



## HYPOTHYROID GRAVES DISEASE – REPORT OF CASE WITH REVIEW OF LITERATURE

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### ABSTRACT

**Background:** TAO is seen in about 80% of patients with Graves' disease; it may also occur in patients with thyroid cancers or autoimmune hypothyroid due to Hashimoto's thyroiditis in about 10% of TAO, while individuals with no thyroid disease were found to have orbital lesions in 10 percent of total cases. **Case presentation:** A 46-year-old male patient who is a known case of hypertension and hypothyroidism attended to medical OPD of SVS Hospital with foreign body sensation in both eyes, bulging of eyeballs and excessive watering in both eyes. He was on 40 mg of telmisartan and 50 micrograms of thyroxine daily for about 6 months. Pulse was 56 per minute and a blood pressure of 146/96 mmHg. The patient was treated with methyl prednisolone initially weekly intravenous doses followed by oral medication along with increased levothyroxine to 150 micrograms, selenium and statins. He was symptomatically better after 6 weeks of therapy. **Summary and conclusion:** Hypothyroid grave disease is very rare that too in a male patient. Treatment does not differ from Hyperthyroid Graves' disease except the supplementation of levothyroxine instead of anti-thyroid measures. The literature has been reviewed.

**KEYWORDS :** Hypothyroidism, Exophthalmos, Proptosis, Methyl Prednisolone, Male patient.

### INTRODUCTION:

Thyroid-associated Ophthalmopathy (TAO) is an ocular condition that frequently manifests with thyroid dysfunction and is the most common extrathyroidal manifestation of Graves' disease. TAO is seen in about 80% of patients with Graves' disease; it may also occur in patients with thyroid cancers or autoimmune hypothyroid due to Hashimoto's thyroiditis in about 10% of TAO, while individuals with no thyroid disease were found to have orbital lesions in 10 percent of total cases<sup>1</sup>.

Ophthalmopathy is reported to occur in 25-50% of patients with Graves' disease and 2% of patients with Hashimoto's thyroiditis. About 3-5% of these patients have severe ophthalmopathy<sup>2,3,4</sup>. Graves' orbitopathy has an incidence rate of 16 women and 3 men per million<sup>5</sup> 100,000. Graves' ophthalmopathy develops in hypothyroid subjects without a history of treatment with anti-thyroid therapy is called hypothyroid Graves' disease<sup>6</sup>.

### Case Presentation:

A 46-year-old male patient who is a known case of hypertension and hypothyroidism attended to medical OPD of SVS Hospital with foreign body sensation in both eyes, bulging of eyeballs and excessive watering in both eyes.

He was on 40 mg of telmisartan and 50 micrograms of thyroxine daily for about 6 months. Pulse was 56 per minute and a blood pressure of 146/96 mmHg. Weight of the patient initially was 102 KGs.

**Table 1 Showing the eye signs in the present case**

Proptosis	Bilateral
Chemosis	Bilateral
Kocher sign	Spasmodic retraction of upper eye lid on retraction
Dalrymple sign	Upper lid retraction
Gifford sign	Difficulty in eversion of upper eye lid
Enroth sign	Edema of lower lid
Ballet's sign	Paralysis of one of extra-ocular muscles



**Fig 1** Facial features showing marked proptosis (consent from the patient was obtained and preserved in the records)

**Table 2 Showing The Investigations**

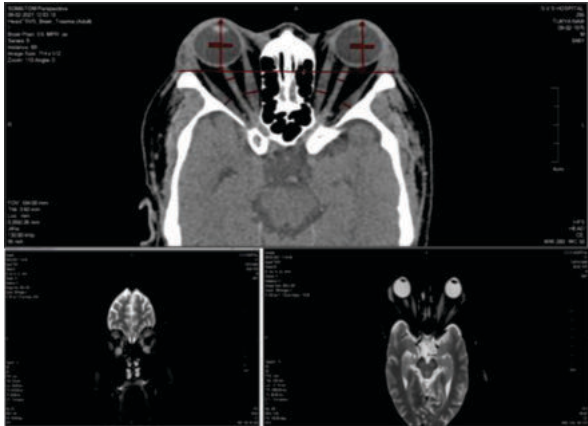
Investigation	Results	Normal range
Total leukocyte count	17,400 cells /mm <sup>3</sup>	4000 – 10,500 cells /mm <sup>3</sup>
Neutrophils	52 %	55 – 68 %
Lymphocytes	46 %	20 – 35%
Eosinophils	2 %	0.5 – 5%
Free T3	2.63 pg/ml	2.3-4.2pg/ml
Free T4	0.55 ng/dl	0.89-1.76ng/dl
TSH	140 micro IU	0.4-4.2microIU/L
Thyroid peroxidase antibody (TPOAb)	482 IU/mL	normal < 35 IU/mL
Thyroglobulin antibody (TgAb):	486.3 IU/ml	normal < 20 IU/mL
Thyroid-stimulating immunoglobulin antibody (TSI):	Less than 140% of basal activity	
Thyroid-stimulating hormone (TSH) receptor binding inhibitor immunoglobulin (TBII)/TRAb	34 IU/L	normal < 1.75 IU/L
Total cholesterol	240 mg/dL	<200 mg/dL
Triglyceride	248 mg/dL	< 160 mg/dL
LDL Cholesterol	194 mg/dL	100 – 130 mg/dL
HDL Cholesterol	28 mg/dL	40 – 60 mg/dL

**USG of NECK:**

Altered echo texture in bilateral lobes of thyroid noted with 2 cystic spaces and fibrous septations. Increased flow on application of color Doppler. All features are suggestive of Hashimoto's thyroiditis.

**MRI of ORBITS and BRAIN:**

Bilateral proptosis with symmetric fusiform extraocular muscle enlargement predominantly inferior, medial, superior recti with tendons typically spared. Increased bilateral orbital fat volume is noted. The space around left optic nerve is diminished.



**Fig 2** MRI of the patient bilateral proptosis with symmetric fusiform extraocular muscle enlargement

**Management:**

Patient was treated with Tab Thyroxine 150 mcg, Artificial tears, oral selenium, statins and intravenous methyl prednisolone 500 mg once a week for 6 weeks and 250 mg of methyl prednisolone weekly for another 6 weeks. Symptoms and proptosis relatively subsided after 12 weeks of glucocorticoid therapy. Weight of the case at this stage was 88 Kgs. And requirement of artificial tears was reduced to only bed side only.

**DISCUSSION:**

The pathogenesis of TAO is not clearly understood, but it has been confirmed that the autoimmunity develops antigens common to the thyroid gland and the orbit. Most speculated mechanism causing Graves' orbitopathy is that autoantibodies are formed against thyrotropin receptors that are found in both the thyroid gland and orbit. This causes activation of T lymphocytes with subsequent release of inflammatory mediators<sup>5</sup>. The muscles are infiltrated with inflammatory cells and hyaluron causing enlargement of the EOMs and an increase in the orbital fat volume<sup>7</sup>. Ultimately, collagen deposition leads to fibrosis. In hypothyroidism accumulation the mucopolysaccharides and water in the dermis were causes because of the reduced activity of enzymes in the cholesterol sulfate cycle, causing the changes in the skin barrier and increased capillary permeability, decreased androgenic tone and increased serotonin metabolism<sup>8,9</sup>. Apart from age and gender, cigarette smoking is the strongest modifiable risk factor for developing TAO. There is strong evidence for a causal association between smoking and development of TAO<sup>10-13</sup>.

Cardiac calsequestrin gene had been detected to presented in TAO patient and antibodies against orbital fibroblast membrane antigen collagen XIII were found to be presented in thyroid orbitopathy cases<sup>14,15 and 16</sup>. Michelson and Young<sup>17</sup> reported a 27-year-old female case with hypothyroidism, pretibial myxedema and exophthalmos way back 1970. There are few cases of TAO in treated hyperthyroid states and in hypothyroid status. But very few cases were reported in cases of hypothyroidism status had Graves Ophthalmopathy (Hypothyroid Graves Ophthalmopathy) from all over the

world<sup>18,19,20and21</sup>.

Sixty-three men and 105 women were reported by Savku and Gündüz<sup>22</sup> from Turkey noticed euthyroid was the most common thyroid status (64.9%), followed by hyperthyroidism (27.4%) and hypothyroidism (7.7%). Among patients with thyroid disease, 135 patients (80.4%) had Graves' disease, while the remaining 33 patients had other thyroid diseases (Hashimoto's thyroiditis in 8.3%, multinodular goiter in 8.3% and thyroid cancer in 3%). Li et al reported 354 cases from China of whom hyperthyroidism was noted in 84.18%, euthyroidism in 11.30% while 4.52 % cases were of hypothyroidism. There was an equal distribution of TED with hyperthyroid 22 patients (34.95%) euthyroid status in 22 cases (34.95%) while 19 (30.2%) had hypothyroidism in a Nepal study. In a study from Japan<sup>26</sup>, 58 patients diagnosed with EGD, 24.1% developed hyperthyroidism, while 3.4% developed hypothyroidism. A total of 72.4% of the 58 patients remained euthyroid throughout the entire follow-up period. Treatment suggested by EUGOGO association is as follows<sup>24</sup>.

**Table 4:** Treatment algorithm for thyroid-associated ophthalmopathy<sup>24</sup>

All patients	1. Restore euthyroidism 2. Urge to quit smoking	
Severity	Active	Inactive
Mild	Artificial tears Sunglasses Elevating head of bed Prismatic glasses	Artificial tears Prismatic glasses Surgical Müllerectomy Blepharoplasty
Moderate-severe	Intravenous methylprednisolone In patients resistant to steroids: cyclosporin A plus oral steroid, immunosuppressive therapies, anti-cytokine/lymphocyte agents If motility dysfunction is pronounced: orbital radiotherapy	Orbital decompression Strabismus surgery Palpebral surgery
Threat to vision 1. Optic atrophy	Intravenous methylprednisolone, 1 gr for 3 days If nonresponsive: orbital decompression +/- intravenous steroid +/- radiotherapy	Urgent surgical decompression
Threat to vision 2. Severe Corneal ulceration	Intravenous steroid, lubrication, tarsorrhaphy orbital decompression	Lateral tarsorrhaphy, orbital decompression, amniotic membrane transplant, Keratoplasty

The intravenous glucocorticoid (iv GC) represents the mainstay of therapy for Graves' ophthalmopathy (GO), but uncertainty remains concerning the optimal regimen. Although the European Group on Graves' Orbitopathy (EUGOGO) regimen has been commonly employed, evidence for its superiority to other regimens is still lacking. The aim of this meta-analysis was to compare the efficacy and safety of the EUGOGO regimen with higher-dose regimens in the management of GO.

**SUMMARY AND CONCLUSION:**

A rare case of hypothyroid male had been reported here with essential review of the literature.

**Conflicts:** Nil

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