Case report

Thyrotoxicosis presenting with pancytopenia

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Abstract

Thyrotoxicosis can present with a wide array of clinical manifestations, among which pancytopenia is a rare entity. The disease itself, as well the treatment, can result in pancytopenia which makes the diagnosis more difficult and crucial. The mechanisms underlying are poorly understood currently. Antithyroid drugs which are well known to produce cytopenias as a side effect can safely be implemented in the management. Pancytopenia of thyrotoxicosis should completely reverse with the establishment of euthyroid state. We report a rare case of thyrotoxicosis presenting with pancytopenia which completely resolved with antithyroid treatment.

Key words: Thyrotoxicosis, Pancytopenia, Sri Lanka, Rare presentation

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Introduction

Introduction

Pancytopenia is an important common clinical entity with a vast differential diagnosis. It can be due to marrow suppression or peripheral destruction of all three-cell lines. Thyrotoxicosis can rarely present with pancytopenia. The diagnosis and the management is equally challenging as most antithyroid drugs are well known to cause cytopenias as a drug side effect. Thus correct diagnosis; pretreatment proper evaluation and follow up are cornerstones of management. We report a patient presenting with pancytopenia due to thyrotoxicosis which completely resolved with antithyroid treatment and restoration of euthyroid state.

Case report

A 49-year-old previously healthy male presented with loss of weight with tremulousness for six months duration. He also complained of episodic palpitations. He had preserved appetite and normal bowel habits without fever or chronic cough. He complained of mild ankle oedema but there was no orthopnoea or paroxysmal nocturnal dyspnoea. There was no history of drenching night sweats, easy bruising or bleeding manifestations. No history of episodic yellowish discolouration of eyes or body, dark coloured urine or recent febrile illnesses accounting for transient bone marrow suppression. He was not on any long-term medications. On examination he was anxious, thinly built and had fine tremors on both hands with sweaty palms.

On general examination he was pale, afebrile and was anicteric. Mild bilateral pitting ankle oedema was noted. There was no lymphadenopathy or bone tenderness suggesting hematological malignancy. There were no eye signs of Graves' disease such as exophthalmos, proptosis or chemosis. He had no evidence of pretibial myxoedema. Neck examination revealed a multinodular thyroid goiter with bruits. Pulse rate was 140 beats per minute and was irregularly irregular. Blood pressure was 110/60mmHg. Cardiac apex was felt in the fifth intercostals space lateral to mid clavicular line and was thrusting in nature. The other system examinations were unremarkable. Full blood count revealed pancytopenia with WBC 3 × 10^9/L, Haemoglobin 9.6 g/dL and platelets 98 × 10^9/L. Blood picture showed pancytopenia without any evidence of haemolysis or malignancy. Coombs test was negative, TSH was less than 0.15 µIU/L (Normal values 0.4 - 4 µIU/L) and free T4 was above 70 pmol/L (normal values 9-23 pmol/L). Thyroid autoantibodies were not performed due to the lack of resources. ESR was 28 mm/hr (<20mm/hr) and CRP was 9 mg/dl. Corrected calcium level was 2.2 mmol/L (2.2-2.6mmol/L). Blood cultures were negative. Liver and renal profiles were normal. AST was 52 IU/L, ALT 49 IU/L and INR was 1.1. Serum total bilirubin was 18 µmol/L (<21µmol/L). Serum creatinine was 76 µmol/L (<126 µmol/L). Ultrasound scan of the abdomen was normal and 2D echocardiogram showed good left ventricular systolic function with EF 60%. ECG showed atrial fibrillation at a rate of 120 beats/min. Bone marrow biopsy was done for further evaluation of pancytopenia. Trephine biopsy revealed a normocellular marrow with erythroid hyperplasia. He was started on Carbimazole 15mg three times per day with rate controller drugs. On follow up his pancytopenia completely resolved in six weeks review with restoration of euthyroid state and was confirmed haematologically and biochemically.

Discussion

Our patient presented with loss of weight despite a preserved appetite together with tremulousness and increased sweating. Examination revealed a multinodular goiter with bruits and atrial fibrillation. His investigations confirmed thyrotoxicosis and revealed pancytopenia. The history or examination did not reveal any causes that may have attributed to the pancytopenia such as recent febrile illnesses, features of hematological malignancies, autoimmune hemolysis or use of any drugs. Blood picture and bone marrow examination excluded the possibilities of hematological malignancy and bone marrow infiltrations. The possibility of thyrotoxicosis predisposing to pancytopenia was thus considered. After the bone marrow evaluation, patient was started on Carbimazole which rendered him euthyroid and the pancytopenia also improved with the treatment, confirming our diagnosis.

Pancytopenia is a rare complication of thyrotoxicosis. It can also be a complication of antithyroid medication. The mechanisms underlying are not clearly understood. Possible mechanisms include reduced red cell life span due to functional hyperactivity of reticuloendothelial system, ineffective erythropoiesis caused by excess thyroid hormones, autoimmune processes and due to toxicity of thyroid hormone to bone marrow stem cells (1,2,3). Additionally folic acid deficiency, vitamin B12 deficiency and iron metabolism disorders may also play a role. In some cases of Graves' thyroid disease, autoimmune haemolytic anaemia has also been reported (4).

Anaemia has been reported in up to 10-15% of patients with hyperthyroidism and in 22% of Graves' patients (5,6). Thyroxin increases the tissue metabolic rate and tissue oxygen consumption resulting in tissue hypoxia. This results in increased erythropoietin secretion and in turn can give rise to polycythemia (7).

Leucopenia is seen in up to 15-30% patients with Graves' disease. This is usually associated with pancytopenia (8). The suggested mechanisms for leucopenia include a cross antigenicity between TSH receptors and polynuclear neutrophils, reduced marrow granulocyte reserve and a decreased circulating time of granulocytes (7,10). Kocher's blood picture is a term used to describe characteristic haematologic findings in Graves' disease showing relative lymphocytosis with normal or slightly low white cells (9).

Thrombocytopenia is relatively rare, accounting for only up to 4.3% of cases with Graves' disease (9). The mechanisms may be immunologically mediated or due to reduced lifespan resulting from functional hypersplenism with or without splenomegaly (7,11). Antiplatelet antibodies are identified in 50% of patients with Graves' disease and Hashimoto's thyroiditis. Graves' disease can also be associated with idiopathic thrombocytopenic purpura (12).

All these patients have been successfully and safely started on antithyroid drugs and the pancytopenia has been observed to completely reverse with re-establishment of euthyroid state. Thus a bone marrow assessment is warranted prior to starting antithyroid treatment and a re-evaluation of bone marrow is necessary if the pancytopenia remains unresolved despite euthyroid state. Also in clinical setting, a proper haematological workup prior to starting antithyroid treatment is essential to prevent erroneous diagnosis of antithyroid drug induced pancytopenia in place of thyrotoxicosis induced pancytopenia. Similarly, in patients with pancytopenia, a thyroid evaluation can be helpful even in the absence of related symptoms.

Conclusion

Pancytopenia can be a rare complication of thyrotoxicosis as well antithyroid treatment. Thus a

proper diagnosis of the causative factor is essential for the correct management. In certain patients a complete haematologic work up including bone marrow assessment is warranted and complete recovery of cytopenia is expected with antithyroid treatment and restoration of euthyroid state. In patients with unexplained pancytopenia, a thyroid assessment may prove beneficial even in the absence of symptoms. To the best of our knowledge this is the first reported case of thyrotoxicosis presenting with pancytopenia in Sri Lanka.

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