

# GRAVES ORBITOPATHY COURSING WITH HYPOTHYROIDISM: A CASE-REPORT

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## INTRODUCTION

- Graves's orbitopathy (GO) is usually associated with Graves's Disease, which is typically characterized by hyperthyroidism and goiter.
- However, in rare situations, GO can also present with hypo or euthyroidism (prevalence 1.6 and 8.6%)

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Left eye ptosis. No other ophthalmologic complaints.

**General Practitioner Evaluation**  
Normal Cranial CT Scan

**Referenced to Ophthalmology Consultation**

## CLINICAL CASE

- IDENTIFICATION:** Male, 38 years old.
- PAST MEDICAL HISTORY:** Overweight; Unilateral Renal Agenesis; Haemorrhoids.
- Smoker – 10 cigarettes/day since 14 years old: 12 pack-year.
- No regular medication.



**Conjunctival hyperaemia**

**Exophthalmia RE>LE:** RE: 25mm | LE:23mm

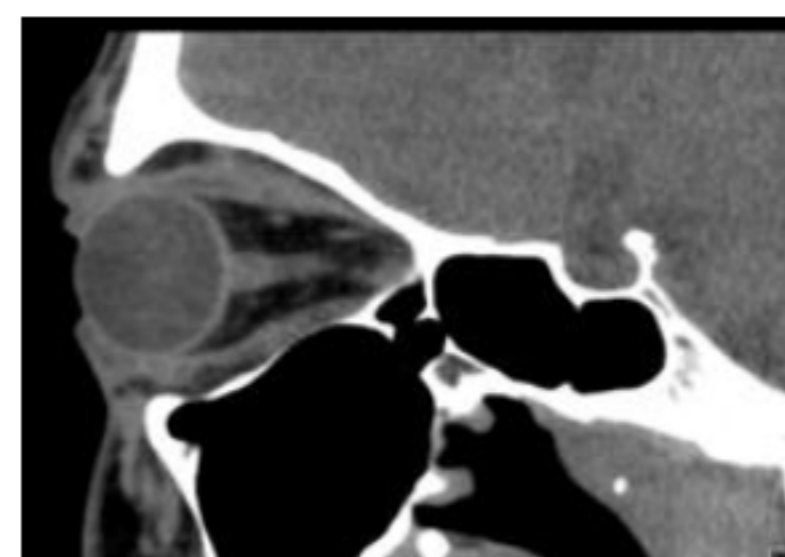
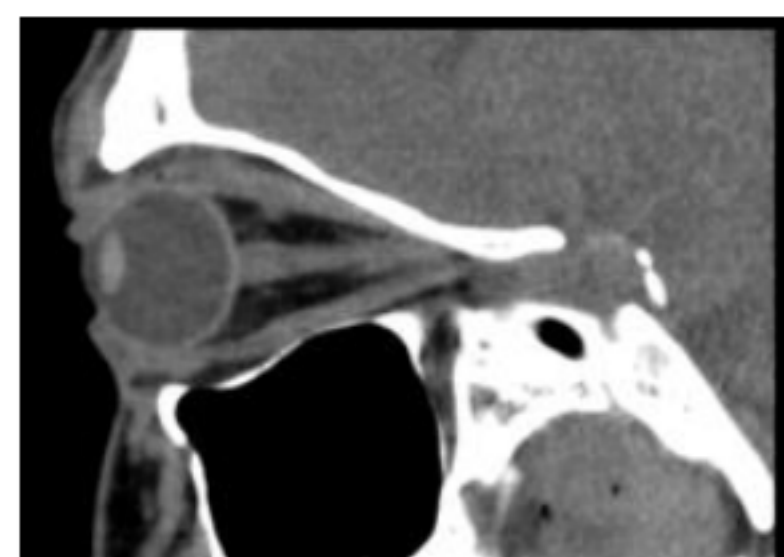
**MDR 1(Margin Reflex Distance):** RE: 5mm | LE: 3mm

**Visual acuity:** 10/10sc in both eyes

**Ocular Tension:** 20 mmHg in both eyes

### ORBITS CT 07/03/2013:

Optic nerves and eyeballs without significant changes in their morphology or their densitometry. **Intra and extraconical fat without obvious changes in their densitometry.** Bony walls apparently preserved. Small focus of high density in the adjacent soft tissue on the right side of the nasal bones - to correlate with clinical history.



Sagittal – Left Eye

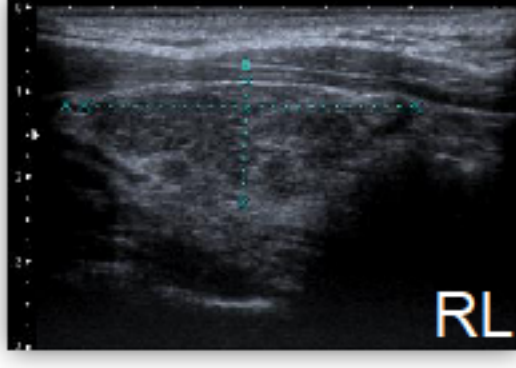
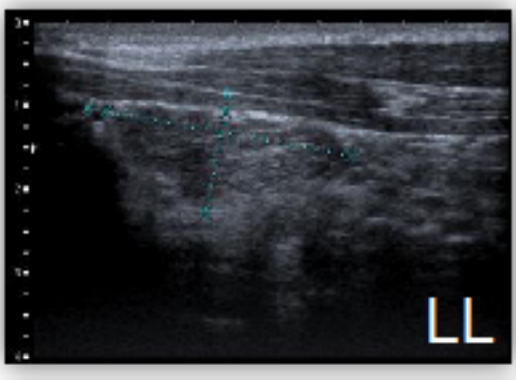
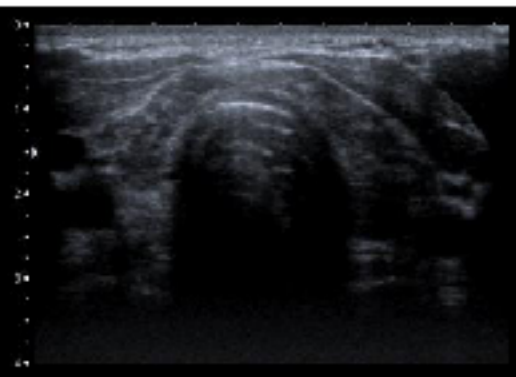
Coronal

Sagittal – Right Eye

	RESULT	REFERENCE VALUES
Hemoglobin	16.0	13.0-18.0 g/dL
WBC	8.94	4.0-11.0 x 10 <sup>9</sup> /L
Platelets	213	150-400 x 10 <sup>9</sup> /L
AST	24	10-37 U/L
ALT	26	10-37 U/L
GGT	15	10-49 U/L
AP	63	30-120 U/L
CT	237	<200 mg/dL
HDL	37	>60 mg/dL
LDL	161	<130 mg/dL
Triglycerides	195	<150 mg/dL
Glucose	88	75-100 mg/dL
Urea	35	10-50 mg/dL
Creatinine	1.15	0.8-1.3 mg/dL
TSH	62.75	0.35-4.94 uIU/mL
FT4	0.70	0.70-1.48 ng/dL
FT3	2.95	0.35-4.94 pg/mL
TSH receptor antibodies	5.2	0-1.8 U/L

### THYROID ULTRASOUND 05/03/2013:

Thyroid with preserved dimensions: RL-14x14x39mm(TxAPxL), LL-11x12x3 (TxAPxL). The parenchyma presents diffuse heterogeneous echostructure with decreased echogenicity and pseudonodular areas with diffuse increase in vascularization, suggestive of inflammatory changes in the context of thyroiditis. There are no enlarged lymph nodes in the lateral-cervical chains.



**GRAVES ORBITOPATHY + HYPOTHYROIDISM**

**ENDOCRINOLOGY**

- Symptoms:** asthenia and weight gain (10 kg) along the last year.
- No cervical compression complaints.
- No cervical irradiation history.
- No known family history of thyroid disease

→He started therapy with levothyroxine (75 µg/day) and the dose was increased as needed.

### Levothyroxine

75 µg    88 µg    88 µg    100 µg 4x 88 µg 3x    100 µg 5x 112 µg 2x    125 µg

	RV	Feb/13	Jul/13	Nov/13	Mar/14	Jun/14	Sept/14	Nov/14
TSH	0.35-4.94 uIU/L	62.75	7.88	3.48	4.66	14.71	17.50	3.47
FT4	0.70-1.48 ng/dL	0.70	1.10	1.18	1.19	0.89	1.05	1.08
FT3	0.35-4.94 pg/mL	2.95	3.47	3.13	3.35	2.08	2.56	3.04
TSH receptor antibody	0-1.8 U/L	5.2	2.6	3.9	9.3	>40.0	13.9	-
Thyroglobulin Antibody	<4.11UI/mL	-	46.5	-	-	-	28.9	-
Thyroid Peroxidase Antibody	<5.61UI/mL	-	584.5	-	-	-	416.5	-

**Symptoms Relapse**

## CONCLUSIONS

- There are different types of TRAbs, capable of inducing distinct clinical syndromes, according to their functional influence - stimulating, blocking, or neutral.
- In this patient with Graves's orbitopathy, a predominance of blocking type TRAbs could be a possible explanation for the presence of hypothyroidism. However, TRAbs blocking and stimulating activity were both in the normal range. So, neutral TSH-receptor antibodies, which do not block TSH binding and are unable to induce cAMP via Gs, may be present in this patient. However they may induce other signaling cascades with important implications for the generation and persistence of chronic inflammation.
- In conclusion, hypothyroidism in this particular case may be a consequence of the associated thyroiditis (suggested by high titers of anti-peroxidase/anti-thyroglobulin autoantibodies and ultrasonographic findings), while orbitopathy may be a result of neutral TRAbs' effects.

### ANALYSIS OF BIOLOGICAL ACTIVITY OF TSH RECEPTOR ANTIBODIES<sup>1</sup>:

TRAB concentration: 15.5 UI/L (normal <1.5)

- Blocking activity: <10% (normal <10%)
- Stimulating activity: 115% (normal 80-140%)

<sup>1</sup>Biossay involving CHO (chinese hamster ovary) cells expressing the recombinant human TSH receptor.

## REFERENCES

- Eckstein AK et al. Br J Ophthalmol. 2009 Aug;93(8):1052-6  
Gupta MK. Clin Chim Acta. 2000 Mar;293(1-2):1-29  
McLachlan SM et al Thyroid. 2013 Jan;23(1):14-24.  
Zophel K et al. Autoimmun Rev. 2010 Aug;9(10):695-700.

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