

Case Report

# Successful Subcutaneous Allergen-Specific Immunotherapy in Refractory Atopic Keratoconjunctivitis: A Case Report

Passara Jongkhajornpong<sup>a</sup> Wannada Laisuan<sup>b</sup>

<sup>a</sup>Department of Ophthalmology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; <sup>b</sup>Division of Allergy, Immunology, and Rheumatology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

## Keywords

Atopic keratoconjunctivitis · Subcutaneous immunotherapy · Steroids · Immunomodulators

## Abstract

**Purpose:** We report a case of refractory atopic keratoconjunctivitis (AKC) which was successfully treated with subcutaneous immunotherapy (SCIT). **Case Report:** A 22-year-old woman presented with severe allergic conjunctivitis for one and a half year. She failed to respond to conventional topical anti-allergic medications, topical corticosteroid, as well as topical cyclosporine A. Therefore, oral corticosteroids had to be prescribed to control the exacerbation for 1 year. Due to refractory AKC and to avoid long-term corticosteroid use, we referred her to an allergy clinic for considering the role of SCIT. Allergology investigations showed positive skin prick test and strongly elevated serum-specific IgE to *Dermatophagoides farinae* (Der f) and *Dermatophagoides pteronyssinus* (Der p). She received a conventional protocol of SCIT using Der f and Der p allergen extracts. **Results:** The patient's ocular signs and symptoms were dramatically improved 2 months after the initiation of SCIT, and oral corticosteroids could be discontinued within 3 months of the treatment. She was maintained with mast cell stabilizers and preservative-free tears without any episodes of exacerbation. **Conclusions:** SCIT may contribute to successful outcomes in controlling symptoms and preventing exacerbation in AKC patient. It should be considered as an alternative or even a primary treatment

for patients with refractory AKC. However, the optimal SCIT protocol must be discussed with an allergist on an individual basis for the best outcome.

© 2017 The Author(s)  
Published by S. Karger AG, Basel

## Introduction

Atopic keratoconjunctivitis (AKC) is one of the most severe forms of chronic ocular allergy. Moreover, in the worst case, it leads to corneal blindness requiring corneal transplantation [1, 2]. This particular type of ocular allergy is characterized by chronic allergic conjunctivitis resulting in conjunctival scarring, fornix shortening, symblepharon, corneal ulceration, and corneal neovascularization [3]. Patients with AKC frequently present with eczema of the lids and other parts of the body [3]. The pathologic phenomena in AKC are related to a mixed IgE- and non-IgE-mediated mechanism, which is propagated by T helper 2 cells resulting in specific allergic inflammation, polyclonal IgE (and IgG4) activation, as well as an increase in mast cell, basophil, and eosinophil populations [3]. The optimal management of this condition aims to prevent permanent visual impairment by controlling symptoms and reducing recurrence and exacerbation [4]. Conventional treatment for ocular allergy such as cromones and antihistamine drugs, which are usually effective in seasonal allergic conjunctivitis and perennial allergic conjunctivitis, are often inadequate for controlling AKC [3]. Steroids are then required for combatting this condition, especially during an active phase. Several studies reported the efficacy of alternative treatments for combatting AKC, including tacrolimus and cyclosporine A [5–8], although, in challenging cases who are refractory to conventional treatments and resist to immunomodulatory medications, the appropriate treatment has yet to be established. Limited case reports demonstrated the efficacy of omalizumab (anti-immunoglobulin E, IgE) and plasmapheresis [9, 10], but difficult accessibility and high treatment cost are still major barriers to overcome.

Immunotherapy has been indicated as a treatment option for several allergic conditions including allergic rhinitis, allergic conjunctivitis, or allergic asthma [11]. However, clinical evidence in terms of specific roles and outcomes of immunotherapy for treating AKC is unclear and remains to be illustrated. We present a case of refractory AKC who was successfully treated with subcutaneous immunotherapy (SCIT).

## Case Report

A 22-year-old woman presented with severe allergic conjunctivitis for one and a half years prior to her visit. Her symptoms included itching, foreign body sensation, tearing, and photophobia. Ocular examination revealed thickened lid margins, conjunctival hyperemia with moderate thick ropy discharge, cobblestone-like papillary reaction at the palpebral conjunctiva, and dense punctate corneal epithelial erosion in both eyes (Fig. 1). Visual acuity was 20/40 in the right eye and 20/50 in the left eye. Apart from the eyes, she also had erythematous keratotic plaque at flexor areas, which was compatible with atopic dermatitis, and clinical symptoms of allergic rhinitis. She was diagnosed with AKC and was treated with 0.2% olopatadine hydrochloride once a day, 1% preservative-free methylprednisolone 4 times per day, and frequent preservative-free artificial tears. After 1 month of treatment, her condition had not improved; therefore, 20 mg of oral prednisone per day and 1% cyclosporine A twice daily were added. However, we were unable to stop oral and topical steroids due to wax and wane exacerbations for over a year. Her visual acuity varied from 20/25 to

20/70 depending on disease activity, which extremely disturbed her daily living activities. Other allergic conditions, including rhinitis and dermatitis, were well controlled by using oral antihistamine and topical steroids.

Due to refractory AKC, we referred her to an allergy clinic for considering the role of SCIT. Allergy investigations showed positive skin prick tests to *Dermatophagoides farinae* (Der f), *Dermatophagoides pteronyssinus* (Der p), cat hair, and cockroach. The levels of IgE in peripheral blood were 1,636 kUA/L of total IgE, 58.2 kUA/L of specific IgE for Der p (class 5, strongly positive), 45.2 kUA/L of specific IgE for Der f (class 4, strongly positive), 0.51 kUA/L of specific IgE for German cockroach (class 1, weakly positive), and <0.35 kUA/L of specific IgE for cat (negative).

According to the positive results of skin prick tests and serum-specific IgE in this patient, conventional SCIT for Der f and Der p was performed by using standardized Der f and Der p commercial extracts (ALK Laboratories, Port Washington, NY, USA). The conventional protocol for SCIT started with 0.1 mL of 10 AU/mL of each allergen extract, then the treatment dose was adjusted weekly until it reached the monthly maintenance dose at 0.5 mL of 1,000 AU/mL of each allergen extract within 12 weeks. The ocular symptoms and signs were significantly improved in terms of lid inflammation, conjunctival reactions, and punctate epithelial erosion on the corneas 2 months after initiation of SCIT, as shown in Figure 2. We were able to taper the patient off oral and topical steroids within 3 months and maintained with topical mast cell stabilizers and preservative-free tears, without any episodes of exacerbation. Her vision was maintained at 20/40 in the right eye and 20/50 in the left eye. Moreover, her skin and nasal conditions gradually improved. No adverse effects were noted during SCIT.

## Discussion

In this case, immunotherapy appears to have been effective for the treatment of AKC refractory to standard therapy, including systemic and topical steroids and topical cyclosporine. AKC was first described by Hogan in 1952 [12]. The diagnosis is based on the following criteria: (a) hereditary history of allergies, (b) associated allergies such as asthma, rhinitis, and urticaria, (c) typical persistent dermatitis which exacerbates and remits over a period of years, (d) keratoconjunctivitis associated with the skin condition, and (e) eosinophilia in blood and in conjunctival secretion [12]. It is considered one of the most severe spectrums of ocular allergy that can potentially lead to long-term visual impairment due to corneal and lenticular complications [2]. The clinical course is always consistent all year long. Basically, AKC management begins with adjusting environmental factors, dietary control for those with food sensitivity, and anti-allergic medications [12]. However, conventional topical antihistamines or mast cell stabilizers are often insufficient in controlling AKC. Patients with refractory AKC may require long-term use of steroids, which can lead to steroid-induced cataract and glaucoma. Currently, treatment trends are shifting from constant steroid use to steroid-sparing measures, with immunomodulating agents to help controlling exacerbation. Although some studies showed benefits of topical cyclosporine A in treating AKC [5], our patient was refractory to the combination of topical steroid and topical cyclosporine A. She required low-dose oral steroid for controlling episodic exacerbations; therefore, we decided to consult an allergist for immunotherapy.

Basically, immunotherapy is indicated for the treatment of patients with allergic rhinitis, allergic conjunctivitis, allergic asthma, atopic dermatitis if associated with aeroallergen sen-

sitivity, and stinging insect hypersensitivity [13]. The immunotherapy schedule is classified into two phases, the initial build-up phase and the maintenance phase. In the initial build-up phase, the dose and concentration of specific allergen extracts are increased until reaching the effective therapeutic dose. There are various protocols for allergen immunotherapy in the initial build-up phase, including the conventional, cluster, and rush regimens. The appropriate protocol should be customized with consideration of three factors including the patient, the physician, and the specific allergen used for immunotherapy. As for our case, we considered the conventional protocol for the initial build-up phase due to the patient's preference. Her ocular signs and symptoms dramatically improved within 2 months. Previous studies showed different durations between the initiation of immunotherapy and a significant ocular response, varying from months to even years [14–17]. We speculated that the differences in types and numbers of the specific allergens, treatment protocols, and evaluation intervals among studies were responsible for the variations in clinical response intervals.

We found the following advantages of immunotherapy in refractory AKC: (1) offering steroid-sparing effects for long-term disease control, (2) providing persistent effects after discontinuation of therapy for as long as 3 years [18], (3) producing systemic improvement, including dermatologic and nasal conditions, and (4) directly advocating for the core pathogenesis of the disease as a disease modifier. Nonetheless, it should be noted that approximately 50% of AKC patients show negative allergological screening [3]; thus, immunotherapy may not be applicable for AKC patients with unidentified aeroallergen sensitization.

In conclusion, AKC is a severe spectrum of ocular allergy which frequently resists conventional medications. This case report sheds light on the therapeutic role of SCIT for controlling this condition. SCIT should be considered an alternative treatment or even a primary treatment for patients with refractory AKC who have at least one certain aeroallergen accounted for the disease. However, the optimal SCIT protocol must be discussed with an allergist on an individual basis for the best outcome.

### Statement of Ethics

This study obtained ethics approval from the Institutional Review Board of Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

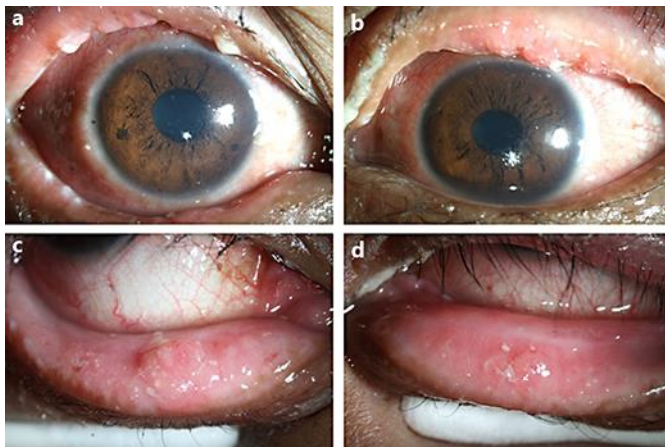
### Disclosure Statement

The authors have no financial interests to declare.

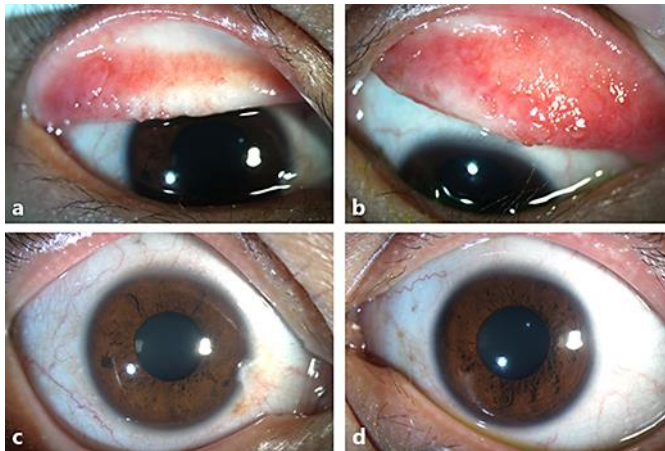
### References

- 1 Koçluk Y, Yalniz-Akkaya Z, Burcu A, Örnek F: Atopic keratoconjunctivitis: long-term results of medical treatment and penetrating keratoplasty. *Arq Bras Oftalmol* 2016;79:376–379.
- 2 Power WJ, Tugal-Tutkun I, Foster CS: Long-term follow-up of patients with atopic keratoconjunctivitis. *Ophthalmology* 1998;105:637–642.
- 3 Bonini S: Atopic keratoconjunctivitis. *Allergy* 2004;59(suppl 78):71–73.
- 4 Chen JJ, Applebaum DS, Sun GS, Pflugfelder SC: Atopic keratoconjunctivitis: a review. *J Am Acad Dermatol* 2014;70:569–575.
- 5 González-López JJ, López-Alcalde J, Morcillo Laiz R, Fernández Buenaga R, Rebolledo Fernández G: Topical cyclosporine for atopic keratoconjunctivitis. *Cochrane Database Syst Rev* 2012;9:CD009078.

- 6 Wakamatsu TH, Tanaka M, Satake Y, et al: Eosinophil cationic protein as a marker for assessing the efficacy of tacrolimus ophthalmic solution in the treatment of atopic keratoconjunctivitis. *Mol Vis* 2011;17:932–938.
- 7 García DP, Alperete JI, Cristóbal JA, et al: Topical tacrolimus ointment for treatment of intractable atopic keratoconjunctivitis: a case report and review of the literature. *Cornea* 2011;30:462–465.
- 8 Tzu JH, Utine CA, Stern ME, Akpek EK: Topical calcineurin inhibitors in the treatment of steroid-dependent atopic keratoconjunctivitis. *Cornea* 2012;31:649–654.
- 9 Taillé C, Doan S, Neukirch C, Aubier M: Omalizumab for severe atopic keratoconjunctivitis. *BMJ Case Rep* 2010;2010:bcr0420102919.
- 10 Aswad MI, Tauber J, Baum J: Plasmapheresis treatment in patients with severe atopic keratoconjunctivitis. *Ophthalmology* 1988;95:444–447.
- 11 Huggins JL, Looney RJ: Allergen immunotherapy. *Am Fam Physician* 2004;70:689–696.
- 12 Hogan MJ: Atopic keratoconjunctivitis. *Trans Am Ophthalmol Soc* 1952;50:265–281.
- 13 Cox L, Nelson H, Lockey R, Calabria C, et al: Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol* 2011;127(1 suppl):S1–S55.
- 14 Jutel M, Jaeger L, Suck R, Meyer H, Fiebig H, Cromwell O: Allergen-specific immunotherapy with recombinant grass pollen allergens. *J Allergy Clin Immunol* 2005;116:608–613.
- 15 Corrigan CJ, Kettner J, Doemer C, Cromwell O, Narkus A: Efficacy and safety of preseasonal-specific immunotherapy with an aluminium-adsorbed six-grass pollen allergoid. *Allergy* 2005;60:801–807.
- 16 Frew AJ, Powell RJ, Corrigan CJ, Durham SR; UK Immunotherapy Study Group: Efficacy and safety of specific immunotherapy with SQ allergen extract in treatment-resistant seasonal allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 2006;117:319–325.
- 17 Walker SM, Pajno GB, Lima MT, Wilson DR, Durham SR: Grass pollen immunotherapy for seasonal rhinitis and asthma: a randomized, controlled trial. *J Allergy Clin Immunol* 2001;107:87–93.
- 18 Durham SR, Walker SM, Varga EM, et al: Long-term clinical efficacy of grass-pollen immunotherapy. *N Engl J Med* 1999;341:468–475.



**Fig. 1.** **a, b** Ocular examination revealed a thickened lid margin, conjunctival hyperemia, moderate thick ropy discharge, and dense punctate corneal epithelial erosion on the cornea in both eyes (**a** right eye; **b** left eye). **c, d** Cobblestone-like papillary reaction at the right lower palpebral conjunctiva (**c**) and linear subepithelial fibrotic scar at the left lower palpebral conjunctiva (**d**).



**Fig. 2.** **a, b** Two months after the initiation of subcutaneous immunotherapy, inflammation at the lid margin was significantly decreased, and no eye discharge was found in both eyes (**a** right eye; **b** left eye). **c, d** No conjunctival hyperemia or punctate epithelial erosion were observed in both eyes (**c** right eye; **d** left eye).