Who is the culprit in neutropenia associated with Graves' disease?

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Introduction:

Thyroid hormone abnormalities and autoimmune diseases in general are associated with various haematological manifestations. Neutropenia is a well recognised side effect of anti-thyroid drugs(ATDs) .

Case history:

We present a 41 year old Nepalese lady who was referred by her GP with a three month history of weight loss, insomnia, irritability, sweating, palpitations, tiredness and proximal muscle weakness. Past medical history revealed pyelonephritis six months ago and recurrent ear infections. There were no other medical problems and she was not on any regular medications. Her English speaking was limited.

Examination revealed diffusely enlarged thyroid gland without opthalmopathy.

Laboratory investigations revealed hyperthyroidism with T4 of 64 mol/L (9-24 mol/L) T3 of 20 mol/L (3.5-6.5mol/L) and TSH 0f <0.03mol/L (1.5- 5). Full blood count prior to commencement of any treatment revealed neutropenia with a neutrophil count of 0.7x 10^9/L(3.5-7.5 0.7x $10^{9)}$ with normal cell counts in other cell lines. TSH receptor antibodies were elevated 6.5 (<0.4) suggestive of graves disease and technetium scan showed homogeneous uptake supporting this diagnosis. Haematology advice was sought to investigate neutropenia and it was decided to start on carbimazole 10mg with close monitoring of blood counts.

There was an improvement in her neutrophil count as the thyroid disease was controlled. Subsequently she discontinued her carbimazole therapy as she felt better and her thyroid function tests deteriorated associated with a drop in her neutrophil count. On restarting the carbimazole therapy her thyroid function improved as did her neutrophil count.

All the haematological investigation results were negative except an incidental finding of this patient being a thalassemia trait. These include autoimmune screen (ANA, P-ANCA, Lupus screen), Viral screen (HIV,CMV, EBV, Hep B, C), Negative DAT(direct antiglobulin test) /Coombs test, Negative lupus anticoagulant and normal B12,Folate,ferritin,B2 macroglobulin,LDH levels. Incidental finding of this lady being a thalassemia trait was identified with haemoglobin of 11.4 g/dL (normal range 11.5-16g/dL).

Time	Carbimazole dose	T4 (mol/L) (normal value 9-24)	Neutrophil count 10^9 (normal value L(3.5-7.5 0.7x $10^{9)}$
1st review (week 1)	10mg	67	0.7
Week 2	10mg		1.3
Week 3	10mg		1.5
Week 4	10mg	32	2.4
Week 5	10mg	26	2.8
Week 6	Poor compliance with ATDs		
Week 8	Poor compliance with ATDs	Missed follow up.	1.6
3 months	10mg (back on therapy)	12.7	2.2
4 months	10mg	11.6	3.0

Discussion:

Carbimazole and Propylthiouracil are the initial treatment in adults presenting with Graves' disease. However there is a rare (1:1000) risk of agranulocytosis (neutropenia) secondary to bone marrow suppression caused by these drugs which remains a concern. In this lady, untreated graves' disease itself was thought to be the reason for neutropenia and improvement noted once thyroid disorder became controlled. Therefore low dose anti-thyroid medications can be cautiously used as first lime treatment in these situations with careful monitoring of blood counts.

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