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Case Report

Cholestatic Jaundice Induced by Sequential Carbimazole and Propylthiouracil Treatment for Thyrotoxicosis-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 dangerous adverse effects can occur in 3-12% of treated patients. Cholestatic jaundice is a rare but potentially fatal complication secondary to the use of antithyroid drugs like carbimazole and propylthiouracil. We report a case of 46 year old male patient who developed cholestatic jaundice following sequential administration of carbimazole and propylthiouracil treatment for thyrotoxicosis.

Keywords: Thyrotoxicosis; Cholestatic jaundice; Carbimazole; Propylthiouracil.

INTRODUCTION

Grave's disease is an autoimmune disease and is the most common cause of thyrotoxicosis in 80-90 % of patients. Antithyroid drugs are usually well tolerated. Cholestatic jaundice is a rare but potentially dangerous complication following the use of antithyroid drugs. The underlying mechanism of pathogenesis is still unclear. We report a case of 46 year old male developing cholestatic jaundice shortly after receiving sequential carbimazole and propylthiouracil treatment for thyrotoxicosis.

CASE REPORT

A 46 year old man presented with anorexia, heat intolerance, palpitation, and skin rash since 10 days. He was taking carbimazole 10 mg thrice daily for control of thyrotoxicosis since 1 month. On physical examination, he had anxious look, fine tremors of hands, bilateral exophthalmos and urticarial skin rash. Neck examination revealed thyromegaly. Vitals were stable BP 130/80 mmHg, Pulse 112 beats/min. In view of urticarial rash we stopped carbimazole and started propylthiouracil in dosage of 100 mg three times daily. There was no history of hepatitis, alcohol intake or drug abuse. After taking propylthiouracil for 8 weeks, he developed jaundice and itching over body.

Abdominal examination revealed firm hepatomegaly 4 cm below the right costal margin. Spleen was not palpable. He had no skin rash or any sign of chronic liver disease. Cardiovascular, central nervous system and respiratory system examination was unremarkable. Laboratory investigations revealed haemogram, renal and lipid profile within normal limits. ECG showed sinus tachycardia. Thyroid function revealed T3 295 ng/dl (N 80-201), T4 65

ng/dl (N 5-14), TSH 0.10 mIU/l (N 0.27-5 IU/ml), S.bilirubin 4.2 mg/dl (N 0.3-1.2), SGOT 115 U/l (N 5-40), SGPT 125 u/l (N 12-38), S.alkaline phosphatase 465 U/l (N 40-126), S.albumin 3.4 g/dl (N 4-5), gamma glutamyl transferase 590 U/l (N9-58), Prothrombin time 15 sec (N12-18).. Ultrasound abdomen showed hepatomegaly with prominent intrahepatic biliary ducts of left lobe without evidence of obstruction, Antinuclear antibodies and Viral markers for hepatitis A, B, C and E were negative. The laboratory findings were suggestive of cholestatic jaundice. The patient refused liver biopsy. Keeping in view of possible drug induced cholestasis, patient was started on oral prednisolone 0.5 mg/kg for 10 days. As a result his serum alkaline phosphatase decreased to 165 U/l but to our surprise there was rise in serum bilirubin to 12.6 mg/dl with unchanged prothrombin time. On stoppage of prednisolone at 10 days, he developed high grade fever, non productive cough and worsening dyspnea. X-ray chest revealed evidence of interstitial fulminant pneumonitis. But he was negative for malaria, acid fast bacilli. Due to financial constraints, he could not be tested for fungi, herpes simplex virus and cytomegalovirus. Ultimately he was started on broad spectrum antibiotics and intravenous immunoglobulin's but he expired 7 days after developing respiratory symptoms.

DISCUSSION

Antithyroid drugs are being used in clinical practice since more than 50 years for the management of hyperthyroidism. Antithyroid drugs including carbimazole and propylthiouracil can rarely induce liver toxicity in 0.1-0.2 % of cases. [1] The induced liver toxicity is usually in the form of acute hepatitis with rise of liver enzymes. [2] The development of acute cholestasis is more commonly observed with carbimazole as compared to propylthiouracil. [3,4] Cross reactivity between carbimazole and propyl thiouracil leading to development of cholestatic jaundice may occur in few cases. [4,5] Our patient fulfilled the diagnostic criteria of drug induced hepatotoxicity as proposed by Hansen in 1984[2]characterised by absence of chronic liver disease, absence of alcohol intake, or drug abuse, absence of serological evidence of viral hepatitis infection with a temporal relation to drug therapy. The persistent ultrasound findings could be explained by severe cholestasis. Cholestasis usually appears many weeks after starting carbimazole but it may appear as early as 1 day after start of propylthiouracil. [6] But in our case, cross reactivity of the two drugs may be responsible as reported in other studies. [4,5] Antithyroid drugs induced fulminant hepatitis has been successfully treated with steroids. [7] The mechanism of pathogenesis of hepatotoxicity is unclear but it may be due to peripheral lymphocyte sensitisation in vitro [8] or immune mediated as symptoms progressed rapidly on rechallenge with antithyroid drugs. [9] Liver biopsy in such patients showed evidence of portal inflammatory changes, glycogen inclusion bodies, hepatocyte necrosis with or without intra canalicular cholestasis. [3,10] The development of interstitial pneumonitis in our case could be explained on basis of either superadded opportunistic infections during treatment with steroids or immune mediated reaction involving liver and lung, which could be responsible for patient death.

CONCLUSION

The aim of presenting this rare case is to enlighten the fact that cross reactivity may develop to the other antithyroid drugs in the causation of allergy to one type of antithyroid drugs. So extreme caution should be observed while sequentially prescribing carbimazole and propylthiouracil for the management of thyrotoxicosis patients.

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