

Epidemic Keratoconjunctivitis Treatment and Management

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Abstract

Epidemic keratoconjunctivitis (EKC) is a viral conjunctival and corneal inflammation with high contagiousity, which, if is not adequately treated, may cause blurred vision for several years. The purpose of this study was to describe the clinical and epidemiological characteristics of adenoviral keratoconjunctivitis, as well to present the latest news regarding diagnosis, treatment and prophylaxis.

Are known two well-defined clinical syndromes of adenoviral keratoconjunctivitis: epidemic keratoconjunctivitis and faringococcal fever, which are caused by various serotypes of adenoviruses. The exact incidence of adenoviral keratoconjunctivitis is not known. However, it mainly occurs during the winter months. Infection can occur during direct contact or through equipment, devices in ophthalmologic ambulances, etc. The virus is extremely resistant to various chemical and physical agents. Symptomatology is similar to other types of conjunctivitis, with high incidence of conjunctival pseudo membrane formation. In the cornea, the changes varying from epithelial punctate keratitis to sub epithelial infiltrates and the creation of nummular keratitis that leads to visual impairment. Diagnosis is mainly clinically decided, and etiology can be confirmed based on cell culture analysis.

Conclusion: Until now there is no approved therapy against epidemic adenoviral keratoconjunctivitis. Uncontrolled use of antibiotics, particularly corticosteroids, which reduce tissue resistance, is responsible for the deterioration of such conditions. Priority in prevention EKC is the rigorous application of hygienic disinfectant measures in hospital areas, respectively medical devices in ophthalmologic ambulatory services.

Keywords: Epidemic Keratoconjunctivitis, Adenoviruses, Epithelial Punctate Keratitis, Nummular Keratitis.

Introduction

Epidemic keratoconjunctivitis (EKC) is a viral conjunctival and corneal inflammation with high contagiousity that affects the eye surface, which, if it is not adequately treated, may cause blurred vision for several years. It is called 'epidemic' because of epidemic spread of infection. Almost every kind of microorganism can cause inflammation of the eye, but about 92% of them are thought to be caused by viruses, mainly adenovirus [1]. This adenovirus family contains various serotypes which cause epidemic adenoviral keratoconjunctivitis (EKC), pharyngoconjunctival fever and non-specific follicular conjunctivitis. About 50% of patients with adenoviral keratoconjunctivitis are associated with upper respiratory tract infections that often precede EKC. At some of those patients the disease can be generalized with fever or gastrointestinal disorders with diarrhoea and vomiting [2].

Epidemiology

Acute epibulbare infections in humans are one of the most commonly diagnosed eye diseases, and compose 2.3-10% of all ophthalmologic diagnoses, with a prevalence of 0.6 - 3.5 per 1000 patients [3].

Adenovirus keratoconjunctivitis generally includes adults between age of 20-40 years and are more common in males than in females (2:1). The incubation of the virus is 2 to 12 days. The disease is very contagious, perhaps before the symptoms of the infection appears, and of course remains as long as the virus can be isolated in body fluids; for tears this period usually lasts two to three weeks from the day the virus is being transmitted [4]. Human Adenovirus (HAdV) belongs to the Adenoviridae family, in the genus of Mast adenovirus that causes a variety of diseases including respiratory infections, gastroenteritis, and eye infections [5].

There are 51 types of adenoviruses classified in 6 groups, from A to G, determined on the basis of oncogenicity, hemagglutination model of erythrocytes, and DNA homology [5,6].

Table 1: Ophthalmological significance of adenovirus species in Europe

Follicular conjunctivitis	Ad3, 4, 7
Epidemic keratoconjunctivitis	KKE Ad8, 19, 37
Acute respiratory disease	ARD Ad1-3, 4, 6, 7, 14, 21
Pharyngoconjunctival fever	Ad3, 7, 1

They are highly resistant to external influences and can survive even after contact with ordinary disinfectants. They remain contagious for weeks at room temperature and have high ability to cause nosocomial infections. This demonstrates the need for proper selection and application of germicides for the disinfection of medical devices and instruments, especially tonometers, in order to prevent epidemic keratoconjunctivitis.

Human Type 19 Adenovirus (HAdC-19) is the leading etiologic agent of EKC while subgroups B and C are isolated from the respiratory tract [5].

The spread of infection is observed in places where people are in groups such as: schools, kindergartens, health institutions, including ophthalmologic ambulances. EKC can touch any age group at any time of the year. Adenoviruses are transmitted from human to human through contact with infected hands, face and secretions, mainly tears. The virus can also be spread by ophthalmologic contaminated instruments, dropper bottles, tonometers, and contaminated hands of medical personnel, which is the main risk factor for a nosocomial infection.

Clinical Presentation

Infection usually begins with unilateral sensation of foreign body and in most cases the other eye is infected a few days later. Patients usually showing for contact with someone who has had an eye infection or upper respiratory tract infection. Besides the feeling of foreign body in the eye, the patients may have also photophobia, watery discharge, and blurred vision if there is corneal involvement, ocular pain and redness of the eye [6].



Figure 1: Epidemic keratoconjunctivitis, a patient with the appearance of conjunctival hyperemia

During clinical examination, we can notice swelling of eyelids, conjunctival hyperemia and chemosis, follicular conjunctivitis of lower eyelid, and subconjunctival hemorrhage (Figures 1 and 2).



Figure 2: Epidemic keratoconjunctivitis, redness and subconjunctival hemorrhage, chemosis of conjunctiva, caruncula and plica lacrimalis

Follicular hypertrophy is more pronounced in the upper palpebral conjunctiva and may be present for 2 to 4 weeks (Figure 3). Occasionally the follicular reaction may continue for several months [7].

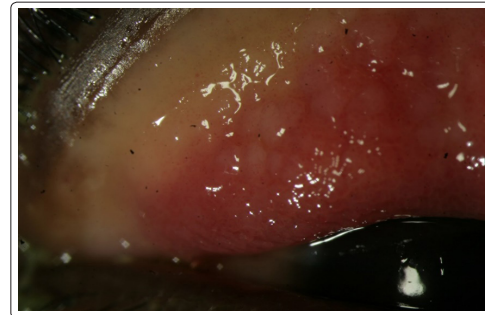


Figure 3: Follicular reaction of upper palpebral conjunctiva

In healthy eyes, most of these infections are limited and do not leave seizures, but pseudomembranes can be created in cases with compromised eyepieces (Figure 4).

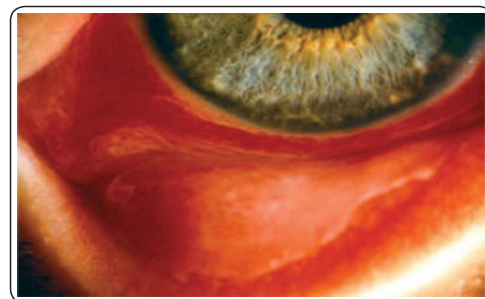


Figure 4: Epidemic keratoconjunctivitis, the appearance of subcutaneous hemorrhage and the creation of pseudomembranous tarsale.

Keratitis is common in adenoviral infections, usually occurring around the fourth day. Epithelial punctate keratitis (KEP) (characterized by the appearance of small infiltrates in the form of points in the cornea) may be created at the early stage of infection by all types of adenoviruses. The duration of KEP is less than 3 weeks, except with type 8 and 19 adenovirus where it may last longer. While the sub epithelial punctate keratitis (SEPK) is characterized by large and dense sub epithelial opacities in the cornea. After several days in 95% of cases, may appear nummular, multifocal, avascular corneal infiltrates with central localization. These consist of immune complexes deposited under epithelium of the cornea [8,9]. Nummular infiltrates when enlarged may reduce the visual acuity. SEPK can resolve spontaneously within three months [8].

Stromal diffuse infiltrates and corneal edema may be present in severe keratitis. In addition, an anterior uveitis can be manifested at the cases with adenovirus type 8 and 19.

Similarly, but usually less pronounced, the symptoms appear in the other eye, two to seven days later. The severity of the disease varies from subclinical conjunctivitis to a very severe disease with bacterial super infection, keratitis and with systemic symptoms such as fatigue, arthralgia along with signs of an upper respiratory tract infection [10].

The acute phase is can last about three to six weeks. Nummuli may

persist even after this stage, continuing to reduce the visual acuity (but only in the first affected eye in most cases). Nummuli that damage the vision can be resolved within weeks, but in rare cases, can persist for years [10].

More rarely, in patients who have undergone fulminant disease with the formation of pseudomembranes, it comes to the persistence of corneal irritation and the feeling of ocular pain. Also, as one of the most serious sequelae at the patient with dry eye syndrome with persistent infection and inflammation, pseudomembranous conjunctivitis, is formation of symblepharones (adhesion between the palpebral and bulbar conjunctiva).

In all cases with adenoviral infection, there is a preauricular, submandibular and cervical lymphadenopathy 48 hours after the appearance of the first symptoms. Any cytopathogenic agent that infects the ocular surface, including adenoviruses, results with dry eye due to loss of goblet cells [9, 10].

Diagnosis

The disease is usually diagnosed on the basis of a clinical signs, careful ophthalmological examination (bio microscopy, fluorescence test, corneal sensitivity test) and supplemented by laboratory tests such as conjunctival cytology with Giemsa stain to look for intranuclear inclusions and lymphocytes to identify the cause of the corneal and conjunctival sample.

Adequate agents for detecting the infective agent are also antigen detection, nucleic acid detection, polymerase-chain reaction and cell culture [11]. To confirm the diagnosis, viral culture is the criterion standard.

Differential diagnosis also includes other types of conjunctivitis as well as all cases of “red eye” such as uveitis, (epi-) scleritis, trauma, glaucoma, and so on.

Contagiosity

Adenoviruses are particularly resistant to various physical and chemical agents, and even in unfavorable pH environments are able to survive for a long time outside of the human body. Therefore, it comes the high rate of spread of these infections by ophthalmologic ambulances. For example, HAdV19 resists 8 days on paper, 9 days on the tonometer, 10 days on textile and metal materials, and up to 35 days on plastic materials [12]. These findings increase the need for adequate and rigorous application of germicides to disinfect space and medical devices [13]. Studies have shown greater efficacy of disinfectant agents such as hydrogen peroxide and isopropyl alcohol for the elimination of adenoviruses.

Treatment

Epidemic keratoconjunctivitis has not an effective treatment. Antiviral medications have not been shown to be effective against viral conjunctivitis, especially to adenoviruses that are responsible for epidemic keratoconjunctivitis [14].

The management of epidemic keratoconjunctivitis includes: the use of artificial tears, cold compresses, cycloplegic in severe cases of photophobia, topical corticosteroids (for short periods of time), and topical anti-inflammatory and anti-viral agents. Depending on the severity of clinical signs and symptoms, patients should be followed up a few days to weeks later. Patients on topical corticosteroid therapy

should be observed regularly to monitor side effects, including increased intraocular pressure and cataract formation. In rare cases with cicatricial conjunctivitis and symblepharon, surgery is recommended for fornix reconstruction and repairs the entropies [14].

The local use of steroids as eye drops almost always shows success during short-term use because of reducing corneal and conjunctival inflammatory signs, but does not have any significant effect at the time of recovery [12]. Topical corticosteroids can relieve subjective symptoms and may delay or prevent the formation of corneal infiltrates. However, in 30% of cases, recurrence of disease after discontinuation of corticosteroids has been observed due to increased adenovirus replication from corticosteroids [15]. The use of corticosteroids is only allowed in fulminant infections when loss of vision is at risk, in order to prevent symblepharon formation and pseudo membranes, sub epithelial corneal infiltrates and iridocyclitis [15].

Consensus on the use or dosage of corticosteroids does not exist. Only in one study, the use of cyclosporine A has been reported to be effective in relieving or eliminating corneal infiltrates [4]. While resistant cases are treated surgically with excimer laser, to improve visual acuity.

Scientific researchers are directed at the treatment of adenoviral keratoconjunctivitis with antiviral agents. In clinical studies for ribavirin, it is founded that ribavirin has a limited vitroactivity and low efficacy on three dominant serotypes of adenoviruses related with EKC [16,17].

During the topical administration of 0.15% ganciclovir in the form of ophthalmic gel, is reached the therapeutic level in humor aqueous and cornea, and is known as effective treatment for epithelial herpetic keratitis. Ganciclovir is recommended against the EKC because it has shown efficacy in vitro to specific adenovirus serotypes [17].

Promising results have been noted in the treatment of adenoviral conjunctivitis with providence iodine. Povidone-iodine has a broad spectrum in vitro, and is effective in eradication of bacteria, fungi, viruses and protozoa. A study by Pelletier et al. has reviewed the topical combination of povidone-iodine 0.4% as an antiviral agent and 0.1% dexamethasone as a potent steroid [18]. The results have shown that all eyes had rapid improvement of conjunctival injection with lowering of antiviral titers at the same time, thus guaranteeing the need for further studies of application of this combination [19].

Prevention

Medical staff should be rigorously advised for hand disinfection with 80% ethanol or 1% or 2% tosylchloramide salt. It is also recommended that eye drops and eye ointment to be used one time for each patient. Disinfection of ophthalmologic instruments is also needed mainly with chlorhexidine which is more preferable than 70% isopropyl alcohol [20].

Close co-operation with infection control specialists can prevent the potential spread of infection in the healthy population as well as limiting laboratory costs for the diagnosis of the infection [21]

Conclusion

Corneal and conjunctival viral diseases present an increasing problem due to frequent occurrence, recurrence and resistance to medication. Uncontrolled use of antibiotics, particularly corticosteroids, which

reduce tissue resistance, is responsible for the deterioration of such conditions.

Based on the fact that epidemic should be eradicated as soon as possible by taking adequate treatment, it is recommended first to report the epidemic disease and to apply recommendations from relevant referent institutions. Priority in treatment of patients with EKC is the rigorous application of disinfectant hygiene measures in hospitals, respectively ophthalmology departments, because there is still no adequate treatment for this disease. Until there is an effective antiviral therapy for EKC treatment, clinicians should be very careful in the use of corticosteroids considering the risk of infection duration.

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