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A CASE REPORT ON CARBIMAZOLE INDUCED AGRANULOCYTOSIS

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ABSTRACT

Drug induced agranulocytosis is encountered in patients on anti-thyroid medications, ranging from mild forms to life threatening situations. Expeditious discontinuation of the offending drugs helps to resolve agranulocytosis. Various parametric values are evaluated to monitor the side effects of Carbimazole. One main parameter includes the evaluation of TLC (Total Leukocyte Count). In this case report we are going to emphasize carbimazole induced agranulocytosis. Clinicians should be extremely conscious about such events and complete blood count monitoring helps to circumvent such situations.

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INTRODUCTION

Hyperthyroidism is a pathophysiological state of the endocrinology system in which overproduction of thyroid hormones occurs. Hyperthyroidism can be treated by using anti thyroid drugs, radioactive iodine or by subtotal thyroidectomy. Anti-thyroid drugs are one of the predominant therapies which includes thioamides such as propylthiouracil, methimazole and carbimazole. Carbimazole is a prodrug which gets rapidly converted to its active form methimazole, which inhibits the thyroid peroxidase enzyme, thereby exerting the anti- thyroid action. Initial dose ranges from 10 to 20mg. Major side effects include agranulocytosis (<1.5%), SLE(Systemic Lupus Erythematosus) like syndrome, hepatotoxicity etc. Various blood values are investigated to evaluate the agranulocytosis caused by Carbimazole. The Total Leukocyte Count initially reduced drastically and over time under hospital evaluation, the offending drug was identified on reconciliation and discontinued, subsequently the values began to rise and came back to normal state. Thus in view of any major side effects, the drug should be withheld and should not be restarted in such patients.

CASE REPORT

A 62 year old female patient with a history of Hyperthyroidism diagnosed 5 months ago was on Tab. Neomercazole (Carbimazole) 15mg once daily, presented with complaints of sore throat, generalized tiredness, giddiness and rhinorrhea for one week. She was also a known case of Systemic Hypertension, Dyslipidemia for 2 years and Allergic Rhinitis for the past 20 years. She had a history of recent admission to the Emergency Department for the above mentioned complaints along with mild productive cough with white sputum, which was symptomatically managed and discharged with advice to review with blood reports. The blood reports showed that total leukocyte count was below the normal range with neutropenia and lymphocytosis. The reports of laboratory investigations is shown in Table 1. Direct Coomb's test and Dengue test were negative. Serum cortisol and thyroid hormones were in the normal range. HbA1C was 6.2%. Considering the possibility for Carbimazole induced agranulocytosis, the offending drug was stopped and planned for administering GCSF (Granulocyte Colony Stimulating Factor). Since blood counts were improving after discontinuing carbimazole, GCSF was withheld. The patient was symptomatically treated with antihistamines and other supportive measures. Endocrinology consultation was obtained for the further management of Hyperthyroidism and they planned for Iodine ablation therapy after a week. The condition of the patient was improved and discharged with an advice to review after a week with blood reports and the latter shows improvement in blood counts.

Table 1: Laboratory Investigations.

PARAMETER	During hospital stay				On review	REFERENCE RANGE
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 11	
TLC	2300	2500	3200	4000	4500	4000 - 11000/ μ L
Polymorphs	28	32	32	26	38	43 - 72%
Eosinophil	05	05	04	05	04	0 - 4%
Lymphocyte	51	60	60	62	51	20 - 50%
Monocytes	06	03	04	07	07	0 - 10%

DISCUSSION

Anti-thyroid drugs are one of the predominant therapies for hyperthyroidism which includes thioamides such as propylthiouracil, methimazole and Carbimazole. Carbimazole is a prodrug which gets converted to its active form methimazole rapidly. It reduces thyroid hormone synthesis by inhibiting thyroid peroxidase enzymes that catalyse the iodination of tyrosine residues in thyroglobulin and the oxidative coupling of iodinated tyrosine. The conversion of thyroxine to triiodothyronine is also reduced. Typical maintenance dose is 5 to 30 mg/day. [1]

Minor side effects associated with Carbimazole therapy include fever, urticaria and more while reported potential side effects include agranulocytosis and hepatotoxicity. According to projections from various studies, carbimazole induced can occur within the first three months after initiation of therapy and delayed for upto one year in certain cases. Cumulative incidence ranges from 0.3% to 0.6%. [2] Immune mediated mechanism is one of the proposed mechanisms leading to carbimazole induced agranulocytosis. [4,5] Also the possible interaction between the thyroid peroxidase enzyme and myeloperoxidase of neutrophils leads to the formation of reactive metabolites in neutrophils resulting in the formation of modified proteins which act as antigen's contributing to agranulocytosis. [5] According to various evidences, if a patient on an anti-thyroid drug develops with major side effects, the causative drug should be stopped and not restarted. [3,8] Total count returns to normal range within a week after discontinuing the offending drug but may vary upto 56 to 60 days. Recovery of Neutrophil count depends on age, comorbidities, no. of myeloid precursor cells present in the bone marrow and GCSF was found to be beneficial for the same. [3, 6, 7]

CONCLUSION

Carbimazole induced agranulocytosis is one of the major adverse drug reactions which can range from mild forms to even life threatening situations. Carbimazole with its marked potential adverse reactions may cause a variety of co- morbid conditions. Patients on anti- thyroid drugs should be closely monitored and seek consultation from physician if any uneven side effect is observed. Thus clinicians should be cautious of such events and monitor complete blood counts which helps to avoid the same. In case, such reactions occurs, discontinuing the offending drug is of vital importance. Vigilant monitoring and reporting on the adverse effects of anti- thyroid drugs should be continued to circumvent such adverse events in the future.

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CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

ABBREVIATIONS

SLE : Systemic Lupus Erythematosus
TLC : Total Leukocyte Count
GCSF : Granulocyte Colony Stimulating Factor

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