

Atopic keratoconjunctivitis

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ABSTRACT

Atopic keratoconjunctivitis (AKC) is a chronic allergic inflammatory disease that is at the severe end of a spectrum of allergic conjunctival diseases. AKC can involve the cornea and conjunctiva bilaterally, and at times can lead to visual loss from corneal complications. The classification, histology, ocular examination findings and complications of AKC are described herein, as well as the roles and interactions of inflammatory cells involved. Finally, current treatment options for AKC is reviewed and presented as a stepwise, multidisciplinary approach that involves the allergist/immunologist's medical interventions of topical and systemic immunomodulating agents, as well as the surgical skills of the ophthalmologist.

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Atopic keratoconjunctivitis (AKC) is a chronic allergic inflammatory disease that bilaterally involves the cornea and conjunctiva, primarily affecting adults, but has its onset during adolescence. Of the allergic conjunctival diseases, AKC is one of the most debilitating conditions owing to its ability to cause visual loss from corneal complications.¹

AKC is at the severe end of a spectrum of allergic conjunctival diseases that includes several subtypes²: 1. seasonal (<4 weeks) allergic conjunctivitis (SAC) or intermittent allergic conjunctivitis, 2. perennial or persistent (>4 weeks) allergic conjunctivitis (PAC), 3. vernal keratoconjunctivitis (VKC), and 4. giant papillary conjunctivitis (GPC). Figure 1 illustrates this spectrum of allergic conjunctival diseases, the severity of which correlates with increased involvement of inflammatory cells. In SAC or PAC, proliferative changes seen in the more severe forms of allergic conjunctival disease are absent. VKC is characterized by proliferative changes in the conjunctiva and corneal lesions such as superficial punctate keratitis, corneal erosions, corneal ulcers, or corneal plaques, primarily occurring in the pediatric population. AKC is clinically associated with keratoconus, retinal detachment, and the formation of giant papilla. In GPC, corneal lesions are absent, but proliferative changes are seen in the upper palpebral conjunctiva that are thought to occur by mechanical irri-

tation from contact of foreign bodies such as contact lenses, ocular prosthesis, or surgical sutures.³

Although AKC is classified under allergic conjunctival diseases, clinical and pathophysiological features distinguish it from the other subtypes.⁴ SAC and PAC are predominantly dependent on IgE-mast cell hypersensitivity with widespread mast cell activation, while AKC and VKC integrates a mixture of IgE-mast cell with proliferation of the Th₂-type allergic inflammation.⁵

In 1942, AKC was classically described as having unique dense yellow infiltrates named Trantas dots within the limbus, which represent areas of necrosis in the superficial and middle layers of the corneal stroma and contain neutrophilic and eosinophilic debris.⁶ The most frequent conjunctival finding in AKC is conjunctival hyperemia with dilated conjunctival vessels. Conjunctival follicles, which are lymphoid follicles seen under the lower palpebral conjunctival epithelium, can develop and evolve from the chronically inflamed conjunctival epithelium *via* hypertrophy and increasing vascularity forming at the center of the prominence, generating a conjunctival papilla. These lesions appear to progress to develop giant papillae, >1 mm composed of fibrous tissue and inflammatory cells that bridge innate and adaptive immunity and are also found in VKC or GPC. Chemosis, caused by vascular leakage, is common. Corneal complications (from mild to severe) include superficial punctate keratitis, exfoliated superficial punctate keratitis, corneal erosions, and shield ulcers³ progressing to ulceration and neovascularization, conjunctival subepithelial fibrosis, fornix shortening, and symblepharon.¹ Eyelid involvement is commonly associated with edema and spongiotic changes with lichenification leading to the formation of Dennie-Morgan lines in the lower eyelid. Some clinical signs are more specific to AKC than others (Table 1).³

HISTOLOGY

Histological and immunohistochemical staining of conjunctival biopsy specimens in AKC patients indicate ep-

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Cellular Involvement in Ocular Allergy

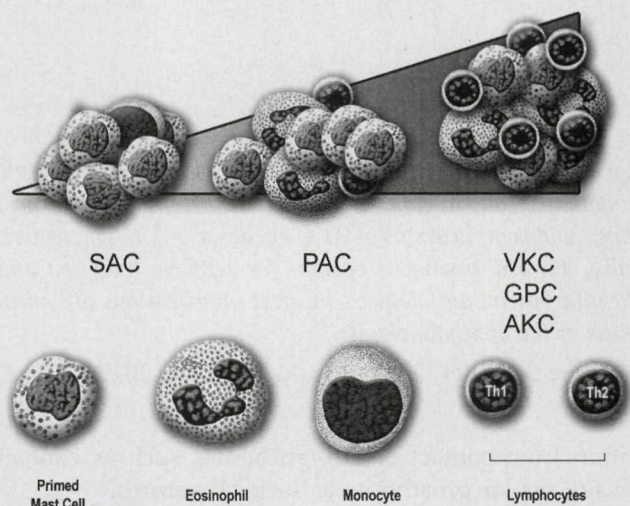


Figure 1. Cellular involvement in ocular allergy.

ithelial pseudotubular formation,⁷ significant squamous metaplasia, goblet cell proliferation with reduced goblet cell density.⁸ Confocal scanning laser microscopy of the cornea in AKC demonstrates a lower density of basal epithelial cells and corneal nerve abnormalities (i.e. increased tortuosity, thickening) compared to normal eyes.⁹ The conjunctival epithelium is infiltrated by T lymphocytes, eosinophils, macrophages, dendritic cells, and mast cells (Fig. 1). The substantia propria of the conjunctiva also shows infiltration by T lymphocytes, B cells, macrophages, and dendritic cells, sometimes accompanied by granuloma formation.⁷ AKC is commonly associated with a ropey white discharge that may correspond to increased mucin mRNA expression MUC1, 2 and 4 mRNA,¹⁰ MUC16 mRNA, and a lower MUC5AC mRNA expression.⁸

Conjunctival Epithelium

Conjunctival epithelial cells promote inflammation in chronic ocular allergic disease by a number of mechanisms: antigen presentation, expression of adhesion molecules, and expression of inflammatory cytokines. The inflammatory response seen in AKC epithelium seems to bridge the innate and adaptive immune systems.

Allergic inflammation is associated with increased human leukocyte antigen-DR (HLA-DR) and intracellular adhesion molecule (ICAM) 1 expression in the AKC epithelium.¹¹ Other cellular adhesion molecules that have been studied in AKC include ICAM1, vascular cell adhesion molecule-1 (VCAM1),¹² and P-selectin ligand¹³ that recruit, retain, and locally concentrate neutrophils and especially eosinophils with eotaxin.

Epithelial cells also express RANTES (regulated upon activation normal T cell, expressed and secreted,

chemokine ligand 5 [CCL5]), a chemotactic cytokine for T lymphocytes, eosinophils, and basophils, which is up-regulated in all allergic disorders induced by TNF- α and further augmented by interferon (IFN) γ ¹⁴ and thymic stromal lymphopoietin (TSLP), associated with the T-lymphocyte maturation through activation of antigen-presenting cells. TSLP, with IL-33, induces IL-13 mRNA expression in mast cells and TSLP⁺ cells in the giant papilla of conjunctiva reflect the potential role in the activation of dendritic and mast cells.^{15,16} In addition, $\gamma\delta$ -T lymphocytes (gamma delta cells) found in the conjunctival biopsy specimens of chronic forms of conjunctivitis (e.g., AKC) possess an alternative T-cell receptor as opposed to CD4⁺ and CD8⁺ $\alpha\beta$ -T lymphocytes that share characteristics of helper, cytotoxic, and natural killer lymphocytes placing them at the interface between innate and adaptive immunity.¹⁷

Fibroblasts

Conjunctival fibroblasts are involved in AKC development expressing ICAM1 and VCAM1, which are up-regulated by IFN- γ . Eosinophils primed with IL-5 have been shown to adhere to conjunctival fibroblasts treated with IL-4, and TNF- α ¹² also express eotaxin 1.¹⁸ The tear film bathing the AKC conjunctival surface contains IL-6, IL-8, monocyte chemotactic protein 1, and RANTES that may be derived from the conjunctival fibroblasts.¹⁹ The AKC chronic "red eye" may be caused by the production by conjunctival fibroblasts of vascular endothelial growth factor generating the neovascularization and formation of giant papillae in AKC, in concert with transforming growth factor β 1, IL-1 β , IL-4, and IL-13.²⁰

T-Lymphocytes

The AKC conjunctival surface shows an increased percentage of T-helper and a decreased T-suppressor lymphocyte concentration (i.e., high CD4/CD8 ratio) that may enhance IgE production of B cells²¹; increased numbers of CD4⁺, CD45RO⁺, and HLA-DR⁺ T cells²²; increased memory Th-cell/naïve Th-cell ratio in tear samples, suggesting a localized accumulation of memory T-helper cells²³; increased production of cytokines such as IFN- γ , IL-10, and IL-13,²⁴ as well as IL-4; infiltration by IL-4-producing T¹³; and increased expression of P-selectin ligand assisting the innate immune cells to access to the AKC surface.¹³ Because atopic states are primarily recognized as a Th₂ linked disorder, the finding that the expression of IL-2 mRNA and IFN- γ expression (more than VKC and GPC) indicates a potential shift and hybridization to a nonallergic phase with a potential Th₁ pattern in patients with AKC, compared with VKC and GPC.²⁵ In addition, the chemokine receptors CXCR4 and CCR4, which are proteins with potent chemotactic

Table 1 Specificity of AKC signs

High Specificity	Intermediate Specificity	Low Specificity
Giant papillae	Conjunctival edema	Conjunctival hyperemia
Limbal proliferation (including limbal gelatinous hyperplasia and Horner-Trantas dots)	Conjunctival follicles	Superficial punctate keratitis
Shield ulcers	Papillary hyperplasia	
	Corneal epithelial abrasions (corneal erosions and exfoliated superficial punctate keratitis)	

AKC = atopic keratoconjunctivitis.

activity for lymphocytes, were found to be increased in the papilla of AKC patients, suggesting that these chemokine receptors play a role in the formation of giant papillae.²⁶

Eosinophils and Other Cells of the Innate Immune System

Eosinophils play a critical role in the destructive nature of AKC that can lead to sight-threatening complications. Light microscopy and immunofluorescence of the cornea of patients with AKC show linear deposition of eosinophil granular substance subepithelially above Bowman's membrane and along the edge of corneal ulcers. Indirect immunofluorescence has identified this material as major basic protein (MBP) and eosinophil cationic protein (ECP) that lead to epithelial cell dehiscence, thus generating punctate keratitis and epithelial ulcers, but these depositions are not limited only to the area of ulceration, but are also found underneath intact corneal epithelium.²⁷ The corneal surface that is bathed in tears shows significantly higher levels of ECP in patients with AKC and VKC compared with GPC and SAC. The tear levels of ECP values correlated to disease severity, further supporting the role of eosinophil in visual complications of AKC and VKC²⁸ but they are not seen in other anterior surface sight-threatening disorders such as Sjögren syndrome.²⁹

Eosinophil expression of cell surface antigens such as ICAM-1, CD4, IL-2R, and HLA-DR is noticeably greater in AKC and VKC (*i.e.*, corneal surface involvement) than in GPC. Greater expression of eosinophil surface antigens imply greater cell activation suggesting that eosinophil function, rather than cell numbers, may be important in keratopathy. The spectrum of cytokines produced by eosinophils was noted in AKC and includes IL-4, IL-8, and granulocyte macrophage-colony-stimulating factor; and IL-3, -5, -6, and granulocyte macrophage-colony-stimulating factor were more prominent in VKC; and IL-5 was more prominent in GPC.³⁰ Like eosinophil activation, neutrophil activa-

tion has been shown in tears of patients with AKC with increased production of neutrophil myeloperoxidase³¹ and the extracellular deposition of neutrophil elastase, in addition to eosinophil MBP in patients with AKC and VKC.³²

In addition, macrophage activation as evidenced by osteopontin, which mediates cell activation and cytokine production, is elevated in tears of AKC patients and correlates to the severity of allergic conjunctival diseases.³³

Mast Cells

Several studies have described the densities of mast cells in normal and pathophysiological states of the eye. Differences in fixation and staining methods, as well as location and thickness of tissue sections, preclude comparison of mast cell densities, but they show the absence of mast cells in the normal epithelium, and increasing numbers of mast cells in the epithelium as well as the substantia propria of patients with ocular allergies, with the severe forms presenting with significantly higher mast cell densities.³⁴⁻³⁸ In normal human conjunctiva, mast cells are seldom found in the epithelium, and, when present, they are typically limited to the MC_T phenotype. On the other hand, the substantia propria of the normal human conjunctiva contains large numbers of mast cells (~5,000-11,000/mm³), primarily the MC_{TC} (mast cell subtypes that stain positive for both tryptase and chymase) phenotype (95%). The total numbers of mast cells are increased in the substantia propria of ocular allergies,³⁹ and more significantly in both bulbar and tarsal substantia propria of AKC patients. Animal studies show a correlation between mast cell density and the development of AKC-like signs.⁴⁰ Of note, mast cells in AKC show marked reduction in the amount of proteases other than tryptase.^{35,38} In the chronic and fibrosing conditions of AKC, the MC_{TC} subtype predominates, suggesting a transition from a simple mediator-driven disorder to that of chronic inflammation leading to conjunctival fibrosis.⁴¹

COMPLICATIONS OF AKC

Chronic inflammation of the conjunctival epithelium and cornea leads to several complications, including formation of giant cell papilla, conjunctival concretions, conjunctival scarring, corneal epitheliopathy, conjunctival scarring, keratoconus, retinal detachment, and visual loss.

The major difference between non-sight-threatening allergic conjunctivitis and sight-threatening AKC was the occurrence of T lymphocytes and the activated forms of eosinophils and their associated destructive enzymes that are absent in the former and prominent in the latter. In SAC and PAC, there exists a heavy increase in mast cells, caused by infiltration of mucosal type mast cells, but the extent of eosinophils is low and lymphocytes are almost nonexistent. In sight-threatening AKC (and VKC), on the other hand, the allergic responses are primarily directed by T-lymphocytes and its driven eosinophilia with increased expression of adhesion molecules.⁴² Conjunctival concretions appear as yellow spots in the tarsal conjunctiva and are composed of finely granular material and membranous debris that accumulates in the conjunctival subepithelium that stain strongly positive for phospholipid and elastin; weakly positive for neutral polysaccharides and lipid; and negative for amyloid, collagen, glycogen, iron, mucopolysaccharides, RNA, and DNA. This finding supports the hypothesis that concretions associated with chronic conjunctivitis represent products of cellular degeneration.⁴³

Cataract, the first ocular complication of atopic dermatitis, which was reported in 1914,^{44,45} is the most common and documented complication and retinal detachment is considered relatively rare. Because cataracts have been observed in patients with atopic dermatitis that includes retinal detachment,⁴⁶⁻⁴⁸ the pathogenesis of breaks and retinal detachments in patients with atopic dermatitis was originally thought to be caused by mechanical trauma from the excessive scratching and rubbing as many patients would slap their eyes/eyelids to relieve the itching. Interestingly, it had been shown that there are similarities between traumatic retinal detachments and those associated with atopic dermatitis, suggesting some form of defect within the connective tissue.⁴⁹⁻⁵² One of the earlier theories suggested that the skin, lens, vitreous, and retina were derived from the ectoderm and thus could be affected by atopic dermatitis, but these tissues do not completely share the same origin.^{53,54} However, this does not exclude defects in filaggrin or keratin that may be common to the retina, skin, and lens and thus may be part of the proposed epithelial defect in allergic disorders.⁵⁵⁻⁵⁸

AKC cataracts are uniquely situated at the anterior portion of the lens that may completely opacify within

6 months, but can also involve posterior portions of the lens that mimic steroid-induced cataracts⁵⁹ caused by the use of oral or prolonged topical corticosteroid therapy. There is no consistent correlation between distribution of atopic dermatitis cutaneous involvement or asthma with the development of cataracts. However, there is a suggestion that high levels of IgE⁶⁰ or the rapid rise of IgE levels may portend the development of atopic cataracts.⁶¹ In patients diagnosed with an atopic cataract on the first visit, IgE levels were ~25,000 IU/mL and those who did not have cataracts had IgE levels of ~4000 IU/mL that increased to 13,000 IU/mL at the time of cataract development.⁶¹ External eye disease such as chronic conjunctivitis (32%) or superficial keratitis (7%) is seen in over one-third of patients with cataracts. There appears to be no difference in the clinical features of the patients with or without cataracts, suggesting that it may be caused by genetic disposition. Total lens opacities had shown rapid progression at the time of exacerbation of the skin lesions (reported in two patients).^{62,63} The etiology of atopic cataracts is unclear although immunohistochemical investigation showed lens epithelial MBP deposition in 100% ($n = 3$) of atopic cataracts when compared with senile cataracts. Similarly, MBP was detected in the aqueous fluid by radioimmunoassay in 25% (4/12) of atopic cataract eyes and ranged in concentration from 11 to 70 ng/mL and senile cataract eyes contained no MBP.⁶⁴ Essential fatty acids in plasma phospholipids have been reported in AD, which was similar to atopic cataracts patients.⁶⁵ Increase in lipid peroxide levels and decrease in superoxide dismutase inducibility have been reported in severe AD patients. The lipid peroxides apparently attach to the stratum corneum, promoting loss of skin moisturization and resulting in the worsening of AD. Excessive lipid peroxide formation seems to correlate to severe, adult-type AD with cataract formation.^{66,67} Although galactosemia has been suggested as a contributory factor in the pathogenesis of some presenile and senile cataracts, it was not found in patients with atopic dermatitis with cataracts.⁶⁸

Retinal detachment appears to be increased in patients with AKC as well as in atopic dermatitis in general.^{47,48,54,69} Additional complications of AKC including blepharoconjunctivitis, cataract, corneal disease, and ocular herpes simplex are commonly associated with older patients and have been reported to be as high as 42.5%.⁷⁰⁻⁷² Herpes simplex keratitis is often bilateral with high recurrence rates that are more severe. Many patients may develop secondary staphylococcal blepharitis. It appears that AKC patients have a higher incidence of bacterial superinfections especially with *Staphylococcus*,^{73,74} leading to a chronic inflammatory response of conjunctival epithelial cells through pathways that involve Toll-like receptor 2 (TLR-2) and

receptor for platelet-activating factor.⁷⁵ In a recent study, *Staphylococcus aureus* was isolated from 67% of the AD patients, and finding any type of bacteria was isolated from 86% of the patients was significantly higher than those of nonatopic control participants (6% *S. aureus* and 25% any bacteria). However, no significant relationship between the frequency distribution of bacteria and the grade of atopy or associated ocular diseases was noted in this small population of atopic dermatitis patients ($n = 36$).⁷⁶ Conjunctival epithelial cells in patients with AKC have been shown to express TLR-2, and may be involved in the inflammatory response to *S. aureus* infection through pathways that involve TLR-2 and platelet-activating factor.⁷⁵

Keratoconus is a progressive noninflammatory corneal ectasia that occurs in a small percentage of patients with atopic dermatitis.^{77,78} Progressive thinning and ectasia occurs in the corneal stroma that is mainly composed of collagen.⁷⁹ Conjunctival mast cell hyperplasia with release of proteolytic enzymes may play a role in the pathogenesis of this complication.³⁶

Visual loss is one of the most dreadful complications of AKC. In sight-threatening AKC and VKC, T-lymphocyte-driven eosinophilia with increased adhesion molecules may be the primary cause for the impact on the cornea⁴² and is noted when AKC starts earlier in life.⁸⁰ Conversely, severe AKC associated with complications such as blepharoconjunctivitis, cataract, corneal disease, and ocular herpes simplex are primarily associated in 40% of the older patients with the peak incidence occurring in the 30- to 50-year old age group.^{70,71,81}

TREATMENT

In a stepwise approach, topical and systemic antihistamines can be used to control allergic symptoms in the eyes. Systemic drugs may result in adverse effects such as drowsiness and dry mouth, tipping the favor to second-generation antihistamines to avoid these unwanted sedative and anticholinergic effects. Topical vasoconstrictor agents provide rapid relief of ocular erythema, but the relief is often temporary, and overuse of these agents may lead to rebound hyperemias and irritation (Fig. 2).⁸²

Topical Steroids

Steroid eye drops (betamethasone, dexamethasone, fluorometholone, and hydrocortisone) have been effective in AKC but may increase intraocular pressure and also increase risk of corneal infection through local immunosuppression. Steroid use can also induce cataracts and delay wound healing.^{3,83} Other complications that limit steroid use include herpes simplex keratitis and atrophy of the derma of the eyelids.¹ Ointment

Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Quiescent	Mild Intermittent	Moderate Persistent	Severe	Very Severe	Remodeling (scarring)
No Treatment	Oral Steroids				
	Short bursts of Topical Steroids				
	Topical cyclosporine or tacrolimus				
	Topical Vasoconstrictors / lubricants / Cool compresses				
	Disposable contact lenses Oral antihistamines Avoidance Treatment of comorbidities (e.g. atopic dermatitis, allergic rhinitis) that includes immunotherapy, intranasal steroids				
					Surgery for Keratoconus

Figure 2. Stepwise approach to the management of AKC.

preparations applied at nighttime are an alternative when ophthalmic drops can not be used.³

Topical Cyclosporine

Cyclosporine A (CyA) is an immunophilin that inhibits activation of T lymphocytes *via* inhibition of IL-2 receptor expression, as well as activation of eosinophils and mast cells, thereby preventing the release of inflammatory mediators.^{83,84} *In vitro* effects of CyA are caused by reduction in T cells, normalization of CD4⁺CD8⁺ ratio, decrease in T-lymphocyte activation, and reduction in T-lymphocyte cytokine expression, especially IL-2 and IFN- γ . There were fewer B cells, but the number of plasma cells, mast cells, or eosinophils were not significantly reduced.⁸⁵

A large prospective observational study ($n = 594$) of VKC or AKC patients evaluated the efficacy of CyA 0.1% aqueous ophthalmic solution. Over the course of 6 months 30% were able to discontinue topical steroids. The most common adverse complaint being eye irritation (12%) with >1% ($n = 5$) reporting infectious complications (bacterial corneal ulcer or herpetic keratitis).⁸⁶ In patients with steroid-dependent AKC ($n = 18$) CyA 0.05% did not show any benefit versus placebo as a steroid-sparing agent in drug score, symptoms, or clinical signs scores.⁸³ A more prolonged course with topical CyA 0.05% in the treatment of severe, steroid-resistant AKC patients ($n = 22$) for a period of 28 days, six times daily for 2 weeks and four times daily for 2 weeks, showed improvement in signs and symptoms of AKC with the treatment group without adverse events.⁸⁴ An earlier study using 2% CyA four times daily for 3 months in addition to their usual therapy had a greater steroid-sparing effect than placebo, and clinical signs and symptom scores were reduced for CyA group, despite difficulties in patient tolerance.⁸⁷ CyA (2%) in AKC patients ($n = 26$) who did not improve with conventional therapy, showed reduction in sub tarsal papilla 69%; reduction or disappearance of Trantas dots in 50% and overall subjective symptoms

improvement while reducing the need of adding topical steroids.⁸⁸ Thus, higher concentrations of topical CyA appear to be more beneficial.

Systemic Cyclosporine

The use of systemic cyclosporine has been studied in AKC patients ($n = 8$) who were resistant to conventional management with doses between 50 and 300 mg daily (in divided doses), given for a duration between 5 months and 7 years. The drug was effective as a steroid-sparing agent, and systemic corticosteroids were stopped in half of the cases. Papillary blepharoconjunctivitis and punctate keratopathy completely resolved after a few weeks, and corneal ulcers resolved after 5–10 weeks of treatment. The incidence of side effects from systemic CyA was low, suggesting that CSA is an effective and safe option in treatment of severe cases of AKC resistant to conventional management.⁸⁹ In an earlier AKC study ($n = 4$) that evaluated systemic CSA therapy, a daily dosage of oral CSA at 3–5 mg/kg treated for a mean of 37 months resulted in complete response in three patients and partial response in one patient. Treatment with cyclosporine resulted in renal toxicity in one patient, which was transient and resolved with reduction of CSA dosage.⁹⁰

Tacrolimus

Tacrolimus is another calcineurin inhibitor that inhibits the release of inflammatory cytokines including IL2, IL3, IL4, IL5, IL8, IFN- γ , and TNF- α and down-regulates the IgE receptor I expression on Langerhans cells. Tacrolimus shares some properties with CyA but is considered to be 10–100 times more potent.^{1,91}

Several case reports of severe AKC established the efficacy and relative safety of topical tacrolimus in the treatment of severe, longstanding AKC. Topical tacrolimus (0.02–0.03%) ointment applied to the conjunctival fornix daily after 6–8 weeks of continuous treatment resulted in decreased papillary size, suppression of corneal melting, remission of scleroperikeratitis, reduction of epithelial defect, and decreased in conjunctival eosinophils, neutrophils, and lymphocytes. These case reports reported no occurrence of severe adverse events.^{91–93} Comparing tacrolimus 0.1% ointment to clobetasone butyrate 0.05% ointment in a double-masked crossover AKC study ($n = 25$) applied twice daily for 3 weeks, both treatments were effective in reducing signs and symptoms of eyelid eczema, but with tacrolimus showing superiority to clobetasone.⁹⁴ Low-dose systemic tacrolimus given for 1 year has also been shown in a retrospective study to be effective and safe in the treatment of severe AKC unresponsive to conventional therapy.⁹⁵ The ECP has been investigated as a marker for assessing the efficacy of treatment of AKC because levels correlates strongly with clinical

signs.^{1,96} Although relatively safe, treatment with tacrolimus is not completely without risks. One case report described an increased risk of infection with herpes simplex virus keratitis after 1 week of topical tacrolimus, but this may be normal for patients with atopic dermatitis because they can have secondary viral infections.⁹⁷

Surgery

When symptoms are unresponsive to pharmacologic treatment, and conjunctival papillary hyperplasia aggravates the corneal ulcers, surgical treatment such as tarsal conjunctival resection may be considered. Corneal plaques may also be removed by surgical curettage.³ Surgical removal of corneal plaque with administration of autologous fibronectin eyedrops has been shown to ameliorate inflammation and resurface the corneal epithelium.⁹⁸ In patients with severe allergy with corneal complications, papillary resection followed by intraoperative conjunctival application of 0.02–0.05% mitomycin C can result in resolution of corneal and conjunctival complications. Papillary regrowth has been shown to be decreased with combined resection and mitomycin C application compared with simple resection.^{99,100} Amniotic membrane implantation has also been shown to help with the reepithelialization of corneal defects associated with ulcers of chronic AKC.^{101,102}

Finally, nonpharmacologic interventions are important adjuncts to the treatment of AKC. This includes the use of goggle-type glasses and avoidance of contact lens use during high-pollen periods to reduce allergen contact to the epithelium and use of artificial tears without preservatives instead of tap water to prevent loss of tear layer stability.³

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