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Carbimazole-induced Agranulocytosis

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ABSTRACT

This is a-46 years-old female was admitted in Qurayyat general hospital with Cardiomyopathy and Hyperthyroidism, was put on Carbimazole 60 mg orally daily.

Background: *Hyperthyroidism four weeks back on Carbimazole 60 mg orally daily.*

Presentation: *This patient presented with few days of palpitation and general fatigue, found have Cardiomyopathy, with severe neutropenia (Agranulocytosis), managed by cardiac team for Cardiomyopathy, with internal medicine team for her neutropenia. Carbimazole was stopped immediately. Started on Filgrastim a Granulocyte colony-stimulating factor (G-CSF) 300 mcg SC daily, with neutropenic antibiotic coverage and application of isolation precautions. But there was no response to Filgrastim initially. However, after 7 days of administering Filgrastim, WBC with neutrophil started to recover and increase in number, returned to normal range on day 9 of treatment, so Filgrastim was stopped. However, WBC and Neutrophil showed rebound increase in the next three days until reached 50.600/ cmm, and then returned again to normal range on day 13.*

Her cardiac condition stabilized on cardiac medication.

Conclusion: *Carbimazole is used to treat hyperthyroidism; however, Agranulocytosis is a rare but potentially life-threatening side effect occurs during the first few months of treatment. If patients develop symptoms such as fever or a sore throat, blood tests should be performed immediately, and Carbimazole should be discontinued if Agranulocytosis is suspected.*

Keywords

Carbimazole, Induced, Antithyroid, Agranulocytosis, Hyperthyroidism, Filgrastim.

Abbreviations

AIA: Antithyroid drug-induced Agranulocytosis; ALC: Absolute Lymphocyte Count; ANC: Absolute Neutrophil Count; ATD: Antithyroid Drugs; ATT: Antithyroid Therapy; BID: Two times a day; CBC: Complete Blood Count; cm: centimeter; cmm: cubic millimeter; CNS: Central Nervous System; CVS: Cardio Vascular System; ECG: Electro Cardio Gram; g/dL: gram/decilitre; FDA: Food and Drug Administration; G-CSF: Granulocyte Colony-Stimulating Factor; GD: Grave's disease; Hb: Hemoglobin; HLA: Human Leukocyte Antigen; HLA DRB1: Human Leukocyte Antigen class I Beta chain; LFT: Liver Function Test; mcg: microgram; mm: millimeter; µL: microliter; OD: Once Daily; pmol/L: Picomole/ liter; PLT: Platelet; PO: Per Oral; RAI: Radioactive Iodine; RBC: Red Blood Cell; RFT: Renal Function Test; SC: Subcutaneous; S1: first heart sound; S2: second heart sound; TFT: Thyroid Function Test; TI-RADS: Thyroid Imaging

Reporting and Data System; TP: Total protein; TSH: Thyroid Stimulating Hormone; WBC: White Blood Cell; WNL: Within Normal Limits.

Introduction

Carbimazole is a pro-drug used to treat patients with Hyperthyroidism through conversion to its active metabolite form (Methimazole). It may take four to eight weeks for symptoms to completely resolve, and typical maintenance dose ranges from 5 to 30 mg/day. Patients on higher doses of Carbimazole (> 30 mg/day) for more than two months and aged > 40 years are at risk of developing Agranulocytosis [1].

The incidence of this Carbimazole-induced Agranulocytosis has been reported to range from 0.3% to 0.6% and is associated with a very high mortality rate of up to 21.5% [1,2].

Some studies showed that Agranulocytosis from Carbimazole occurs in patients usually in the first two to three months, and it usually happens in patients on higher doses. Other study has reported the incidence of Agranulocytosis from Carbimazole up to a year after the initiation of the therapy [1]. The incidence of Agranulocytosis was 6.4 times higher in patients aged > 40, although few cases have also been reported in younger patients [1].

The common clinical features of Carbimazole-induced Agranulocytosis include fever (92%), sore throat (85%), painful mouth ulcer (15%), ulcer (8%), and reduced immune response making individuals prone to infections [1] [3]. More serious presentations are severe deep tissue infections, septicemia, and septic shock [3]. Agranulocytosis and hepatotoxicity are two very rare but life-threatening side effects of Antithyroid therapy (ATT). Signs may vary, and the most common signs in patients with Agranulocytosis include ulcerative changes in the upper respiratory tract mucous membranes, ulcerative-necrotic tonsillitis, gastrointestinal side effects, fever, regional lymphadenopathy, and fungal infections [1].

Minor side effects of Antithyroid drugs like, skin rash, fever, and arthralgia occur in up to 5% of patients. These usually resolve spontaneously or after stopping and substituting with an alternative Antithyroid drugs (ATD) [3].
Other Rare but serious and life-threatening side effects of Antithyroid drugs include Hepatitis, and Vasculitis, which occur in 0.2–0.3% of adult patients taking ATDs [3].

Agranulocytosis defined as absolute neutrophil count < 500/mm^3) [3].

Patients with a neutrophil count less than 100/μL have a greater risk of serious infectious and fatal complications than do patients with a higher neutrophil count. In our case, her initial granulocyte count was 30/μL which in addition to her age put her in the high-risk category for serious deep tissue infections and death [3].

The pathogenesis of Agranulocytosis is not completely understood. Immunologically mediated responses and direct toxicity were postulated. A specific polymorphism in human leukocyte antigen (HLA) genes has been associated with ATD-induced Agranulocytosis. For example, HLA-B*27:05, HLA-B*38:02, and HLA-DRB1*08:03 alleles increase susceptibility to ATD-induced Agranulocytosis [3].

The leukocyte count usually starts to normalize within 1–2 weeks of drug discontinuation, if there are enough myeloid precursor cells present in the bone marrow; however, with granulocyte precursor aplasia, a prolonged recovery is expected [3]. The mean recovery time in patients with G-CSF therapy is 6.8 days. After recovery from Agranulocytosis, prescribing alternative ATD should be avoided due to common cross-reactions among Thionamides [3]. Treatment of ATD-induced Agranulocytosis by G-CSF has been reported to decrease the mortality rate from 21.5 to 5% [3].

Hyperthyroidism is a condition resulting from the excessive production of thyroid hormones. Graves' disease and toxic multinodular goiter are the most common causes. The initial treatment of hyperthyroidism is with the Antithyroid drug Carbimazole or its active metabolite Methimazole, while for Propylthiouracil, Food and Drug Administration (FDA) have limited its use to the first trimester of pregnancy, and the thyroid storm, due to risk of hepatotoxicity [3].

Literature Review

- **Carbimazole-Induced Agranulocytosis in a Previously Stable Patient: A Case Report and Literature Review [1].**

A 48-year-old female patient with a history of Hyperthyroidism for several years presented with generalized fatigue and chest pain associated with palpitations; the patient was stable on Carbimazole therapy. She was previously on Carbimazole 15 mg once daily (OD) and, three months later, was reduced to 10 mg PO OD as symptoms were controlled. She was taking propranolol, and it was stopped as she was not having any palpitations. This time, however, she presented mainly with palpitations at night associated with chest pain and generalized fatigue on-going for the last one week. Her laboratory results showed Agranulocytosis with reduced white cell count and neutrophil count in the absence of any evidence of infection. Her Carbimazole was stopped, and the patient was referred to ear, nose, and throat surgeons for consideration of thyroidectomy. The patient underwent subtotal thyroidectomy, and her symptoms resolved following surgery.

- **A Lethal Case of Severe Carbimazole-Induced Agranulocytosis [2]**

A 70-year-old female with newly diagnosed Hyperthyroidism (baseline TSH: 0.002 m IU/L, free T4: 58 pmol/L) was initiated on Carbimazole 30 mg once daily at a health clinic. After approximately one month on Carbimazole, she developed fever, sore throat, and multiple oral ulcers. On examination, she exhibited a spiking temperature of 39.4°C, injected throat, and multiple oral ulcers over the hard palate, tongue, and lower lip, and a diffuse goitre. She had leucopoenia with total white blood cell count of 1.0, with immeasurable absolute neutrophil count (ANC) and no blast cells.

Repeat TSH was 0.003 m IU/L and fT4 was 39.55 pmol/L. Chest radiograph showed consolidation over the right lower lung zone. Initial treatment included intravenous Piperacillin Tazobactam, subcutaneous granulocyte colony-stimulating factor (G-CSF) 300 mcg daily, Cholestyramine, Lugol's iodine, and propranolol. Due to the deterioration in her clinical condition, we promptly escalated her antimicrobials to Meropenem, Micafungin and increased her G-CSF dosing to 300 mcg two times a day. Her ANC remained at 0.01- 0.02 (109 /L). Despite treatment escalation, she succumbed to severe sepsis after 8 days of admission.

- **Agranulocytosis: a rare complication of the Thionamides [3].**

A 66-year-old female 3 months back was diagnosed with Hyperthyroidism. She was started on Methimazole 30 mg/day and a beta-blocker for symptom management, prescribed by an endocrinologist in her city.

Two months later, her Methimazole dose was increased to 60 mg/day, because of a persistent symptom. One month later, she presented to her local doctor with fatigability, fever, headache, and sore throat. Azithromycin was prescribed with no improvement. Her CBC showed neutropenia. She was advised to stop ATD and referred to the endocrine department, at the university hospital.

Laboratory tests showed microcytic hypochromic Anemia. Her hemoglobin was 9.13 g/dL (reference range, 12–18 g/dL), and platelet count was $214 \times 103/\mu L$ (reference range, $150–350 \times 10^3/\mu L$). Total leukocyte count was $1.14 \times 10^3/\mu L$ (reference range, $4–9 \times 10^3/\mu L$), and the absolute neutrophil count was $0.03 \times 10^3/\mu L$ (reference range, $1.10–7.0 \times 10^3/\mu L$). Differential showed the following: 2.99% neutrophils, 93.21% lymphocytes, 0.00% monocytes, 3.35% eosinophils, and 0.45% basophils.

Thyroid ultrasound examination showed a hypoechoic round nodule 11 mm × 12 mm × 14 mm in the left thyroid lobe and a cystic lesion in the right thyroid lobe measuring 3 mm × 3 mm × 4 mm.

The patient was diagnosed with Methimazole-induced Agranulocytosis. Methimazole was discontinued immediately, and the patient was admitted to the hospital, in an isolation room, and started empirically on an intravenous broad-spectrum antibiotic (4th-generation parenteral cephalosporin) Cefepime 2-g q8h. On the 4th admission day, she was started subcutaneous Filgrastim (G-CSF) 300 µg once daily for 3 days. On day 11, her total leukocyte count was 4.91 $10^3/\mu L$, and differential count was as follows: neutrophils 1.55 (31.56%), lymphocytes 2.54 (51.7%), monocytes 0.74 (15.16%), eosinophils 0.0 (0.0%), and basophils 0.08 (1.58%). On day 12, she was discharged on her medication and beta-blockers.

- **Severe Neutropenia Due to Carbimazole and the Importance of Early Recognition and Management [4].**

This is a-51year-old female patient who was recently diagnosed with Graves' disease, Hyperthyroidism and started on Carbimazole 40 mg daily and propranolol. After 4-5 weeks of treatment, she developed a fever, sore throat, and fatigue. A routine blood test ordered revealed severe neutropenia, consistent with Agranulocytosis. Carbimazole was immediately discontinued, and she was treated with broad-spectrum antibiotics and granulocyte colony-stimulating factor (G-CSF), leading to a gradual recovery.

A diagnosis of Carbimazole-induced neutropenia was made, Carbimazole was discontinued, and the patient was started on granulocyte colony-stimulating factor (G-CSF).

The patient was treated with intravenous broad-spectrum antibiotics (teicoplanin, metronidazole, and gentamicin) due to the risk of neutropenic sepsis, her neutrophil count improved, and she became afebrile. She was discharged on oral antibiotics with endocrinology follow-up for the definitive management of her hyperthyroidism.

- **A Case Report of Carbimazole Induced Agranulocytosis [5]**

This is a-52-year-old female, was admitted with complaints of painful swelling in the scalp, neck and right hand. She was hyperthyroid and taking Neomercazole 10 mg twice daily. Laboratory examination showed the possibility of Carbimazole induced Agranulocytosis. The drug was stopped, and with the treatment she received, her counts gradually showed an improving trend and she was discharged.

Agranulocytosis is the most serious adverse effect of Carbimazole drug therapy and is characterized by fever, malaise, gingivitis, oro-pharyngeal infection, and a granulocyte count less than 250/mm. This drug is concentrated in granulocytes, and this reaction can represent a direct toxic effect rather than hypersensitivity. The toxic effect is higher in patients older than age 40 years receiving a Methimazole dose greater than 40 mg/day and is linked to HLA class II genes containing the DRB1*08032 allele. Agranulocytosis almost always develops in the first 3 months of therapy. Once Antithyroid drugs are discontinued, clinical improvement is seen over several days to weeks.

- **A case of Graves' disease with Agranulocytosis secondary to Carbimazole [6].**

A 39-year-old female was referred to the emergency department with a sore throat, fever, myalgia and odynophagia. She had presented to her physician three months previously with palpitations, erratic mood and fatigue and had been diagnosed with hyperthyroidism. She had been started on Carbimazole 20 mg OD and was awaiting review in endocrinology OPD. She had no other past medical history and was a non-smoker. On examination she was tachycardic with a heart rate of 113. She had cervical lymphadenopathy and oropharyngeal exam revealed tonsillitis with exudate. Laboratory work up showed neutropenia with a total white cell count of 0.8 (ref 4-11 x 10^9/l) and neutrophils of <0.1 (ref 2-7.5 x 10^9/l). Her thyroid function tests had improved with a TSH of <0.05mU/L (ref 0.3-4.2mUl) and free thyroxin of 13.6 pmol/l (ref 12-22 pmol/l) which had been 66.8 pmol/l three months prior. TSH receptor antibody was positive-

14.4IU/l (ref <1.8IU/l). She was diagnosed with neutropenic sepsis and Agranulocytosis secondary to Carbimazole. She was treated with antibiotics and granulocyte colony stimulating factor (G-CSF) 30mu once daily as per haematology advice. Thyroid ultrasound showed 'diffuse thyroid enlargement with increased vascularity in keeping with thyroiditis' and technetium 99m pertechnetate scan showed 'high uptake of radionuclide in both lobes, appearances suggest graves'. Her white cell count returned to normal and GCSF was stopped after 6 days. Her thyroid function tests deteriorated while she was off Carbimazole: She was commenced on lithium 200 mg BID and discharged home with close outpatient follow up to monitor thyroid function tests and lithium levels. Unfortunately, she did not attend her follow up appointments and was poorly compliant with lithium therapy. When she engaged with the service again, she had clinical and biochemical evidence of thyrotoxicosis with a free thyroxin of 80 pmol/l and evidence of thyroid eye disease with left eye proptosis, lid retraction and exophthalmos and mild right eye proptosis. Lithium therapy was restarted and a plan was made for definitive therapy. Surgery was preferred over radioactive iodine treatment given the presence of thyroid eye disease and the patient's plans for pregnancy in the near future. She was electively admitted prior to surgery for treatment with lugol's iodine and close monitoring of thyroid function tests. She ultimately had a successful thyroidectomy and is now well on thyroxin replacement therapy.

- **Therapeutic Management and Long-Term Outcome of Hyperthyroidism in Patients with Antithyroid-Induced Agranulocytosis: A Retrospective, Multicenter Study [7].**

Background: Antithyroid drug-induced Agranulocytosis (AIA) (neutrophils <500/μL) is a rare but serious complication in the treatment of hyperthyroidism. Methodology: Adult patients with AIA who were followed up at 12 hospitals in Spain were retrospectively studied. A total of 29 patients were studied. The etiology of hyperthyroidism was distributed as follows: Graves' disease (n = 21), Amiodarone-induced thyrotoxicosis (n = 7), and hyperfunctioning multinodular goiter (n = 1). Twenty-one patients were treated with Methimazole, as well as six patients with Carbimazole and two patients with Propylthiouracil. Results: The median (IQR) time to development of agranulocytosis was 6.0 (4.0–11.5) weeks. The most common presenting sign was fever accompanied by odynophagia. All of the patients required admission, reverse isolation, and broad-spectrum antibiotics; moreover, G-CSF was administered to 26 patients (89.7%). Twenty-one patients received definitive treatment, thirteen patients received surgery, nine patients received radioiodine, and one of the patients required both treatments. Spontaneous normalization of thyroid hormone values occurred in six patients (four patients with Amiodarone-induced thyrotoxicosis and two patients with Graves' disease), and two patients died of septic shock secondary to AIA. Conclusions: AIA is a potentially lethal complication that usually appears around 6 weeks after the initiation of Antithyroid therapy. Multiple drugs are required to control hyperthyroidism before definitive treatment; additionally, in a significant percentage of patients (mainly in those treated with Amiodarone), hyperthyroidism resolved spontaneously.

- **A case of severe Agranulocytosis induced by Carbimazole in a patient with graves' disease requiring thyroidectomy [8]**

This is a 74-year-old lady with a background of rheumatoid arthritis and Felty's syndrome was diagnosed as having Grave's Thyrotoxicosis few months back. She was commenced on Carbimazole. She had repeat blood tests which showed neutropenia. The levels of neutrophils were 0.01 and WCC was 0.4. She was otherwise asymptomatic, her weight had been stable and there were no concerns regarding any infection. Rest of her infectious screen including blood cultures, Respiratory screening and COVID were all negative. The cause of the neutropenia was Carbimazole. She was also on Hydroxychloroquine due to her Rheumatoid Arthritis which was stopped along with Carbimazole. After stopping her Carbimazole, her T4 started rising and it was 45 at one point. In order to maintain euthyroidism she was started on Lugol's iodine, potassium iodide, propranolol and Cholestyramine. These medications were not initiated all at once but were introduced gradually over time. She also developed AF due to her hyperthyroidism and needed anticoagulation. She was also given Filgrastim to help with the levels of neutrophils. Her thyroid functions improved, and she was transferred for total thyroidectomy. She had successful thyroidectomy done and was started on Levothyroxine. Previous studies have demonstrated that risk of developing Agranulocytosis is higher in the first two to three months and patients aged >40. This was the classical case where she was in her 70s and recently diagnosed as having Grave's disease. It is important to recognize the medications as a cause of neutropenia and also to look for any effects of neutropenia experienced such as infections.

- **Case Report: Agranulocytosis as a Side-Effect of Carbimazole [9].**

A 40-year-old female presented to the Endocrinology Outpatient Department after being referred by her general practitioner with a diagnosis of Grave's disease (GD). Her initial thyroid-stimulating hormone (TSH) level was <0.01 (0.27–4.2 mIU/L) and her free thyroxin (fT4) was >100 (12–22 pmol/L). TSH receptor antibody levels were elevated with a titre of 8.84 (0.27–4.20 U/L). She was initiated on Carbimazole at a dose of 20 mg orally three times daily. At the1 month follow-up visit, clinical and biochemical improvement was observed, and her fT4 levels had decreased to 27.9 pmol/L. The dose of Carbimazole was reduced to 20 mg once daily. Ten days later she presented to the Emergency Department with a fever, sweating and vomiting. There was pyrexia, tachycardic, diaphoresis and tremulous. Given her history of GD, she was clinically assessed to be thyrotoxic and thus treated with Carbimazole while awaiting further laboratory investigations. Laboratory investigations revealed a severe neutropenia, and the working diagnosis was revised to that of neutropenic sepsis. Her white cell count was 1.81 × 109 /L (3.9– 12.6 × 109 /L) with an absolute neutrophil count (ANC) of 0.05 × 109 /L. Other parameters of the full blood count showed a haemoglobin level within normal limits and an elevated platelet count of 675 × 109/L (186–454 × 109/L). Carbimazole was thought to be the most likely agent to cause Agranulocytosis, and the patient was managed

with neutropenic measures, which included isolation, infection control and empiric antibiotics. Despite an extensive work-up for the source of infection, none was identified. Carbimazole was immediately discontinued, and the patient was started on granulocyte-colony stimulating factor (G-CSF). A bone marrow aspirate and trephine was performed and revealed a hypocellular bone marrow with markedly under-represented granulopoiesis. Erythropoiesis and megakaryopoiesis was adequately represented. Following 4 days of withdrawal of Carbimazole and treatment with G-CSF, her ANC had returned to within-normal limits She was referred for definitive thyroid therapy, specifically radioactive iodine (RAI) of the thyroid gland.

Carbimazole Monitoring [10]

- Before starting; required:
  Baseline Free T, Free T4, Full blood count including white cell count (WCC), Thyroid stimulating hormone, Liver function tests, White blood cell differential.
- Continued until stable; required every 6 weeks:
  Free T3 continued until TSH in reference range, Free T4 · continued until TSH in reference range
  Thyroid stimulating hormone · continued until TSH in reference range
- Consider periodically; Full blood count · including white cell count and differential, if clinical suspicion of Agranulocytosis, Liver function tests if clinical suspicion of liver dysfunction
- On-going once stable; required
  Every 3 months: Thyroid stimulating hormone
- Consider; periodically: Free T3 · if TSH below reference range, Free T4 · if TSH above reference range. Creatine phosphokinase · if patient experiencing myalgia. Full blood count · in patients who may be confused or have poor memory.

Current Case Presentation

Situation: This is a-46 years-old female was admitted in Qurayyat general hospital with Cardiomyopathy and recent diagnosis of Hyperthyroidism four weeks back, was put on Carbimazole 60 mg orally daily.

Background: Hyperthyroidism four weeks back, on Carbimazole 60 mg orally daily.

Assessment: conscious, oriented. Abdomen: soft, lax, Chest: clear, CVS: S1, S2,0 tachycardia, CNS: WNL, Lower limbs: no edema. Normal vital signs. ECG: sinus tachycardia

Brief Radiology Findings: Chest x-ray: mild cardiomegaly

Thyroid Ultrasound: Diffusely enlarged thyroid gland mainly in left side. Right lobe measuring 1.6x1.6x4.6 cm. Left lobe measuring 2x2.2x5.2cm. Isthmus is 1 cm.

Multiple solid & cycstic nodules in both lobes more in left. In right lobe largest on in lower pole measuring around 1x1cm & largest one in left seen in middle third measuring 2 x 0.7cm.

The described largest ones are mostly heterogeneous / iso to hyper echoic with suspicious of macro calcifications, picture mostly coming with TI-RADS 3 to 4. One small nodule in left lobe around 05 x 0.5 cm with mural calcification. No clear retrosternal extension seen.

Prominent cervical lymph nodes, however looked benign with fatty hilum.

Laboratory investigations:

CBC: see next, RFT: WNL, LFT: WNL, TFT: WNL, TP: WNL, Albumin: WNL

Series of laboratory investigations for CBC samples are demonstrated in the following table (Table 1):

The patient found to have severe neutropenia (Agranulocytosis) on admission, her Carbimazole was stopped immediately. Started on Filgrastim (Granulocyte colony-stimulating factor) 300 mcg SC daily, with neutropenic antibiotic coverage by Piperacillin & Tazobactam and Vancomycin with application of isolation precautions. But there was no response to Filgrastim initially.

Table 1: Series of laboratory investigations for CBC samples.

No.	WBC	Neutrophil %	ANC	Lymphocyte%	ALC	Hb	PLT	1st Blood film
1st	2.67	13.90	0.371	76.8	2.055	10.3	188	RBC: Hypochromic microcytic WBC: Neutropenia, no abnormal cells PLT: Normal
2nd	2.32	0.80	0.02	88.80	2.06	10.4	223	
3rd	2.96	0.40	0.01	86.10	2.55	10.6	202	
4th	0.72	1.40	0.01	91.70	0.66	10.9	231	
5th	0.94	1	0.01	94.70	0.89	11.5	287	
6th	0.85	1.2	0.01	94.10	0.80	11.8	137	
7th	0.48	0	0.01	97.2	0.86	10.7	290	2nd Blood film
8th	0.47	0	0.01	98.1	0.87	10.7	212	RBC: Hypochromic microcytic WBC: Reduced on film, neutrophils are significantly reduced with relative lymphocytosis and normal morphology PLT: adequate in number and morphology
9th	0.46	2.2	0.01	82.60	0.38	10.5	239	
10th	2.34	22.60	0.53	51.30	1.20	11.2	256	
11th	10.09	61.70	6.22	16.90	1.71	10.5	249	
12th	44.03	82.90	36.52	3.52	1.71	10.5	277	
13th	50.60	82.20	41.59	10.10	5.12	10.5	251	
14th	26,69	81.30	23.8	13.10	3.12	10.7	197	
15th	19.77	76.10	15.04	16.70	3.31	10.3	182	
16th	8.65	65.6	23.6	23.90	2.05	10.2	177	

However, after 7 days of administering Filgrastim, WBC with neutrophil started to recover and increase, returned to normal range on day 9 of treatment, so Filgrastim was stopped. But WBC and Neutrophil showed rebound increase in number in the next three days until reached 50.600/cmm, and then returned again to normal on day 13th after starting with Filgrastim

Discussion

Carbimazole is a pro-drug that gets converted to its active metabolite (Methimazole) used for the treatment of Hyperthyroidism alone or in combination with other medications. mild Leukopenia to severe complications such as Agranulocytosis and, in rare cases, Aplastic Anemia. Agranulocytosis and hepatotoxicity are two very rare but life-threatening side effects of Antithyroid therapy (ATT). The common clinical features of Carbimazole-induced Agranulocytosis include fever (92%), sore throat (85%), painful mouth ulcer (15%), ulcer (8%), and reduced immune response making individuals prone to infections. Signs may vary, and the most common signs in patients with Agranulocytosis include ulcerative changes in the upper respiratory tract mucous membranes, ulcerative-necrotic tonsillitis, gastrointestinal side effects, fever, regional lymphadenopathy, and fungal infections [1].

Antithyroid drugs (ATDs), particularly Propylthiouracil and Carbimazole, can cause hematological effects such as mild Leukopenia, Agranulocytosis, and Aplastic Anemia, although the reported incidence is rare. These effects can result from direct toxic effects of the medications and immunological reactions, and ATDs affect oxygen and glucose utilization in cells through oxidized metabolites after penetrating the bone marrow. It may take two to eight weeks for the Agranulocytosis to appear in patients after being started on ATD. The WBC can return to normal in patients over one to two weeks' time period after discontinuation of the offending medication, but it can take up to one to eight weeks sometimes [1].

Carbimazole-induced Agranulocytosis has an incidence of approximately 0.3-0.6% with a mortality rate of 21.5%. Studies indicate that the risk of Agranulocytosis is significantly increased in patients receiving Methimazole doses ≥30 mg/day, particularly in individuals over the age of 40.

Hyperthyroidism is a common endocrine disorder, with a higher prevalence in women (1-2%) compared to men (0.1-0.2%). While ATDs remain the first-line treatment, research suggests that Carbimazole-induced Agranulocytosis typically manifests within the first two to three months of therapy especially in patients receiving higher doses. Given the serious nature of this complication, it is imperative for clinicians to educate patients on recognizing early warning signs, such as fever and sore throat, which may indicate neutropenia or Agranulocytosis.

The precise pathophysiology of ATD-induced Agranulocytosis remains incompletely understood, although several immunological mechanisms have been proposed. One hypothesis suggests that antibodies form against the drug when it binds to granulocyte cell membranes, leading to accelerated neutrophil destruction. Another theory proposes that antibodies target a drug-metabolite complex adsorbed onto neutrophil granulocytes, triggering autoimmune destruction. Additionally, ATDs may stimulate the production of autoantibodies, or an interaction between a granulocyte antigen and the drug may induce an immune response, resulting in neutropenia.

The clinical presentation of Agranulocytosis varies, but the most commonly observed signs include ulcerative lesions of the upper respiratory tract mucosa, ulcerative-necrotic tonsillitis, gastrointestinal symptoms, fever, regional lymphadenopathy, and opportunistic infections such as fungal infections. If a patient on ATDs develops these symptoms, immediate discontinuation of the drug is essential, along with a full blood count assessment to evaluate neutrophil levels. In cases where neutropenic sepsis is suspected, prompt initiation of broad-spectrum antibiotics is warranted, and the administration of G-CSF should be considered. G-CSF plays a crucial role in stimulating granulocyte proliferation and accelerating neutrophil recovery, thereby reducing the risk of severe infections and complications. Early recognition and intervention are essential for improving patient outcomes and preventing life-threatening consequences. Studies have demonstrated that treating ATD-induced Agranulocytosis with G-CSF can reduce mortality rates from 21.5% to 5%.

The average recovery time in patients receiving G-CSF therapy is approximately 6.8 days. Following recovery from Agranulocytosis, reintroducing an alternative ATD is not recommended due to the high likelihood of cross-reactivity among these medications. For patients who have developed ATD-induced Agranulocytosis, alternative treatment strategies such as radioactive iodine therapy or thyroidectomy are advised to prevent recurrence and provide long-term disease control.

Conclusions

Antithyroid medications, including Carbimazole, are commonly used to treat hyperthyroidism; however, Agranulocytosis is a rare but potentially life-threatening side effect that may occur during the first few months of treatment. Close monitoring and regular follow-ups are crucial in this period to identify any adverse effects. If patients develop symptoms such as fever or a sore throat, blood tests should be performed immediately, and Carbimazole should be discontinued if Agranulocytosis is suspected.

This case report presents a well-structured and clinically relevant discussion of a rare but serious adverse effect of Carbimazole therapy in a patient with Graves' disease. The case highlights the importance of early recognition and prompt discontinuation of the drug, which are crucial to preventing severe complications

Recommendations

1. Patients taking Antithyroid drugs; Thionamides must be instructed to stop taking the medication immediately and contact their physician if they develop sore throat, fever, or malaise. In hospital admission, a broad-spectrum antibiotic is

indicated. G-CSF may hasten the recovery.

2. A complete blood cell count with a differential leukocyte count is recommended before Antithyroid drug therapy is initiated. A transient Agranulocytosis (granulocyte count, < 1500/mm3) can be a manifestation of thyrotoxicosis itself, may occur during the first few weeks of Antithyroid therapy, but can also be a herald of Agranulocytosis. If serial measurements of the WBC count remain constant or return to normal, treatment can be continued. But if the WBC count shows a downward trend, the Antithyroid drug should be stopped.
3. In patients taking Methimazole it is recommended to check blood counts every 2 weeks for the first 2 months of therapy for early detection of granulocytes disorder.
4. Patients who have developed ATD-induced Agranulocytosis, definitive therapy with radioactive iodine or surgery is recommended.

References

1. Zahid Khan, Waleed Afifi, Syed Aun Muhammad, et al. Carbimazole-Induced Agranulocytosis in a Previously Stable Patient: A Case Report and Literature Review. Cureus. 2022; 14: e24115.
2. WY Wan Nur Hidayah, WA Siti Sanaa, MA Masliza Hanuni. A Lethal Case Of Severe Carbimazole-Induced Agranulocytosis. Journal of the ASEAN Federation of Endocrine societies. 2024.
3. Hawa Juma El-Shareif. Agranulocytosis: a rare complication of the Thionmides. The Egyptian Journal of Internal Medicine. 2023; 35.
4. Anup Banerjee, Ahmed Jamil. Eazaz Ali Khan. Severe Neutropenia Due to Carbimazole and the Importance of Early Recognition and Management. Cureus. 2025; 17: e81867.
5. Anns Mariya, Sreenath R, Dona Maria. A Case Report of Carbimazole Induced Agranulocytosis. Indian Journal of Pharmacy Practice. 2023; 16: 262-263.
6. Caoimhe Casey, Anne McGowan. A case of Graves disease with Agranulocytosis secondary to Carbimazole. Endocrine Abstracts. 2023.
7. Carlos García Góme, Elena Navarro, Victoria Alcázar, et al. Therapeutic Management and Long-Term Outcome of Hyperthyroidism in Patients with Antithyroid-Induced Agranulocytosis: A Retrospective, Multicenter Study. J Clin Med. 2023; 12: 6556.
8. Shahzad Akbar, Khurram Qayyuum, Abdelmajid Musa, et al. A case of severe Agranulocytosis induced by Carbimazole in a patient with graves' disease requiring thyroidectomy. Endocrine Abstracts. 2025.
9. Stacey Norsworthy, Frederick Raal, Farzahna Mohamed. Case Report: Agranulocytosis as a Side-Effect of Carbimazole. Wits Journal of Clinical Medicine. 2022; 4: 61-63.
10. Justine Scanlan, Ben Rehman, Helen Davis, et al. Carbimazole monitoring. 2024.