

# Thyrotoxicosis associated with severe hypoalbuminemia and hyperbilirubinemia

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Thyrotoxicosis is a known cause of nonspecific abnormalities in liver function tests: most commonly mild elevations in serum bilirubin and liver enzymes, and rarely decreases in serum albumin levels. We report a case of severe hyperbilirubinemia and hypoalbuminemia secondary to thyrotoxicosis in a 64-year-old woman who presented to our emergency department with complaints of jaundice, pruritis, and chronic diarrhea. In our case, the symptoms and signs of various abnormalities in liver function tests such as serum albumin and bilirubin normalized after euthyroid state. We think that these findings are related to thyroid dysfunction. Every hyperbilirubinemia and hypoalbuminemia, which can be seen in many serious diseases, may unexpectedly appear in the long-term progression of thyrotoxicosis. Whether thyrotoxicosis is present in patients with hyperbilirubinemia and hypoalbuminemia should be evaluated.

## Keywords:

cholestasis, hyperbilirubinemia, hyperthyroidism, hypoalbuminemia, jaundice

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## Introduction

The term thyrotoxicosis refers to the clinical syndrome resulting from serum elevations in thyroid hormone levels. The cause of hepatic dysfunction in hyperthyroidism may be multifactorial, occurring solely as a result of hyperthyroidism, drugs used to treat hyperthyroidism, hepatic congestion from thyrotoxic heart failure, autoimmune hepatitis, primary biliary cirrhosis, viral hepatitis, alcohol abuse, sepsis, and cholangitis. Medications such as oral contraceptives, propylthiouracil, acetaminophen, isoniazid, and rifampicin can also be implicated [1–5].

Thyrotoxicosis is known to cause a variety of nonspecific abnormalities in liver biochemistries, but there has been no evidence to suggest that thyroid hormones have a direct toxic effect on the liver. The liver is the primary organ of thyroid hormone metabolism, which may explain how thyroid disorders can result in liver profile derangements. Hepatic dysfunction associated with hyperthyroidism has been documented in literature for over 100 years, but the pathophysiology is yet to be determined. Modest elevation in transaminases is the most common liver manifestation of thyroid disease. However, severe hyperbilirubinemia and hypoalbuminemia may rarely occur [5].

To our knowledge, we report a rare case of severe hypoalbuminemia with thyrotoxicosis in literature.

## Case report

A 64-year-old woman (71 kg body weight; BMI 19 kg/m<sup>2</sup>) presented to our emergency department

with complaints of jaundice, pruritis diffuse edema, palpitation, shortness of breath, irritability, confusion, and chronic diarrhea. Her past medical history included only multinodular goiter. About 15 years ago, a multinodular goiter was diagnosed, which is the cause of thyrotoxicosis, but she did not have a regular control. She was not taking any prescribed medications.

The patient denied any history of hepatitis, international travel, blood transfusions, intravenous drug use, or high-risk sexual behavior. She denied heavy alcohol or over-the-counter/herbal medication use. She denied family history of liver or autoimmune diseases.

At presentation, vital signs were temperature of 37.1°C, arterial blood pressure of 110/68 mmHg, irregular heart rate of 170 beats/min, and respiratory rate of 19 breaths/min. On her physical examination, she had significant scleral icterus and generalized edema. Her neck was soft and asymmetric with palpable prominence of the isthmus and pyramidal lobes of the thyroid. A thyroid bruit was not appreciated. There was no hepatosplenomegaly or stigmata of chronic liver disease other than jaundice.

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Transthoracic echocardiography revealed left ventricular ejection fraction of 58%; mild mitral, aortic, and tricuspid insufficiency; pulmonary artery pressure of 35 mm/Hg; and biatrial dilatation. Our patient was hospitalized to the Department of Internal Medicine for further examination and treatment.

On admission, her blood analysis revealed thyroid-stimulating hormone of 0.001 IU/ml (0.2–4.4), free T3 of 11.83 pg/ml (2.88–4.55), free T4 of 8.12 pg/ml (0.62–1.2), albumin of 2.3 g/dl (3.5–5.3), total bilirubin of 4.3 mg/dl (0.3–1.2), direct bilirubin of 2.4 mg/dl (0–0.4), alkaline phosphatase of 158 U/l (36–92), alanine aminotransferase (ALT) of 45 U/l (0–35), aspartate aminotransferase (AST) of 67 U/l (0–35),  $\gamma$ -glutamyl aminotransferase of 61 U/l (0–49), amylase of 95 U/l (0–130), lipase of 53 U/l (<95), and lactate dehydrogenase of 125 U/l (60–100). Other parameters such as urea, creatinine, sodium, and potassium were normal. The acute-phase reactant levels, hepatitis markers, anti-endomysial and anti-gliadin antibodies, Rose Bengal test, gaita culture, and microscopy were negative. The 24-h urine analysis was free of proteinuria. Complete blood count has revealed normocytic normochromic anemia. Abdominal ultrasound revealed ascites and liver tissue with mild congestion. Upper gastrointestinal endoscopy revealed normal mucosal findings.

Total thyroidectomy was performed after treatment with high-dose methimazole and propranolol. L-Thyroxine treatment was started after surgery. In the follow-up, bilirubin and albumin levels returned to normal limits.

## Discussion

The liver has an important role in the metabolism of thyroid hormones. Therefore, thyroid functions may be affected by liver diseases. Conversely, thyroid diseases may cause alterations in liver morphology and functions. The pathophysiologic effects of thyrotoxicosis on the liver remain unclear.

In the first half of the 20th century, there were numerous reports in the literature concerning abnormal hepatic function and pathologic changes in the liver of patients with thyrotoxicosis. Morphologically, the liver has received abundant attention in fatal cases of diffuse toxic goiter. The lesions found are various; there are fatty changes, parenchymatous degeneration, venous congestion, and, finally, cirrhosis of such a distinctive character as to be pathognomonic of this disorder. These lesions occur singly or in various combinations. In an

appreciable percentage of cases, no lesion of the liver is found. Acute yellow atrophy has been reported by Raab and Terplan [6], Kerr and Rusk [7], Zeldenrust and van Beek [8], and Beaver and Pemberton [9]. Foci of necrosis have been reported by Beaver and Pemberton [9], Haban [10], Rössle [11], and Cameron and Karunaratne [12].

Sola *et al.* [13] presented liver biopsies of five patients with hyperthyroidism that revealed nonspecific changes including mild to moderate intrahepatic cholestasis, lobular inflammation of eosinophilic origin, and Kupffer cell hyperplasia. There was no correlation between the severity of the histologic damage and thyroid function tests [4,13]. Although various liver lesions associated with thyrotoxicosis and liver cirrhosis have been reported [9,12,14,15], further investigations indicate that liver changes in thyrotoxicosis are not very significant. Whether these changes are caused by thyroxine or are secondary to metabolic alterations of the hyperthyroid state could not be determined in ultrastructural studies of liver biopsy specimens in patients with thyrotoxicosis. These changes appeared to be adaptive in nature and were not reflected in abnormalities of hepatic tests [16–18]. Currently, hepatic lesions detected in hyperthyroid patients are linked to secondary causes such as heart failure, infections, hypoxia, and malnutrition, rather than the direct effect of thyroid hormones on liver [19,20]. There is no conclusive evidence that thyroid hormones have direct toxic effects on the liver.

In patients with thyrotoxicosis, various abnormalities have been reported: decrease in liver function tests such as serum albumin, and increase in serum bilirubin, AST, ALT,  $\gamma$ -glutamyl aminotransferase, and alkaline phosphatase levels. Kim *et al.* [21] found up to 40% of patients with hyperthyroidism having increased alkaline phosphatase. Similarly, Tibi *et al.* [22] documented mild elevations in AST, ALT, and/or alkaline phosphatase in 30% of untreated hyperthyroid patients, with most of these cases normalizing following hyperthyroidism treatment.

In our case, various abnormalities in liver function tests such as serum albumin and bilirubin are normalized after euthyroid state. We think that these findings are associated with thyroid dysfunction.

## Conclusion

This case demonstrates that hyperthyroidism can result in cholestasis, generalized edema, and may even cause severe hyperbilirubinemia and hypoalbuminemia. Hyperthyroidism should be considered in the differential

diagnosis of a patient presenting with abnormal liver biochemistries. Prompt recognition and treatment of hyperthyroidism should result in clinical improvement and avoidance of unnecessary testing.

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#### Conflicts of interest

There are no conflicts of interest.

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