

Orbital irradiation for thyroid orbitopathy: 4 years experience

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Abstract

Objective: To review the practice of orbital irradiation in thyroid orbitopathy.

Methods: Review of the records of patients who received orbital irradiation for thyroid orbitopathy between June 1995 and June 1999. Twenty four patients were treated with a radiotherapy protocol. The practice of radiotherapy was analyzed and various clinical parameters were measured to document the response during follow up.

Results: Radiotherapy was used as first-line treatment for 7 patients (29%) and as second-line treatment for 9 (38%), while 8 patients (33%) had combined therapy with steroids. Soft tissue signs and compressive optic neuropathy showed the most favorable outcome while ocular motility and proptosis had a less positive outcome. No ocular complications were detected during follow-up.

Conclusion: Orbital irradiation is a safe and effective way of treating active thyroid orbitopathy.

orbital tissue. Following inflammation and congestion, the clinical outcome is symptoms and signs of proptosis, soft tissue swelling, exposure keratopathy, or compressive optic neuropathy.

To alleviate the effects of thyroid orbitopathy, either reduction of the retrobulbar tissue volume and inflammation, or expansion of the volume of the bony orbit is required. The latter can be achieved by surgical removal of the orbital wall while medical decompression helps to reduce inflammation and orbital tissue volume. Traditionally, corticosteroids were shown to be effective as first-line immunosuppressive treatment.² However, side effects of gastrointestinal disturbance, glucose intolerance, and psychiatric disturbance are frequent. Orbital irradiation has been used worldwide for more than 70 years with variable results.³⁻⁶ Radiotherapy can be used either alone or, more commonly, combined with systemic corticosteroids. In Hong Kong, the use of radiotherapy has been increasing in recent years. In this retrospective study, we summarize our experience of the management of thyroid orbitopathy with orbital irradiation.

Methods

The medical records of 43 patients who received orbital irradiation in the Radiotherapy and Oncology Unit at Queen Elizabeth Hospital between June 1995 and June 1999 for thyroid orbitopathy were reviewed. Since the unit is a tertiary referral center, the patients were referred from and followed up in different ophthalmology units. Therefore, only the 24 patients who were followed up at the Hong Kong Eye Hospital were included in the study. Follow-up ranged from 2 to 45 months and all patients were followed up by ophthalmologists and clinical oncologists. Radiotherapy was offered to patients by ophthalmologists or radiotherapists for various indications.

Key words: Corticosteroid, Radiotherapy, Thyroid orbitopathy

Introduction

Thyroid orbitopathy is thought to be autoimmune in origin and is closely linked to autoimmune thyroid disease. The core problem is a discrepancy between increased volume of retrobulbar soft tissues and the fixed space of the bony orbit.¹ The trigger for the autoimmune response in the orbit remains unknown. The final pathway is the mononuclear infiltration of the orbital soft tissue and extraocular muscle. Hydrophilic glycosaminoglycans laid down by activated fibroblasts cause a vast increase in the volume of the

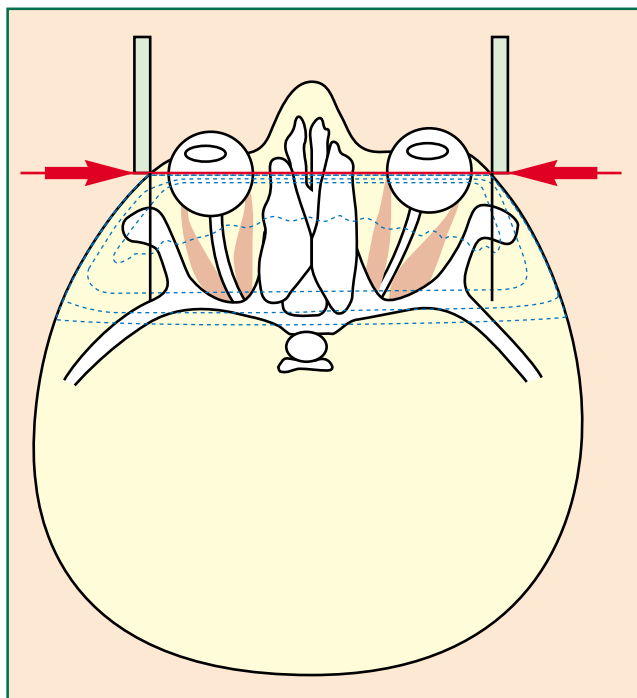


Figure 1. Isodose distribution of radiotherapy.

The clinical parameters of eye change recommended by the American Thyroid Association were monitored during follow up.⁷ The clinical response to radiotherapy, with or without systemic corticosteroids, was noted, with particular attention to the primary problems necessitating irradiation. Since thyroid orbitopathy runs a natural course, it generally improves with no intervention,⁸ clinical improvement occurring 6 months after radiotherapy was instigated did not count as a response to treatment

All 24 patients were treated with a standard orbital radiotherapy treatment protocol, in the supine position, and immobilized by a head cast. The clinical target volume was limited to the retrobulbar orbital content, sparing the lens, lacrimal gland, and the sella turcica. A central dose of 20 Gy was delivered in 20 fractions over 2 weeks with a 6 MV photon beam. Lateral opposing fields with the center on the outer bony canthus were used. The fields measured 4 x 4 cm for 20 patients, 3.5 x 4 cm for 2 patients, 3.75 x 4 cm for 1 patient, and 4 x 5 cm for 1 patient. A half-beam block at the anterior border was used to decrease the dose to the lens. The isodose distribution of the radiation technique is shown in **Figure 1**. In 8 of 24 patients, the portals

of beam were further modified by multileaf collimation to decrease the dose to nearby cranial structures. A thermoluminescent dosimeter (TLD) was used to estimate the lens dose for each patient.

Results

There were 10 men and 14 women in the study. The age of the men ranged from 41 to 67 years (mean, 59.7 years). The average follow up time was 21.8 months. The age of the women ranged from 26 to 75 years (mean, 50.5 years). The average follow up time was 19.4 months.

Radiotherapy was used as a first-line treatment without systemic corticosteroids for 7 patients (29%). Two patients were offered radiotherapy instead of steroids because they had psychiatric disturbance. The other 5 patients had radiotherapy (administered by radiotherapists) as primary treatment because of extraocular muscle problems. The results are summarized in **Table 1**. Eight patients (33%) had combined treatment with radiotherapy and systemic steroids, while 9 (38%) had radiotherapy as a second-line treatment when prior therapy with systemic steroids failed (**Figure 2**). An analysis of the patients in whom prior steroid treatment failed is shown in **Table 2**.

The responses of major ocular problems to radiotherapy with or without systemic steroids are summarized in **Figure 3** —

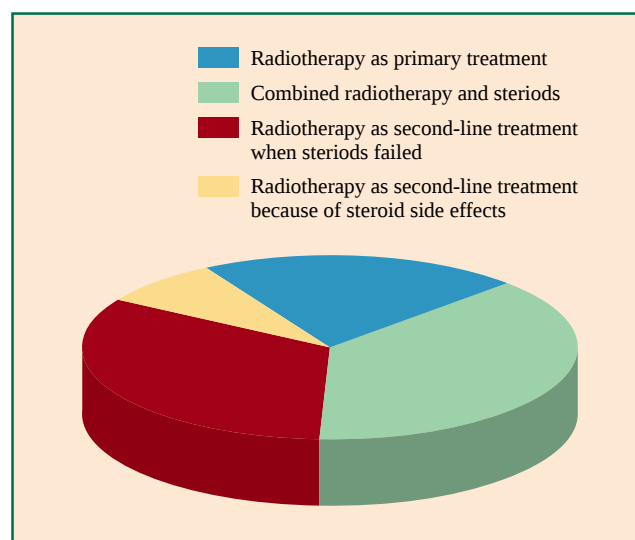


Figure 2. Use of radiotherapy.

Table 1. Summary of the 5 patients who had radiotherapy as primary therapy.

	Indication for therapy	Clinical response
Patient 1	Diplopia/right hypotropia (25 D) and esotropia	No improvement
Patient 2	Diplopia/right hypotropia (23 D)/lid edema	Muscle problem — no improvement. Lid edema — improved
Patient 3	Proptosis/diplopia	Proptosis reduced from 25 mm OU to 22 mm OU/subjective good binocular single vision
Patient 4	Diplopia with reduced right elevation	No improvement
Patient 5	Proptosis/diplopia with reduced right elevation and abduction in both eyes	Proptosis reduced by 2 mm OU. Diplopia only on extreme gaze

Abbreviations: D = prism dioptre; OU = both eyes.

Table 2. Analysis of the 9 patients who had radiotherapy because of previous failure with corticosteroids

Indication	Number of patients	Number of patients improved after radiotherapy (%)
Choroidal folds	3	0 (0)
Proptosis	1	0 (0)
Compressive optic neuropathy	4	2 (50)
Increased intraocular pressure	1	1 (100)

each patient may have had more than 1 problem requiring radiotherapy. The results of exposure keratopathy to treatment were not evaluated since other treatment modalities such as topical lubricant and/or tarsorrhaphy had a better effect on the clinical outcome than medical decompression.

Soft tissue involvement and compressive optic neuropathy had the most favorable outcome. All 11 patients with soft tissue involvement subjectively reported relief of tightness and sensation of swelling of the orbit after treatment. Treatment failed for 2 patients since the problem recurred within 6 months of radiotherapy, necessitating further steroid treatment. The visual acuities of the 7 patients with compressive optic neuropathy ranged from 6/36 to hand movement. Five of the 7 patients (71%) regained their premorbid visual acuity and color vision after treatment, while 2 patients had permanent visual loss. One patient eventually underwent surgical decompression of the orbital wall and the other refused surgical intervention.

Nine patients had significant proptosis, with less than half having a satisfactory response. Four of the 9 patients (44.4%) had a reduction of proptosis of 1 to 3 mm on the Hertel exophthalmometer measurement, while only 1 had a reduction of more than 3 mm.

Ocular motility improved for 4 of 11 patients with significant ocular motility problems. Persistent diplopia remained for 7 patients. The other 4 patients reported improved diplopia in the primary position with a satisfactory field

of binocular single vision, with or without the help of prism glasses.

Ten patients with raised intraocular pressure were already taking antiglaucoma medications (1 to 3 drugs). Seven of the 10 patients (70%) achieved reduced intraocular pressure after radiotherapy, which was thought to be due to alteration of topical medication for some patients. One patient who had a premorbid intraocular pressure of 48 mm Hg in both eyes with maximal topical medications, was given systemic steroids, but this treatment failed. However, the intraocular pressure dramatically reduced to 25 mm Hg in both eyes after radiotherapy, with the same topical medications.

None of the patients with choroidal folds responded to radiotherapy, although 1 patient had spontaneous resolution of the folds after 1 year. However, no patients with choroidal folds experienced any significant visual loss.

The mean lens doses, estimated by TLD measurement, were 46.6 cGy to the right eye and 46.2 cGy to the left eye. No patients developed radiation-induced cataract, retinopathy, or neuropathy during the follow-up period.

Discussion

Supervoltage orbital irradiation has been used to treat thyroid orbitopathy for more than 70 years. During the past few decades, the technique has been refined to deliver radiation energy more precisely to the orbit. Development

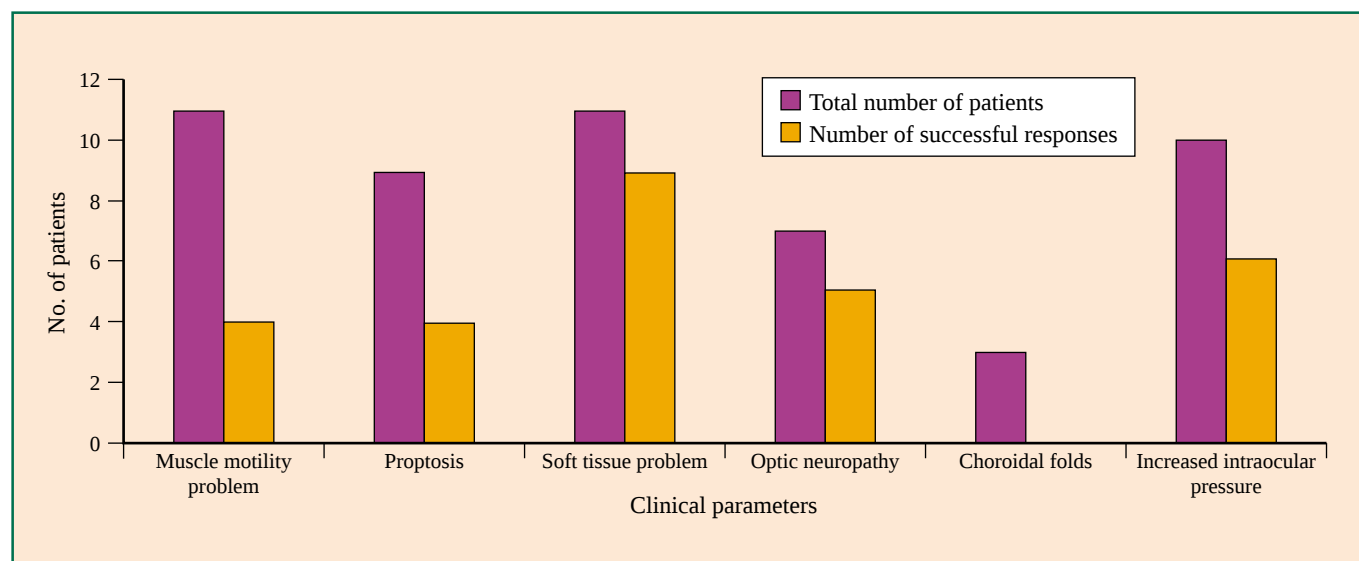


Figure 3. Summary of clinical response to orbital radiotherapy.

of the linear accelerator has enabled radiotherapists to use a collimated energy beam that effectively treats target tissue while limiting radiation to nearby vital structures.⁹

Radiotherapy has been used either as a primary therapy or combined with systemic steroids for the treatment of active thyroid orbitopathy. According to a survey by Weetman and Wiersinga, most respondents recommended disease-modifying treatment but the majority still favored steroid treatment and only a minority (23%) preferred orbital radiotherapy.¹⁰ Most studies show radiotherapy to be most useful at the active inflammatory phase of thyroid orbitopathy,¹¹ and Kazim et al claimed that radiotherapy has even greater efficacy and fewer complications than systemic steroids.⁴

Our study showed radiotherapy to be most useful for the treatment of compressive neuropathy and soft tissue involvement. Comparable results have also been demonstrated in other major series.^{5,6} This observation is comprehensible as these 2 conditions are related to the active inflammatory state of the disease. In our study, all the patients with compressive optic neuropathy had prior systemic corticosteroid therapy or combined therapy. The most common problem with steroids is the deterioration of optic nerve function during reduction of the dosage. However, the dosage required for achieving adequate decompression often induces intolerance to the drug. Radiotherapy plays a vital role in stabilizing the orbit in the long term. None of the patients who were successfully treated had another episode of optic neuropathy during follow-up. The 2 treatment failures were probably due to prolonged compression.

In contrast, our study did not show a similar success with radiotherapy alone or combined with systemic steroids for patients with proptosis and muscle motility as the primary problem. Although there is a general belief that radiation improves proptosis and ocular motility function to a lesser extent than soft tissue signs,¹² Claridge et al showed that orbital radiotherapy and medical immunosuppression reduced the requirement of major orbital surgery or muscle surgery later in life.⁸ These researchers noted that early application and long-term medical immunosuppression may improve the outcome. The reduction of proptosis in our patients was low (mostly below 3 mm) when compared with surgical decompression of the orbit.¹³ The 1 to 2 mm reduction of proptosis for most patients probably did not significantly improve the cosmetic appearance. When applied to muscle motility problems, patients may have a better range of eye movement but the primary problem, binocular diplopia, remains despite the reduction in muscle imbalance. Only few people with this condition do not require prism glasses. Nevertheless, orbital radiotherapy still has a role since it may shorten the

active phase and earlier definite corrective surgery may be performed.

The response of intraocular pressure to radiotherapy is worth mentioning, since 70% of our patients achieved better control of intraocular pressure. Increased intraocular pressure in thyroid orbitopathy is probably due to the inflamed orbit and muscle tightness. Medical decompression addresses the problem more directly than antiglaucoma medication, which mainly reduces the production of aqueous humor. A well-designed clinical trial may confirm this theory.

In general, we found radiotherapy to be efficient for relieving patients' inflammatory signs within 4 weeks of the end of treatment. Regression of the eye condition is more significant if treatment is initiated in the early stage of the disease (this includes refractory problems such as proptosis and muscle motility disorder). Once inflammatory infiltration has been replaced by fibrosis, radiotherapy is usually less effective. It is therefore recommended that treatment should start during the active phase.

Corticosteroids are effective for treating active thyroid orbitopathy. Some radiotherapists routinely give a short course of low-dose steroids while the patient undergoes irradiation since exacerbation of eye problems during the treatment period is common. The side effects of corticosteroids are cushingoid features, diabetes, and depressive psychosis. Steroids are therefore most useful for severe orbitopathy since radiotherapy takes 3 to 4 weeks to take effect and the fast action of steroids alleviates acute symptoms, while irradiation stabilizes the orbit in the long term. Radiotherapy may be used alone for moderate thyroid orbitopathy but we prefer to use combination therapy for the severe form of the disease.

The dose of radiation used in our protocol has been widely studied and shown to be safe, with a low risk of inducing cataract, retinopathy, or neuropathy.^{5,6} The estimated lens dose was below the internationally-accepted limit for radiation-induced cataract. Although no radiation-induced tumor has been reported during the past 30 years, the minimal risk still justifies follow-up of treated patients. The clinician should ensure that the irradiated volume remains small and localized and some authorities suggest radiotherapy is avoided for young patients.^{6,14}

Conclusion

Orbital irradiation, in conjunction with systemic corticosteroids, is a safe and effective way of treating some patients with thyroid orbitopathy.

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