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A highly exaggerated response to Warfarin Therapy in a patient with Thyrotoxicosis

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Introduction

- Thyrotoxic atrial fibrillation (AF) occurs in 10% to 35% of patients with thyrotoxicosis with high risk of embolisation [1,2,3].
- In addition to AF, the high risk of embolic events may be related to the thrombotic environment created by thyrotoxicosis[4].
- Therefore anticoagulation of thyrotoxic patients with atrial fibrillation is advised, this can be stopped after restoration of euthyroidism and reversion to sinus rhythm[5].

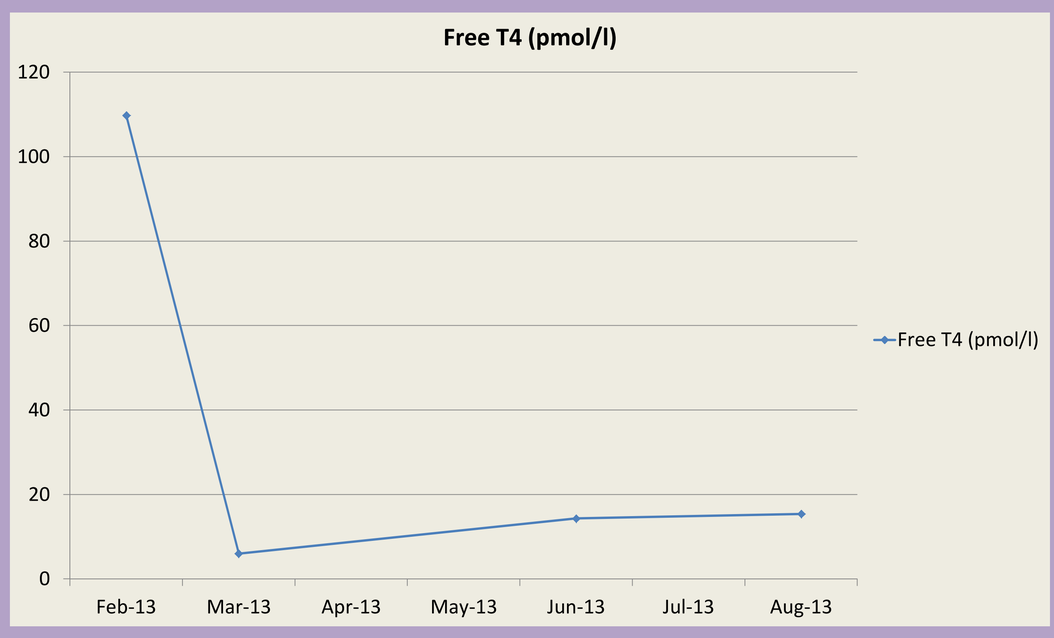
Case History

A 22 year old lady was referred to our joint ophthalmology clinic with bilateral proptosis following a routine visit to the opticians. She had a two year history of thyrotoxic symptoms which included sweats, palpitations, weight loss and anxiety, particularly pronounced in the 4 months prior to her presentation . Her past medical history included alopecia totalis and there was no family history of thyroid disease or autoimmunity.

On examination she had clear signs of thyrotoxicosis and was clinically in atrial fibrillation (AF) with a central heart rate of 195 beats/mins. Neck palpation revealed a moderate-sized smooth and symmetrical goitre with no bruits or lymphadenopathy. There was evidence of active thyroid eye disease with conjunctival injection, periorbital oedema and bilateral proptosis. Her investigations revealed severe thyrotoxicosis with a Free T4 109.8 pmol/l, Total T3>12.3 nmol/L and TSH< 0.05 miu/L. Her TSH-R antibodies were positive at 100u/L, consistent with a diagnosis of Graves' disease, and her electrocardiogram confirmed AF.

She was commenced on Carbimazole 20mg three time daily and 40 mg/day of prednisolone was added for the management of thyroid eye disease. A cardiology opinion was sought for her AF and she was started on 5mg bisoprolol and warfarin using a loading dose of 10mg/d for two days then 5 mg on the third day. Her INR on the fourth day before warfarin ingestion was 18.7 but the patient did not exhibit any symptoms or signs of bleeding.

Warfarin was stopped and the dose was subsequently adjusted to achieve an INR of 2-3. She became euthyroid in 6 weeks and reverted spontaneously into sinus rhythm. This was confirmed by repeat ECG and a 24 hour tape which also ruled out paroxysmal arrhythmias.



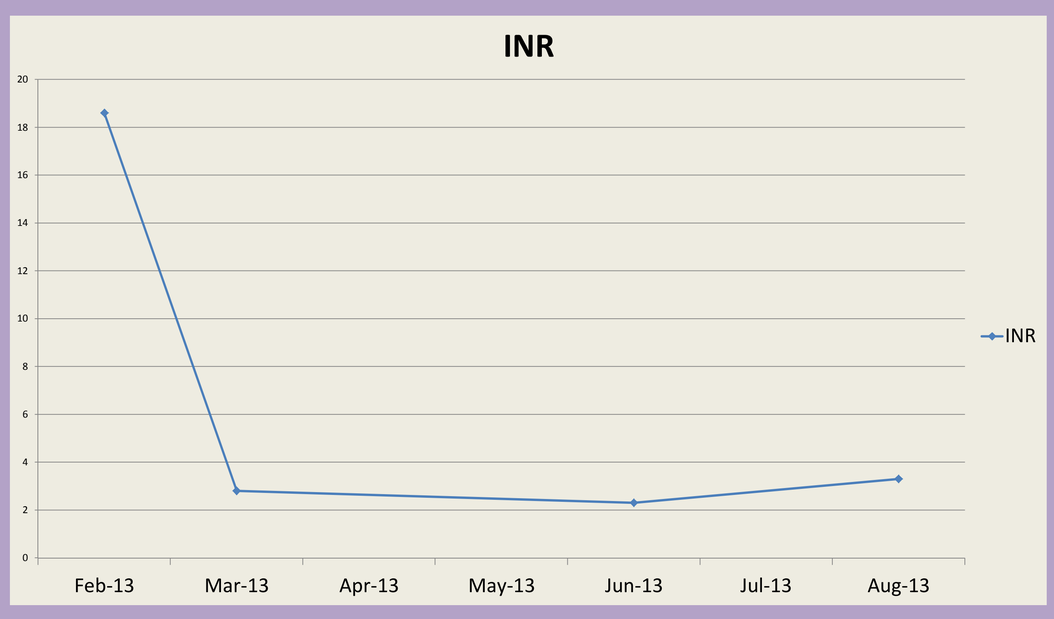


Fig. 1: Free T4 levels at presentation and following treatment with Carbimazole

Fig 2: INR 3 days after treatment with Warfarin and following dose adjustment

Discussion

- A limited number of reports have shown an increased sensitivity to oral anticoagulants in thyrotoxicosis, but to our knowledge, the case described represents the most extreme case described to date[4-7].
- The mechanism remains unclear, although some have suggested thyroxine induced alteration in clotting factor kinetics with decreased protein binding of the drug or an altered metabolism of warfarin[6-8] .
- This highlights the need for a different anticoagulation regimen in patients with thyrotoxicosis and atrial fibrillation.
- We suggest more frequent and earlier checks of INR in case warfarin therapy is needed in patients with hyperthyroidism, particularly in those with severe thyrotoxicosis.

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