ORIGINAL RESEARCH PAPER

Radiotherapy

GRAVES' OPHTHALMOPATHY: A CASE REPORT AND THE ROLE OF RADIOTHERAPY IN MANAGEMENT

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ABSTRACT

Graves' ophthalmopathy (GO) is a complex autoimmune orbital disorder often associated with thyroid dysfunction. It may present with proptosis, diplopia, and soft tissue inflammation, significantly impairing visual function and quality of life. We report a 43-year-old male with active moderate-to-severe GO refractory to corticosteroid therapy. Despite orbital decompression, symptoms persisted. He underwent orbital radiotherapy (20 Gy in 10 fractions using 3DCRT), resulting in substantial symptomatic improvement within 3 months of completion of radiotherapy. Orbital radiotherapy remains a valuable modality in managing moderate-to-severe GO unresponsive to medical and surgical therapy. Early intervention within the active phase, alongside thyroid control and lifestyle modification, enhances outcomes.

INTRODUCTION

Graves' ophthalmopathy (GO), also known as thyroid eye disease (TED), is an organ-specific autoimmune disorder that primarily affects the orbital and periorbital tissues. It is characterized by orbital inflammation, accumulation of glycosaminoglycans, adipogenesis, and subsequent fibrosis, leading to varying degrees of proptosis, lid retraction, diplopia, and, in severe cases, compressive optic neuropathy. While commonly associated with hyperthyroidism secondary to Graves' disease, GO can precede or follow thyroid dysfunction and, occasionally, present in euthyroid individuals. The pathophysiology involves the aberrant stimulation of orbital fibroblasts by autoantibodies targeting the thyrotropin receptor (TSHR) and insulin-like growth factor 1 receptor (IGF-1R). This immune activation promotes cytokine release, hyaluronan production, and tissue remodeling, ultimately compromising both function and appearance. Risk factors such as cigarette smoking, radioactive iodine therapy, and genetic predisposition exacerbate disease onset and progression. Management requires a stage-specific and severity-based approach, encompassing conservative measures, immunosuppressive therapies, radiotherapy, and, in some cases, surgical intervention. This case highlights the multidisciplinary challenges in managing moderate-to-severe GO, unresponsive to standard medical therapy, emphasizing the utility of orbital radiotherapy.

Case Report

A 43-year-old male with significant smoking history and multiple comorbidities presented with progressive periorbital discomfort, ocular redness, tearing, and binocular diplopia. Clinical examination revealed bilateral eyelid edema (Enroth's sign), upturned eyelashes (Dalrymple's sign), grade 3 proptosis (Stellwag's sign), ecchymosis, restricted extraocular movements, and a Clinical Activity Score (CAS) of 7, indicating an active and moderate to severe state of disease.

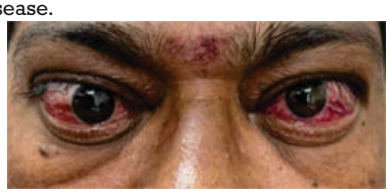

Figure 1: Pre Radiotherapy clinical presentation of Graves' ophthalmopathy showing bilateral proptosis, periorbital edema and conjunctival injection.

Initial management with anti-thyroid agents, systemic corticosteroids and immunosuppressants yielded inadequate symptomatic relief. Imaging studies, including MRI of the orbits, demonstrated significant enlargement of the medial and lateral rectus muscles with retrobulbar fat stranding.

Figure 2A-T2 Fat Saturation Axial Image Shows Bulky Extra Ocular Muscles Predominantly Involving Muscle Belly With Sparing of Insertion With Prominent Peri Optic Sheath and Adjacent Fat Stranding (coke Bottle Appearance).

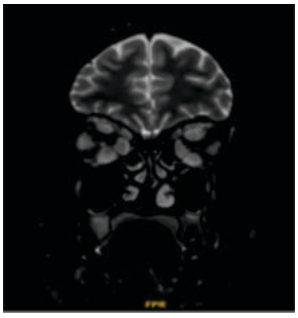

Figure 2B- T2 Fat Saturation Coronal Image Shows Bulky Extraocular Muscles With Adjacent Fat Stranding.

A Technetium-99m thyroid scan confirmed thyroid gland enlargement, and biochemical assays revealed elevated free T3 (166 pg/dL), free T4 (17 ng/dL), and suppressed TSH (0.05 mIU/L). Due to persistent symptoms and anatomical progression, the patient underwent bilateral orbital decompression via an endonasal endoscopic approach. Histopathological evaluation of the resected tissues revealed chronic inflammation without malignancy.

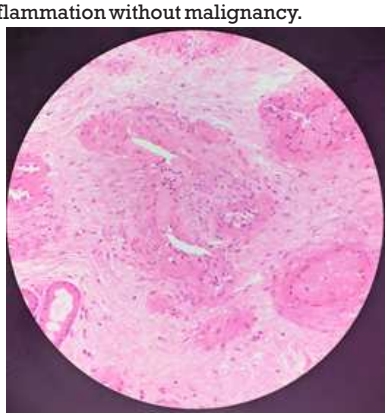

Figure 3: Post Orbital Decompression Microscopic Image Showing Inflammatory Cells Composed of Lymphocytes, Plasma Cells, Eosinophils, Mast Cells With no Evidence of Granuloma or Malignancy.

Despite surgical intervention, symptoms persisted. Subsequently, the patient received orbital radiotherapy with a total dose of 20 Gy administered in 10 fractions (2 Gy per fraction) using three-dimensional conformal radiation therapy (3DCRT). He was counseled to cease smoking and advised on the importance of achieving euthyroid status to stabilize the disease course. At a 3-month follow-up, the patient exhibited marked clinical improvement, including reduction in proptosis and resolution of diplopia, allowing resumption of routine activities.

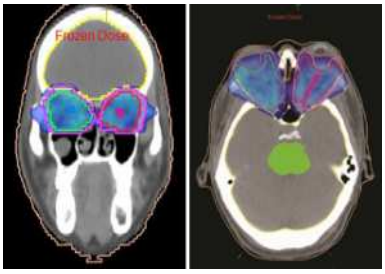

Figure 4: Radiation Treatment Planning Image Demonstrating Target Volume Delineation And Isodose Distribution.

DISCUSSION

Graves' ophthalmopathy (GO), a key manifestation of autoimmune thyroid disease, presents a distinct clinical challenge due to its unpredictable natural course and variable severity. It often occurs alongside Graves' disease, though both entities can manifest independently. GO is driven by an autoimmune response targeting orbital fibroblasts expressing TSH and IGF-1 receptors, leading to fibroblast activation, hyaluronan deposition, and adipogenesis, resulting in extraocular muscle enlargement and orbital fat expansion. These structural changes account for the hallmark features of proptosis, eyelid retraction, and diplopia.

The incidence of GO peaks between the second and sixth decades of life and shows a clear female preponderance. Smoking is a well-established modifiable risk factor, not only increasing disease incidence but also exacerbating its severity. Genetic predispositions, including HLA-DR3 and HLA-B8, further contribute to susceptibility.

The pathogenesis involves the activation of T-helper lymphocytes and the release of inflammatory cytokines in response to TSH receptor-stimulating autoantibodies. This cascade culminates in orbital inflammation, connective tissue remodeling, and, in severe cases, optic nerve compression—termed dysthyroid optic neuropathy (DON). This biphasic disease course is characterized by an initial inflammatory ("active") phase lasting approximately 6–18 months, followed by a fibrotic ("inactive") phase.

Disease activity and severity are assessed independently. The Clinical Activity Score (CAS) remains a practical tool for assessing inflammatory burden, although it lacks prognostic value for long-term outcomes such as DON. The European Group on Graves' Orbitopathy (EUGOGO) classification offers a three-tiered severity grading system-mild, moderate to-severe, and sight-threatening-which helps guide treatment decisions.

In this case, the patient exhibited moderate-to-severe disease with a CAS of 7 and radiological evidence of extraocular muscle involvement. First-line treatment with intravenous corticosteroids was insufficient, necessitating the use of adjunctive modalities. Radiotherapy (RT), especially when delivered during the active phase, has demonstrated efficacy in halting disease progression by modulating the immune response and reducing inflammatory cell infiltration in orbital tissues. RT was administered using a 3D conformal technique at a dose of 20 Gy over 10 fractions, which aligns with established protocols aimed at optimizing therapeutic outcomes while minimizing toxicity. Post-treatment imaging indicated structural improvement, and the patient showed significant symptomatic relief. The reason for avoiding RT in the management of benign disorders or conditions in routine practice is because of the risk of developing second malignancies, but the latter has been reported rarely. Emerging targeted therapies—such as teprotumumab, an IGF-1 receptor inhibitor—offer promising avenues for disease control, though cost and availability remain limiting factors in resource-constrained settings. Immunomodulatory agents such as rituximab and tocilizumab have shown variable success and may be considered in steroid-refractory cases. Selenium supplementation has shown benefit in early, mild cases, particularly in selenium-deficient populations.

CONCLUSION

Graves' ophthalmopathy remains a complex clinical entity with heterogeneous manifestations and unpredictable progression. In patients who are unresponsive to corticosteroids and surgery or unsuitable for surgery, orbital radiotherapy offers an effective therapeutic option, particularly during the active phase of the disease. Delivered appropriately, RT reduces orbital inflammation, mitigates compressive symptoms, and improves functional outcomes with a favorable safety profile. Multidisciplinary management remains essential, incorporating endocrinology, ophthalmology, radiation oncology, and immunology to tailor treatment across disease phases. Early intervention, cessation of risk factors like smoking, and patient education significantly influence long-term outcomes. Optimal management requires a multidisciplinary approach tailored to disease severity and phase, with early intervention and patient compliance playing critical roles in achieving long-term remission.

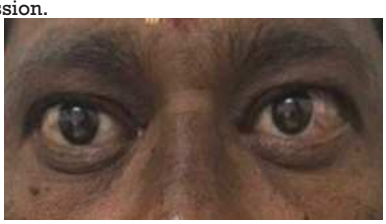

Figure 5: Post Radiotherapy Clinical Image Showing Reduction in Periorbital Edema and Proptosis With

Improvement in Conjunctival Injection and Eye Lid Retraction.

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