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Case Report

Ophthalmology Section

A Case Report on the Thyroid and Eye Connection: A Deep Dive into Evaluation and Treatment Strategies

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ABSTRACT

Thyroid-Associated Orbitopathy (TAO), also known as Graves' ophthalmopathy or Thyroid Eye Disease (TED), is an autoimmune condition often linked to hyperthyroidism, particularly Graves' disease. It causes inflammation and swelling of the eye muscles and surrounding tissues, leading to symptoms such as proptosis, diplopia, and discomfort. The condition is six times more prevalent in females as compared to males. Among individuals diagnosed with TAO, about 90% have Graves' hyperthyroidism, while a smaller percentage may have primary hypothyroidism, Hashimoto's thyroiditis, or normal thyroid function. These patterns emphasise the importance of recognising thyroid dysfunction in orbitopathy management which includes treating the underlying thyroid dysfunction, using corticosteroids to reduce inflammation, and applying artificial tears for symptomatic relief. Severe cases may require orbital decompression surgery, strabismus correction, or eyelid surgery. Smoking cessation and selenium supplementation are recommended for improved outcomes in mild-to-moderate cases. A case involving a 42-year-old man is presented here with a history of hyperthyroidism who demonstrated signs of proptosis, diplopia, and upper eyelid retraction in both eyes. Clinical evaluations confirmed inflammation in the orbital tissues, which was substantiated by imaging studies, culminating in a diagnosis of TAO. The patient received intravenous corticosteroids for 12 weeks, reporting significant symptom relief afterward. This case underscores the effectiveness of tailored treatment strategies that combine medical and supportive interventions for managing severe active TED.

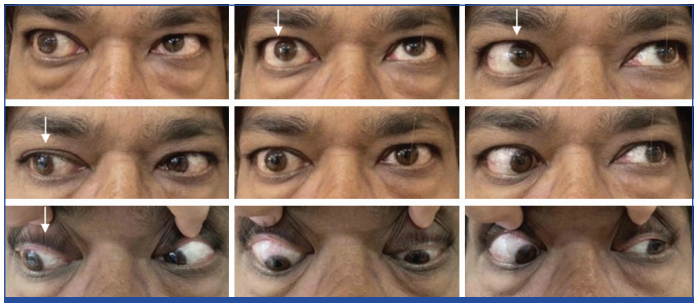
Keywords: Clinical activity score, Graves ophthalmopathy, Hyperthyroidism, Proptosis, Thyroid associated orbitopathy, Thyroid eye disease

CASE REPORT

A 42-year-old man presented to the Ophthalmology outpatient clinic with a three-month history of gradual protrusion of the right eye and intermittent diplopia. He had no prior history of ocular trauma or conditions. Nine months earlier, he was diagnosed with hyperthyroidism and was undergoing treatment with tablet carbimazole 10 mg thrice daily. His vital signs were stable, with a best corrected visual acuity of 20/20 in both eyes and intact colour vision. Upon examination, eyelid retraction and swelling were noted bilaterally [Table/Fig-1]. Proptosis was measured at 27 mm for the right eye and 24 mm for the left, using Hertel's exophthalmometer, with intraocular pressure remaining normal.

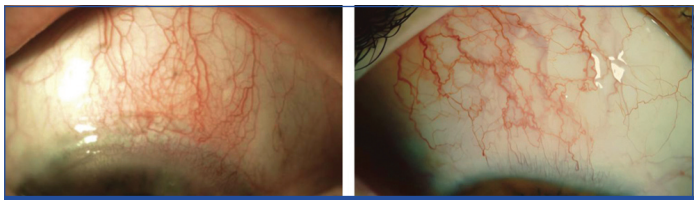
[Table/Fig-1]: Picture depicting the various signs of Thyroid Eye Disease (TED). On the right eye: Dalrymple sign (upper eyelid retraction), Vigoroux sign (eyelid fullness/swelling), Enroth sign (lower eyelid edema), Kocher sign (staring gaze).

Ocular motility assessments revealed restricted movements in the right eye during abduction, elevation, and depression [Table/Fig-2] [1] The Clinical Activity Score (CAS) was three out of seven, indicating active ophthalmopathy. The severity was classified as severe according to the European Group on Graves Orbitopathy (EUGOGO) criteria [2] and as Class 4 under the NOSPECS (N for no signs or symptoms, O for only signs like lid retraction, S for soft tissue involvement such as edema and redness, P for proptosis (eyeball protrusion), E for extraocular muscle restriction causing diplopia, C for corneal involvement like keratopathy, and S for sight loss due to optic neuropathy) classification [2]. The anterior



[Table/Fig-2]: Picture depicting restricted ocular movements of both eye. Ballet sign (EOM restriction) [1], Jendrassik Sign (Abduction limitation of the eyeball) [1].

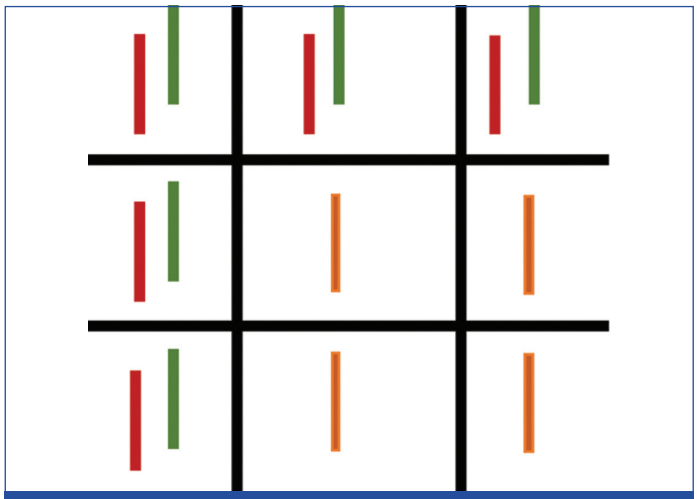
segment examination using a slit lamp showed superior limbal keratoconjunctivitis and chemosis in both eyes [Table/Fig-3]. Pupils were equal, round, and responsive to light. A posterior segment examination indicated a normal fundus.



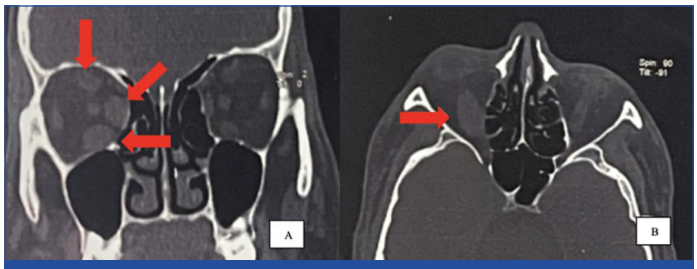
[Table/Fig-3]: Bilateral superior limbal keratoconjunctivitis.

Diplopia charting was done which showed under action of right superior rectus, middle rectus and inferior rectus [Table/Fig-4]. A Computed Tomography (CT) scan of the orbit showed thickening of the medial, inferior, and superior rectus muscles while sparing the tendinous insertions. Mild prominence of the retrobulbar fat and slight proptosis of the right eye was noted, corroborating the diagnosis of thyroid-related ophthalmopathy [Table/Fig-5]. Routine laboratory tests returned normal results. Thyroid function tests showed elevated T3 (5.1 pg/mL) and T4 (4 ng/dL) levels, alongside

a suppressed TSH level (0.01 mIU/L) and elevated anti-Thyroid Stimulating Hormone (TSH) receptors of 10.2 IU/L. Although the Erythrocyte sedimentation rate was mildly elevated (20 mm/hr), C-Reactive Protein (CRP) levels were within normal limits. Liver function tests, renal function tests, blood glucose levels, and Electrocardiogram (ECG) results were also normal. Based on the clinical and investigatory results, a diagnosis of active and severe Graves' ophthalmopathy, with restrictive myopathy and corneal involvement was made.



[Table/Fig-4]: Diplopia charting depicting under action of right superior, middle and inferior rectus.



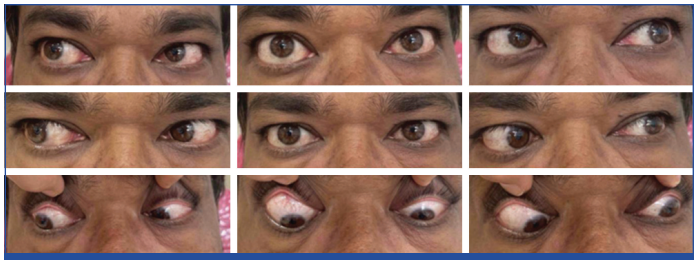
[Table/Fig-5]: Plain CT orbit suggestive of right eye thyroid related ophthalmopathy. a) Coronal section of plain CT orbit showing thickening of medial, inferior and superior rectus; b) Axial section of plain CT orbit showing thickening of superior rectus sparing the tendinous insertion.

The treatment protocol involved administering intravenous methylprednisolone at a dosage of 500 mg in 100 mL of normal saline once weekly for six weeks, followed by 250 mg weekly for another six weeks. Ongoing monitoring of liver function and serum electrolytes was conducted. Additionally, the patient received preservative-free carboxymethyl cellulose eye drops and 10 mg of Carbimazole daily. At the three-month follow-up appointment, the patient reported marked improvement in proptosis, ocular motility and double vision [Table/Fig-6-8]. Proptosis in the right eye measured 17 mm and in the left it was measured 16 mm. Visual acuity remained stable at 20/20.

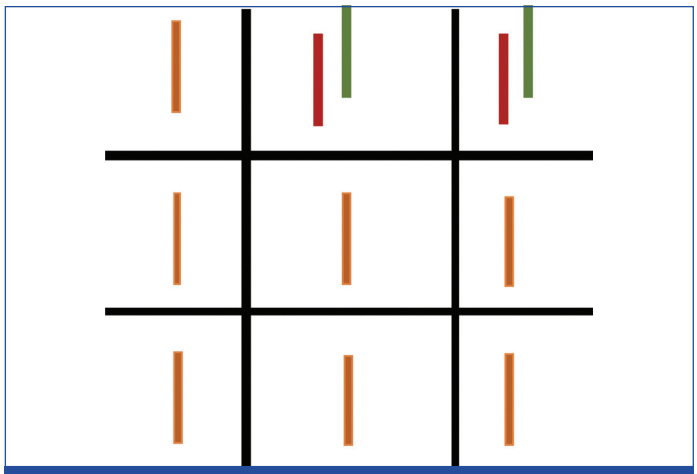
[Table/Fig-6]: Picture showing improvement in right eye proptosis after three month follow-up.

DISCUSSION

This case confirms a diagnosis of active, severe thyroid-related ophthalmopathy, primarily affecting the right eye. Restrictive myopathy



[Table/Fig-7]: Picture depicting improvement in the ocular movements in all nine gazes.



[Table/Fig-8]: Diplopia charting post treatment showing improvement of under action of middle and inferior rectus.

and corneal involvement posed significant functional and structural risks. The condition responded well to high dose intravenous corticosteroids and concurrent thyroid management, demonstrating reduced inflammation, improved motility, and normalised proptosis. This case uniquely illustrates the asymmetric yet severe presentation of thyroid related ophthalmopathy with preserved vision, absence of comorbidities and the effectiveness of early corticosteroid therapy. It emphasises the importance of individualised management strategies and the potential for non surgical resolution in severe cases, contributing to nuanced understanding and patient care in thyroid-related ophthalmopathy.

Thyroid-related orbitopathy, also known as Graves' ophthalmopathy or TED, is primarily an autoimmune condition associated with hyperthyroidism, particularly in Graves' disease. However, it may also occur in those with Hashimoto's thyroiditis or primary hypothyroidism [3]. This disorder predominantly affects the orbit, causing inflammation and swelling of the ocular muscles and surrounding tissues. Common manifestations include eyelid retraction, proptosis and extraocular muscle dysfunction [4]. The condition predominantly affects women, with an incidence ratio of approximately 6:1 compared to men. The condition is six times more common in females, accounting for 86% of cases, compared to 14% in males. Incidence peaks in females at ages 40-44 and 60-64 years, and in males at 45-49 and 65-69 years. Thyroid dysfunction is closely associated, with 90% of patients diagnosed with Graves' hyperthyroidism. A smaller percentage is linked to primary hypothyroidism (1%), Hashimoto's thyroiditis (3%), or euthyroid status (5%) [5]. TAO often exhibits a biphasic progression, sometimes referred to as "Rundle's Curve" [6]. The pathophysiology involves a complex interplay of genetic factors, environmental triggers, and immune system dysregulation. In Graves' disease, antibodies targeting the TSH receptor lead to excess thyroid hormone production, which can also affect orbital tissues, resulting in inflammation, muscle enlargement, and possible optic nerve compression [7]. The underlying cause is mainly autoimmune, with various risk factors influencing its development. These include ethnicity (more prevalent among African Americans), gender, genetic factors, systemic autoimmune diseases, smoking, radioactive iodine therapy, psychological stress, pregnancy, and trauma [8]. Clinical

assessments often utilise the CAS [2] and the European Group on Graves Orbitopathy (EUGOGO) system to evaluate severity [2]. The clinical presentation of TAO can vary widely, with common symptoms including proptosis, epiphora, diplopia, eye discomfort, and eyelid retraction [9].

Diagnosing TAO involves a comprehensive evaluation that includes a detailed medical history, clinical examination, and various diagnostic tests. Thyroid function tests are critical for determining the underlying thyroid status, as many patients with TAO may present as hyperthyroid, euthyroid, or hypothyroid. Imaging techniques, such as CT or Magnetic Resonance Imaging (MRI), are useful for visualising muscle enlargement and assessing disease extent [2,3,5]. Management of TAO is multifaceted and should be tailored to disease severity. Patients are encouraged to cease smoking, and stable euthyroidism should be achieved promptly. For individuals receiving radioactive iodine therapy, prophylactic prednisone is often initiated. Mild cases can be managed with local therapies and risk factor modification, with selenium supplementation proving beneficial. For moderate to severe cases, intravenous glucocorticoids are the first-line treatment, typically administered as an intermediate dose regimen of methylprednisolone. High-dose protocols may be reserved for the most severe instances. Patients who do not respond to glucocorticoids may require second-line treatments such as additional glucocorticoids, orbital radiotherapy, or immunomodulatory therapies. Elective rehabilitative surgery is advised for inactive cases with significant visual impairment lasting six months or more [2].

Treatment of TED has advanced with a focus on both symptom management and targeting disease mechanisms. Corticosteroids remain a first-line treatment, with orbital radiotherapy used for more severe cases. The introduction of Teprotumumab, a monoclonal antibody, has significantly improved outcomes by targeting the insulin-like growth factor receptor involved in TED. Other immunosuppressive drugs like methotrexate and azathioprine are used in cases where steroids are ineffective. For severe TED with significant proptosis, orbital decompression surgery is an option, while strabismus and eyelid surgeries can correct eye misalignment and eyelid retraction. Supportive care, including smoking cessation and selenium supplementation, also plays a crucial role. These evolving treatments, particularly biologics, have significantly improved TED management and patient Quality of Life (QoL) [10].

A study by Burch HB et al., outlined the management of TED, focusing on severity, activity, QoL, and tailored treatment plans based on individual patient factors. In mild cases, monitoring or use of selenium is advised, while surgery is reserved for inactive phase. In moderate to severe cases, active cases may require intravenous glucocorticoids, teprotumumab, radiotherapy, or selective surgeries while inactive cases focus on corrective surgeries. In sight threatening cases, urgent intravenous glucocorticoids and orbital decompression is done [11].

There have been various studies with different treatment modalities, one study where intravenous methylprednisolone for 12 weeks showed suboptimal response by Macovei ML and Azis U, another study where intravenous steroids with orbital decompression showed significant improvement [12,13]. A study by Daniel J et al., showed marked improvement in retrobulbar pain and reduction in extraocular muscle size after eight cycles of teprotumumab infusion at three weeks interval [14].

The differential diagnosis of TED includes conditions causing similar orbital or ocular symptoms, such as proptosis and diplopia. These include orbital tumours (e.g., lymphoma, meningioma, or metastases), inflammatory conditions like Idiopathic Orbital Inflammatory Syndrome (IOIS), sarcoidosis, or granulomatosis with polyangiitis. Infectious causes, such as orbital cellulitis or fungal infections, and congenital or structural disorders like orbital varices and arteriovenous malformations, may mimic TED. Blow out fracture of the orbit, postsurgical changes, and vascular causes such as carotid-cavernous fistula are also considerations. Diagnosis requires a combination of clinical evaluation, imaging, thyroid function tests, and sometimes biopsy to distinguish TED from other orbital pathologies effectively [15].

This case highlights few deviations and adaptations from standard management protocols. Proactive use of intravenous corticosteroids, avoidance of surgical or radiational therapies, emphasis on systemic monitoring to mitigate steroid related side-effects, strong focus on multidisciplinary team approach of endocrinology, ophthalmology and radiology and prioritisation of early intervention to prevent progression rather than waiting for vision threatening complications. A multidisciplinary approach is important between specialists to address both systemic and local complications. An endocrinologist, to optimise thyroid function to reduce disease activity and preventing recurrence, an ophthalmologist for vision threatening complications, radiologist for orbital imaging- to confirm diagnosis, assessing muscle involvement and monitoring response to treatment, an immunologist for managing systemic immunosuppressive therapy, a psychologist for support to address patient's impact on QoL and improve adherence to treatment. Continued research for understanding asymmetric disease pattern, efficacy of early interventions, biomarker development, exploration of novel therapies such as teprotumumab are essential.

CONCLUSION(S)

This case of active TED highlights the critical importance of early diagnosis and individualised treatment approaches tailored to the specific needs of the patient. The initial symptoms of proptosis and diplopia were significantly alleviated through corticosteroid therapy, leading to meaningful improvements in QoL. Ongoing monitoring and a multidisciplinary approach are vital in managing active thyroid-related orbitopathy, ensuring comprehensive care to address the complex nature of the condition. Continued research and increased awareness are essential for optimising treatment strategies and enhancing outcomes for individuals with thyroid-related orbitopathy.

REFERENCES

[1] Saraci G, Treta A. Ocular changes and approaches of ophthalmopathy in basedow-graves-parry-Flajani disease. Maedica (Bucur). 2011;6(2):146-52. PMID: 22205899; PMCID: PMC3239395.
[2] Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, et al; European Group on Graves' Orbitopathy (EUGOGO). The 2016 European Thyroid Association/European Group on graves' orbitopathy guidelines for the management of graves' orbitopathy. Eur Thyroid J. 2016;5(1):09-26. Doi: 10.1159/000443828. Epub 2016 Mar 2. PMID: 27099835; PMCID: PMC4836120.
[3] Bahn RS. Graves' ophthalmopathy. N Engl J Med. 2010;362(8):726-38. Doi: 10.1056/NEJMra0905750. PMID: 20181974; PMCID: PMC3902010.
[4] Sahlı E, Gündüz K. Thyroid-associated ophthalmopathy. Turk J Ophthalmol. 2017;47(2):94-105. Doi: 10.4274/tjo.80688.
[5] Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota. Trans Am Ophthalmol Soc. 1994;92:477-588. PMID: 7886878; PMCID: PMC1298522.
[6] Bartley GB. Rundle and his curve. Arch Ophthalmol. 2011;129(3):356-58. Doi: 10.1001/archophthalmol.2011.29.
[7] Maheshwari R, Weis E. Thyroid associated orbitopathy. Indian J Ophthalmol. 2012;60(2):87-93. Doi: 10.4103/0301-4738.94048.
[8] Bartalena L, Piantanida E, Gallo D, Lai A, Tanda ML. Epidemiology, natural history, risk factors, and prevention of graves' orbitopathy. Front Endocrinol (Lausanne). 2020;11:615993. Doi: 10.3389/fendo.2020.615993. PMID: 33329408; PMCID: PMC7734282.
[9] Du B, Wang Y, Yang M, He W. Clinical features and clinical course of thyroid-associated ophthalmopathy: A case series of 3620 Chinese cases. Eye (Lond). 2021;35(8):2294-301. Doi: 10.1038/s41433-020-01246-7. Epub 2020 Nov 2. PMID: 33139874; PMCID: PMC8302589.
[10] Szelog J, Swanson H, Sniegowski MC, Lyon DB. Thyroid eye disease. Mo Med. 2022;119(4):343-50. PMID: 36118816; PMCID: PMC9462910.
[11] Burch HB, Perros P, Bednarczuk T, Cooper DS, Dolman PJ, Leung AM, et al. Management of thyroid eye disease: A consensus statement by The American Thyroid Association and the European Thyroid Association. Thyroid. 2022;32(12):1439-70. Doi: 10.1089/thy.2022.0251. Epub 2022 Dec 8. PMID: 36480280; PMCID: PMC9807259.

[12] Macovei ML, Azis U. A case report of a patient with severe thyroid eye disease. Rom J Ophthalmol. 2022;66(2):153-57. Doi: 10.22336/rjo.2022.30. PMID: 35935091; PMCID: PMC9289779.
[13] Ismailova DS, Belovalova IM, Grusha YO, Sviridenko NY. Orbital decompression in the system of treatment for complicated thyroid eye disease: Case report and literature review. Int Med Case Rep J. 2018;11:243-49. Doi: 10.2147/IMCRJ.S164372.
[14] Ozzello DJ, Kikkawa DO, Korn BS. Early experience with teprotumumab for chronic thyroid eye disease. Am J Ophthalmol Case Rep. 2020;19:100744. ISSN 2451-9936, Available from: https://doi.org/10.1016/j.ajoc.2020.100744. (https://www.sciencedirect.com/science/article/pii/S2451993620300955).
[15] Shah SS, Patel BC. Thyroid eye disease. [Updated 2023 May 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK582134/.

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