Case Report

Carbimazole Induced Cholestatic Hepatitis in Grave's Disease – A Case Report

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Abstract

Grave's disease is the most common cause of hyperthyroidism. Antithyroid drugs are usually well tolerated in majority of patients but serious side effects in the form of allergy, agranulocytosis, aplastic anaemia, vasculitis, hepatitis etc occur in 3 – 12% of treated patients. Carbimazole is extensively used as the drug of choice except in pregnancy, where propylthiouracil is preferred. We report a case of 35 year old female patient with Grave's disease, who developed cholestatic jaundice following administration of carbimazole for 2 months. Symptoms and laboratory abnormalities subsided on withdrawal of carbimazole and Grave's thyrotoxicosis was managed with propranolol and propylthiouracil.

Keywords: Grave's disease; Thyrotoxicosis; Carbimazole; Cholestatic hepatitis.

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Introduction

Grave's disease is an autoimmune disorder and is the most common cause of thyrotoxicosis in 80 – 90% of cases. Treatment modalities include anithyroid drugs, radioactive iodine and surgery. Antithyroid medicines are usually well tolerated. The most common side effects are agranulocytosis,[1] fulminant hepatic failure,[2,3] cholestatic hepatitis,[4,5] aplastic anaemia and vasculitis.[4] We present a case of 35 year old female patient of acute cholestatic hepatitis with underlying Grave's disease secondary to carbimazole.

Case Report

A 35 year old female patient with Grave's thyrotoxicosis presented with anorexia, malaise, heat intolerance, palpitation, mild itching over body, loose stools and yellow discolouration of eyes since 7 days. She was a known case of thyrotoxicosis taking 60 mg carbimezole daily for 1 month. Physical examination revealed anxious look, fine tremors of both hands, bilateral prominent and bulging eyes (exophthalmos) and jaundice. Hands were warm and moist. Neck examination revealed thyromegaly.

Vitals were BP 130/80 mmHg andPulse rate 110 beats/min, her weight was 45 kg. Abdominal examination revealed tenderness in right hypochondrium without hepatosplenomegaly. Laboratory findings revealed hemogram, renal and lipid profile within normal lmits. ECG showed sinus tachycardia. Rest of thyroid function tests T_3 310 (N 80 – 200 ng/dl), T_4 30 (N 5 – 14 ng/dl), TSH < 0.013 (N 0.27 – 5.5 mIU/ml), S.Bilirubin 5.2 mg/dl (N 0.3 – 1.2), SGOT 130 U/l (N 5 – 40), SGPT 145 U/l (N 12 – 38), S.alkaline phosphatase 270

U/l (N 40 – 126), S.albumin 3.6 g/dl (N 4 – 5), GGT 215 U/l (N 9 – 58), Prothrombin time 14 sec (N 12 – 18). Antinuclear antibodies and viral markers for hepatitis A, B, C, and E were negative. Ultrasound abdomen showed normal liver size and texture, normal inter hepatic biliary ducts with no evidence of obstruction. The laboratory findings were suggestive of cholestatic jaundice. The patient refused liver biopsy. Since there was no obvious cause for her cholestatic hepatitis apart from carbimazole we stopped carbimazole. In the mean time she was started on propranolol and propyl thiouracil. Her liver functions started improving and become normal after 4 weeks. She was discharged in a satisfactory condition and is on regular follow up. Her thyroid functions tests repeated at 3 months were normal showing euthyroidism.

Discussion

Antithyroid drugs are in clinical use since more than 50 years for the management of hyperthyroidism. It has been shown that methimazole and its pro drug carbimazole has better efficacy, more compliance and lesser toxicity when prescribed in lower doses as compared to propylthiouracil.[4] All antithyroid drugs including carbimazole and propyl thiouracil can rarely cause liver toxicity in 0.1 – 0.2% patents.[4-7] Hyperthyroidism per se can affect the liver and causes mild elevation of liver enzymes which became normal with treatment[8]. Both carbimazole and propylthiouracil exhibit different mechanisms in causing liver toxicity. Carbimazole/methimazole causes cholestatic hepatitis without evidence of hepatic necrosis on liver biopsy[9] while propyl thiouracil causes hepatocellular toxicity.[7] Carbimazole has been recommended to be first line antithyroid drug for primary treatment or to prepare the patient for radioactive therapy or surgery. But exception to this rule is in pregnancy where propyl thiouracil is preferred over carbimazole because of rare reports of birth defects associated with carbimazole induced toxicity as well as life threatening thyrotoxicosis in view of its additional inhibition of T_4 to T_3 conversion.[2]

The treatment of choice in our patient was either radioactive iodine or thyroid surgery but as she was taking treatment for depression. So radioactive iodine could not be started and she also refused thyroidectomy. So the only option with us was to start propylthiouracil, since the mechanism of liver toxicity is different in cases of carbimazole[9] and propylthiouracil.[7] Our patient responded well on withdrawal of carbimazole, as she was taking large dose of 60 mg of carbimazole daily. The hepatotoxic effect with carbimazole is dose dependent.[10]

Conclusion

Hepatic toxicity is a dangerous side effect of antithyroid medications although it is rare. Routine liver function tests must be performed in patients taking antithyroid drugs to overcame these rare toxic effects. The offending drug must be stopped immediately and alternative treatment in the form of radioactive iodine or thyroidectomy should be started. But our patient was not a candidate for radioactive iodine due to depression, while she refused thyroidectomy. The aim of reporting this rare case is to sensitise the doctors about occurrence of these dreadful complications within the use of antithyroid drugs.[3]

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