CARBIMAZOLE INDUCED CHOLESTATIC HEPATITIS

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ABSTRACT

Thyrotoxicosis is a common disorder especially in women. Most of the patients tolerate antithyroid medications very well with very few developing life threatening side effects. A 64 years old gentleman was diagnosed with hyperthyroidism secondary to Grave's disease (autoimmune). He was treated with Carbimazole 20 mg daily. With in a month, he presented with acute cholestatic hepatitis. The patient's symptoms and laboratory abnormalities resolved after withdrawing the offending drug and controlling his thyroid status first with beta blocker and subsequently with propylethioracil. Since the mechanism of liver damage is different, antithyroid medications can be interchanged without increasing the risk of further liver damage.

Key Words: Thyrotoxicosis, Grave's Disease, Carbimazole, Colestatic Hepatitis

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INTRODUCTION

Antithyroid drugs are usually well tolerated. Side effects occur in 3-12 % of the treated patients. The most dangerous side effects are; agranulocytosis[1] which occurs in 0.2% to 0.3% of the patients treated with antithyroid drugs, cholestatic hepatitis[4], fulminant liver failure[2], aplastic anaemia and vasculitis. The most common adverse effect is a maculo-papular pruritic rash, at times accompanied by fever[3].

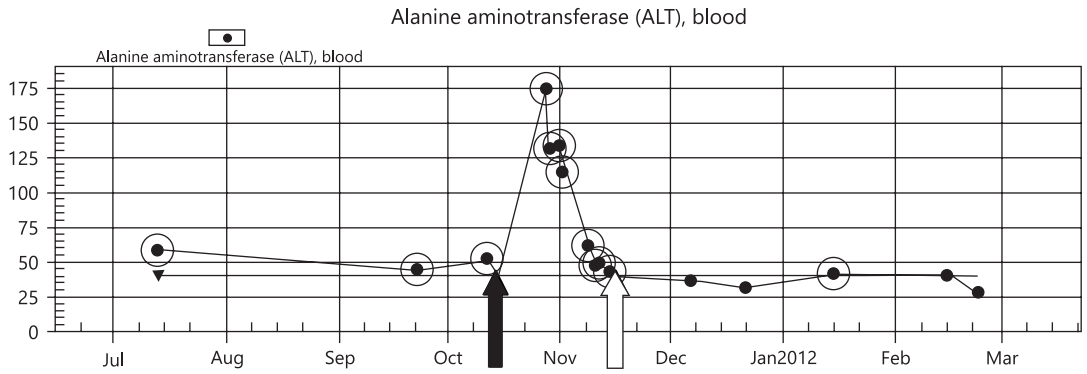
We describe our experience of managing a case of acute cholestatic hepatitis secondary to Carbimazole.

CASE REPORT

A 63 years old gentleman with Grave's thyrotoxicosis (TSH<0.05 mIU/L Free T4= 30 pmol/L) was prescribed Carbimazole 20mg daily in Sept. 2011. After a month, he presented with reduced oral intake, abdominal pain and malaise.

The physical examination showed blood pressure of 110/60, dry mucous membrane and right hypochondrium tenderness. The rest of the physical examination was normal.

Figure 1: Alanine transaminase levels (ALT). Black arrow indicates start of Carbimazole treatment while the white arrow shows start of Propylthiuracil treatment



The investigations showed normal urea and electrolytes, adjusted calcium, haemoglobin, platelets and white cell count. However, his bilirubin was 12µmol/L(normal 0-17µmol/L), alkaline phosphatase 433µ/L(normal 40-150 µ/L), albumin 30g/L(normal 34-50g/L), alanine aminotransferase 173 µ/L(normal 0-40 µ/L) [Figure 1]. His serum ceruloplasmin was 0.33 g/L(normal 0.2-06g/L),normal autoimmune screen and iron studies. His viral hepatitis screen for A, B and C was negative.

The ultrasound of the liver was normal.

Since there was no obvious cause for his cholestatic hepatitis apart from Carbimazole so, it was stopped. Meanwhile he was given beta blockers to control his symptoms. His liver functions improved and after 10 days, we started propylthiouracil. He has been on it for three months and his liver function tests were normal.

DISCUSSION

Both classes of antithyroid agents, Propylthiouracil and Carbimazole, can cause liver dysfunction, which is among the small number of their idiosyncratic toxic effects. The frequency of this condition probably ranges from 0.1 to 0.2 %.[4]

Both Carbimazole and Propylthiouracil differ in their mechanisms of causation of liver damage. Propylthiouracil has hepato-cellular toxic effects and cholestatic changes are seen in case of Methimazole/Carbimazole[3]

Antithyroid drugs have been used for the treatment of hyperthyroidism for more than 50 years. Observations over several decades have shown that Methimazole and its prodrug Carbimazole are better than Propylthiouracil in controlling more severe hyperthyroidism, having higher compliance rates, and causing less toxicity, especially when prescribed in lower doses[4]. This has led to the recommendation that Carbimazole should be the first-line drug when antithyroid drug therapy is initiated, either for primary treatment or to prepare a patient for radioiodine or surgery. An exception to this rule has been pregnancy, during which Propylthiouracil has been preferred because of rare reports of birth defects associated with Carbimazole[5]. Propylthiouracil has also been used in patients who had minor reactions to Carbimazole. Propylthiouracil may also be preferable in patients with life-threatening thyrotoxicosis because of its additional inhibition of T_4 to T_3 conversion.

In our case, the patient was initially started on carbimozle but with in month his liver functions deteriorated. His antithyroid medications were stopped and he was started on high dose propranolol. The definitive treatment of thyrotoxicosis in this case could either be radio active iodine or thyroid surgery. Unfortunately the patient was in a psychiatry unit for his severe depression. So, he could not have radioactive iodine. Similarly he was not keen for thyroidectomy either.

Substitution of Propylthiouracil for Carbimazole was the only choice we had. We started Propylthiouracil and monitored the liver functions closely. They remained stable three months after starting Propylthiouracil. Thus substituting one thionamide for another can be carried out without any increased risk of hepatotoxicity as the mechanism of liver injury is different in both the groups.

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