

# Subconjunctival injection of triamcinolone in the treatment of lid retraction of patients with thyroid eye disease: a case series

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## Abstract

**Purpose** To report the results of subconjunctival injection of triamcinolone in the treatment of thyroid eye disease-related lid retraction.

**Intervention** Patients with either unilateral or bilateral upper lid retraction, secondary to thyroid eye disease, diagnosed during the period of February 2004 to June 2005 were recruited. An injection of 0.5 ml of triamcinolone acetonide (40 mg/ml kenalog) with 0.1 ml of 2% lignocaine was injected into the subconjunctival region of the lid between the conjunctiva and Muller's muscle under topical anaesthesia on upper lid eversion.

Pre- and post-procedure measurements included lid aperture, marginal reflex distance, the amount of lagophthalmos, and intraocular pressure measurements. Photographs were also obtained before the procedure and at subsequent visits. Follow-up was done at 2 weeks, 1, 3, 6 months and at 1 year.

**Results** Three of the four patients had resolution of their upper lid retraction within 1 month of treatment, with one patient requiring a repeat triamcinolone injection. The patient who had fibrotic muscles did not respond to triamcinolone injections and required surgical correction.

**Conclusion** Upper lid subconjunctival triamcinolone appears to be an effective treatment option in reducing lid retraction in patients with recent onset of thyroid eye disease.

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**Keywords:** subconjunctival; triamcinolone injection; lid retraction; thyroid eye disease

## Introduction

Upper lid retraction has been attributed to various proposed mechanisms. The mechanisms include increased sympathetic tone in the Muller's muscle,<sup>1,2</sup> levator muscle fibre enlargement,<sup>3</sup> levator muscle contracture or fibrosis, abnormal adhesions between the levator and adjacent structures<sup>3</sup> or fixation duress that results from contracture and restriction of the inferior rectus muscle with resultant increase in tone of the superior rectus and levator muscle when the affected eye attempts to fixate.<sup>4,5</sup> The typical histopathological findings of the extraocular muscles and orbital connective tissue that are seen in these patients show inflammatory cell infiltration, oedema, fatty degeneration, and collagen proliferation leading to muscle enlargement,<sup>5</sup> supporting an immune-mediated inflammatory process.

To date there have been various surgical and medical options, for the treatment of lid retraction secondary to thyroid eye disease. Treatment however has been relatively ineffective and difficult in many cases. Surgical options are irreversible and invasive and are often reserved as a last resort. Medical therapy includes treatment of the hyperthyroid status, to treatment with oral steroids. Apart from the systemic side effects of steroids, there have been reports of recrudescence of disease after steroid

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**Table 1** Summary of patient characteristics

Patient	Age	Timing of treatment (months)	Duration of effects (months)	Maximum follow-up (months)	Complications
1	33	4	7	7	Nil
2	34	11	4	12	Nil
3	40	1	11	2	Nil
4	42	72	No improvement	5	Nil

**Table 2** Summary of patients' marginal reflex distance (MRD) and lagophthalmos

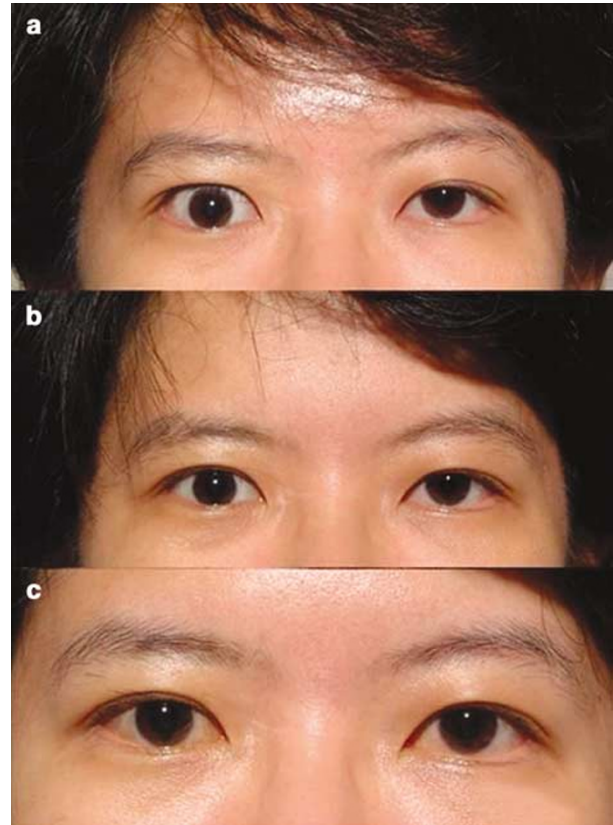
	Patient 1	Patient 2	Patient 3	Patient 4
<i>MRD (right, left)</i>				
Pre	6, 2 mm	6.5, 6 mm	6, 4.5 mm	7, 7.5 mm
Post (2 months)	4, 2 mm	4, 4 mm	5, 4.5 mm	8, 8 mm
<i>Lagophthalmos</i>				
Pre	2, 0 mm	2, 3 mm	1, 0 mm	1, 3.5 mm
Post (2 months)	0, 0 mm	1.5, 2 mm	0, 0 mm	1, 3.5 mm

dosage reduction or discontinuation, with persistence of lid retraction in the late stages.<sup>6,7</sup> Periocular steroids have also been tried in the treatment of orbitopathy.<sup>8</sup> However it has not been shown to be effective in the treatment of lid retraction. There have also been recent reports of the trial of Botulinum A toxin. Although there were improvements in lid retraction, results were unpredictable and short lived.<sup>9</sup>

Although we know the main pathology is inflammatory in nature and lies within the Muller's muscle itself, no effective method to treat lid retraction has been found. Herein, we present the results of a series of patients with upper lid retraction, treated with subconjunctival injections of triamcinolone acetoneide placed adjacent to the Muller's muscle.

**Case report**

Between the period of February 2004 and June 2005, patients diagnosed with thyroid eye disease with features of either unilateral or bilateral lid retraction were recruited. Patients who had features of myopathy, proptosis, optic nerve compression, prior thyroid eye disease treatment other than lubrication, or history of a steroid response, were excluded. After an informed consent was obtained, measurements of the upper marginal reflex distance, lid aperture, lagophthalmos, and baseline intraocular pressures were taken. Photographic documentation was also done before the treatment. The treatment was conducted in the procedure room in the outpatient setting under topical and local anaesthesia. A volume of 0.5 ml of triamcinolone acetoneide (kenalog 40 g/ml) was injected with 0.1 mls of 2% lignocaine into the subconjunctival



**Figure 1** (a) Pre-treatment. (b) 2 months post-treatment. (c) 6 months post-treatment.

area, between the conjunctiva, and the Muller's muscle, upon lid eversion. As far as possible, the patient was followed up at intervals of 2 weeks, 1, 3, 6 months and at 1 year. Similar measurements and photographs were taken post-procedure for comparison, while intraocular pressure measurements were done to monitor for potential rise in intraocular pressures secondary to steroid response (Tables 1 and 2).

**Case 1**

A 33-year-old Chinese woman presented with left superior limbic keratoconjunctivitis and subsequently developed left upper lid swelling, bilateral lid lag, and retraction. She also had lagophthalmos of the right eye, measuring 1.5 mm (Figure 1a). She was a known thyrotoxic patient who had been treated for 6 months

and was euthyroid at the time of presentation. She underwent subconjunctival triamcinolone injection for the right upper lid retraction 4 months after presentation of active thyroid eye signs. Improvement in the right upper lid retraction and resolution of the lagophthalmos of the right eye, was seen 1 month after the treatment (Figure 1b). At 6 months after treatment (Figure 1c), she was noted to have absence of lid retraction and scleral show.

### Case 2

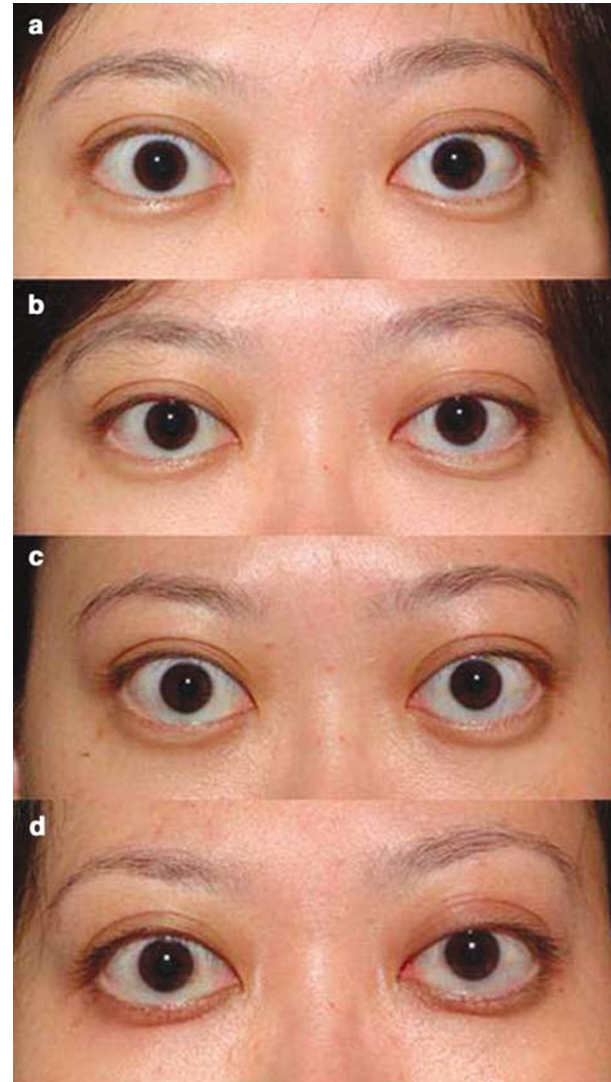
A 34-year-old Chinese woman presented with bilateral upper and lower lid retraction, lagophthalmos of 2 mm in both eyes, and had a marginal reflex distance of 7.5 mm both sides (Figure 2a). She was diagnosed to be thyrotoxic and was started on treatment. Her lid retraction persisted despite achieving a normalization of the thyroid function. The patient then received 0.5 ml of triamcinolone injection to both upper eyelids 11 months after the diagnosis of lid retraction. The patient responded well with signs of improvement starting as early as 12 days from treatment. At 1 month there was still residual scleral show, and she achieved complete resolution of the scleral show subsequently at 2 months post-treatment (Figure 2b). However 4 months after the initial injection, her bilateral upper eyelid retraction recurred (Figure 2c), requiring two repeat injections of 0.5 ml each time into the same area. The patient had received a total of three injections to the upper lid and remained stable (Figure 2d).

### Case 3

A 40-year-old Chinese woman who had been euthyroid for 4 months, presented with right lid retraction of one month's duration. Clinical examination revealed upper lid retraction and 1 mm of lagophthalmos on the right associated with mild right lid lag. She underwent treatment of the right eye 1 month after presentation. During a subsequent review 1 month later, she had subjectively improved and the lid retraction had reduced. Triamcinolone was no longer visible in the subconjunctival region on eversion of the upper lid and her intraocular pressures were normal. She did not have any recurrence of the lid retraction. The patient was contacted via phone and reported no recurrence of the upper lid retraction 1 year after treatment.

### Case 4

A 42-year-old Chinese woman presented with left eyelid retraction of 6 years duration. She had received only ocular lubricants from her previous ophthalmologist and



**Figure 2** (a) Pre-treatment. (b) 2 months post-treatment. (c) 4 months post-treatment. (d) 9 months after third Triamcinolone injection to the upper lid.

had been biochemically euthyroid and stable. She was initially not keen on surgery and consented to bilateral upper lid subconjunctival injection of triamcinolone. She was observed up to 2 weeks post-treatment, but there was no improvement in the lid retraction bilaterally. She subsequently underwent bilateral lid recession and right Mullerectomy. Intraoperatively, it was noted that there was residual triamcinolone between the conjunctiva and the fibrotic Muller's muscle fibres.

### Discussion

The four patients were treated with subconjunctival injections at varying intervals after the onset of upper eyelid retraction. The first three patients, who had onset

of upper lid retraction of less than 12 months, showed a relatively dramatic response, improving by 2 weeks post-injection; with complete resolution of their lid retraction within 1 to 2 months of treatment. The fourth patient did not respond to subconjunctival triamcinolone at all, even though the triamcinolone was visualized at the time of surgery and identified at the right target location, between the conjunctiva and the Muller's muscle. This was likely because of the fact that the Muller's muscle was already fibrotic and no longer had active inflammation. This rapid response to injection in euthyroid patients suggests that triamcinolone is likely to be effective in reducing lid retraction in lids with active inflammation. There is probably a window period for treatment as the inflammation generally reaches the burnt out plateau phase beyond 12 months.<sup>10</sup> Triamcinolone acetonide is a relatively insoluble compound and allows one to achieve a prolonged local steroid concentration while minimizing systemic side effects. Periocular injection of triamcinolone in the treatment was first described by Ebner<sup>11</sup> in the treatment of thyroid orbitopathy with promising results. However, to date, this is the first report of direct localized therapy in the treatment of lid retraction.

The first patient required only one injection while the second patient required three injections per lid at 3–4 month intervals. This may be explained by the fact that targeting the inflammation during the acute phase before it becomes chronic is more likely to achieve complete resolution. In patient 2, chronic inflammation had already developed at 11 months after the onset of the upper lid retraction, and hence required a longer duration of anti-inflammatory therapy. Patient 3 did not have complete resolution of lid retraction, but declined further injections as she was satisfied with the outcome. In cases that require repeat injections, the dose of medication should be adjusted, as 0.5 ml (20 mg) of the triamcinolone may still have been insufficient. More inflamed lids probably require higher doses, but this may be technically more difficult to administer as such lids are difficult to evert. Furthermore, these swollen lids are less able to accommodate larger volumes of the drug. It is important to ensure that the injected triamcinolone does not leak out through the needle entry point, thereby reducing the retained dose. A cotton swab is therefore used to press on the injected site as the needle is withdrawn.

Our small series suggests that the patients with thyroid-related upper lid retraction who were treated early in the course of their disease, during the active inflammatory phase, possibly within 6 months of their presentation, had a sustained response to subconjunctival injection of triamcinolone.

None of the patients developed any complications during the injection and it was relatively painless and

well tolerated. Close follow-up of these patients allowed the authors to quickly detect and treat any steroid response-induced raised intraocular pressures. None of the patients developed glaucoma or cataract.

While the mechanism of effect of triamcinolone on lid retraction is presumed to be due to an anti-inflammatory and anti-fibrotic effect, it has been well reported that the steroids may cause myopathic ptosis. However, our second patient had relapse of the retractions, requiring repeat injections. This suggests that the mechanism of action is its anti-inflammatory effect rather than the myopathic or aponeurotic dehiscence effect on the upper lid. Any injection to the upper lid, which can cause the tissues to swell, may detach the levator aponeurosis from the tarsal plate, inducing an aponeurotic ptosis. However, in our series only small volumes of triamcinolone were injected, and the site of administration was between the conjunctiva and Muller's muscle, and not between the tarsal plate and aponeurosis, as demonstrated by the intraoperative findings in patient 4. Thus aponeurotic ptosis as a possible effect in reducing the lid aperture is less likely.

There are several limitations to this case series. Our sample size was small and our method of treatment may not apply to the general thyroid population who may have features of thyroid orbitopathy as well. In severe lid retraction, eversion of the upper lid may prove difficult and hence may not be amenable to such treatment. Despite the short follow-up, we feel that repeat injections of triamcinolone can be safely administered.

Although triamcinolone may not address all the possible mechanisms of lid retraction, it appears to be effective for the treatment of active thyroid upper lid retraction avoiding the need for surgical correction. However, proper case selection is important in ensuring the success of this procedure.

In summary this case series illustrates that there is a future for targeted medical treatment of upper lid retraction. Future randomized-controlled trials with a larger sample size and longer follow-up are needed to determine the safety and efficacy of this mode of therapy.

#### Conflict of interest

None of the authors have any financial interests to disclose.

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