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Major review

Adenoviral keratoconjunctivitis

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ABSTRACT

Viral conjunctivitis caused by adenovirus is the most common infectious conjunctivitis. Adenoviruses are highly contagious pathogens. The modes of transmission are mainly through hand to eye contact, ocular secretions, respiratory droplets, and contact with ophthalmic care providers and their medical instruments. The most frequent manifestation of ocular adenoviral infection is epidemic keratoconjunctivitis, followed by pharyngoconjunctival fever. Epidemic keratoconjunctivitis is also the most severe form and presents with watery discharge, hyperemia, cheosis, and ipsilateral lymphadenopathy. Pharyngoconjunctival fever is characterized by abrupt onset of high fever, pharyngitis, bilateral conjunctivitis, and periauricular lymph node enlargement. Isolated follicular conjunctivitis without corneal or systemic involvement also occurs. The rate of clinical accuracy in diagnosing viral conjunctivitis is less than 50%. Rapid diagnostic tests now being used decrease unnecessary antibiotic use. Treatment for viral conjunctivitis is mostly supportive. The majority of cases are self-limited, and no treatment is necessary in uncomplicated cases.

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1. Introduction

Adenoviruses are icosahedral, non-enveloped, double-stranded DNA viruses that can cause an array of diseases including conjunctivitis, gastroenteritis, hepatitis, myocarditis, and pneumonia.[97] Adenovirus is a highly contagious pathogen with over 50 known serotypes with unique antigenic determinants.[A] The most frequent manifestation of ocular adenoviral infection is epidemic keratoconjunctivitis (EKC), followed by pharyngoconjunctival fever (PCF). The distinguishing feature of presentation of EKC is the involvement of the entire ocular surface, including both the conjunctival and corneal epithelia. In severe cases, there may be formation of pseudomembranes and symblephara as well as multifocal

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subepithelial infiltrates that can reduce vision for years.[9,12,18] PCF is characterized by fever, pharyngitis, acute follicular conjunctivitis, and preauricular adenopathy. Isolated adenoviral conjunctivitis without corneal or systemic involvement also occurs. The modes of transmission are mainly through hand to eye contact, ocular secretions, respiratory droplets, and contact with ophthalmic care providers and their medical instruments.[8] Adenoviral conjunctivitis a biphasic disease that begins with an infective phase that is then followed by an inflammatory phase, which tends to begin 7–10 days after the initial infection as the virus continues to shed. The patient remains infectious for up to 2–3 weeks.[49]

2. Epidemiology

Adenoviruses are the most common cause of acute viral infection of the conjunctiva, accounting for up to 75% of case of conjunctivitis.[120] In Japan, adenoviral conjunctivitis affects approximately 1 million individuals each year, and epidemics are monitored by the National Surveillance Center.[48] Precise statistical data on the actual prevalence and incidence at the international level, however, is not available as cases may go undetected because patients do not seek medical care. According to data from Germany, the infection is more common in adults, though all age groups may be affected. There is no sex predilection.[2] In general, EKC typically occurs in the 20–40 year age group, whereas PCF typically occurs in children.[28,29]

Adenoviruses are classified into seven species (A to G) and different serotypes according to their immunochemical properties, nucleic acid similarities, hexon and fiber protein length, biological properties, and phylogenetic analysis.[4,100,A] Adenoviral conjunctivitis may occur epidemically or sporadically throughout the year. The spectrum and severity of disease varies based on the serological subtypes. Serotypes 8, 19, and 37 (species D) are associated with EKC; serotypes 3, 5, 7, and 11 (species B and C) cause PCF; serotypes 1–11 (species B to E) frequently cause isolated follicular conjunctivitis characterized by conjunctivitis without the sore throat or preauricular lymph node enlargement.[2,6,25,95,112] In an epidemiological study in Japan, adenoviral conjunctivitis related to serotypes 3, 4, and 37 increased in summer with temperature rises.[5] Data from Germany also suggest that adenoviral conjunctivitis is more frequent during warmer months.[28] EKC outbreaks can occur in the general population, in hospital environments (especially the ophthalmological units),[17,36,94] in neonatal intensive care units,[10,26] and in nursing homes.[20,27] PCF outbreaks, on the other hand, are more common in schools, kindergartens, and summer camps.[29]

Both EKC and PCF tend to occur in closed institutions. Direct contact with ocular secretions is the most common mode of transmission. The infection may be also spread through contact with eye care providers and instruments like tonometers, lid specula, and slit lamps. In one study, 46% of infected persons had positive hand swab cultures.[8] The risk of infection from domestic contact is approximately 10%, increasing in cases with prolonged infection.[35] Nosocomial EKC infections are common, and outbreaks in ophthalmology units may impose restrictions on clinical practices, including delay of eye surgery, early release of inpatients from hospital, and closure of ophthalmology wards.[48] In the United States, a nosocomial outbreak involving 41 individuals cost a hospital $29,527 ($1,085 for medical costs, $8,210 for investigative costs, $3,048 for preventive measures, and $17,184 for lost productivity), indicating a substantial expenditure that could have been prevented by proper infection control measures.[74]

3. Clinical symptoms and disease spectrum

3.1. *Epidemic keratoconjunctivitis*

Of the 60 or so serotypes of adenovirus that have been isolated, at least 19 can cause EKC. The most frequently associated serotypes are adenovirus 8, 19, and 37; less common serotypes include 2–5, 7, 9, 10, 11, 14, 16, 21, and 29.[B] The incubation period varies between 4 to 24 days, and the symptoms tend to last for 7–21 days. The patient may remain infectious for 10–14 days. The virus is not usually detectable by polymerase chain reaction (PCR) of ocular secretions prior to the onset of symptoms.[51] EKC is predominantly a unilateral condition in its initial phase, but can become bilateral in up to 70% of cases.[29] The most common symptoms are “pink eye” or “red eye”, excessive tearing, foreign body sensation, and photophobia. In more severe cases, patients can present with ocular or periorbital pain and decreased visual acuity. There is usually a recent history of an eye examination, an affected family member, or an occupational exposure. The infection may occasionally be preceded by flu-like symptoms such as fever, malaise, myalgia, respiratory symptoms, nausea and vomiting, and diarrhea. The ocular signs are predominantly bulbar conjunctival redness, chemosis, tarsal follicular reaction, petechiae, or even subconjunctival hemorrhage (Fig. 1).

3.2. *Pharyngoconjunctival fever*

PCF is most frequently caused by adenovirus serotypes 3, and less commonly by serotypes 2, 4, 7, and 14. Sporadic outbreaks occur in association with serotypes 1, 5, 6, 8, 11, and 19.[7,41,62] PCF is an acute and highly contagious disease characterized

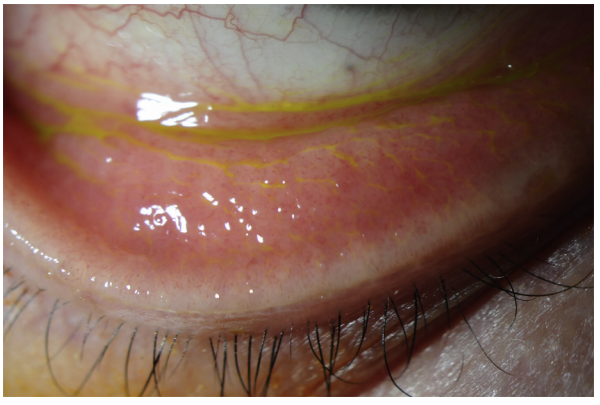

Fig. 1 – Slit lamp photography showing a case of epidemic keratoconjunctivitis. Prominent follicular reaction was demonstrated on the inferior palpebral conjunctiva.

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