Beware Carbimazole induced Agranulocytosis in Amiodarone Induced thyrotoxicosis: recovery with Filgrastin

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Introduction

Agranulocytosis (granulocyte count < 100 x 10^6/l) is a rare life threatening complication of carbimazole, a thionamide first line therapy for hyperthyroidism. Prevalence is 1/300 patients with greater risk at higher doses and in older patients. Mortality can be 15% with sepsis.

Amiodarone is a 2nd line agent for both intractable atrial fibrillation and malignant ventricular arrhythmias. It may cause thyrotoxicosis in 3-6% of patients depending on their background and iodine intake.

Amiodarone induced thyrotoxicosis (AIT) is classified as Type 1 AIT usually with a previous history of thyroid disease causing hyperthyroidism and is not responsive to steroids. Type 2 AIT is an inflammatory /destructive thyroiditis which is responsive to steroids. Some patients have a mixture of both types called mixed AIT.

High dose carbimazole and prolonged therapy sometimes may be necessary .

We report 2 cases of AIT with agranulocytosis associated with sepsis. Therapy of thyrotoxicosis is challenging.

We describe our experience with the granulocyte stimulating factor Filgrastin.

Case 1

- 63 yr. old male, ischaemic cardiomyopathy
- Amiodarone treatment x 3 years –stopped
- 6 months later hyperthyroidism. No prior history
- Carbimazole 60mgs/day
- 3 months later: sepsis, granulocytes: 100 x 10^6/l
- Tc Scan uptake low
- Treated with antibiotics, Filgrastin
- Granulocyte count 1000x 10^6/ day 9
- Hyperthyroidism managed with low dose propylthiouracil
  + Corticosteroids +
  +short course of potassium perchlorate
- Euthyroid after month 5

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Case 2

- 72 yr. female, atrial fibrillation, diabetes ES renal disease
- Amiodarone x 2 years
- No prior thyroid disease
- Carbimazole 60 mgs/ day
- At 2 months sepsis + granulocytes 100 x 10^6/l
- Antibiotics + Filgrastin
- Granulocytes 1000 x10^6 day 6
- Euthyroid on prednisone at 1month, probable type 2 AID

Discussion

When Sepsis strikes in patients with thyrotoxicosis and cardiomyopathy/atrial fibrillation there is a high risk of thyroid storm.

The options to promptly manage this cause of thyrotoxicosis are limited because high dose antithyroid drug cannot be employed.

Patients are usually not fit for surgery and iodine cannot be administered. Radioiodine may have limited effectiveness and take many weeks to work. Low dose propylthiouracil can be employed but with limited effect . Potassium perchlorate may be of use in AIT Type 1 but probably not in AIT Type 2. Corticosteroids can be used empirically but with caution in the face of sepsis.

The benefits of Granulocyte Colony Stimulating Factor are debated. We chose to use it given the risks in these cases.

Our report raises the need for caution with high dose carbimazole in AIT and we suggest multi- mode therapy early including radioiodine as has been recently suggested.

Take Home Points

- Risk of agranulocytosis may be higher in AIT due to use of high dose carbimazole and age.
- AIT + sepsis risks thyroid storm.
- Caution with high dose Carbimazole advised:

  -Consider multimode AIT therapy early
- Filgrastin may accelerate recovery from agranulocytosis

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Thyroid non-cancer

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