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# Thyroid Storm in the Presence of Acute Liver Failure - A Management Dilemma

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## Abstract

**Introduction:**

Hyperthyroidism presenting in conjunction with liver impairment leads to diagnostic and therapeutic dilemmas. This case report explores the intricate management challenges presented by the co-occurrence of thyrotoxicosis and liver impairment

**Case Description:**

A 58-year old gentleman presented with features of cardiac and liver failure compounded by palpitations, weight loss, and a goiter suggestive of hyperthyroidis. Clinical findings unveiled features of Graves' disease, right heart failure, and acute liver failure. Laboratory results confirmed acute-on-chronic liver cell disease (CLCD) and portal hypertension, coupled with hyperthyroidism indicative of a thyroid storm. Management challenges arose in initiating antithyroid drugs due to escalating liver enzymes. Therapeutic interventions encompassed propranolol for rate control, hydrocortisone, cholestyramine, Li2CO3, and early total thyroidectomy.

**Conclusion:**

This case highlights the multifaceted nature of thyroid-liver interactions, emphasizing the need for a tailored therapeutic approach in addressing both endocrine and hepatic complications. The complexities surrounding autoimmune liver diseases and the impact of antithyroid drugs on liver function are discussed. Through this exploration, valuable insights are provided into the nuanced management of this challenging clinical scenario.

**Keywords:** case report, thyrotoxicosis, hyperthyroidism, Acute liver failure, chronic liver cell disease

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## Introduction

Thyrotoxicosis presenting in conjunction with liver impairment poses a challenging management dilemma, requiring a nuanced approach to address both endocrine and hepatic complications. This case report delves into the intricacies of such a scenario, shedding light on diagnostic intricacies and therapeutic conundrums.

## Case presentation

A 58-year-old manual worker with a history of Chronic Obstructive Airway Disease (COAD) presented with worsening dyspnea (modified Medical Research Council dyspnea scale 4), bilateral lower limb swelling, and abdominal distension over the past 2 weeks.Accompanying symptoms included orthopnea, paroxysmal nocturnal dyspnea, palpitations, and yellowish discoloration of the eyes with dark urine. Notably, he reported a recent weight loss of 10kg in 2 months, along with heat intolerance, loose stools, and irritability. His urine output was normal, and there was no heamatemesis or melena.

His past medical history was significant for a hospital admission with worsening shortness of breath 4 years back, where he was diagnosed with COAD.

Prior to this presentation, he had a history of 20 packs years of smoking and a history of alcohol use disorder, drinking 3-4 units of arrack per day for the past 40 years. He has had a binge drinking episode 3 days before the presentation. He denied any intake of any hepatotoxic drugs or herbal remedies. Family history of liver disease.

The examination was significant for icterus, gross anasarca, asterixis, exophthalmos, and a large non tender goiter with a bruit. Cardiovascular examination revealed atrial fibrillation with a rate of 130-140/min, elevated JVP with systolic pulsations, displaced apex beat, loud S2 and murmurs suggestive of mitral and tricuspid regurgitation. Abdominal examination revealed hepatosplenomegaly with free fluid in the abdomen suggestive of right heart failure.

Laboratory investigations indicated elevated liver enzymes, bilirubin, and prothrombin time, low platelet count and macrocytosis consistent with acute on chronic liver cell disease (CLCD). An ultrasound of the abdomen confirmed cirrhosis of the liver with portal hypertension. Further assessments revealed hyperthyroidism, with a Burch-Wartofsky point scale of 55 indicative of a thyroid storm.

He was started on propranolol 40 mg 8 hourly and titrated up to 80 mg 8 hourly for rate control together with routine management for acute on chronic liver failure. However, starting Carbimazole/ propylthiouracil was problematic due to the rising liver enzymes.

He was treated with intravenous hydrocortisone100mg 6 hourly, oral cholestyramine 4g 6 hourly, and oral Li2CO3 300mg 8 hourly. Anticoagulation was not started due to labile INR. Repeat FT4 level in 4 days was 3.62, and he improved symptomatically. Carbimazole was started in a dose of 10mg mane when liver functions improved and INR normalized in 5 days and slowly up titrated up to 30mg/day while monitoring liver functions. He was referred for early surgery, given the severity of the presentation and underwent total thyroidectomy with uneventful recovery. The psychiatry team was involved in the management of severe alcohol use disorder.

## Discussion

Thyroid storm is a life-threatening endocrine emergency that manifests as multiorgan failure in the background of an exacerbation of thyrotoxicosis with a mortality around 10-30% [1]. It is associated with hyperthermia, neurological, cardiac, gastro-intestinal and hepatic manifestations and can share significant overlap with other medical emergencies including infections. Burch- Wartofsky point scale can be used to calculate the probability of a thyroid storm objectively and a score of more than 45 is considered as highly possible in having a thyroid storm. [2]

Pathophysiology of liver dysfunction in thyroid disease can be multifactorial. Lipophilic thyroid hormone enters the liver cell and acts on mitochondria increasing cellular metabolism and ATP consumption causing relative hepatic anoxia. Glucuronidation and sulfation of thyroid hormone occur in the liver before excretion via bile, and the overwhelming demand for these pathways results in hepatocyte injury. Furthermore, congestive cardiac failure due to thyrotoxicosis can result in congestive hepatopathy. Preexisting liver disease due to other aetiology can get worsened with thyrotoxicosis as well. Given the autoimmune nature of Graves disease coexistence of autoimmune liver disease such as autoimmune hepatitis and primary biliary cholangitis can also occur. Adding to the mix, antithyroid drugs may also result in liver derangement.

**Table 1**: Baseline investigations of the patient

| Parameter | Result |
|---|---|
| TSH (mIU/L) | <0.008 |
| fT4 (pmol/L) | 4.92 |
| Neck ultrasound scan | Multinodular goiter with background thyroiditis |
| ECG | Atrial fibrillation (AF), rate 130-140/min |
| 2D Echocardiogram | - Preserved left ventricular (LV) systolic function, EF 55%<br>- Dilated left atrium (LA), right ventricle (RV), right atrium (RA)<br>- Grade 11 mitral regurgitation (MR)<br>- Severe tricuspid regurgitation (TR) with TR peak gradient (TRPG) 38 mmHg |
| Abdominal ultrasound scan | Cirrhosis of the liver with portal hypertension |
| Liver function tests | - INR 3.5<br>-ALT 170<br>- AST 185<br>- Albumin 2.7<br>- ALP 196<br>- Total bilirubin (TBIl) 2.8<br>- Direct bilirubin (D bil) 2.1 |

Mild derangements in LFTs are common even in patients with hyperthyroidism but that hepatic failure is rare.[3,4,5]Higher free T4 level and TrAb antibody level were found to be independent risk factors associated with liver derangement in some studies.[3] Pathological assessment of animal and human hepatocytes in the background of thyrotoxicosis has demonstrated structural changes in mitochondria, hepatocyte apoptosis, fatty infiltration and hyperchromasia.[6] Severe liver impairment and fulminant hepatic failure are more common in the setting of congestive/ right heart failure associated with hyperthyroidism and can present with coagulopathy, ascites and hepatomegaly compared to those without heart failure.[6]

Initiating therapy for thyrotoxicosis in the presence of liver impairment poses a dilemma. The patient received propranolol for rate control and routine management for acute-on-chronic liver failure. However, initiating Carbimazole/Propylthiouracil was challenging due to rising liver enzymes. Thionamides act by inhibiting thyroid hormone synthesis. Propylthiouracil (PTU) is the preferred antithyroid drug over carbimazole or methimazole in treating thyroid storm due to its ability to inhibit peripheral T4 to T3 conversion. Though rare, propylthiouracil can result in fulminant liver necrosis in some patients [7]. Furthermore, methimazole has also been associated with liver dysfunction. However, meta-analysis has shown improvement in liver enzymes after starting antithyroid drugs in the majority of patients when the cause for the liver derangement is the underlying thyroid disease [5]. Initiating antithyroid drugs in the presence of liver impairment requires careful consideration, especially in patients with a history of alcohol use disorder, biochemical features suggestive of chronic liver cell disease (CLCD), and limited access to liver transplant, as observed in our patient.

Beta-blockers, steroids, iodine, cholestyramine, and lithium carbonate are alternative drugs that can be used in patients unable to take thionamides. Beta-blockers counteract the hyperadrenergic state associated with thyrotoxicosis and are important for controlling atrial fibrillation, though they should be used with caution in patients with systolic dysfunction. Steroids inhibit the peripheral conversion of T4 to T3, treating autoimmunity associated with Graves' disease. Furthermore, steroids may counteract impaired adrenal hormone reserve that occurs due to increased cortisol metabolism in the presence of hyperthyroidism. However, steroids have not shown a mortality benefit in thyroid storm[8].

High doses of iodine inhibit the binding of iodide to thyroglobulin in the thyroid gland due to the Wolff-Chaikoff effect. However, this effect is transient, and worsening hyperthyroidism can occur with prolonged use of iodine9. Similarly, lithium inhibits thyroid hormone production by inhibiting the coupling of iodothyronines but should be used with caution in patients with renal impairment[9]. Glucuronidated and sulfated thyroxine metabolites are excreted in bile into the intestine, and free hormones are released from these conjugated metabolites and are reabsorbed. Cholestyramine binds to conjugated thyroxine metabolites, inhibits enterohepatic circulation, and promotes the excretion of thyroid hormones. Plasma exchange is another mode of treatment in thyroid storm, especially as a bridging therapy until definitive management, such as surgery, when thionamides are contraindicated.

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