

A Case in Which Tranilast Ophthalmic Solution Was Thought to Be Effective for the Prevention of Symblepharon and Recurrence after Pterygium Surgery

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We report our experience of a case in which a combination of conjunctival symblepharon detachment, conjunctival granuloma excision, and conjunctival free flap transplantation was performed for the treatment of symblepharon after pterygium surgery, with satisfactory outcomes.

The patient was referred to our hospital with pterygium recurrence, symblepharon and granuloma formation after pterygium surgery in the right eye at another hospital. We performed conjunctival symblepharon detachment along with conjunctival autograft transplantation, and started instillation of tranilast ophthalmic solution immediately after the surgery, to inhibit proliferation and adhesion formation. During the 6 months' follow-up of the patient at our hospital, the postoperative course was satisfactory, and no recurrence of symblepharon, pterygium or granuloma was observed. There were no adverse drug reactions associated with the instillation of tranilast ophthalmic solution.

Tranilast ophthalmic solution may be effective not only for prevention of pterygium recurrence, but also for inhibition of symblepharon and granuloma formation.

Key words: Tranilast, Pterygium Surgery, Conjunctival Free Flap, Conjunctival Granuloma, Symblepharon

INTRODUCTION

Pterygium is a disease characterized by abnormal growth of the subconjunctival tissue that commonly occurs on the nasal aspect, causing conjunctival tissue to extend from the nasal edge of the eye to the cornea. The recurrence rate after simple pterygium excision is reported to be 23% to 75% [1]. We report our experience of a case of recurrent pterygium associated with symblepharon, in whom further recurrence was prevented by pterygium excision and combined conjunctival flap transplantation, followed postoperatively by instillation of tranilast ophthalmic solution.

CASE AND METHODS

The patient was a 45-year-old man who underwent pterygium surgery in the right eye at another hospital in June 2009. He was also treated with levofloxacin and betamethasone ophthalmic solution for symptoms of infection. Later, a conjunctival tumor-like growth was found on the surgical wound; thus, instillation of tranilast ophthalmic solution was initiated to inhibit the formation of granulation tissue. However, conjunctival symblepharon, granuloma formation, and a tendency towards pterygium recurrence were observed, and the patient was referred to our hospital on July 28, 2009. Because his symptoms were not relieved during the observation of his clinical course at our hospital, we performed a combination of conjunctival symblepharon detachment, conjunctival granuloma excision, and conjunctival free flap transplantation on October 7,

2009. Fig. 1 shows the preoperative findings; conjunctival symblepharon, conjunctival granuloma formation, and a slight tendency towards pterygium recurrence are observed at the nasal edge of the right eye.

Surgical Procedures

First, the recurrent pterygium was detached from the cornea using a 3.0-mm spoon blade knife (Fig. 2). While the pterygium on the conjunctiva was excised with conjunctival scissors, all of the proliferative tissue, including the symblepharon and the conjunctival granuloma, were removed (Fig. 3). Then, a piece of healthy conjunctiva comparable in size to the area of the exposed sclera was covered with the conjunctival autograft obtained from the temporal portion of the bulbar conjunctiva of the same eye to form a conjunctival free flap, after carefully smoothed with conjunctival forceps, and sutured with 8-0 vicryl thread (Fig. 5). The excised area was sutured with 8-0 vicryl thread (Fig. 4). We confirmed that no part of the sclera was exposed. The surgery was then completed.

Fig. 6 shows the pathological findings in the excised tissues. While mild hyperplasia of the conjunctival epithelium, vascularity of the overall stroma, and denaturation of collagen fibers in a part of the stroma were observed, inflammatory cell infiltration was only mild.

The surgical sites was protected with a soft contact lens for 1 week after the surgery. Instillation of levofloxacin, fluorometholone and tranilast ophthalmic solutions was started immediately after the surgery.

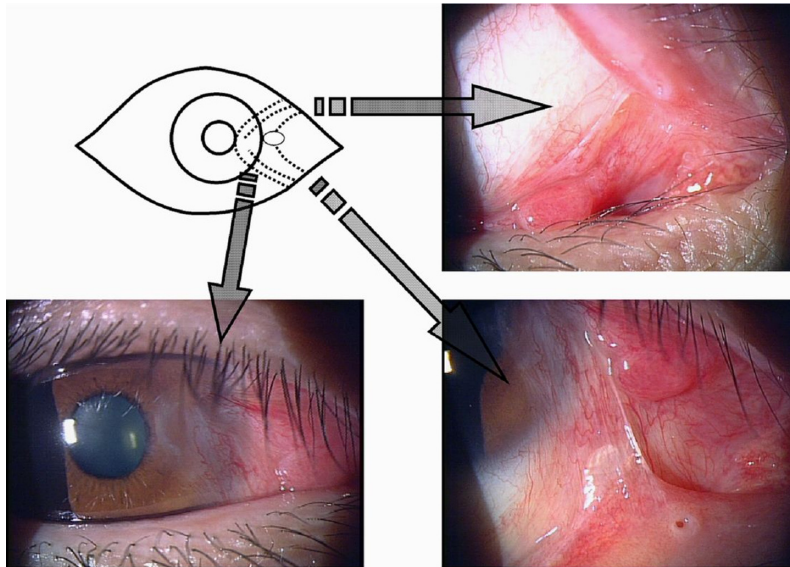


Fig. 1 Findings before the reoperation (September 29, 2009)

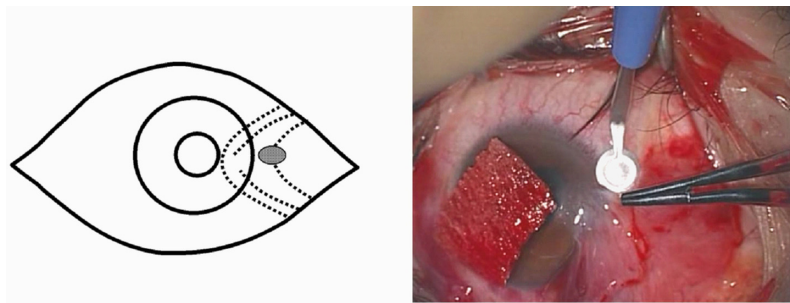


Fig. 2 Detachment of the recurrent pterygium and the adhesion site

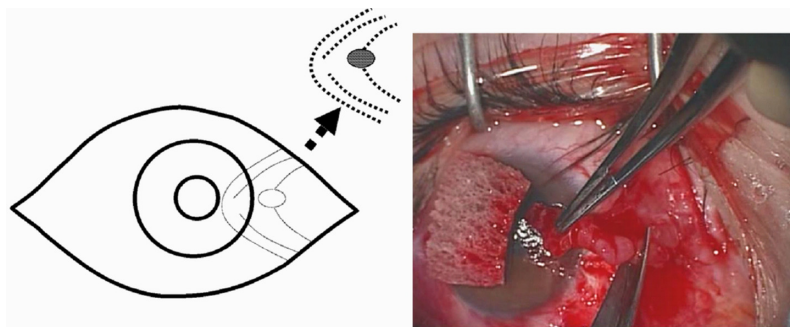


Fig. 3 Excision of the conjunctival granuloma and the adhesiolysis site

RESULTS

The postoperative course was satisfactory, and the clinical course remained satisfactory until the end of the 6 months' follow-up after the surgery (Fig. 7), no evidence of recurrence of the conjunctival symblepharon, pterygium or granuloma formation was observed. There were no proliferative changes at the site of the graft transplantation.

DISCUSSION

Recurrence is known to be very common after pterygium surgery. In our present patient, we performed transplantation of a conjunctival free flap, followed immediately by initiation of tranilast ophthalmic solution instillation, which resulted in the prevention of recurrence for at least 6 months after the surgery.

Tranilast inhibits calcium entry into inflammatory cells, such as mast cells [2], thereby inhibiting the release of histamine and other chemical mediators [3]; thus, an ophthalmic solution of this drug is used for

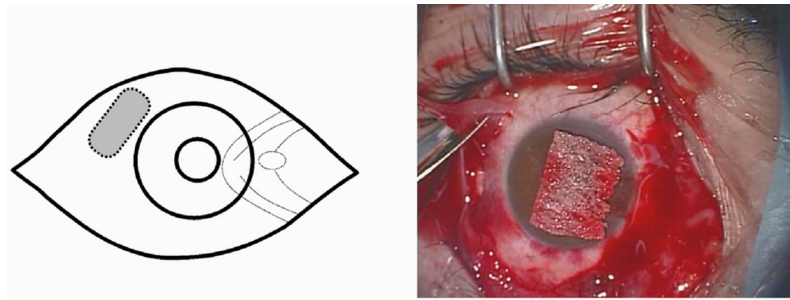


Fig. 4 Harvest of a free graft from the conjunctiva at the temporal edge

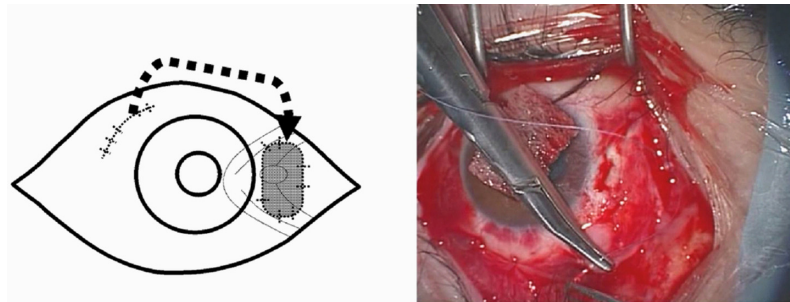


Fig. 5 Suture of the free graft to the site of conjunctival granuloma excision and adhesiolysis

the treatment of allergic conjunctivitis. Moreover, the drug shows an inhibitory effect on the production and release of cytokines such as transforming growth factor β [4], and on collagen synthesis in the fibroblasts [5]; thus, in addition to being used for the treatment of allergic diseases of the eye, oral formulations of this drug are also used in the treatment of keloids and hypertrophic scars. In the field of ophthalmology, previous reports have shown the efficacy of tranilast in the prevention of postoperative pterygium recurrence [6], **consistent with the therapeutic effect in our present case**. In addition, the inhibitory effect of the drug on postoperative adhesion formation has also been reported in animal studies [7, 8], and there are reports of cases in which oral administration of steroids and tranilast was effective in the treatment of granulomatous blepharitis [9].

At the previous hospital, instillation of tranilast ophthalmic solution was not initiated immediately after the pterygium surgery, but only after a conjunctival tumor-like growth was found on the surgical wound, and no relief of symptoms was achieved. On the other hand, transplantation of a conjunctival free flap and early initiation of postoperative instillation of tranilast ophthalmic solution at our hospital resulted in a satisfactory postoperative course in the patient. It has been reported from studies on the therapeutic effects of oral tranilast administration following excision of keloids and hypertrophic scars, that preoperative prophylactic administration is effective for the prevention of postoperative recurrence [10, 11]. Thus, early postoperative initiation of tranilast ophthalmic solution instillation might have been effective for the prevention of pterygium recurrence and formation of granulation tissue

and adhesions in our patient.

On the basis of above findings, we consider that initiation of tranilast ophthalmic solution instillation soon after pterygium surgery is effective for the prevention of recurrence. On the other hand, we routinely use topical steroid and topical anti biotics after most of ocular surgery. Therefore we cannot put aside the effect of steroid because steroid also shows strong anti inflammatory effect so that theoretically it is able to reduce the scarring and the recurrence after the pterygium excision. Even though we routinely use both topical steroid and topical antibiotics after the pterygium excision, we faced recurrence of pterygium many times. Thus we thought the anti-inflammatory effect of steroid is not enough to reduce the recurrence rate in pterygium surgery. In this case reported here, we have added the topical instillation of tranilast immediately after the surgery. We thought the additive effect of tranilast was apparent and significant. Immediate instillation of tranilast is also thought to be important. This patient received topical tranilast more than one month after the first pterygium surgery was performed. We thought it was too late to expect the effect of tranilast. Again, we have used tranilast immediately after the second surgery and seen no recurrence for at least 6 months after the surgery. It is necessary that further close observation of this case in order to evaluate the long term effect of tranilast.

CONCLUSION

We have presented a case in which tranilast ophthalmic solution was thought to be effective for the prevention of conjunctival symblepharon and recurrence of pterygium in a patient who presented with recurrence

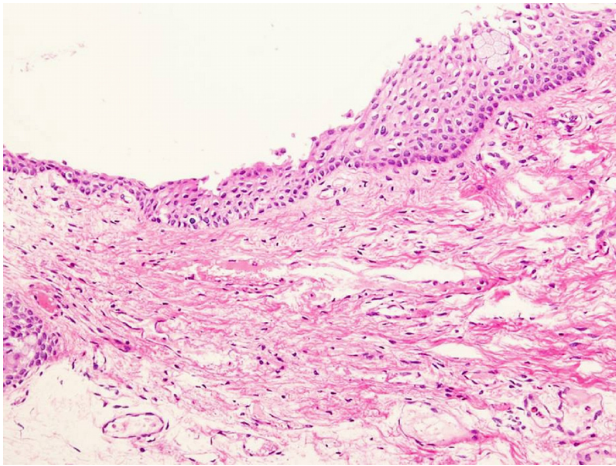


Fig. 6 Pathological findings of the excised tissue

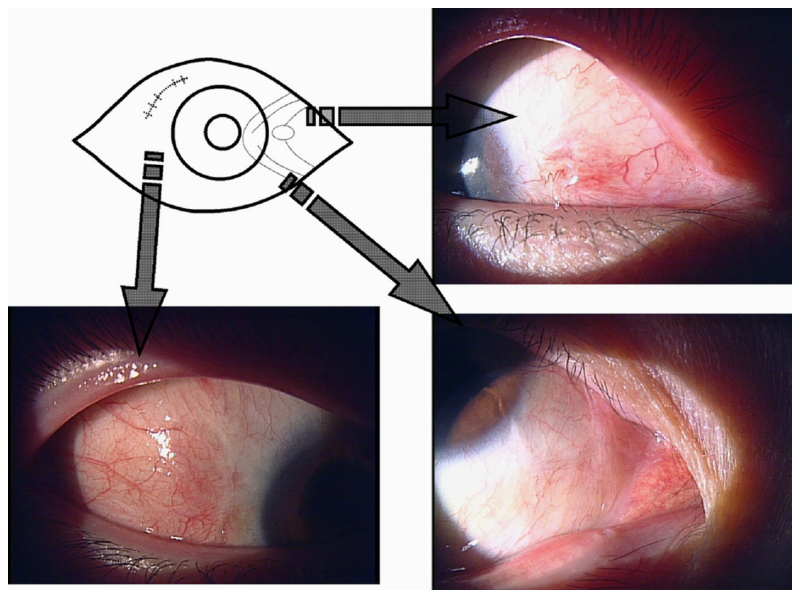


Fig. 7 Findings 6 months after the surgery (April 27, 2010)

after pterygium surgery.

It is suggested that initiation of tranilast ophthalmic solution instillation immediately after surgery might prevent recurrence of pterygium, conjunctival symblepharon, granuloma formation, etc.

REFERENCES

- 1) Shimazaki J: Pterygium Surgery. *Ganka* 47: 403-408, 2005 (in Japanese).
- 2) Komatsu H *et al.*: Mechanism of Inhibitory Action of Tranilast on the Release of Slow Reacting Substance of Anaphylaxis (SRS-A) In Vitro: Effect of Tranilast on the Release of Tranilast on the Release of Arachidonic Acid and Its Metabolites. *Japan J Pharmacol* 46: 53-60, 1999.
- 3) Sakuma Y *et al.*: Inhibitory Effects of Tranilast Eyedrops on the Release of Chemical Mediators. *Journal of the Eye* 13: 621-623, 1996 (in Japanese).
- 4) Kikuchi S *et al.*: Effects of Tranilast and Other Anti-allergic Drugs on the Collagen Synthesis and the Release of Cytokines. *The Clinical Report* 26: 4377-4383, 1992 (in Japanese).
- 5) Suzawa H *et al.*: The Mechanism Involved in the Inhibitory Action of Tranilast on Collagen Biosynthesis of Keloid Fibroblasts. *Japan J Pharmacol* 60: 91-96, 1992.
- 6) Fukui C *et al.*: Effect of Tranilast in Preventing Recurrence After Pterygium Surgery. *Japanese Journal of Ophthalmic Surgery* 12: 547-549, 1999 (in Japanese).
- 7) Adachi S *et al.*: The Prevention of Postoperative Intraperitoneal Adhesions by Tranilast: N-(3',4'-dimethoxycinnamoyl) Anthranilic Acid. *Surg Today* 29: 51-54, 1999.
- 8) Cooper K *et al.*: Reduction of Post-Surgical Adhesion Formation with Tranilast. *Journal of Surgical Research* 141: 153-161, 2007.
- 9) Mayumi A *et al.*: A case of blepharitis granulomatosa. *Japanese Journal of Clinical Dermatology* 63: 191-193, 2009 (in Japanese).
- 10) Iwahira Y *et al.*: Preventive Effect of Tranilast on Keloid and Hypertrophic Scar Formation or Exacerbation. *Journal of Clinical Therapeutics & Medicines* 8: 225-232, 1992 (in Japanese).
- 11) Fujino T *et al.*: Effect of Tranilast in Preventing Recurrence and Keloid and Hypertrophic Scar Formation After Surgery. *The Japanese journal of clinical and experimental medicine* 69: 903-913, 1992 (in Japanese).