An Update in Allergic Conjunctivitis

By

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Ocular allergic disease is typically associated with IgE mediated mast cell activation (type I immediate hypersensitivity reaction) in the conjunctival tissue.
Allergic conjunctivitis is typically divided into five types:

- **Seasonal**
  - allergic conjunctivitis (SAC)

- **Perennial**
  - allergic conjunctivitis (PAC)

- **Vernal**
  - keratoconjunctivitis (VKC)

- **Atopic**
  - keratoconjunctivitis (AKC)

- **Giant Papillary**
  - Conjunctivitis (GPC)

Seasonal & Perennial Allergic Conjunctivitis
Seasonal & Perennial Allergic Conjunctivitis

• SAC and PAC are linked to allergic rhinitis (more commonly known as allergic rhinoconjunctivitis)

• SAC is the most common form of allergic conjunctivitis
• 79% of patients who have PAC experience a seasonal exacerbation.

Symptoms

• Low-grade ocular and periocular itching (pruritus) (characteristic)
• Redness
• Tearing (epiphora)
• Burning
• Stinging
• Photophobia
Mild to moderate eyelid edema
- Dilatation of conjunctival vessels
- Minimal to moderate conjunctival chemosis
- May be a small amount of mucus
- Small papillae may be present under the upper lid, but there are never large papillae or follicles
- Lid swelling may be accompanied by venous congestion, causing the lids to have a dark color called an “allergic shiner.”
- Cornea is seldom involved
- Vision is not significantly affected
Bilateral, seasonal, external ocular inflammatory disease of unknown cause

**vernal catarrh** or **spring catarrh**.

- Most commonly begins in the spring
- Primarily affects children (5-25 y)
- May be related to atopy
- Usually self-limited (burns itself out by the early twenties)
- Can result in potentially blinding corneal complications

**Symptoms**

- Itching (severe) (93%)
- Burning (90%)
- Redness (90%)
- Tearing (83%)
- Photophobia (80%)
- Discharge is common: an accumulation of ropy mucus can be found in the conjunctival fornix
- Can become chronic or perennial
Signs

• Bilateral disease (but can present asymmetrically)
• Periorbital skin is usually unaffected (≠ AKC)

1. Palpebral (tarsal) signs
• Predominantly in the superior tarsal conjunctiva
• Papillary reaction large 1-8 mm, “cobblestone” appearance
• Mechanical ptosis
• Thick (ropy), mucoid, white discharge

2-Limbal signs

• Horner-Trantas dots:
  Single or multiple gelatinous, pale infiltrates (Aggregates of degenerating eosinophils)
• Conjunctival cysts (rare)
3- Corneal signs

- Sight-threatening complications (< in AKC)
- Punctuate epithelial erosions
- Larger erosions: “shield” ulcer
- Pannus or opacification
- Significant astigmatism
- Keratoconus

Atopic Keratoconjunctivitis
• Males > females
• Bilateral, Usually symmetric disease
• Chronic inflammatory process
• Often a personal or family history of other atopic diseases
• Symptoms are perennial (less intermittent)
• Atopic dermatitis (eczema), present in 95% of patients with AKC
• 25–40% of atopic dermatitis patients have AKC
• Begins in the late teens and early twenties (Peak 30-50)
• Can lead to blindness

**Symptoms**

• Bilateral itching of the eyelids and periorbital skin
• Tearing
• Photophobia
• Burning
• Blurred vision
• Stringy discharge
• Foreign body sensation and pain
**Signs**

1- **Conjunctiva**

- Papillary reaction (more prominent inferior)
- Non-specific signs of inflammation such as hyperaemia or chemosis
- Papillary hyperplasia of the limbal conjunctiva (rare)
- Horner- Trantas dots
- Conjunctival cicatization (shallowing of the fornix and symblepharon)

2- **Cornea**

- Corneal scarring in AKC may result from vascularization, infection or keratoconus
- Punctate epithelial erosions
- Peripheral corneal vascularization (pannus)
- Non-infectious corneal ulcers
- Chronic eye rubbing may be an important factor in the association between AKC and keratoconus
3- Eyelids

- Periorbital skin: dry, indurated, scaly appearance of eczema
- Eyelid swelling causes fold in the lower lid skin (Dennie-Morgan fold)
- Fissures at lateral canthus
- Lid margins may be thickened (tylosis)

- Meibomian gland dysfunction
- Staphylococcal blepharitis

Other Causes of Visual Deterioration in AKC

- Premature bilateral cataracts; anterior subcapsular “shield” cataract

- Retinal detachment (v. rare)

- Posterior subcapsular cataracts and glaucoma (due to chronic use of topical steroids)
Giant Papillary Conjunctivitis

• Inflammatory disorder of the external eye that describes the advanced stages of the conjunctival response to the prolonged presence of a foreign body on the ocular surface

• First observed and characterized in contact lens (CL) wearers

• Later reported in patients with ocular prostheses and exposed suture ends
**Symptoms**

- Mucus discharge in the morning
- Itching on removal of CL
- Foreign body sensation
- Redness
- Burning
- Blurred vision as a result of coating of CL with mucus and increasing lens mobility and instability
- Increasingly intolerant of their contact lenses

**Signs**

- Bulbar conjunctival injection superior corneal pannus
- Corneal opacities
- Fluorescein stain ex.
**Stage 1**

**preclinical giant papillary conjunctivitis**

(A) Minimal hyperemia of the upper tarsal plate  
(B) Papillary reaction in same patient  
(flourescein instilled and photographed with cobalt filter)

**Stage 2**

**mild giant papillary conjunctivitis**

(A) Injection and thickening of the conjunctiva.  
(B) Enlargement and elevation of papillary reaction  
(flourescein instilled and photographed with cobalt filter)
• **Stage 3**
  
  **Moderate giant papillary conjunctivitis**

(A) Marked injection, thickening, and obscuration of the normal vascular pattern of the upper tarsal plate
(B) Papillae are between 0.5 and 1 mm in size

(flurorescein instilled and photographed with cobalt filter)

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• **Stage 4**

**Severe giant papillary conjunctivitis**

(A) Marked injection, thickening, and total obscuration of the normal vascular pattern.
(B) Large papillae with apical staining

(flurorescein instilled and photographed with cobalt filter)
Treatment

Advisory Nonprescription Interventions

• Environmental control
• Cold compresses
• Lubrication
• Contact lenses
Antihistamines

• Oral antihistamines:

Loratadine (a second generation anti-histaminic)

Emedastine (a second generation anti-histaminic, selective H1 blocker)

• Topical antihistamines:

Levocabastine 0.1% (selective second-generation H1 receptor antagonist)

Emedastine: 0.05% (selective H1 antagonist with no apparent effect on adrenergic, dopaminergic, or serotonin receptors)

Mast Cell Stabilizing Agents

Sodium Cromoglycate 4%

• Prototypic MC secretion inhibitor
• Four to six times daily, with the dosage decreased incrementally to twice daily as symptoms permit.
• The major adverse effect is burning and stinging

Lodoxamide 0.1%

• MC stabilizer that has been shown to be approximately 2500 times more potent than sodium cromoglycate in preventing histamine release
• Four times daily, may be used continuously for 3 months

Pemirolast 0.1%

A specific inhibitor of MC degranulation inhibiting the release of chemical mediators
Topical Multiple Action Agents

Olopatadine
Ketotifen
Azelastine
Nedocromil
Epinastine HCl 0.05%
Mizolastine
Picumast

Topical Multiple Action Agents

Olopatadine

• MC stabilizing effects and H1-receptor binding effect
• Decreasing cytokine secretion and tumor necrosis factor (TNF)-α.

Ketotifen

MC stabilizing effect; several anti-mediator properties, including strong H1-receptor antagonism, inhibition of leukotriene formation
S.E.: mild stinging affect
Azelastine

- Inhibit early allergic response and histamine release from MCs
- Inhibition of superoxide generation by neutrophils and eosinophils
- Inhibition of leukotriene synthesis
- Inhibition of TNF-α secretion, IL-6 from human leukemic mast cells
- S.E.: bitter taste and some application site stinging

Topical Corticosteroids

**Soft corticosteroids**
- clobetasone
- desonide
- fluorometholone
- loteprednol
- Rimexolone

**Harder corticosteroids**
- prednisolone
- dexamethasone
- betamethasone

- First corticosteroid preparations to be used carefully.
- A “pulsed” corticosteroid treatment is recommended, in addition to the continuous use of MC stabilizers and/or topical antihistamines.
- Doses are chosen based on the inflammatory state. *Instillation frequency of 4 times/day for 5–10 days*
**Non-steroidal Anti-inflammatory Agents**

**Ketorolac 0.5%**
- Mechanism of action is on the arachidonic acid cascade, where it binds cyclooxygenase to block the production of PGs, but it does not inhibit lipoxygenase or the formation of leukotrienes.

**Diclofenac**
- May have similar features in the treatment of SAC.
- Transient stinging and burning on instillation.
- Allergic reactions, corneal edema, iritis, ocular inflammation, ocular irritation, superficial keratitis, and superficial ocular infections.

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**Immunomodulatory Agents**

**Cyclosporin A**
- Fungal anti-metabolite and anti-CD4+ agent that decreases the clinical signs and symptoms of the chronic forms of VKC and AKC.
- Acts to control ocular inflammation by blocking Th2 lymphocyte proliferation and IL-2 production, by inhibiting histamine release from MCs and basophils, and by reducing the production of IL-5.

**Tacrolimus**
- Macrolide antibiotic with potent immunomodulatory properties.
- Acts on T lymphocytes to block the production of lymphokines, such as IL-2, IL-5, TNFα and interferon γ a. It also blocks the degranulation of MCs and several MC cytokines, such as IL-3 and IL-5.
Excimer laser phototherapeutic keratectomy (PTK) and CO2-assisted removal of giant papillae have been attempted in the treatment of shield ulcer with or without plaque (Belfair et al, 2005).

Amniotic membrane grafts following keratectomy have been described as a successful treatment in deep ulcers, in cases with slight stromal thinning. (Pelegrin et al, 2008).
**Future Drug Developments**

- Focus on steroid-sparing agents that control the immune response
- The study of the genetics of ocular allergy
- The use of immunostimulatory DNA sequences that can inhibit the allergic response

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**Take home message**

*Take your time with every patient.*

Always prescribe an *artificial tear.*

Depend mainly on the new *multiple acting drugs.*

Choice of *steroids depends on the severity of the case*  
(not given for all allergic patients)

On using steroids *start with the soft ones as a 1st choice*

Always use pulsed doses and better with *gradual withdrawal*

On prescribing steroids *tell the patient or his parents about its its dangers and why you had prescribe it and to stop it on the schedule and never use it again unless you say this.*