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CARBIMAZOLE INDUCED AGRANULOCYTOSIS WITH HYPO-THYRIODISM – A CASE REPORT

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ABSTRACT

Agranulocytosis is a rare adverse effect of anti-thyroid drugs; the reported incidence being ~0.17%-0.23%. Agranulocytosis has been reported with all antithyroid drugs including Propylthiouracil, Methimazole and Carbimazole. Drug-induced agranulocytosis can be caused by direct marrow toxicity or be immune mediated. The antithyroid drugs Carbimazole (Neo-Mercazole) and Propylthiouracil carry a relatively high risk of haematological dysfunctions including agranulocytosis. Females and those aged over 65 may have an increased risk. Patients taking antithyroid drugs should be told to notify their doctor at once if they experience fever, a sore throat, mouth ulcers, bruising, malaise or nonspecific illness. Because these are the complications associated with the use of antithyroid drugs and such reports should be treated as medical emergencies.

KEYWORDS: Drug-induced agranulocytosis, Antithyroid drugs, Carbimazole.

INTRODUCTION

Thyrotoxicosis is a common endocrine disorder. It affects mainly women of child-bearing age (prevalence, approximately 2%),[1] and is approximately five times more common in females than in males. Patients are usually treated with antithyroid drugs, the most common of which is carbimazole. Antithyroid drug therapy, however, is associated with a potentially fatal complication namely, agranulocytosis.[2]

Agranulocytosis is a rare adverse effect of anti-thyroid drugs; the reported incidence being ~0.17%-0.23%.[3,4]Agranulocytosis has been reported with all antithyroid drugs including proplythiouracil, methimazole and carbimazole. Agranulocytosis occurs within first 90 days of starting antithyroid drugs usually but cases occurring even after 1 year of exposure have been reported.

Hyperthyroidism can be associated with various haematological disorders. The prevalence of anaemia among patients with hyperthyroidism ranged from 10 to 15%. Slight leucopenia, neutropenia, and thrombocytopenia are common events in thyrotoxicosis and are usually of an autoimmune origin.[5]

Antithyroid drugs are associated with many complications, of the known complications, antithyroid drug induced agranulocytosis, although rare, is the most severe and life-threatening.[6]

The incidence of this particular side effect has been reported to range from 0.3% to 0.6%.[7]Although antithyroid drug-induced agranulocytosis is rare, it has been associated with a mortality rate of 21.5%.[8]

CASE PRESENTATION

A 38years old female was a known case of Hyper-thyroidism was admitted in General Medicine department presented with chief complaints of generalised weakness, sore throat, abdominal distension and shortness of breath since 4 days.

Physical Examination

On examination, Patient was found to be conscious & drowsy, and was found to be Obese. Pulse Rate 72/min, Heart- $S_{1+,}S_{2+}$ with irregular rhythm, lungs clear and abdominal examination revealed no abnormalities. Blood pressure: 80/60mm Hg was found to be low.

Past History

On her Past medical history she was known to be hypertensive and with type-2 Diabetes mellitus since 5 years and a case of Hyper-thyroidism since 1 year. Past medication history revealed use of Tab.Carbimazole 10mg/POTID since 1 year.

Social history revealed that she is a moderate toddy consumer and have any no abusive habits of pan masala and tobacco or gutkha chewing.

Laboratory Investigations

General Random Blood Sugar: 149gm/dl (80-120 mg/dl) Blood Urea Nitrogen (BUN):56mg % (7- 20mg/dl). Complete blood picture (CBP) revealed low, Haemoglobin: 10gms% (12-16gms %), RBC: 3.2Cells/µmm (4.2-5.4millioncells/µmm) WBC: 3,800Cells/µmm, (5000-10000/mm^3) Polymorphs:38%(40-75%), Lymphocytes: 58%(20-40), Eosinophil: 3%(1-4%), Monocytes: 1%(2-10%), Thyroid test:T_3:0.54ng/ml(0.6-1.81ng/ml), T_4:10.70µg/dl (4.5-10.9µg/dl),TSH:1.19µIU/ml (0.35- 5.5µIu/ml).

The provisional diagnosis was made as Carbimazole induced hypothyroidism with morbid obesity with obstructive sleep apnoea (OSA). Then the final diagnosis was made as metabolic syndrome (hyperthyroidism with OSA) DM and HTN.

Treatment

Initially symptomatic treatment has been started; Tab.Carbimazole has been stopped because which has been lead to this condition. Inj.Ceftriaxone 1gm/IV/BD, Tab.Pantoprazole 40mg/OD, Tab.B Complex OD, Syp.Gutclear (lactitol monohydrate) 20ml/H/S Syp.Cremaffin (paraffin) 10ml/PO/TID, Tab.Telmasartan 40mg BD, Tab. Glycomet GP (Glimepiride+ Metformin) with IV fluids for 5 days.

Finally patient was discharged with the decreased dose of Tab.Carbimazole10mg/OD from thrice a day to once a day, with Tab.Telmasartan 40mg/OD, Tab. Glycomet GP (Glimepiride+Metformin) BD and Tab. Beplex fort (vitaminB supplement).

DISCUSSION

Profound reductions in granulocytes and a neutrophil count of less than $0.5x10^9$ per litre indicate agranulocytosis. Drug-induced agranulocytosis can be caused by direct marrow toxicity or be immune mediated. The antithyroid drugs carbimazole (Neo-Mercazole) and propylthiouracil carry a relatively high risk of haematological dysfunctions including agranulocytosis.[9] Because the occurrence of antithyroid-drug induced agranulocytosis is sudden and explosive, it is potentially fatal It is reasonable to obtain a baseline leukocyte count before initiation of antithyroid drug therapy. When therapy is begun the patient should be instructed to notify the physician immediately if fever or sore throat develops and the leukocyte count must be checked. Discontinuation of the offending antithyroid drugs should be considered when the leukocyte count falls below 1500×10^6/l.[4]

Females and those aged over 65 may have an increased risk. Although some have argued for routine blood monitoring, the balance of opinion is that monitoring is not considered worthwhile due to the rapid onset of the adverse effect that monitoring would not capture. Recurrence of agranulocytosis has also been reported when switching from Carbimazole to Propylthiouracil.[10]

CONCLUSION

Approximately half the fatalities caused by Carbimazole and Propylthiouracil reported as agranulocytosis and neutropenia. Patients taking antithyroid drugs should be told to notify their doctor at once if they experience fever, a sore throat, mouth ulcers, bruising, malaise or nonspecific illness.

Because these are the complications associated with the use of antithyroid drugs and such reports should be treated as medical emergencies, as in this patient agranulocytosis is also associated with hypothyroidism due to chronic use of high dose Carbimazole; which is a rare reported condition.

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