American Academy of Optometry: Case Report #1

Diagnosis, Treatment, and Management of Seasonal and Perennial Allergic Conjunctivitis

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Abstract: Allergic conjunctivitis is an ailment that optometrists encounter nearly every day. Understanding the immunologic mechanisms, clinical features, and differential diagnoses is key to providing patients with the best care possible. This case report outlines a discussion of the various forms of, associations with, and treatment options for this prevalent disease.

Keywords: allergic conjunctivitis, ketotifen, olopatadine

Introduction

There are several forms of allergic conjunctivitis and collectively, they affect a significant proportion of the population. The signs and symptoms of the condition have a remarkable impact on the daily lives of those afflicted, and having allergic conjunctivitis actually puts them at a higher risk of having other conditions. Thankfully, there are many treatment options and additional means of managing allergic conjunctivitis are being researched. The more information healthcare providers have on allergic conjunctivitis, the better they can diagnose, treat, and manage the condition.

Case Report

Initial Visit, Brief Eye Exam, 01/03/2020

A seven-year-old Hispanic female accompanied by her mother presented for a problemspecific eye exam with the complaint of a red left eye for one week with multiple intermittent episodes in each eye for the past month. Her chief complaint was a gritty foreign body sensation in the left eye, and a general itchiness of both eyes. She admitted to rubbing her eyes frequently. In addition, the patient reported ocular hyperemia and epiphora. She denied pain or any changes in visual acuity. No methods of relief had been employed.

The patient's last eye exam was a comprehensive eye exam about one year ago at another office; this was the first time she presented to our office. There was no remarkable medical, ocular, family, or social histories. The patient denied any history of ocular surgeries or trauma. She was not taking any medications and had no known drug allergies. The patient and parent denied being ill recently or being around someone who was sick. The patient denied photopsias or floaters, and reported no headaches or diplopia. She was oriented to time, place, and person, and her mood was appropriate, albeit noticeably anxious and nervous about the examination.

The patient's uncorrected distance visual acuity was 20/20-2 each eye; she had no habitual spectacle correction. Pupils were equal, round, and responsive to light, with no relative afferent pupillary defect. Confrontation fields were full to finger counting in each eye. Function of extraocular muscles were found to be smooth, accurate, full, and extensive with no pain nor diplopia. Unilateral and alternating cover testing revealed orthophoria at distance and near. There was no palpable preauricular lymph node.

Examination of the anterior segment revealed several remarkable findings. The eyelashes of the right eye were normal, whereas the left eye's eyelashes on the inferior lid nasally were truncated, appearing to have been broken or cut off (Figure 1). Eyelids were clean and clear, without lesions, but the left lower lid displayed trace edema and redness. All puncta were patent and normal in appearance. The right bulbar conjunctiva was white and quiet, whereas the left exhibited 1+ mild diffuse injection. The palpebral conjunctiva for both eyes had a 1+ fine papillary reaction. There were no follicles. Upon everting the upper eyelids, a similar fine papillary reaction was noted; there was no foreign body observed. A sodium flouresceing strip was instilled OU. The right cornea was clear, but the left cornea had a 1 mm area of vertical

track-like sodium fluorescein staining (Figure 2). The scleras were clear in each eye. The anterior chambers were deep and quiet with no evidence of cells or flare, and angles were estimated to be 4/4 via the Van Herick method. The irides were brown, flat, and clear.



Figure 1: truncated lashes nasally OS

Figure 2: 1 mm area of corneal staining OS

Measurement of intraocular pressures were attempted with the iCare tonometer, but the patient was extremely apprehensive and did not cooperate. On palpation, the orbits felt soft and equal.

Differential diagnoses considered at this point include:

- Allergic conjunctivitis
 - Seasonal allergic conjunctivitis
 - Perennial allergic conjunctivitis
 - Vernal keratoconjunctivitis
 - Atopic keratoconjunctivitis
 - Giant papillary conjunctivitis
- Bacterial conjunctivitis
- Viral conjunctivitis
 - Epidemic keratoconjunctivitis
 - Herpes simplex virus conjunctivitis
- Corneal abrasion
- Dry eye syndrome
- Blepharitis
- Episcleritis

The clean eyelashes ruled out blepharitis and the clear scleras ruled out episcleritis. The lack of a palpable preauricular node pointed away from a viral conjunctivitis, and the lack of discharge besides increased lacrimation suggested that the etiology was not of a bacterial origin. The complaint of itch points to one of the types of allergic conjunctivitis. The lack of giant papillae, Horner-Trantas dots, and a shield ulcer make the diagnosis of vernal keratoconjunctivitis unlikely. The patient is also outside the usual age range for atopic keratoconjunctivitis and did not report any signs of eczema. Because it was wintertime and pollen levels were low, the patient's tentative diagnosis was determined to be perennial allergic conjunctivitis. A corneal abrasion and truncated eyelashes were secondary to frequent eye rubbing.

Both the patient and the parent were educated on the findings. The treatment protocol included beginning one drop of over-the-counter Zaditor or Alaway (ketotifen fumarate ophthalmic solution 0.035%) in each eye twice daily. The patient and parent were counseled on the nature of allergic conjunctivitis, and the patient was instructed to never rub her eyes and to use cold compresses instead. To assist in the healing of the corneal abrasion, the patient was to also begin using lubricating artificial tears several times daily for the next few days. They were instructed to return to the office in one week for a follow-up.

Follow up #1, Brief Eye Exam, 01/11/2020

The patient returned about one week later for a follow-up appointment and reported vast improvement in the pruritus with the use of Zaditor. Her mother reported that she noticed her daughter rubbing her eyes less often. Instillation of sodium fluorescein and slit lamp examination revealed complete resolution of the corneal abrasion. The eyelid edema improved, but a trace conjunctival papillary reaction remained.

The patient and parent were instructed to continue the present management of the allergic conjunctivitis and reminded about the importance of not rubbing the eyes. They were instructed to return to the office at the next availability for a comprehensive eye examination.

Follow-up #2, Comprehensive Eye Exam, 01/17/2020

The patient returned to the clinic about one week later for a comprehensive eye exam. The patient and parent reported complete resolution of previous symptoms and compliance with the recommended medical therapy. Her last complete eye exam was one year ago, during which she had an unremarkable dilated fundus examination. The patient and parent reported no changes to the patient's history since the last exam. Her uncorrected visual acuity was 20/20 for each eye at distance and near. The autorefractor showed a refractive error of -0.75DS OD and -0.50-0.50x074 OS. Autokeratometry readings were 43.00@176 and 45.00@086 OD, and 42.75@002 and 43.25 @092 OS. Manifest subjective refraction was plano sphere OD with a visual acuity of 20/20+1, and +0.25DS OS with a visual acuity of 20/20+1. Color vision testing with Hardy Rand and Rittler Pseudoisochromatic Plates was normal in each eye. Stereoacuity measured with the Random Dot 3 stereopsis test was 20 seconds of arc. Pupils were equal, round, and reactive to light with no relative afferent pupillary defect, and extraocular muscles were unrestricted in all gazes. Cover testing revealed orthophoria at distance and near, and confrontation fields were full to finger counting each eye. Intraocular pressures were again attempted with iCare and

Goldmann applanation tonometry, but the patient was not cooperative. On digital palpation, the orbits were soft and equal.

Anterior segment evaluation revealed resolution of the papillary reaction in both eyes and all findings were within normal limits except for the short lashes on the lower left eyelid. The patient's posterior segment evaluation was unremarkable. The patient and parent were explained the importance of a dilated fundus examination, but they declined dilation and understood that retinal findings could be missed. The crystalline lenses and vitreous of both eyes were optically clear. Slit lamp evaluation with a 90D lens revealed that the optic nerves were flat with deep cups, distinct margins, pink and healthy rims, and had a cup-to-disc ratio of 0.30 round each eye. The maculas were flat and clear. Retinal vasculature was normal, with an artery to vein ratio of 2/3. Optomap ultra-widefield retinal imaging, obtained as a screening measure performed on all patients, was obtained for both eyes. The retinas were clear with no holes, tears, or detachments to the extent that the image was able to capture.

The patient and parent were educated on the findings and instructed to continue present management of the allergic conjunctivitis. The patient was to return to the office in one year for their next comprehensive eye exam, or sooner if needed.

Discussion

There are four main types of allergic conjunctivitis: seasonal allergic conjunctivitis, perennial allergic conjunctivitis, vernal keratoconjunctivitis, and atopic keratoconjunctivitis. Allergic conjunctivitis is categorized as seasonal or perennial depending on whether the symptoms are triggered by transitory allergens like pollen or those present year-round such as dust mites, mold, or animal dander.¹ Perennial allergic conjunctivitis is less common and milder in presentation. Vernal keratoconjunctivitis usually affects prepubescent males living in warm, dry climates with a history of atopy or asthma.² Atopic keratoconjunctivitis usually presents between the ages of 30 and 50, and atopic dermatitis is present in 95% of cases and asthma in 87% of cases.³ Giant papillary conjunctivitis is traditionally included in the group of ocular allergic diseases, but it is actually a result of non-immune tissue damage from repetitive microtrauma.⁴

In the United States, almost half of the population is affected by symptoms of allergic conjunctivitis.⁵ Seasonal and perennial allergic conjunctivitis, in particular, affect 15-20% of the population.⁶ Seasonal and perennial allergic conjunctivitis result when an allergen causes cross-linkage of IgE that causes mast cells to degranulate, further causing a cascade of allergic and inflammatory mediators including histamine.⁷ Symptoms of allergic conjunctivitis include pruritus, hyperemia, and epiphora. Signs, usually bilateral, include hyperemia and chemosis of the conjunctiva and eyelids, and a relatively mild papillary reaction.¹ An allergic "shiner" is discoloration under the eyes from venous congestion.³ A detailed case history and, in the case of pediatric patients, careful observation by caregivers, assist in not only the diagnosis of allergic conjunctivitis, but a higher chance of identification of the perpetrating allergens.

There are many ways to treat and manage allergic conjunctivitis. The first method of addressing allergic conjunctivitis is by eliminating or reducing exposure to the allergen, if known. For example, air pollution has been found to be associated with severe ocular allergic inflammatory diseases.⁸ The use of air filters and regular cleaning of linens may help reduce the

presence of allergens in the home. Cool compresses several times per day will relieve itch. For mild allergic conjunctivitis, lubricating artificial tears four to eight times per day will dilute the tears and help flush allergens from the eyes; they are especially effective for itch when used refrigerated. Moderate allergic conjunctivitis may be treated with antihistamine and mast cell stabilizer drops. Topical eye drops with daily dosing include olopatadine 0.2% or 0.7% and alcaftadine 0.25%. Twice daily dosing eye drops include olopatadine 0.1%, epinastine 0.05%, nedocromil 2%, bepotastine 1.5%, and ketotifen 0.025%. There are also four times daily dosing eye drops that include pemirolast 0.1% and lodoxamide 0.1%.

For severe allergic conjunctivitis, a mild topical steroid in addition to the antihistamine mast cell stabilizer drops can be helpful to reduce inflammation quickly. If topical steroids are used, tapering is required and the patient should be monitored for side effects, including an increase in intraocular pressure. Topical steroids work by reducing inflammatory cytokine production, mast cell proliferation, and cell-mediated immune responses.⁹ Loteprednol etabonate (0.2% Alrex, 0.5% Lotemax) has been shown to be very effective in allergic conjunctivitis and is preferred due to its quick metabolization, which reduces the risk of adverse side effects.¹⁰ Lotelprednol etabonate 0.2% caused significant intraocular pressure increase in only 1% of patients and has not been shown to correlate with the development of cataracts.¹⁰ Topical nonsteroidal anti-inflammatory drugs (NSAIDs) have been found to significantly decrease conjunctivitis, but caution must be exercised due to the risk of adverse side effects such as corneal melt.¹¹ Oral antihistamines may be helpful as well and include 25 mg of diphenhydramine per oral three times a day and 10 mg loratadine per oral once a day.¹ Intranasal steroids for allergic rhinitis have been shown to improve symptoms of ocular allergies.¹²

Dupuis et al developed a treatment algorithm for seasonal and perennial allergic conjunctivitis.⁹ They consider topical ophthalmic dual-activity agents such as olopatadine, ketotifen, and bepotastine first-line therapies due to their good clinical response and safety profile. If there are signs of inflammation, topical ophthalmic steroids such as loteprednol and fluorometholone may be used short-term. If further treatment is warranted, use of a second generation oral antihistamine such as cetirizine or loratadine can be helpful. If they are contraindicated due to ocular surface drying or central nervous system effects, a nasal steroid such as fluticasone furoate or mometasone furoate may be used off-label for pain and foreign body sensation if the above methods do not provide relief. Immunotherapy including subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) can be used for generalized allergic symptoms and provides long lasting relief of symptoms. Other immunomodulatory treatments include cyclosporine 0.05% which can be used off-label for chronic cases, usually for vernal or atopic keratoconjunctivitis.¹³

Ketotifen, a mast cell stabilizer and antihistamine combination topical solution, was selected as a first-line treatment of the patient's allergic conjunctivitis. Its mechanism of action includes eosinophil activation, generation of leukotrienes, and cytokine release.¹⁴ Ketotifen has a favorable safety and tolerability profile in patients as young as three years old.¹⁵ In a study comparing ketotifen 0.025% versus 0.05%, ketotifen 0.025% was found to be more effective and better tolerated.¹⁶ Ketotifen 0.025% was found to be superior to placebo and levocabastine 0.05% in relieving itching and epiphora.¹⁷ Multiple studies have compared ketotifen to

olopatadine. In a 30-day, randomized, double-masked, artificial tear substitute-controlled trial comparing ketotifen 0.025% and olopatadine 0.1%, both reduced inflammatory markers in conjunctival surface cells, were well tolerated, and were more effective than artificial tears.¹⁸ In another study comparing the two drugs, hyperemia, tearing, itching and photophobia were better relieved with olopatadine than with ketotifen.¹⁹ A study that compared the efficacy and tolerability of olopatadine, ketotifen, and epinastine found that olopatadine was the most effective in relieving signs and symptoms of allergic conjunctivitis.²⁰ One study also showed that itching at day 14 was greatly reduced with olopatadine compared to ketotifen.²¹ However, another study showed no difference in efficacy between the two for itch and hyperemia.²² Ketotifen, available over the counter as the brands Zaditor and Alaway, is the most easily accessible to this patient population. Olopatadine, which is a prescription-only medication at the time of this writing, has been prescribed in the past with unfavorable responses from insurance companies requiring submission of prior authorization before releasing the medication, causing delays in the treatment of the patients' conditions. In the case that ketotifen does not provide enough relief during the first week of treatment, olopatadine is then prescribed.

It is known that eye rubbing can exacerbate keratoconus and research has shown that patients with allergic conjunctivitis do have an increased risk of developing keratoconus.²³ There is also a positive correlation between allergic conjunctivitis and asthma and eczema.²⁴ In most cases, keratoconus, asthma, and eczema are correlated more with atopic keratoconjunctivitis than with seasonal or perennial allergic conjunctivitis. Numerous studies have found that allergic conjunctivitis is a risk factor for other seemingly unrelated problems. Children with allergic conjunctivitis have a higher incidence and risk of migraine.²⁵ Allergic conjunctivitis has also been found to be a risk factor for myopia; upregulation of allergic inflammation promotes the progression of myopia in the animal model and children with allergic conjunctivitis have been found to have a higher incidence and risk of myopia.²⁶ The myriad of associations allergic conjunctivitis has indicates that proper management of the disease is crucial for the wellbeing of patients.

Research continues to be done on novel ways to manage allergic conjunctivitis. Topical cyclosporine has been studied in the off-label treatment of allergic conjunctivitis and has been found to be effective, reducing the use of steroid eye drops in patients with steroid-dependent allergic conjunctivitis.¹³ Tacrolimus 0.03% dermatological ointment applied to the conjunctival sac has been shown to reduce chemosis, tarsal papillary size, corneal staining, tearing, itching, and photophobia in patients with intractable allergic conjunctivitis.²⁷ Mapracorat is a selective glucocorticoid receptor agonist that is non-steroidal and being studied for ocular use with promising effects on allergic conjunctivitis with a lower risk of increasing intraocular pressure, cataract formation, and delayed wound healing compared to traditional corticosteroid eye drops.²⁸

Interprofessional collaboration results in improved healthcare outcomes for patients.⁹ Eyecare specialists are able to examine the ocular adnexa and treat ocular manifestations of allergies, but when a patient presents with symptoms that extend beyond the eyes, consulting with and referring to their primary care provider or an allergist may be a beneficial next step. An allergist is helpful when signs and symptoms remain uncontrolled and allergen identification or immunotherapy is required. Primary care providers can be referred to for management of general allergic disease or when signs of multisystem disease are identified. Providing patients with the

proper resources limits their self-medicating with over-the-counter medications and encourages them to seek help when needed.²⁹ Incorrect or overuse of these medications, especially topical vasoconstrictors, can have adverse side effects such as tachyphylaxis and rebound hyperemia upon discontinuation of use.³⁰

Conclusion

Allergic conjunctivitis comes in various forms and affects a large percentage of the general public. The condition not only causes discomfort, but is also a risk factor for a number of other ailments. Although there is currently a strong array of treatment options for allergic conjunctivitis, research is ongoing and several new methods for the management of the condition have been discovered in recent years. Study of the condition and its associations equip healthcare providers with the knowledge necessary to provide the best care to their patients. This case demonstrates a straight-forward case of allergic conjunctivitis in which the patient responded very well to a traditional treatment of the condition.

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