Hyperthyroidism Presenting as Jaundice in a Child

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Abstract

Hyperthyroidism-related liver disease is an uncommon cause of jaundice in children. There is scarce data on its clinical and histological features and management. We report the case of a five-year-old girl with thyrotoxicosis associated with hepatitis, which was managed solely and successfully with carbimazole and propranolol.

Keywords: Hyperthyroidism; Jaundice; Pediatric; Autoimmune Hepatitis; Carbimazole; Oman

Introduction

Liver involvement in hyperthyroidism is uncommon in children and was first described in 1874.[1] In a recent study on 204 Chinese children with hyperthyroidism, 50 were found to have abnormal liver functions (LFT).[2] However, no histological biopsies or liver disease investigations were conducted in that study.

We describe here the clinical features and liver investigations including the histological features of a child who was successfully treated with carbimazole and propranolol.

Case Report

A five-year-old girl presented with a history of fever and jaundice for one week and intermittent diarrhea for a few months. She was also reported to have lost weight despite having a good appetite. Her parents denied any history of rashes, joint pains, contact with animals, or family history of chronic disorders. She was initially seen in a local hospital where the blood culture was negative, and paracetamol was prescribed.

Clinically the child looked icteric, had proptosis, with a heart rate of 140/min at rest and blood pressure of 127/70 mmHg. She had wet palms and a palpable goitre with no lymphadenopathy. The liver was palpable by 4 cm in the right lobe and 7 cm in the left lobe. The spleen was not palpable. There were multiple branding marks noted over the abdominal wall. The baseline blood investigation results are listed in Table 1.

Table 1: Initial blood investigations.

Test	(range)	**Results**	**Test**	(range)	**Results**
Hb	(11.5–15.5 g/dL)	11.8	Alpha–fetoprotein	(0–20 ug/l)	13.5
Albumin	(57–82 g/l)	20	Ammonia	(11–32 umol/L)	38
ALT	(10–49 IU/L)	1676	Hepatitis A, B		Negative
Bilirubin	(5–21umol/l)	325	CMV IgM		Negative
GGT	(10–30 IU/L)	109	Anti LKM antibodies		Negative

Test	(range)	Results	Test	(range)	Results
INR	(0.82–1.05)	1.4	Autoantibodies		Negative
Serum creatinine (35–65 umol/l)		19	ANA, Ds-DNA ANCA		Negative
TSH	(0.67–4 m[iU]/L)	<0.008	IgG	(4–12 g/L)	22.9
Free T4	(11–18 pmol/L)	83.1	IgG4	(0.01–0.540) g/l	1.35
Free T3	(5–7 pmol/L)	24.3	Ceruloplasmin (0.2–0.6 g/L)		0.54
Thyroid peroxidase antibodies (<60 iU/ml)		177.1	Neonatal screen		Normal
Hepatitis B surface antigen		Negative	Hepatitis C antibodies		Negative

Note. *Hb: hemoglobulin; ALT: alanine amino transferase; CMV: cytomegalovirus; GGT: gamma glutamyl transferase; INR: international normalized ratio; ANA: antinuclear antibody; Ds-DNA: double stranded deoxyribonucleic acid; ANCA: antineutrophil cytoplasmic autoantibodies; TSH: thyroid stimulating hormone; LKM: liver, kidney, microsomal.*

Ultrasound of the thyroid gland confirmed thyroid enlargement, the right lobe being 1.8 × 1.6 × 3.4 cm and the left lobe being 2 ×1.5 × 3.5 cm, with heterogeneous echogenicity.

Ultrasound of the liver showed coarse echotexture and patent portal and hepatic veins. Liver biopsy showed diffuse steatosis both macro and microvascular. There was a marked expansion of the portal areas along with moderate infiltration of lymphocytes, histiocytes, eosinophils, neutrophils, and occasional plasma cells. There was moderate interface inflammation in all the portal tracts. Lobular inflammation with neuroinflammatory foci was noted along with apoptotic hepatocytes, giant cell transformation and ballooning of the hepatocyte. Also seen was mid-focal bile duct injury [Figures 1 and 2].

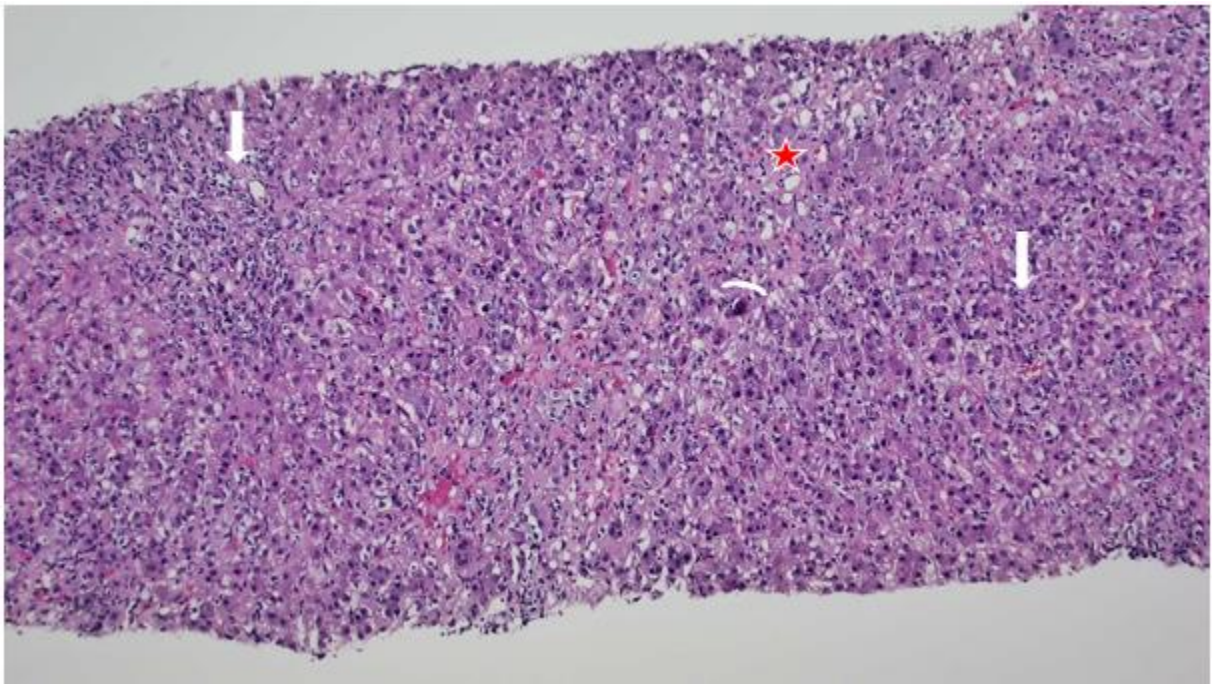

Figure 1: Ssections of the liver show disarray of the architecture with portal and lobular inflammation (arrows), apoptosis (arch) and steatosis (red star), hematoxylin and eosin, magnification = 10 ×.

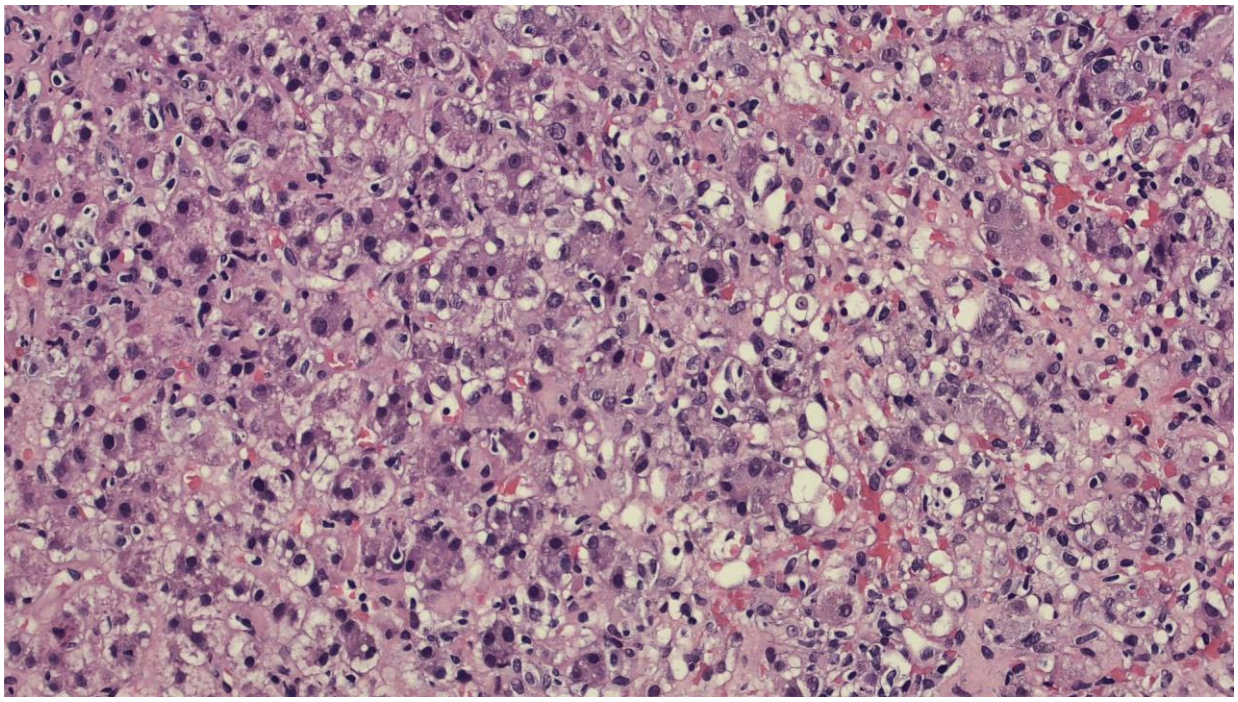

Figure 2: Sections of liver show steatosis with lobular disarray, hematoxylin and eosin, magnification = 40 ×.

The histopathology was not conclusive of viral hepatitis, urea cycle defect, cholesterol ester defect or the relation to thyrotoxicosis. The child in general was well and had no hypoglycemia.

The patient was treated with carbimazole 5 mg three times a day (TID) (0.9 mg/kg/day), propranolol with a gradual increase to a final dose of 10 mg TID in addition to vitamin D supplements for low vitamin D of 48.6 nmol/L (50–250 nmol/L). Table 2 shows the response of liver functions to carbimazole.

Table 2: illustrates the response of ALT and bilirubin to carbimazole therapy alone.

Days of therapy	Day 0	2 weeks	1 month	2 months	3 months
Bilirubin (umol/L)	325	304	84	34	18
ALT (IU/L)	1676	208	57	26	32
TSH (m[iU]/L)	<0.008		<0.008		<0.008
Free T4 (pmol/L)	83.1		29.5		21.1

ALT: *alanine amino transferase*; TSH: *thyroid stimulating hormone*; T4: *thyroid hormone*.

Discussion

The pathophysiology of hyperthyroidism-related liver disease is not yet clear. Factors including ischemia of the hepatocytes secondary to a hypermetabolic state and relative oxygen deficiency, decreased glucuronyl transferase activity, and cardiac failure[3,4] have all been proposed as potential causes. The biochemical and histopathological changes in hyperthyroidism-related liver disease have been commonly described as a mild derangement in the ALT with mild lobular inflammation, and rarely as liver failure.[5]

A liver biopsy is of great value in distinguishing the likely etiology of liver disease. However, the differential diagnosis of any child presenting with autoimmune thyroid disease and liver disease must include autoimmune hepatitis. In our patient, however, histology revealed not a purely autoimmune liver disease, but with the presence of steatohepatitis with moderate necro inflammatory changes, apoptosis, and interface hepatitis. This raised a diagnostic challenge between autoimmune hepatitis and hyperthyroidism-related liver disease. The confusion between autoimmune hepatitis and thyrotoxicosis-related hepatitis was resolved by combining the clinical picture of florid thyrotoxicosis, the absence of autoantibodies against hepatocytes, the histological feature of steatohepatitis, and the presence of apoptotic hepatocytes, which were not typical features of autoimmune liver disease.

Therefore, the management of hyperthyroidism was prioritized. The rapid response to carbimazole within two weeks reassured the physicians of the primary diagnosis of thyrotoxicosis-related liver disease. Propranolol was used to keep the heart rate in a near-normal range of 80–90 beats per minute.

Urea cycle defects and cholesterol ester deficiency suggested from histopathology were not favored due to the patient's age, absence of acidosis or neurological symptoms, and the marked hyperbilirubinemia.

The first line of treatment of thyrotoxicosis in children is with an anti-thyroid drug, usually carbimazole.[6] Our patient responded well to carbimazole and did not have side effects such as hepatitis, arthralgia, or agranulocytosis.

Conclusion

Hyperthyroidism-related liver disease is challenging and uncommon for children. The current case of pediatric thyrotoxicosis associated with hepatitis was diagnosed by clinical signs, liver biochemistry, biopsy, and imaging. The thyroid abnormality was corrected using carbimazole and propranolol, which also resolved the liver issues. In patients with overt hyperthyroidism and hepatitis, thorough hepatitis work up including a liver biopsy is mandatory to clarify the exact aetiology of liver disease. In patients with thyrotoxicosis, thyroid abnormalities need to be corrected first before considering auto-immune hepatitis.

Disclosure

The authors declare no conflicts of interest. Informed written consent was obtained from the patient's father.

References

1. Habershon SO. Exophthalmic goitre, heart disease, jaundice, death. Lancet 1874;1:510-512.

2. Xie H, Chen D, Zhang J, Yang R, Gu W, Wang X. Characteristics of Graves' disease in children and adolescents in Nanjing: a retrospective investigation study. Front Public Health 2022 Oct;10:993733.

3. Van Steenbergen W, Fevery J, De Vos R, Leyten R, Heirwegh KP, De Groote J. Thyroid hormones and the hepatic handling of bilirubin. I. Effects of hypothyroidism and hyperthyroidism on the hepatic transport of bilirubin mono- and diconjugates in the Wistar rat. Hepatology 1989 Feb;9(2):314-321.

4. Fong TL, McHutchison JG, Reynolds TB. Hyperthyroidism and hepatic dysfunction. A case series analysis. J Clin Gastroenterol 1992 Apr;14(3):240-244.

5. Sousa A, Pérez-Rodríguez MT, Páramo C, Álvarez E, Rivera A. Severe acute liver failure and thyrotoxicosis: an uncommon association. Rev Esp Enferm Dig 2015 Sep;107(9):575-576.

6. Léger J, Carel JC. Diagnosis and management of hyperthyroidism from prenatal life to adolescence. Best Pract Res Clin Endocrinol Metab 2018 Aug;32(4):373-386.