Editorial: Adenovirus keratoconjunctivitis

Adenovirus (adeno) is responsible for a large proportion of sporadic cases of keratoconjunctivitis (KC) and for outbreaks of the disease in hospitals, schools, and factories. The eye infection is characterised by a moderate to severe KC, causing in a proportion of the patients hazy vision lasting several years. In the United Kingdom the eye infection is a major economic problem and is probably responsible for the loss of tens of thousands of working days each year.

Epidemic keratoconjunctivitis (EKC) caused by adeno 8 is a well described entity (Bietti and Bruna, 1957; Jawetz et al., 1957; Leopold, 1957; Thygeson, 1957; Davidson, 1964; Imre et al., 1964; Liabson et al., 1968; Grist et al., 1970; Dawson et al., 1972; Hart et al., 1972). Severe outbreaks of EKC are especially common in hospitals and factories (Leopold, 1957; Thygeson, 1957; Davidson, 1964; Liabson et al., 1968). Adenos 3 and 7 are the most common causes of sporadic KC. Other types, i.e., 1, 2, 4, 5, 6, 9, 10, 11, 13, 14, 15, and 29, are also reported to cause moderate to severe KC (Bell, 1957; Hogan, 1957; Huebner and Rowe, 1957; Kendall et al., 1957; Kimura et al., 1957; Ormsby et al., 1957; Jones, 1962; Caldwell et al., 1974; Tanifuji et al., 1974; Muzzi et al., 1975). Adeno 19 has recently been recognised as a cause of KC similar to EKC (Hierholzer et al., 1974; O’Day et al., 1976; Darougar et al., 1977).

Adeno KC commonly affects adults between the ages of 20 and 40 years and is more common in males than females (2:1). No seasonal variation is observed for sporadic cases except for adeno 7, which appears to be more common in the summer.

Man appears to be the only reservoir of the infection. Upper respiratory tract infection due to adenovirus (pharyngoconjunctival fever) is a common disease, especially among children. Adenovirus has also been isolated from the tonsils and adenoid tissues of the throat in patients with no apparent inflammation (Huebner and Rowe, 1957; Vargosko et al., 1965). Transmission from respiratory tract to the eye is responsible for the majority of sporadic adeno KC. Eye-to-eye transmission is the common cause of outbreaks of adeno KC. The virus can commonly be isolated up to 2 weeks from the onset of the keratoconjunctivitis. The virus has also been isolated from chronic papillary conjunctivitis (Darougar et al., 1977). Associated systemic infections occur in 50% of the patients with adeno KC.

The majority of these suffer from a pharyngitis and rhinitis. A few may develop general malaise with a fever or gastrointestinal upset with diarrhoea and vomiting. Preauricular lymphadenopathy occurs in approximately 90% of cases.

The incubation period for adeno KC is usually 7 to 9 days but ranges between 2 and 14 days. The infection starts unilaterally, and in the majority of cases the other eye develops conjunctivitis 2 to 7 days later.

The KC is generally mild to moderate in patients infected with adeno 2, 3, 4, 15, and 29, but slightly more severe in cases of adeno 7 infection. Adeno 5, 8, and 19 cause most severe disease. The average duration of conjunctivitis is 4 to 6 weeks for adeno 5, 8, and 19, and slightly shorter for other serotypes.

Foreign body sensation, photophobia, lachrymation, discharge, swelling, and inflammation are the main symptoms.

On clinical examination, the bulbar conjunctiva is hyperaemic with chemosis. Haemorrhages may occur in the cases of adeno 8 and 19. The major signs in the palpebral conjunctiva are moderate to severe hyperaemia, diffuse infiltration, papillary and follicular hypertrophy. Papillary hypertrophy is more severe in the upper tarsal conjunctiva and may be present for 2 to 4 weeks in most cases except for adeno 5, 8, and 19. Occasionally the papillary reaction may continue for several months (Darougar et al., 1977). Follicular hypertrophy is moderate and is present mainly in the upper and lower fornices. Punctate haemorrhages and pseudomembrane are common in severe cases of adeno 8 and 19 and less in adeno 3 and 7. Moderate to severe scarring may develop 20 to 30 days after the onset of infection in patients who had had well marked pseudomembrane.

Keratitis is common in adenovirus infection. Mild to moderate epithelial punctate keratitis (EPK: small, punctate, slightly elevated corneal infiltrations) (Jones, 1962) may develop in the early stages of infection with all types of adenovirus. The duration of EPK is less than 3 weeks except in cases of adeno 8 and 19. Subepithelial punctate keratitis (SEPK: large, dense, well marked opacities in the subepithelial area of the cornea) (Jones, 1962) may develop in association with adeno 3, 4, 5, 7, 8, and 19. The SEPK may resolve within 3 months in all cases of adeno KC, except for adeno 8 and 19, which may remain for several years. Diffuse stromal
nfiltration (resembling disciform keratitis) and corneal oedema may occur in association with severe keratitis. A mild anterior uveitis may also develop in cases of severe adenovirus 8 and 19.

Outbreaks of adenovirus KC are a continuing problem in hospitals, outpatient departments, surgeries, schools, and in swimming pools. Adeno 3, 7, 8, and 19 are the commonest cause of these outbreaks (Hogan, 1957; Kendall et al., 1957; Leopold, 1957; Thygeson, 1957; Davidson, 1964; Liabson et al., 1968; Caldwell et al., 1974; Tanifuji et al., 1974; O’Day et al., 1976; Darougar et al., 1977). Institutional transmission may result from contamination of eye solutions, instruments, including slit-lamp and tonometers, and by contaminated fingers of doctors and nurses. Transmission among patients may be due to direct contact or by droplet spread. Outbreaks of adenovirus KC are prevented by segregation of patients with infective eye disease, increased care with hand washing with soap before and after examination, the use of single dose eye solutions or change of droppers for each patient, and proper sterilisation of instruments, especially tonometers.

The clinical features of adenovirus KC—a moderate to severe bilateral follicular conjunctivitis, subepithelial punctate keratitis, and associated upper respiratory infection—are helpful in the diagnosis of infection. However, differential diagnosis should be made from herpetic keratoconjunctivitis, epidemic haemorrhagic conjunctivitis (picornavirus), and chlamydial and bacterial conjunctivitis.

Laboratory tests may help diagnosis of adenovirus KC. In the acute stage of infection the presence of profuse mononuclear cells, especially lymphocytes, in conjunctival scrapings is highly suggestive of a viral infection. Fluorescent antibody (FA) staining of conjunctival smears provides a rapid and sensitive method for the detection of adenovirus in conjunctival cells (Imre et al., 1964; Schwartz et al., 1976). Cultural tests for isolation of adenovirus are rather slow and may require between 1 and 8 weeks for detection and identification of the virus. The highest rate of isolation is obtained in the first 2 weeks of KC. The complement fixation test is a standard serological test for detection of group antibody to adenovirus. A four-fold rise in the titre of antibody between the acute and convalescent sera is significant for diagnosis of adenovirus KC.

Although adenovirus is a DNA virus that has some in vitro sensitivity to idoxuridine and trifluorothymidine, no effective chemotherapy has yet emerged for this important cause of ocular and respiratory morbidity. Frequent topical applications of antibiotic drops may soothe the eye and prevent secondary bacterial infection.

References
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