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Case Report

A rare case of neomercazole induced hepatitis

Muralidhar Varma, Jaikaran Mansingh*, Devyani Sivakumar, Rabia Dhalla, Sudha Vidyasagar, Nandakrishna B.

Department of Medicine, Kasturba Medical College, Manipal, Karnataka, India

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***Correspondence:**
Dr. Jaikaran Mansingh,
E-mail: jai.3.mansingh@gmail.com

ABSTRACT

Neomercazole is one of the most commonly used drugs to treat hyperthyroidism. Common side effects include rash, hair loss and agranulocytosis. Hepatotoxicity is a common side effect of Propylthiouracil, the other major antithyroid drug, but it has been rarely described as a side effect of neomercazole. Here, a patient presents with hepatitis 6 months after starting neomercazole therapy for graves disease. Diagnosis is based on excluding other causes of hepatitis, and treatment involves removing the offending drug. This is followed by normalization of liver function. Rechallenging should not be done as it can lead to recurrence of symptoms.

Keywords: Antithyroid drugs, Drug-induced hepatotoxicity, Graves disease, Neomercazole

INTRODUCTION

Thioamides are the major class of drugs used to treat hyperthyroidism, which act by inhibiting thyroperoxidase and prevent the formation of new thyroid hormones. The two major drugs in this class are propylthiouracil and neomercazole. They are usually well tolerated. Commonly seen side effects with both the drugs include nausea, rash, hair loss, and in severe cases, agranulocytosis.[1]

Additionally, severe hepatotoxicity may be seen with Propylthiouracil which presents as an acute rise in liver enzymes associated with jaundice.[2] However, there have been minimal such incidents reported for neomercazole and most such episodes show a cholestatic pattern.[3] In this report, we present a patient with graves disease, who was started on neomercazole, and subsequently developed hepatitis. We also outline the general workup done to diagnose her as neomercazole-induced hepatitis, and the subsequent management of the patient.

CASE REPORT

A 50-year-old woman who presented with weight loss was diagnosed to have graves disease. The patient was started on Propranolol 40mg OD, and neomercazole 20 mg OD. Her liver function was normal on starting these drugs. The patient felt symptomatically better and gained weight following treatment.

A 6 month after starting treatment, she presented at our hospital with yellowish discoloration of eyes since 2 weeks. Her vitals were stable and systemic examination was unremarkable except for hepatomegaly. Liver function tests were suggestive of acute hepatitis (TB:9.1mg/dL, DB:8.6mg/dL, AST:895IU/L, ALT:998IU/L, ALP:275IU/L). She was initially suspected to have viral hepatitis and was worked up for the same. However, HBsAg, IgM Anti-HbC Ab, and anti HCV were negative. ANA profile and liver profile for

autoimmune hepatitis were also negative. Ultrasound abdomen showed features of chronic liver disease with portal hypertension. She was started on a trial of ursodeoxycholic acid, but this did not improve symptoms.

A provisional diagnosis of neomercazole-induced hepatitis was made and neomercazole was stopped. A 4 week after stopping neomercazole, her liver functions returned to normal. Patient was not re-challenged with neomercazole as there is high risk of recurrence in patients with prior chronic liver disease. A 2 week after stopping T. neomercazole, her liver function tests were done and showed TB of 2mg/dL, AST of 16mg/dL, ALT of 50IU/L, ALP of 98U/L. However, the patient started showing symptoms of hyperthyroidism, and was found to have elevated anti-TPO antibodies, following which, patient underwent Iodine 131 ablation of thyroid. She had an uneventful post-ablation period. One month after ablation her thyroid functions and liver functions have returned to normal.

DISCUSSION

Incidence of drug-induced hepatitis is estimated to be 13.9-24 per 10^6 people.[4] Common drugs causing hepatitis are drugs like methotrexate, amiodarone, statins, halothane, isoniazid, rifampicin, and pyrazinamide.[5-7] Common histopathology of drug-induced hepatitis is similar to that of acute viral hepatitis, however some drugs like erythromycin show a cholestatic picture.[8]

Antithyroid drugs can also rarely cause hepatitis.[9] The most common adverse effect of both antithyroid drugs (neomercazole and propylthiouracil) is neutropenia.[1] Propylthiouracil is also known to cause hepatitis in around one third of patients, usually younger patients, but it is usually a very mild (2-2.5 times) elevation in AST and ALT.[2] In contrast, hepatitis due to neomercazole is very rare with a little over 30 cases reported.[3] It can show either a hepatic or a cholestatic picture.[10]

Our patient's liver functions were suggestive of hepatitis. Mean duration of onset of symptoms is 36 days, however onset can vary from 1 day to 18 months after starting neomercazole.[11] Mechanism of hepatitis was proposed to be an allergic reaction.[12]

Neomercazole induced hepatitis is dose dependent which could explain why our patient had hepatitis 6 months after initiating neomercazole.[13] Risk factors which have significant association with neomercazole induced hepatitis are female sex, age more than 40 years and prior liver disease.[10,11]

Cholestatic hepatitis due to neomercazole does not respond to steroids, but reverses on stopping the drug.[10] The disease is usually mild and does not progress after stopping the drug. Normalization of liver functions may take up to 2 months.[14] There have been some case reports of propylthiouracil hepatotoxicity needing liver transplants.[15] While much less common, there have been rare case reports of acute hepatic failure and death from methimazole.[16] Patients who previously had neomercazole induced hepatitis should not be rechallenged as there is a high risk of recurrence.[17]

CONCLUSION

While very rare, neomercazole can cause a dose-dependant hepatitis. This hepatitis is usually due to an allergic mechanism and has a cholestatic picture on histopathology. With a few exceptions, the hepatitis is mild and resolves within a few weeks of stopping the drug.

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