

An atypical presentation of Graves' disease

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INTRODUCTION

Graves' disease is a common cause of hyperthyroidism characterized by the presence of TSH receptor stimulating autoantibodies (TRAb) and an enlarged thyroid with high uptake of radioiodine. Graves' ophthalmopathy occurs in about 50 % of cases. Treatment by antithyroid drugs (ATD) from 12 to 18 months is the most common therapeutic option. Total thyroidectomy or radioactive iodine (¹³¹I) ablation can be proposed especially in case of relapse after medical treatment or as a first choice in the presence of specific medical situations after discussion with the patient.

CASE REPORT

A 25-year-old man was hospitalized for weight loss, abdominal pain and palpitations. Diagnosis of hyperthyroidism caused by Graves' disease was established and methimazol was started. During biological monitoring, despite decreasing methimazol dosage and the addition of L-thyroxine, the patient kept an atypical hormonal profile with very low T4, and normal or slightly elevated T3 and variable TSH levels (see table). The use of propylthiouracil (PTU) instead of methimazol did not significantly change hormonal profile. Given persistent fatigue and abdominal pain, adrenal insufficiency was suspected but a basal morning cortisol of 260 ng/ml excluded this diagnosis. Finally, we kept the diagnosis of T3-predominant Graves' disease. Due to difficulties of normalizing thyroid function, the presence of Graves' ophthalmopathy and of a growing goitre (see pictures), our patient underwent total thyroidectomy 9 months after the diagnosis.

Pictures. On the left, the patient at the time of diagnosis. On the right, the patient few days before surgery. The eyelid oedema and the goitre are much more pronounced on the right picture.

Ultrasound imaging performed 8 months after diagnosis confirmed that goitre size had more than doubled.



Table. Evolution of TSH, thyroid hormones and TRAb levels. Methimazol was started on 10/10/2014 and the switch to PTU was made on 13/04/2015. The patient underwent total thyroidectomy on 02/07/2015.

Notice the particularly low fT4 levels (min 0,19 ng/dl) in contrast to normal or modest elevation of TSH levels (max 9,5-10 mUI/L).

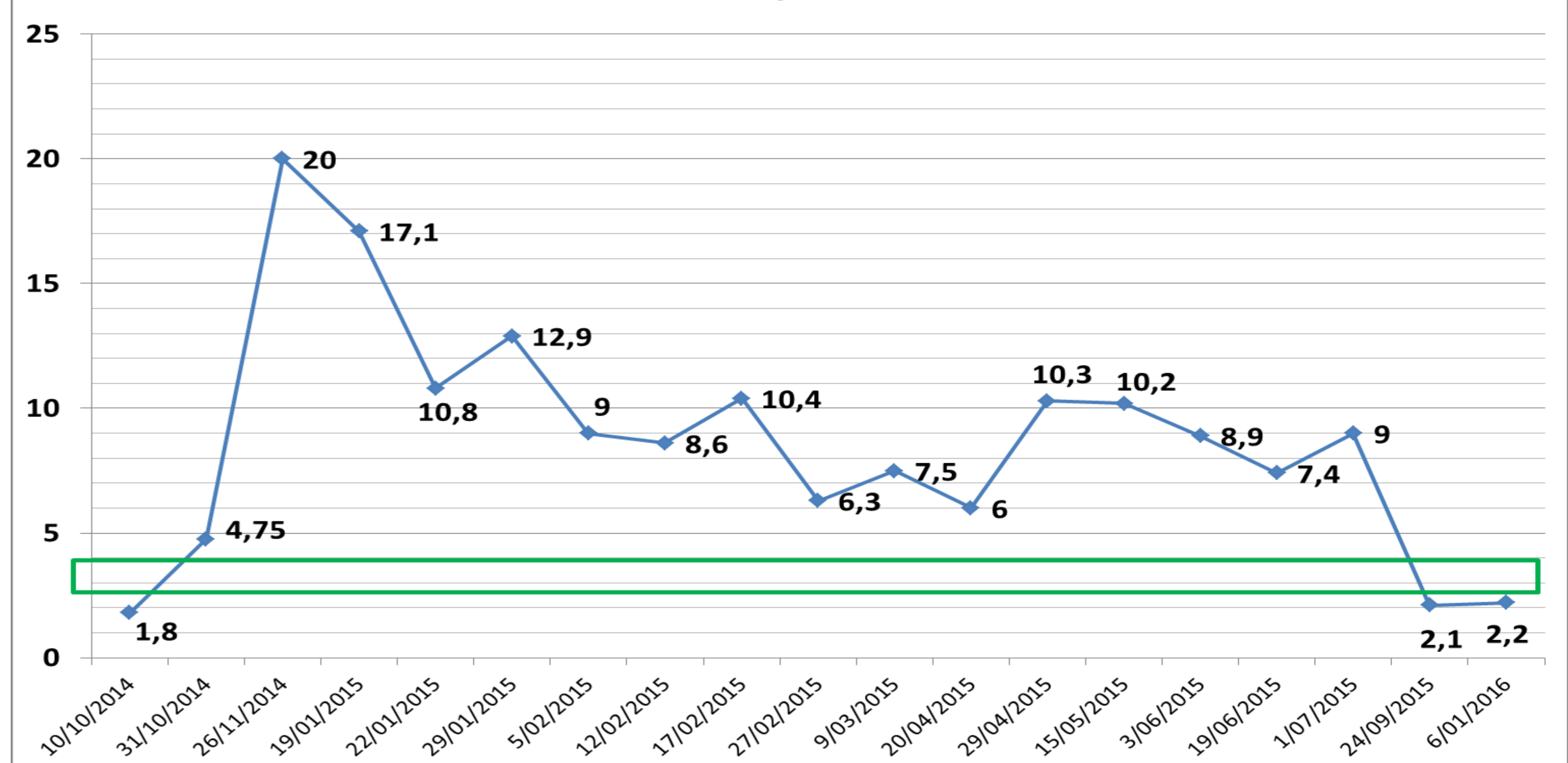
| Dates | 10/10/14 | 31/10/14 | 26/11/14 | 19/01/15 | 22/01/15 | 29/01/15 | 5/02/15 | 12/02/15 | 27/02/15 | 9/03/15 | 20/04/15 | 29/04/15 | 15/05/15 | 3/06/15 | 1/07/15 | 24/09/15 | 6/01/16 |
|-------------|----------|----------|----------|----------|----------|----------|---------|----------|----------|---------|----------|----------|----------|---------|---------|----------|---------|
| TSH (mUI/L) | <0,03 | <0,03 | 9,5 | <0,04 | <0,04 | 0,4 | 12 | 1,8 | 2,2 | 10 | <0,04 | <0,04 | 0,039 | 0,061 | <0,04 | 9 | 2,3 |
| fT4 (ng/dl) | 8,3 | 0,8 | 0,19 | 0,7 | 0,6 | 0,24 | 0,3 | 0,49 | 0,53 | 0,51 | 2,49 | 0,6 | 0,45 | 0,46 | 0,5 | 1,26 | 1,6 |
| fT3 (pg/ml) | 15 | 3,8 | 3,8 | 12 | 6,5 | 3,1 | 2,7 | 4,2 | 3,2 | 3,8 | 14,9 | 6,2 | 4,6 | 4,1 | 4,5 | 2,6 | 3,6 |
| TRAb (IU/L) | 22,8 | | 38 | | 34 | | | 36 | | | | | 30 | | | 11 | 6 |

Reference values: TSH 0,4-4 mUI/L; fT4 0,8-1,7 ng/dl; fT3 1,8-4,6 pg/ml; TRAb < 2 IU/L

DISCUSSION

T3-predominant Graves' disease is characterized by high free T3 (fT3) concentration associated with a normal or low free thyroxine (fT4) concentration and undetectable TSH levels with rising fT3/fT4 ratio after the onset of ATD. This form of severe hyperthyroidism is associated with particularly elevated TRAb levels. High fT3/fT4 ratio seems to be related to an increase in the activity and/or the expression of type 1 and type 2 iodothyronine deiodinases. Usual fT3/fT4 ratios (pg/ml/ng/dl) in T3-predominant Graves' disease as described in literature fluctuate between 4 and 10 (N: 1,8-3,3). In our case we observed much higher fT3/fT4 ratios (up to 20) associated with particularly low fT4 levels (see table and graph). The increase of fT3/fT4 ratio at the beginning of ATD and the normalization after thyroidectomy on L-Thyroxine therapy (see graph) suggest a potential role of ATD in the activation of iodothyronine deiodinases. The recognition of these forms of Graves' disease seems to be important, given the potential development of atypical biological profile after drug initiation and the high risk of recurrence after cessation of medical therapy. T3-predominant Graves' disease is probably underdiagnosed as the determination of fT3 is recommended only in case of low TSH associated with normal fT4 during suspected hyperthyroidism. Thus, we suggest that it might be of interest to measure fT3 in addition to fT4 and TSH, in case of severe Graves' disease with high titer of TRAb or in case of discordant TSH and T4 levels in the follow-up of treated Graves' disease.

fT3/fT4



Graph. Evolution of fT3/fT4 ratio during follow-up. The green rectangle in the bottom of the graph marks the reference values (1.8 to 3.3 pg / ml / ng / dl). Most cases of T3 Graves' disease described in literature showed fT3/fT4 ratios between 4 and 10. Notice the normalization of the ratio after surgery under thyroxine treatment.

REFERENCES

Mitsuru Ito et al. *Eur J Endocrinol* 2011;164:95-100
Matsumo C et al, *European J Endo*, 2013;168(2):137-44
Harvengt J et al, *European J Endo*, 2015; 172(6):715-23

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