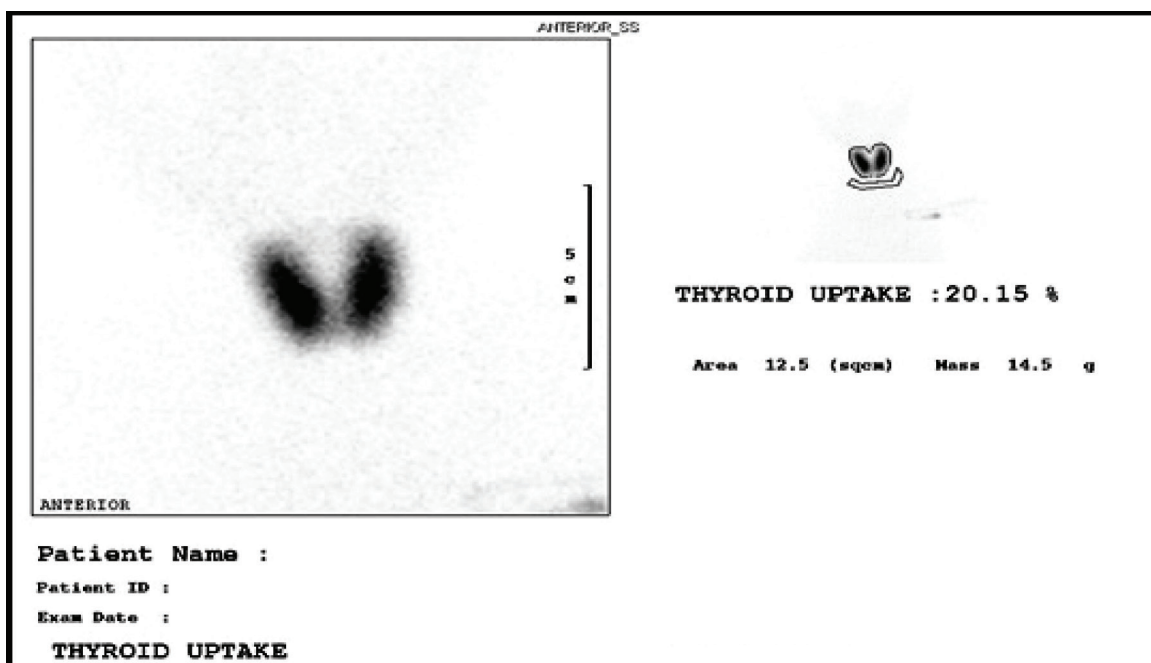


Figure 4 - Radioisotope thyroid scan showing abnormally high thyroid uptake.

Table 1 - Response to treatment and thyroid function test follow-up.

Time/date	At diagnosis	After 2 months	After 1 year	After 2 years	After 3 years
TSH	28.1	10	6.3	3.6	2.1
FT4	10.4	16.68	15.92	18.56	17.92
Notes on treatment	Thyroxin 50 mcg daily	Thyroxin 50 mcg daily	Thyroxin 50 mcg daily	Thyroxin 50 mcg daily	No treatment

(left lobe 3.8 cm, right lobe 3.7 cm) with normal location, shape and blood flow, and uniform intense uptake. Thyroid uptake was abnormally high (20.15%) (Figure 4).

The findings in history and examination, together with the results of investigations and images, pointed to the diagnosis of primary acquired severe hypothyroidism with massive hepatic haemangiomas. Based on this diagnosis thyroxin was started at a dose of 50 µg daily, the oncology team saw the patient and put him on propranolol. The patient then kept regular follow-up with the oncology and the endocrinology teams.

The diagnosis was further confirmed after 3 years when we were able to stop L-thyroxin after complete cure of the liver hemangioma, which was confirmed radiologically by oncology team. The response to treatment and thyroid function test follow-up is illustrated in Table 1.

DISCUSSION

This patient had severe hypothyroidism that did not respond to the usual doses of thyroxin for similar cases of congenital hypothyroidism. The patient had associated multiple hepatic haemangiomas. Other infants with hypothyroidism usually respond to 7 µg of oral levothyroxine per kilogram, given daily. This dose is enough to restore the serum level of TSH. In our patient, we needed three folds as this dose, the cause is that most of the exogenous thyroxin, given orally, was converted to triiodothyronine by the haemangioma tissue [5,6]. While we were following the child, a paediatric oncologist was following the hepatic haemangiomas. We discussed the suitable treatment for these haemangiomas with the paediatric oncologist, as there was no agreed protocol in our hospital. After reviewing literature

and published results in the treatment of infantile haemangioma, the oncologist decided to use propranolol, which gave excellent results [7,8,9].

The thyroid hormone is deactivated massively in the tumour tissue by 3-iodothyronine deiodinase. This is the only explanation of this phenomenon as the enzymatic activity of the haemangiomas consumed the thyroid hormone that was released by the infant and more than that; the tumour also consumed the ordinary exogenous thyroxin dose. In our case, we did not measure the level of 3-iodothyronine deiodinase as its level was very high in most similar reported cases, and our patient responded well to high doses of thyroxin [4,6,10].

It was found in previous studies that the fibroblast growth factors expression is increased in the proliferative phase of hemangiomas [4,11]. These growth factors activate the extracellular receptor of the kinase pathway, which in turn increases the activity of 3-iodothyronine deiodinase. Basic fibroblast growth factors play a major role in the high level of expression of 3-iodothyronine deiodinase in haemangiomas, which is mediated by endocrine or paracrine induction of the enzyme in endothelial cells [12,13]. Untreated hypothyroidism in the first year is very serious as it will lead to permanent deterioration in cognitive functions [14]. The first year is very critical in children with hepatic haemangiomas as this is the time where these tumours are proliferated and carry high risk to cause resistant hypothyroidism with the potential risk of mental retardation in infants. The importance of this case report came from the fact that most of the symptoms and signs of hypothyroidism in these infants may be masked with the severity of other symptoms of haemangioma such as symptoms related to haemostasis failure or those resulting from the hepatic injury.

CONCLUSIONS

The most important message to the clinicians from this case report, and other similar reported cases, is that thyroid function should be assessed

in children with hepatic hemangiomas before any type of therapy is begun. Any detected hypothyroidism should be adequately treated and carefully followed.

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