

Case report of retinoschisis associated with chronic epidemic keratoconjunctivitis (EKC) and a review of the literature

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Abstract

Epidemic keratoconjunctivitis (EKC) is a common, highly contagious, and severe infection of the eye caused by adenovirus. EKC is often described as a healthcare acquired infection (HAI) and well known to cause “runs” in eye care clinics. Typically, acute symptoms of this viral infection manifest as ophthalmalgia, marked erythema, profuse clear ocular secretions, impaired vision, photophobia, edema of the eyelid, and pseudo membrane formation. Although previously thought to be self-limited disease, EKC complications may result in waxing and waning ocular debility, severe dry eye, glare, irregular and variable astigmatism, and less commonly permanent ocular damage and scarring. To date, there is no universally effective cure, vaccine, or treatment available. Thus, EKC prevention through education and enhancement of best practices in sanitation in ophthalmology is paramount in disease eradication. We report an otherwise healthy 52-year-old male who developed newly diagnosed unilateral retinoschisis approximately 5 years after nosocomial contagion of EKC in the same affected eye. In this manuscript, we illustrate the morbidity, chronicity, seriousness, and high prevalence of adenoviral eye disease, and the significance of prevention through enhancing sterilization and regular application of universal precautions in eye care delivery.

The significance of (1) the newly described possible association of retinal disease (retinoschisis), and (2) newly identified chronic waxing and waning nature of EKC spanning more than 7 years, in an otherwise previously thought to be “self-limited” corneal process, as described herein, remain to be studied further and those relationships, if any, determined.

Abbreviations: EKC, epidemic keratoconjunctivitis; CDC, centers for disease control; SEIs, subepithelial infiltrates; HAI, healthcare associated infection; HCI, healthcare caused infection

Epidemic keratoconjunctivitis (EKC) is a common and highly contagious acute infection of the eye caused by various strains of adenovirus. Typically, symptoms of this severe viral infection will manifest after an incubation period of 7-14 days and include severe ophthalmalgia, marked erythema, profuse clear ocular secretions, impaired vision, photophobia, edema of the eyelid, and pseudo membrane formation. EKC complications may result in permanent ocular damage. EKC infections are known to result in positive serology for adenovirus. To our knowledge, there have been no prior reports of retinoschisis in EKC, and none as to chronic EKC disease lasting more than 7 years. The significance of (1) the newly described potential association of retinal disease (retinoschisis), and (2) identified chronic waxing and waning nature of EKC spanning 7 years, in an otherwise previously misclassified as a “self-limited” corneal disease, remains to be studied further and relationships, if any, determined.

There is no universally effective cure, vaccine, or treatment available for EKC; topical corticosteroids, while highly controversial and potentially adverse reaction prone, may provide symptomatic relief in a small subset of patients who have severe and vision limiting

subepithelial infiltrates (SEIs). Ocular corticosteroid use in EKC is more often than not discouraged as it may enhance the adenovirus infectious period and result in lengthening of viral shedding.¹ EKC is extremely contagious and frequently described as a healthcare associated infection (HAI) or healthcare caused infection (HCI).² Thus, EKC frequently results in epidemics or “runs” in eye care offices, clinics, and hospital wards worldwide.²⁻⁵ In particular, the U.S. Centers for Disease Control (CDC) has repeatedly described and reported EKC runs in Southern California ophthalmology clinics and offices, outbreaks not unlike the California HAI which resulted in the subject of this case report.^{2,4,5} Laboratory testing such as viral cultures and PCR testing, and rapid in office testing such as Adenoplus, are available to aid in diagnosis of EKC. Accurate and early diagnosis is mandatory to correctly identify the type of virus and to initiate prevention protocols. For the majority of nosocomial EKC cases, individuals often contract the virus directly through routine eye care examinations.^{1,6} With an average incubation period lasting from 7-14 days, affected individuals often do not make the requisite association of contracting the virus with their recent eye examination.^{1,7} In other indirect HAI cases, EKC can arise in family, friends, or close contacts of those who have recently visited an eye care office. The virus is known to last on surfaces, such a slit lamps and multi-use eye drop

containers, for an average of 4-6 weeks.^{1,6,8,9} We report of an otherwise healthy male patient who became infected with EKC during a routine eye examination in 2011 in a Southern California ophthalmology office, which was experiencing a known EKC outbreak of more than 70 patients.^{2,3}

Case Report

In 2011, a 52-year-old healthy Caucasian male accountant, visited a private ophthalmology practice in Irvine, California for his routine eye examination and eye glass prescription renewal.³ He was tested with 20/30 vision, and required a minor adjustment in his prescription. On or about 7 days (average incubation 7-14 days following EKC exposure) post his eye examination he experienced a sudden onset of pain, redness, profuse watering, impaired vision, and severe discomfort in his right eye. He called his ophthalmologist who was aware of the EKC outbreak in her office¹, and diagnosed him over the phone with EKC. With meticulous hygiene, the patient's EKC remained isolated to the right eye, and he did not infect any coworkers or family during any time. The patient did not use any steroids. A corneal examination in May 2013 confirmed persistent SEIs, with periodic symptomatic outbreaks and remission. The unilateral SEIs continued to affect his eye, vision, and overall quality of life for the better part of four years. In year five after the EKC infection, the patient was diagnosed with retinoschisis of the EKC affected right eye and is continuing monitoring. One additional patient associated with the same ophthalmology office EKC HAI outbreak was newly diagnosed on around 2017 with retinal detachment in the same EKC affected eye. The relationship of EKC and these retinal disease findings remains unknown.

Comment

Epidemic keratoconjunctivitis (EKC) is an acute viral ocular surface infection, which may result in chronic corneal damage, irregular astigmatism, recurring severe dry eyes, glare, and impaired vision. EKC is caused by adenoviruses including but not limited to, types 8, 19, 37, or 53. Although the adenovirus particle was thought to typically be self-limited to 2 weeks as the ocular cells shed,¹⁰⁻¹² controverting evidence shows that EKC is chronic in at least a large subset of patients. While there is controversy on whether the actual viral particles are able to survive after the acute EKC phase, the antigen and antibody response has been shown to last for years, and laboratory testing may reveal positive serology titers of adenovirus with waxing and waning levels. Acute EKC symptoms include but are not limited to marked red eyes, edema of the eyelids, impaired vision, clear ocular secretions, and photophobia.^{10,13} While acute EKC symptoms may mimic other conjunctivitis and viral infections, the distinguishing feature for EKC is the presence of multifocal sub epithelial corneal infiltrates (SEIs).^{1,10} SEIs will typically acutely arise within 7-10 days after EKC symptoms emerge. Slit lamp may reveal tiny dot-like follicular infiltrates surface from the cornea, which may give the cornea a "foggy" or "clouded" appearance.^{1,11} While the SEIs typically fade and shed with the ocular cells, the recent case from this report describes that SEIs may and do persist for years. EKC may also cause permanent and irreversible corneal changes, chronic dry eyes, and irregular astigmatism.¹⁰ EKC is highly contagious, with the individual remaining infectious for up to 2 weeks after the acute phase.

¹ Medicare billing records of the ophthalmologist showed at least 46 Medicare beneficiaries contracted EKC within 7-14 days after their exam and were later diagnosed with EKC in the Irvine, California ophthalmology office.

Viral particles may also remain contagious on inanimate surfaces, including multi-use eye drop containers for up to 2 months (6). Many eye care clinics report that they maintain offices and equipment, particularly tonometers, with 70% isopropyl alcohol; although it has been repeatedly documented that 70% isopropyl alcohol sanitizers are not effective against EKC.^{3-5,10,14} Bleach based, medical grade sanitizers are significantly more reliable in the proper disinfection of eye examination equipment and eye clinics.^{2,4,5,14}



Figure 1 Acute EKC outbreak photo Right Eye (Irvine, California 2011 Outbreak)



Figure 2 Acute EKC outbreak photo Left Eye (Irvine, California 2011 Outbreak)



Figure 3 Acute EKC outbreak photo Left Eye (Irvine, California 2011 Outbreak)

Chronic EKC has a wide range of symptom and severity including dry eyes, corneal surface irregularities, irregular and variable astigmatism, and impaired vision.¹¹ After the viral incubation period, which typically lasts 7-14 days, the individual may begin to feel a foreign grit sensation often in the nasal corner of the eye which may spread laterally, eventually coating the eye, causing corneal xerosis.^{1,7} Other symptoms will begin to follow, edema of eyelids, blurred vision, painful red eyes, and ocular secretions.^{1,10} Typically, on the 7th to 10th day after the initial onset of EKC, the corneas may suddenly become “clouded” or “foggy” due to onset of SEIs.^{10,12} EKC symptoms may resemble other conjunctivitis such as viral or bacterial conjunctivitis, however EKC symptoms are generally more severe, do not respond to antibiotics, and last for a longer period of time. SEIs may wax and wane based on the individual’s immune response. Scarring with SEIs has been described. If centrally located, SEIs can cause significant visual impairment and disability.¹⁰

Early and accurate EKC diagnosis is important in order to prevent and contain outbreaks, as well as to notify local health authorities to assist with clinic decontamination. An inadequate diagnosis may lead to inaccurate healing expectations, increased person-to-person transmission rates, and possible EKC complications.¹⁰ A correct diagnosis distinguishes between viral/bacterial conjunctivitis and epidemic keratoconjunctivitis. There are two categories of tests for EKC, the first being a rapid in-office test that is similar to quick strep test.^{1,10} The second being the more traditional diagnosis of EKC with laboratory testing cell culture in combination with immunofluorescence staining (CC-IFA) and (PCR) which identifies adenoviral infections such as serologic methods, antigen detection, and polymerase chain reaction¹⁰ PCR testing may be available when sent to the Centers for Disease Control (CDC). While both tests are considered the gold standard of EKC diagnoses, they require a swab from the ocular discharge to be sent to different laboratories, as most eye care physicians do not have the necessary equipment at their practice.¹⁰ This time consuming method of diagnosis is therefore often not followed, which heightens the risk of the virus to be inadequately contained, and not timely reported to healthcare officials. An in-office rapid response test similar to the quick strep test is available, where results are available within minutes, called the Adeno Detector™ test kit.^{1,7} However, as with many tests, there are limitations as the rapid test may be less sensitive and less specific.

Treatment for EKC is very limited. There is currently no uniformly effective vaccine, or antiviral medication for EKC. EKC treatment remains palliative with artificial tears or cool compresses, and a few proposed off-label uses of topical medications including povidone-iodine (Betadine), and ganciclovir.^{1,10,12} If symptoms worsen or start to become unmanageable, topical antibiotics and steroids have been prescribed. While some studies have shown ocular steroids may attribute or prolong SEIs, the use of topical steroids in EKC may provide symptom relief and temporarily lessen the acute vision impairment.¹ It is controversial if and how EKC may result in corneal scarring, and if any benefit from treatment of SEIs with laser eye surgery (CPKK) is conferred. Corneal EKC involvement may lead to a number of complications, the predominant result being severe dryness, decreased and fluctuating visual impairment, and potentially decrease in corneal sensitivity. Some studies have postulated that EKC decreases the corneal sensitivity and propose that the main confocal microscopic features are morphologic changes in the infected epithelial cells, infiltration with round inflammatory cells

and dendritic cells, increased brightness in the extra-cellular matrix and the stroma surrounding the corneal nerves, increased keratocyte activity, and extra-cellular bright micro-deposits.¹⁵

The highly contagious and epidemic nature of EKC, its frequent HAI causation, along with the lack of effective treatment, makes EKC prevention a top public health priority.^{1,6,9,2,4,5} In addition to community outbreaks, the primary source of EKC outbreaks are inadequately sanitized eye examination equipment, particularly tonometry and slit lamps, at eye healthcare locations all over the world.^{1,2,6,9,16} During active EKC outbreaks, research has shown that infection rates from ophthalmologist and optometrist offices may develop an average infection rate from 5-8%, and may reach as high as 25%^{2,4,5, 8,9,14} Any single report of EKC at an eye clinic, requires an immediate shut down of the affected room while all semi-critical items such as tables, desk, chairs, and critical items, tonometer, slit lamp, eye drops, are sufficiently sanitized with a medical grade disinfectant.^{1,6,4,5} However, in widespread office outbreak cases, the temporary shutting down of a practice or hospital ward may last sometimes a few days, and less commonly up to 6 weeks to allow for adequate decontamination of adenovirus for all surfaces.⁴⁻⁶ In a research report it was found that a number of outpatient eye care facilities experienced EKC outbreaks with significant numbers, yet the outbreaks were never reported.^{7,3} Ophthalmologist and other eye healthcare providers are highly encouraged to report any case of EKC to their local health department in order to prevent future outbreaks. Proper protocols are meant to be kept in place in order to routinely prevent the transmission of EKC for any facility that offers ophthalmologic and optometric care. The protocols include but are not limited to^{1,6,9,17}:

- 1) Maintain strict hand hygiene at all times for all staff members;
- 2) The eye doctor and staff should use disposable gloves in case of contact with any eye secretions;
- 3) Any single use item, such as eye drop vials, should be disposed of when possible;
- 4) Eye examination equipment, such as tonometry, should be properly disinfected with medical grade antiviral sanitizer as opposed to the typically used 70% isopropyl alcohol sanitizer;
- 5) Separate sign-in area, waiting, and examination room for patients suspected of having any type of conjunctivitis are advised;
- 6) Temporarily removing staff members who show signs and symptoms of EKC;
- 7) It is important that any and all EKC outbreaks be immediately reported to local and state public health authorities.

Conclusion

As this case study demonstrated, EKC is often a chronic, relapsing disease with an unpredictable course. While EKC’s acute phase lasts a few weeks, the chronic phase may last years, if not a lifetime. The significance of (1) the newly described possible association of retinal disease (retinoschisis), and (2) newly identified chronic waxing and waning nature of EKC over 7 years, in an otherwise previously thought to be “self-limited” corneal process remains to be studied further and relationships, if any, determined.

EKC is not a fully “self-limited” corneal process as previously likely misunderstood and classified. EKC is a highly contagious ocular

adenovirus infection that is characteristically propagated through routine eye examinations, particularly through the use of applanation tonometry and multi-use eye drops. EKC can be prevented if ophthalmologist and optometrists and staff regularly maintain a level of reasonable hygiene that is required in medical practices.²⁻⁶ If an EKC outbreak occurs, eye care providers have the responsibility to contact affected individuals, and contain and minimize the outbreak by contacting state and local health authorities for help, which some practitioner including the original ophthalmologist in the case study did not do.^{1,6,3} Ultimately the responsibility falls onto eye care professionals to educate their patients on the severity of EKC infection and to prevent the spread of EKC through proper disinfection protocols.^{2,6,9,17} While there are currently no uniformly effective treatments, vaccines, or antiviral drugs available for EKC, larger studies are needed in order to further determine effective EKC and SEI treatment, as well as the relationship of EKC to non-corneal eye disease including retinoschisis, and other possible systemic manifestations.

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