OCULAR ALLERGY AND DRY EYE DISEASE

Understanding the association between these two conditions and working together to comanage patients is mutually beneficial.

This article is based on presentations given by Marc Labetoulle, MD, and Jeremy Gottlieb, MD, during Quantel Medical's symposium on the value of a multidisciplinary approach to managing complicated dry eye and severe ocular surface pathologies. Quantel Medical's symposium was broadcast online on the European Dry Eye Disease Society (EUDES) website: *https://www.dryeye-society.com/dry-eye-live-talks*.

Ocular allergy, an inflammatory reaction on the eye's surface to particles in the environment such as pollen, ragweed, and pet dander, can affect patients of any age. Patients can be asymptomatic or symptomatic and, in extreme cases, they can present with severe loss of vision. Diagnosing ocular allergy and understanding the association between it and dry eye disease (DED) is essential to helping these patients find long-lasting relief from their ocular symptoms. The most efficient and effective way to achieve this, in our experience, is by comanaging patients.

BACKGROUND

Ocular allergy triggers a cascade of inflammatory events that involve the activation of mast cells and the release of histamine. As histamine is released, the blood vessels in the ocular surface layers can begin to leak fluid, proteins, and inflammatory cells. This cascade is the root cause of the symptoms associated with ocular allergy, which include redness, itching, light sensitivity, tearing, burning, swelling of the eyelid and the conjunctiva, decreased vision, and even runny nose/sneezing (nasal allergy is often associated). The main clinical sign of ocular allergy is the presence of papillae on the underside of the superior eyelid and the conjunctiva on the tarsal part of the eyelid (Figure 1). Follicules may also be visible in the lower part of the conjunctiva, on the acute sac, or around the bulbar conjunctiva. In severe cases in younger patients, a corneal shield or limbal inflammation may be noticeable. With time, eyes that suffer from chronic and severe ocular allergy can also experience limbal stem cell insufficiency.

Figure 1. A common clinical sign of ocular allergy.

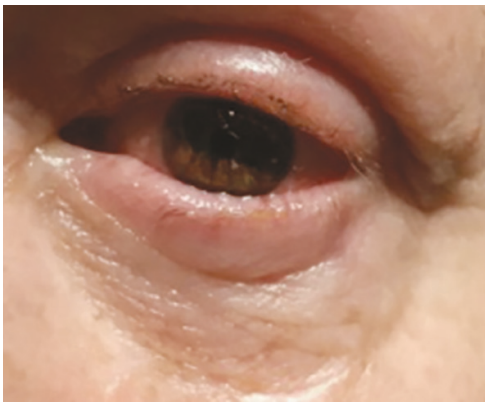

Figure 2. Presence of a Dennie Morgan line could be a sign of atopic dermatitis.

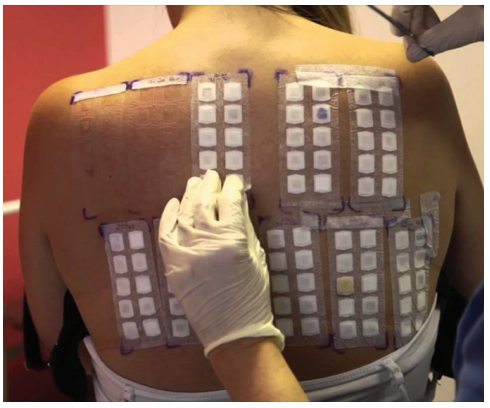

Figure 3. Example panel test to identify possible contact dermatitis.

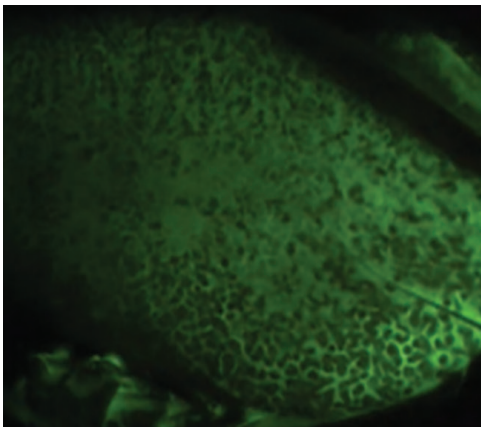

Figure 4. Multiple signs of allergy.

DIAGNOSIS

Diagnosis. Before treatment begins, it is important to identify which of the four types of ocular allergy a patient is experiencing.

- **Type 1**: Seasonal allergic conjunctivitis, which occurs only during the seasons in which environmental allergens are more copious;
- **Type 2**: Perennial allergic conjunctivitis, which occurs year-round (this can be due to a perennial allergen or to successive seasonal allergens);
- **Type 3**: Vernal keratoconjunctivitis (VKC), a severe form of ocular allergy that typically occurs in younger individuals who live especially, but not exclusively, in warm climates. Typical signs of VKC include giant papillae, corneal (Togby) shield ulcer and Trantas dots (limbal inflammation);
- **Type 4**: Atopic keratoconjuntivits (AKC), another severe form that is associated with systemic allergy and more particularly atopic dermatitis.

Besides giant papillae and Trantas dots, signs of AKC include madarosis, thick skin around the eyelashes, and eczematous lesions on the skin around the eye (Dennie-Morgan sign). It can be identified by signs of papillae and mucus discharge.

The last two types, VKC and AKC, are the most severe types of ocular allergy. Chronic and/or recurrent episodes ultimately may lead to conjunctival fibrosis (Figure 2) and limbal stem cell deficiency, which can be severe and sight-threatening in about 1% of cases.

Patch tests and/or ROAT must be performed on patients who are suspected to have severe ocular allergy to search for an associated contact dermatitis that would worsen the underlying inflammatory condition (Figure 3).

Ocular allergy can mimic ocular surface disease (OSD), and it can also worsen the signs and symptoms of some OSDs, such as dry eye disease and herpes simplex keratitis. Ocular allergy can worsen DED symptoms. The association between these two ocular surface conditions should be suspected in patients with a history of burning and stinging sensations in the eyes that is persistent during the year, but is not continuously intense throughout the year. During the periods of exacerbation of ocular symptoms, these patients often experience episodes of rhinorrhea and sneezing.

In these cases, assessment with a multipurpose device such as the LacryDiag (Quantel Medical) is advised, as it provides a complete analysis of all three tear film layers in four non-contact examinations (eg, interferometry, noninvasive tear breakup time, tear meniscus, and meibography). The data gathered allow the clinician to assess the level of ocular surface dysfunction and may help in the diagnosis of the etiological mechanisms. Figure 4 shows multiple signs of allergy.

MANAGEMENT AND FOLLOW-UP CARE

Management. In addition to helping to distinguish between atopic dermatitis/AKC and giant papillary conjunctivitis, dermatologists can help to treat patients with these conditions from a unique point of view. The management of atopic dermatitis often requires systemic treatments due to the involvement of the non-immunoglobulin E (IgE) mediated immune response.

Atopic dermatitis is common in childhood, occurring in up to 30% of children. The condition usually fades and sometimes comes back more severely after the age of 15 years. Adults with atopic dermatitis therefore frequently need systemic treatments. The course of treatment for atopic dermatitis in adults is shown in Figure 5 and described briefly below.

The baseline treatment (ie, basic therapy) for atopic dermatitis includes educational programs, emollients/moisturizing

TREATMENT OF ATOPIC DERMATITIS: ADULT

- For every grade, additional therapeutic options are given
- Add antiseptics/antibiotics in cases of superinfection
- Consider compliance and diagnosis, if therapy has no effect
- Refer to full text for restrictions, especially for treatment marked[1]
- Licensed indication are marked with,[2] off-label treatment options are marked with[3]

SEVERE SCORAD >50 / or persistent eczema
Hospitalization; short course of cyclosporin A,[1,2] dupilumab,[2] short course of oral glucocorticosteroids;[1,2] longer course of systemic immunosuppression: methotrexate,[3] azathioprin,[3] mycophenolate mofetil;[3] PUVA 1; alitretinoin[1,3]

MODERATE SCORAD 25-50 / or recurrent eczema
Proactive therapy with topical tacrolimus[2] or class II or class III topical glucocorticosteroids,[3] wet wrap therapy, UV therapy (UVB 311 nm, medium dose UVA1), psychosomatic counseling, climate therapy

MILD SCORAD <25 / or transient eczema
Reactive therapy with topical glucocorticosteroids class II[2] or depending on local cofactors; topical calcineurin inhibitors,[2] antiseptics incl. silver,[2] silver coated textiles[1] topical crisaborole[3]

BASELINE basic therapy
Educational programmes, emollients, bath oils, avoidance of clinically relevant allergens (encasings, if diagnosed by allergy tests)

1. Darsow U, Lubbe J, Taieb A, et al. Position paper on diagnosis and treatment of atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2005; 19: 286-295.
2. Darsow U, Wollenberg A, Simon D, et al. ETFAD/EADV eczema task force 2009 position paper on diagnosis and treatment of atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2010; 24: 317-328.
3. Wollenberg A, Oranje A, Deleuran M, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. *J Eur Acad Dermatol Venereol*. 2016; 30: 729-747.

Figure 5. The course of treatment for atopic dermatitis in adults depending on disease severity. Adapted from: ETFAD/EADV Eczema Task Force; Wollenberg, A. et al. *J Eur Acad Dermatol Venereol Actions*. 2020;34(12):2717-2744.

creams, bath oils, and avoidance of relevant allergens revealed during the patch test/ROAT. For mild dermatitis, treatment includes reactive therapy with topical class II glucocorticosteroids or, depending on local cofactors, topical calcineurin inhibitors, antiseptics including silver, and silver coated textiles. Topical crisaborale can also be prescribed (not available in every country). It should be noted, however, that topical steroids on the eyelids should be used sparingly.

For moderate atopic dermatitis, common treatments include proactive therapy with topical tacrolimus or class II or III topical glucocorticosteroids, wet wrap therapy, UV therapy, psychosomatic counseling, and climate therapy.

In severe cases, hospitalization may be required. A short course of cyclosporin A or oral glucocorticosteroids in some countries is an effective treatment that produces results rapidly. It may, however, cause adverse events including renal dysfunction, the risk of acute increases of blood pressure, headaches, and hair growth in women. Dupilumab or Janus kinase inhibitors are newer treatments that can be used for long-term management of the disease. Any retinoic acid treatment like alitretinoin (licensed for chronic hand eczema) would increase the risk of eye dryness. It should therefore not be used in patients with DED.

Follow-up care. Patients who are placed on dupilumab for atopic dermatitis are at an increased risk of paradoxical conjunctivitis in the next months and years after initiation. For this reason, constant communication between the dermatologist and the ophthalmologist is crucial. ■

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CONCLUSION

In our experience, the best way to treat patients with ocular allergy is for the ophthalmologist and allergist to collaborate in patients' care. Once an ocular allergy is suspected, the ophthalmologist should seek the help of an allergist, especially in cases of severe ocular allergy such as VKC and AKC, to help patients adopt cutaneous and systemic treatments for these conditions. Ophthalmologists should also be advised to evaluate ocular allergy patients for DED, especially those who do not respond to conventional management.