

Carbimazole Induced Cholestatic Hepatitis

Dr. Hamza Ali Khan*, Dr. Paul Peter#, Dr. Giridhar Tarigopula#, Dr Praveen Partha#

*Specialist Registrar Department of Diabetes & Endocrinology Darlington Memorial Hospital Darlington

#Consultant Department of Diabetes & Endocrinology Darlington Memorial Hospital Darlington

Introduction

Antithyroid drugs are usually well tolerated. Side effects occur in 3-12 % of the treated patients. The most dangerous side effects are; agranulocytosis¹ which occurs in 0.2% to 0.3% of the patients treated with antithyroid drugs, cholestatic hepatitis, fulminant⁴ liver failure², aplastic anaemia and vasculitis. The most common adverse effect is a maculo-papular pruritic rash, at times accompanied by fever³.

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

Case presentation

- A 63 years old gentleman with Grave's thyrotoxicosis (TSH<0.05 Free T4 30) from a psychiatry institution was prescribed Carbimazole 20mg daily in Sept. 2011.
- After a month, he presented with malaise and generally unwell
- His physical examination showed blood pressure of 110/60, dry mucous membrane and right hypochondrium tenderness. The rest of the physical examination was normal

Investigations

- Normal urea and electrolytes adjusted calcium, haemoglobin, platelets and white cell count
- Bilirubin 12 μ mol/L(normal 0-17 μ mol/L), alkaline phosphatase 433 μ /L (normal 40-150 μ /L), albumin 30g/L(normal 34-50g/L), alanine aminotransferase 173 μ /L(normal 0-40 μ /L)
- Serum ceruloplasmin 0.33 g/L(normal 0.2-06g/L)
- Normal autoimmune screen and iron studies
- Viral hepatitis screen for A, B and C negative
- Ultrasound of the liver normal

Progress and Management

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 had been on it for three months and his liver function tests were stable

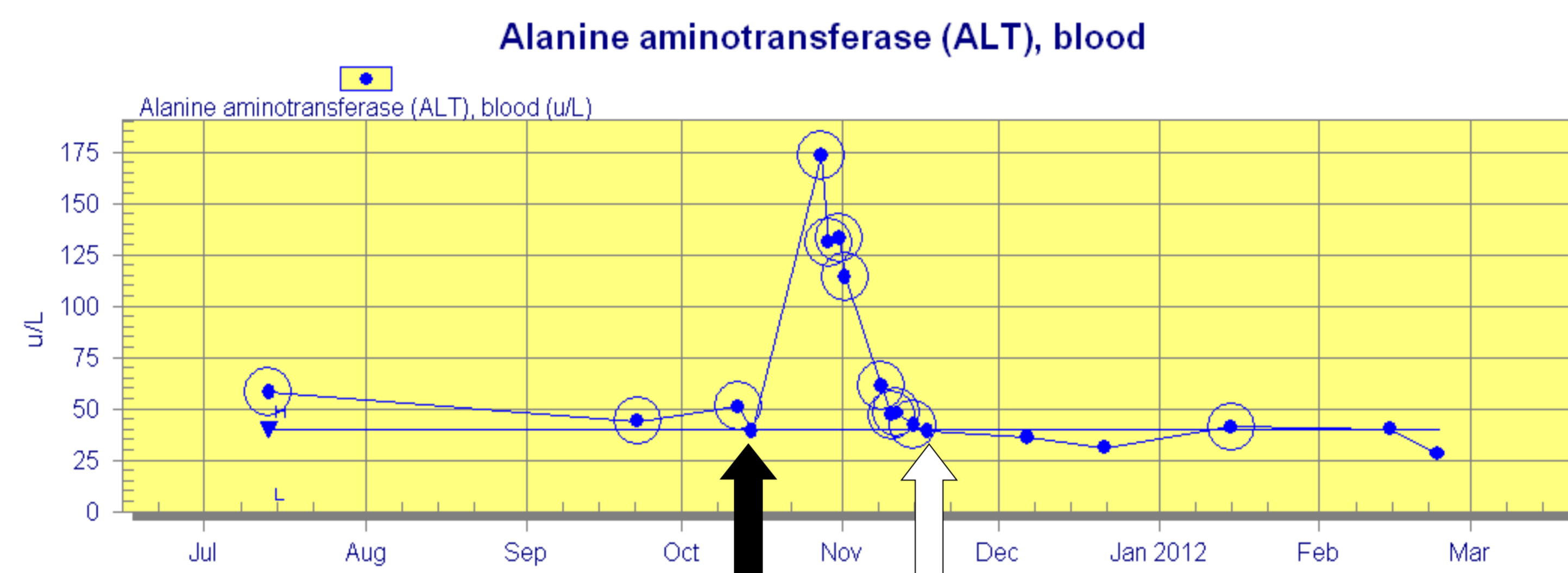


Fig. Alanine transaminase levels (ALT). Black arrow indicates start of Carbimazole treatment while the white arrow shows start of Propylthiouracil treatment

Discussion

- Both Carbimazole and Propylthiouracil can cause liver dysfunction (frequency ranges from 0.1% to 0.2%⁴)
- However, the mechanism is different. Propylthiouracil has hepato-cellular toxic effects and cholestatic changes are seen in case of Methimazole/Carbimazole³
- Observation over several decades have shown that Carbimazole is better than Propylthiouracil in controlling hyperthyroidism having higher compliance rates and causing less toxicity⁴ (except pregnancy where PTU is preferred because of rare birth defects associated with Carbimazole)
- Propylthiouracil may also be preferable in patients with life-threatening thyrotoxicosis because of its additional inhibition of T4 to T3 conversion
- Our patient could not have radio active iodine as he was in a psychiatry unit for his severe depression. Similarly he was not keen for thyroidectomy either

Conclusion

Substitution of one thionamide for an other can be carried out without any increased risk of hepatotoxicity as the mechanism of injury is different in both groups

References

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