Allergic conjunctivitis may be divided into five major subcategories: seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis, giant papillary conjunctivitis, atopic keratoconjunctivitis (AKC), and vernal keratoconjunctivitis (VKC). AKC and VKC are much less common than SAC. Their presentation is often more severe, however, and they are thus more likely to result in permanent structural alterations and visual dysfunction. For these reasons, clinicians must be able to identify and treat AKC and VKC appropriately.

**PATHOPHYSIOLOGY AND EPIDEMIOLOGY**

VKC is a chronic bilateral inflammation of the conjunctiva that is commonly associated with a personal and/or family history of conditions such as asthma, eczema, or seasonal allergic rhinitis, which are termed atopy. More than 90% of patients with VKC exhibit one or more atopic conditions. VKC has a significant male preponderance and typically occurs in areas with tropical and temperate climates such as the Mediterranean, the Middle East, and Africa. The limbal form of VKC commonly occurs in dark-skinned individuals from Africa and India. VKC generally has its onset in the patient’s first decade of life and lasts for up to 1 decade. Its symptoms usually peak prior to the onset of puberty and then subside.

AKC is a bilateral inflammation of the conjunctiva and eyelids, which has a strong association with atopic dermatitis. It is also a type I hypersensitivity disorder with many similarities to VKC, yet AKC is distinct in a number of ways. In 1953, Hogan first described the association between atopic dermatitis and conjunctival inflammation. Atopic dermatitis is a common hereditary disorder that usually has its onset in childhood; symptoms may regress with advancing age.

“...the sine qua non in the clinical history is the symptom of itching. Without it, the diagnosis of any type of allergic conjunctivitis is suspect.”

Approximately 3% of the population is afflicted with atopic dermatitis, and of this group, approximately 25% have ocular involvement.

**CLINICAL HISTORY AND EXAMINATION**

As with seasonal and perennial allergic conjunctivitis, the diagnosis of VKC and AKC generally is made by taking a thorough history and by careful clinical observation. Important historical features include a personal or family history of atopic disease such as allergic rhinitis, bronchial asthma, and/or atopic dermatitis. The sine qua non in the clinical history is the symptom of itching. Without it, the diagnosis of any type of allergic conjunctivitis is suspect. Patients with VKC may also report photophobia, foreign body sensation, tearing, and blepharospasm. The ocular signs of VKC are commonly evident in the cornea and conjunctiva. In contrast to AKC, the eyelid skin usually is not involved, and as the name implies, symptoms are typically seasonal. In AKC, the symptoms are perennial, although they may vary with the seasons (ie, worse in the winter). AKC also has a direct correlation with atopic dermatitis, which may or may not involve the periorbital skin. The most common symptom of AKC is bilateral itching of the eyelids, but watery discharge, redness, photophobia, and pain may be associated.

As with SAC, the classic signs of VKC and AKC include injection of the conjunctival vessels as well as...
varying degrees of chemosis (conjunctival edema) and eyelid edema. The conjunctiva may have a milky appearance due to obscuration of the superficial blood vessels by edema within the substantia propria of the conjunctiva. Edema is generally believed to be the direct result of increased vascular permeability caused by the release of histamine from conjunctival mast cells.

VKC may be subdivided into two varieties, palpebral and limbal. The classic conjunctival sign in palpebral VKC is the presence of giant papillae, which usually occur on the superior tarsal conjunctiva. Giant papillae assume a flat-top appearance, often described as “cobblestone papillae.” In severe cases, large papillae may cause mechanical ptosis. A ropy mucous discharge may be present, which commonly is associated with tarsal papillae. Large numbers of eosinophils are present in the discharge. The limbal form of VKC commonly occurs in dark-skinned individuals. As the name implies, papillae tend to occur at the limbus. They have a thick, gelatinous appearance and are often associated with multiple white spots (ie, Horner-Trantas dots), which are collections of degenerated epithelial cells and eosinophils. Horner-Trantas dots are transient, with each appearance rarely lasting more than 1 week.

Although corneal vascularization is rare, the cornea may be affected in a variety of ways. Punctate epithelial keratopathy may be due to the toxic effect of inflammatory mediators released from the conjunctiva and may be a precursor of the characteristic shield ulcer, which is pathognomonic of VKC. As the areas of punctate epithelial keratopathy coalesce, they may result in frank epithelial erosion that causes shield ulcer, which is typically shallow with white irregular epithelial borders. Although the pathogenesis of shield ulcer is not well understood, a major factor in its development may be chronic mechanical irritation from the giant tarsal papillae. Another type of corneal involvement is vernal pseudogerontoxon, which is a degenerative lesion in the peripheral cornea resembling corneal arcus. Keratoconus may be seen in chronic cases.

AKC may affect the eyelid skin and lid margin, conjunctiva, cornea, and lens. Skin of the eyelids may exhibit eczematoid dermatitis, and the lid margins may show

<p>| TABLE 1. MAJOR DIFFERENTIATING FACTORS BETWEEN VERNAL AND ATOPIC KERATOCONJUNCTIVITIS |</p>
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>VKC</th>
<th>AKC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>Generally presents at a younger age</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Males are affected preferentially</td>
<td>No sex predilection</td>
</tr>
<tr>
<td>Seasonal variation</td>
<td>Typically occurs during spring</td>
<td>Generally perennial</td>
</tr>
<tr>
<td>Discharge</td>
<td>Thick mucoid discharge</td>
<td>Watery and clear discharge</td>
</tr>
<tr>
<td>Conjunctival scarring</td>
<td></td>
<td>Higher incidence of conjunctival scarring</td>
</tr>
<tr>
<td>Horner-Trantas dots</td>
<td>Horner-Trantas dots and shield ulcers common</td>
<td>Presence of Horner-Trantas dots rare</td>
</tr>
<tr>
<td>Corneal neovascularization</td>
<td>Not present</td>
<td>Tendency for development of deep corneal neovascularization</td>
</tr>
<tr>
<td>Eosinophils in conjunctival scraping</td>
<td>Present to a greater degree in VKC than in AKC</td>
<td>Presence of eosinophils less likely</td>
</tr>
</tbody>
</table>
meibomian gland dysfunction and keratinization. Staphylococcal colonization of the eyelid margins is common and may result in blepharitis. The conjunctiva may show chemosis and, typically, a papillary reaction, which is more prominent in the inferior tarsal conjunctiva, unlike that seen in VKC. Hyperplasia of limbal regions may result in a gelatinous thickening, similar to the limbal variant of VKC, and Horner-Trantas dots rarely may be present. Fibrosis or scarring of the conjunctiva may result in a shortened fornix or symblepharon formation with chronic inflammation. Corneal involvement ranges from punctate epithelial keratopathy early in the course of the disease to neovascularization, stromal scarring, and possibly ulceration. There is a strong association between herpes simplex viral keratitis and AKC. Another corneal finding, which may be associated with AKC, is keratoconus, which may stem from chronic rubbing of the eyes. Characteristic lenticular changes in AKC include anterior or posterior subcapsular cataract formation. Lenticular opacities are usually bilateral; they present in the second decade of life but progress slowly. There may be an association with the long-term use of topical corticosteroids (Table 1).

**TREATMENT**

For suspected VKC or AKC, the first step is to refer the patient for evaluation by an allergist/immunologist, who can identify the responsible allergen(s). He or she can help manage systemic therapy, if required. Once identified, the responsible allergen(s) should be avoided. With VKC, besides moving to a cooler climate, which often is not possible, it is important for patients to reduce dust particles at work. Local measures may provide temporary relief. Examples include cold compresses and the periodic instillation of artificial tears, which dilute the allergens.

Pharmacologic intervention for VKC and AKC typically overlaps that of SAC. The exception is vasoconstrictors, which are typically ineffective against atopic and vernal disease. Systemic and/or topical antihistamines may relieve acute symptoms. Topical medications with antihistamine activity can rapidly relieve the signs and symptoms of allergic conjunctivitis. On the other hand, systemic antihistamines can cause drowsiness as well as dry eye and dry mouth, so it is best to avoid them when possible.

Mast cell stabilizers, such as cromolyn sodium and lodoxamide (Alomide; Alcon Laboratories, Inc., Fort Worth, TX) are sometimes used for VKC, because they can prevent the release of inflammatory mediators. Better, however, are drugs that combine a topical antihistamine with a mast cell stabilizer. Agents include bepotastine (Bepreve; Ista Pharmaceuticals, Inc., Irvine, CA), epinastine (Elestat; Inspire Pharmaceuticals, Inc., Durham, NC) and azelastine (Optivar; Meda Pharmaceuticals, Inc., Somerset, NJ), nedocromil (Alocril; Allergan, Inc., Irvine, CA), and ketotifen (Zaditor [Novartis Pharmaceuticals Corporation, East Hanover, NJ] and Alaway [Bausch + Lomb, Rochester, NY]).

One of the most powerful classes of medications for treating VKC and AKC is topical corticosteroids. These agents have a broad spectrum of activity and help limit the inflammatory response. Unfortunately, corticosteroids may delay wound healing and cause secondary infection, elevated IOP, and the formation of cataract. These agents should therefore be used with caution and be prescribed only by qualified eye care professionals.

Relatively weak steroids (eg, rimexolone, medrysone, fluorometholone) tend to have less potency and fewer ocular adverse effects than higher-potency steroids. Agents like prednisolone acetate and difluprednate (Durezol; Sirion Therapeutics, Tampa, FL) are more potent and have a higher incidence of elevated IOP. The steroid loteprednol etabonate (Lotemax 0.05% and Alrex 0.02%; both from Bausch + Lomb) appears to suppress inflammation effectively on the surface of the eye and to have a lower rate of adverse events than prednisolone. As a general rule, topical steroids should be prescribed only for a short period of time and for severe cases that do not respond to conventional therapy. Rarely, oral steroids may be required in cases of AKC. A physician who can monitor the patient for systemic side effects should prescribe these agents.

**CONCLUSION**

VKC and AKC are uncommon conditions, but they can cause severe complications if not treated properly. Local therapies, such as topical steroids and combination antihistamine and mast cell stabilizer agents, can play a positive role in suppressing these conditions.

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