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CASE REPORTOPEN ACCESS

Pancytopenic Thyrotoxicosis: A Management Challenge

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A B S T R A C T

Grave's disease is an autoimmune condition leading to hyperthyroidism which typically presents with a combination of hyperthyroid features. It can lead to a number of haematological alterations and pancytopenia is one such rare complication. The initial management of Grave's primarily resolves around usage of antithyroid drugs like carbimazole. But a common adverse effects of these drugs is marrow suppression. Here we describe a case of Grave's disease who presented with respiratory tract infection and had worsening pancytopenia. Extensive workup failed to identify any explanation for the pancytopenia other than the thyrotoxic state itself. She could not be initiated on antithyroid medications initially and was kept on beta blockers and steroids. GM-CSF analogues like filgastrim and romiplostim were used to bridge the phase of worsening pancytopenia. After resolution of infection and borderline increase in blood counts post therapy with GM-CSF analogues she was started on carbimazole with subsequent radioiodine ablation. Her pancytopenia improved drastically after achievement of euthyroid status. In this case report we highlight the management challenge posed by worsening pancytopenia in a thyrotoxic patient in the clinical backdrop of infection and some therapies which can be used to bridge over this difficult situation.

Keywords: Grave's disease, Hyperthyroidism, pancytopenia, carbimazole, thyrotoxicosis.

INTRODUCTION

Thyrotoxicosis is a clinical state of inappropriately highcirculating thyroid hormones from any cause [1].

Common causes include Graves' disease, toxic multi nodular goitre, toxic adenoma, thyroiditis, excess iodine in diet, overtreated hypothyroidism, pituitarytumors [1].Thyrotoxic state have a wide range of clinical presentations including hematological abnormalities where in single cell lineage disruptions like anemia, leucopenia and thrombocytopenia are common.Thyrotoxicosis induced pancytopenia is a recognized albeit rare complication of Grave's disease [2].

The management of thyrotoxic state involves usage of drugs like beta blockers, steroids and antithyroid agents like carbimazole and propylthiouracil [3].

An important adverse effect of antithyroid drugs which necessitates caution is drug induced pancytopenia or marrow suppression, especially agranulocytosis [7].

The present report deals with a case of Grave's diseasewith concurrent infection where the patient was found to be severely pancytopenic, thus posing a therapeutic hurdle.We describe the problems faced and the strategies adopted to overcome this difficult clinical situation.

Case Presentation

A 60-year-old patientwith no comorbidities presented to the emergency with complaints of fever and cough for 3 days. On enquiry she hadgeneralized weakness andfatigue, difficulty in performing regular household work and a weight loss of around 3 kilos despite normal appetite and diet and had frequent bouts of diarrheafor amonth, associated with intermittentpalpitations.

On examination patient was tachycardic, tachypnoeic, febrile and hadpallor. She had visible thyroid swelling with no palpable nodule .Chest auscultation showed left sided basal coarse crepitations. Neurological examination showed resting tremor,hypertonia andpower was 4/5 in all limbs , deep tendon reflexes were exaggerated with right ankle clonus . Plantar- response was flexor bilaterally and no abnormalities in sensory examination wasfound.No signs of thyroid eye disease or skin changes were found.

With a clinical diagnosis ofthyrotoxicosis, laboratory tests were done which showed very low TSH (<0.01 U) and elevated free T4 and T3. USG of thyroid gland showedbulky thyroid with enlarged left lobe and no definite nodule.

Blood picture revealed pancytopenia(Hemoglobin 7g/dl,total leucocyte 2000/uL and platelet count 80,000/uL) with a normocytic normochromic picture which became a therapeutic challenge since pancytopenia, specially leukopenia is a known adverse effect of antithyroid drugs. She was managed with betablockers initially. Basic blood tests for evaluation of cause of fever including tests for malaria, dengue were negative. Chest X ray showed left lower zone opacities. Hence she was started on antibiotics. She improved symptomatically, but her pancytopenia worsened. Concurrently she was worked up for her pancytopenia. Corrected reticulocyte count was 1.3. Blood iron profile, Vitamin B12 levels, LDH levels were all in normal range. Ferritin was mildly raised.

Her TSHR -antibody and anti -TPO antibody were both positive.A Tc99 thyroid scan showed diffusely increased tracer uptake bilaterally with enlargement of left lobe suggestive of toxic goitre (Figure 1). The diagnosis of Grave's disease was made. Sequential blood counts showed significant decline. Hence antithyroid drugs could not be initiated. After discussion with hematology team, a bone marrow biopsy was done for evaluation of pancytopenia which showedpatchy hypocellular aspirate. For persistent pancytopenia she was given Filgastrim and Romiplostim to improve her blood counts. Her WBC counts slowly improved at a low normal level and based on this antithyroid drug carbimazole was started. She was then discharged and followed up regularly. After 3 weeks of carbimazole therapy, free T4 level reduced from 4.73 to 2.42 ng/dl. Radio iodine ablation was done after a few days of stopping carbimazole. Fifteen days post-Radio iodine ablation patient achieved euthyroid statuswhich permitted stoppage of carbimazole. Her blood counts normalized after restoration of euthyroid status. On follow-up visits she reported resolution of symptoms and a significant increase in subjective wellbeing.

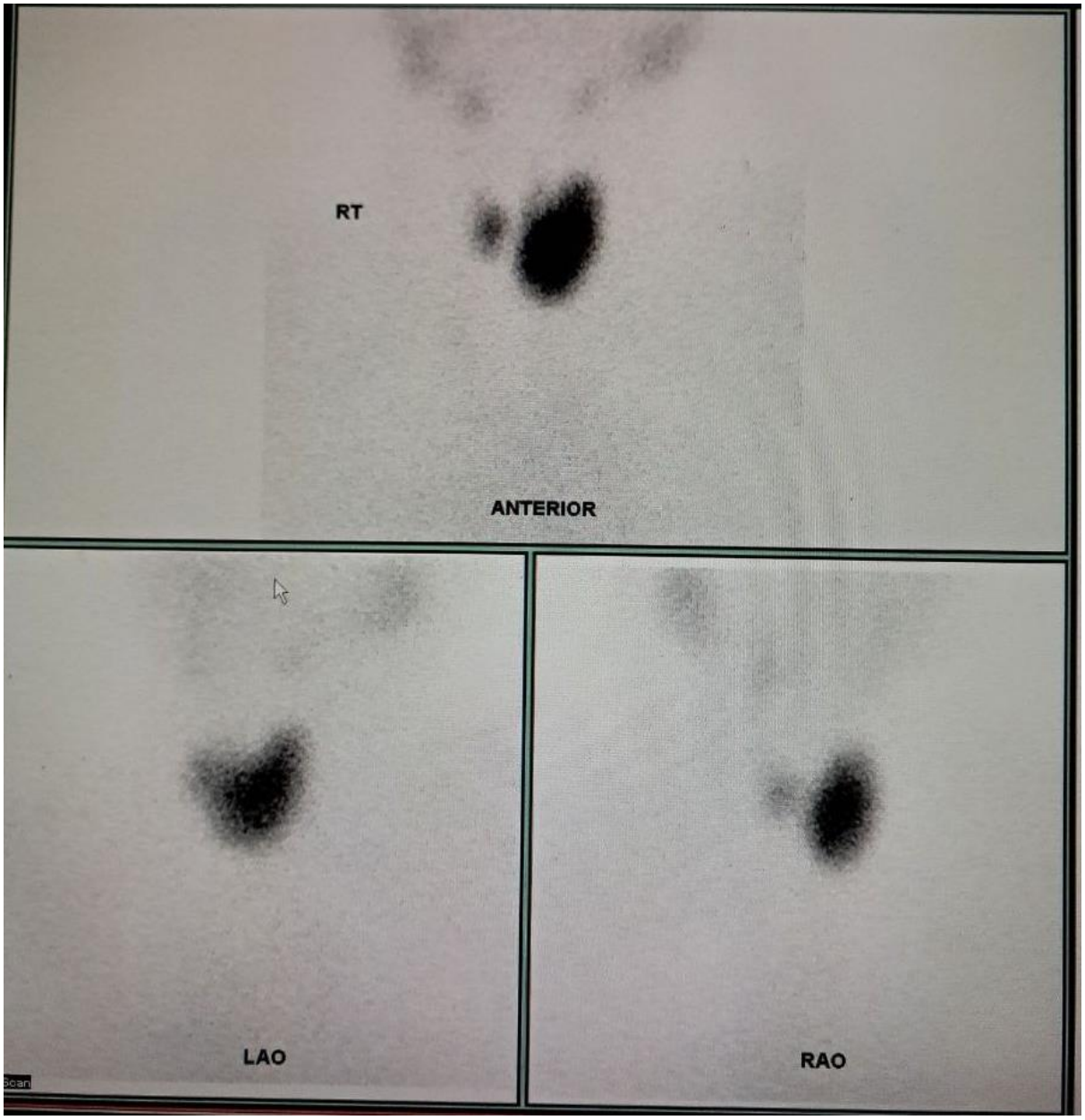

Figure 1: Tc99 thyroid scan showed diffusely increased tracer uptake bilaterally with enlargement of left lobe suggestive of toxic goitre

DISCUSSION

Thyroid hormones impact hematopoietic system in several ways. Although haematological abnormalities are frequently observed in hyperthyroidism, clinically significant ones are rare [5]. Graves' diseaselinked with various single-cell lineagehematological abnormalities, such as anemia, thrombocytopenia, and leukopenia.However, pancytopenia is an exceptionally rare complication of Graves' disease [2]. The underlying pathophysiology behind thyrotoxicosis producing pancytopenia is not fully understood. But there seems to betwo principal pathways: reduced production of hematopoietic cells from the bone marrow and increased destruction or sequestration of mature hematopoietic cells. [6] Thyroid hormones have a stimulating effect on erythropoiesis and excess of thyroid hormones can lead tohyperproliferation of immature erythroid precursors and also cause an increase in secretion of erythropoietin [6].

In our patient who presented with sepsis and subsequently found to have thyrotoxicosis, pancytopenia was noted at the very start of diagnosis. Even after extensive investigation to search for a concurrent cause of pancytopenia, no definite explanation was found. Bone marrow biopsy showed patchy hypocellular aspirate. Hence it was inferred that the possible explanation ofpancytopenic picture wasthyrotoxic state itself.

This clinical context highlights a difficult management challenge as pancytopenia caused by thyrotoxic state hindersusage of antithyroid drugs, since marrow suppression is acommon adverse effect of these agents.

Although pancytopenia without agranulocytosis itself is not a contraindication for starting antithyroid drugs,a cautious approach is neededin initiating antithyroid therapy,keeping in mind the impact ofworseningpancytopenia in the clinical backdrop of concurrent infection.

Hence she was initially managed withbeta blockers and after bone marrow test pancytopenia was corrected with Filgastrim (granulocyte colony stimulating factor) and Romiplostim in close collaboration with endocrinology and hematology teams. Carbimazole was started once there was improvement in blood counts. She was discharged on carbimazole andbeta blocker therapywith close monitoring of WBC counts. Subsequently she underwent Radio-Iodine Ablation.

Several studies have reported thyrotoxicosis as a cause of pancytopenia where the patients were managed with methimazole/carbimazole and subsequent Radio Iodine Ablation treatment [5, 6, 2, 8].

Our study showed that with availability of colony stimulating growth factors, pancytopenia, a rare complication of thyrotoxicosis, can be treatedwith concomitant antithyroid drugs without major adversities which becomes clinically relevant in presence of infection.

Conflict of Interest: No

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