SCIENTIFIC REPORT

Blepharokeratoconjunctivitis in children: diagnosis and treatment

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Aim: Blepharokeratoconjunctivitis (BKC) is a poorly described entity in children. This study characterises this syndrome in childhood and evaluates epidemiology, clinical grading, and treatment strategies.

Methods: 44 children (20 white, 22 Asian, 2 Middle Eastern, median age 5.4 (range 1–14) years) with a diagnosis of BKC were followed for a median of 7 years. Diagnostic criteria included recurrent episodes of chronic red eye, watering, photophobia, blepharitis including recurrent styes or meibomian cysts, and a keratitis. Clinical features were graded as mild, moderate, or severe. The lids and conjunctiva were cultured. The treatment regimen incorporated lid hygiene, topical and/or systemic antibiotics, and topical corticosteroids.

Results: The disease was most severe in the Asian and Middle Eastern children ($p < 0.001$), who had a statistically higher risk of subepithelial punctate keratitis ($p = 0.008$), corneal vascularisation ($p < 0.001$), and marginal corneal ulcerations ($p = 0.003$), than the white group. 15 children had culture positive lid swabs. Most children had a reduction in symptoms and signs with treatment, and progression of disease after the age of 8 was rare.

Conclusions: BKC in children can be defined as “a syndrome usually associated with anterior or posterior lid margin blepharitis, accompanied by episodes of conjunctivitis, and a keratopathy including punctate erosions, punctate keratitis, phlyctenules, marginal keratitis, and ulceration.” BKC is common in children in a tertiary referral corneal and external diseases clinic, with the more severe manifestations in the Asian and Middle Eastern populations. Therapy is effective and loss of sight can be prevented in most cases.

Eyelid margin disease with secondary conjunctival and corneal involvement is well characterised in adults and is termed blepharokeratoconjunctivitis (BKC).^{1,2} Clinical findings typically consist of inflamed eyelids, anterior lid margin telangiectasia, and accumulations of hard, fibrinous, and crusting scales (collarettes) around the base of the cilia. In chronic cases, ulceration, lid notching (tylosis), thinning or loss of lashes (madarosis), or misdirection of lashes (trichiasis) are common. Conjunctival changes in longstanding cases include mild to moderate papillary and follicular hypertrophy of the palpebral conjunctiva. In acute exacerbations, additional inferior corneal involvement (punctate epithelial erosions, marginal infiltrates, sterile marginal abscesses) is also seen. Adult BKC is more responsive to treatment than other forms of chronic blepharoconjunctivitis, the regimen involving lid hygiene together with the use of topical antibiotics.^{3,4}

By contrast, the syndrome of childhood BKC is poorly defined.⁵ In our study, we characterise BKC in children, and

evaluate demographics, clinical features, time course, and treatment strategies.

PATIENTS AND METHODS

Forty four children with a diagnosis of chronic or recurrent BKC were identified from the children presenting to the corneal and external diseases clinic at Moorfields Eye Hospital, London. This hospital is a tertiary referral centre, and has a local catchment area of mixed ethnic origins (white, Asian (Indo-Pakistani), African-Caribbean, Middle Eastern, oriental).

BKC was defined as “a syndrome usually associated with anterior or posterior lid margin blepharitis, accompanied by episodes of conjunctivitis, and a keratopathy including punctate erosions, punctate keratitis, phlyctenules, marginal keratitis, and ulceration.” The diagnosis of BKC required the following features: recurrent episodes of chronic red eye, watering, photophobia, blepharitis including recurrent styes or meibomian cysts, and a keratitis.^{1,2} Children with a history of atopy, perennial allergic conjunctivitis, or vernal keratoconjunctivitis were excluded from the study. The children were followed from presentation to discharge, with frequency of follow up dictated by the disease course. Clinical symptoms and signs were graded as mild, moderate, or severe as detailed in table 1, and figure 1. Swabs were taken with cotton wool tipped swab sticks; these were dipped in tryptic digest broth for the lid margins and used plain for the lower tarsal conjunctiva. Both swabs were plated onto separate blood agar plates for culture and sensitivity studies.

Treatment

The children were treated with a regimen similar to that used in adult BKC. Daily lid hygiene was directed at removing debris and crusts along the lid margin, using cotton wool tipped swab sticks with diluted bicarbonate solution, diluted baby shampoo, or warm water. The child's attendant was advised that the lid hygiene routine had to be maintained for an indefinite period.

Patients with mild or moderate disease were prescribed a short course of topical broad spectrum antibiotics, usually chloramphenicol. Drops were instilled four times daily and ointment applied to the lid margins at night for 1 month, after which they were instructed to use only the ointment at night for a further 2–3 months while maintaining a daily routine of lid hygiene. These patients were examined at 1, 2, 3, and 6 months following presentation, and then at 3 monthly intervals until they were stable using daily lid cleaning alone.

Moderately severe or severe cases were treated with systemic erythromycin 30–40 mg/kg body weight (three divided doses for 3 weeks, then twice daily for 4–6 weeks), topical broad spectrum antibiotic eye drops (chloramphenicol four times daily for 4–6 weeks), and the application of

Abbreviations: BKC, blepharokeratoconjunctivitis

Table 1 Classification of the severity of blepharokeratoconjunctivitis in children

	Lids/conjunctiva	Corneal involvement (degrees)
Mild	Minimal hyperaemia Mild diffuse infiltration Tarsal conjunctival vessels <i>clearly</i> visible Mild papillary hyperplasia and small follicles (<5)	<120
Moderate	Moderate hyperaemia Diffuse infiltration Tarsal conjunctival vessels <i>just</i> visible Moderate papillary hyperplasia and follicles (5–10)	180–240
Severe	Marked hyperaemia Marked diffuse infiltration Tarsal conjunctival vessels <i>not</i> visible Moderate papillary hyperplasia and follicles (>10)	240–360

chloramphenicol ointment to the lid margins at night to reduce the bacterial load. Topical corticosteroids (prednisolone 0.3–0.5%, or fluorometholone 0.1%, four times daily for 4–6 weeks, then decreasing the frequency to once or twice daily over 2–3 months or longer) were used to control the conjunctival and corneal inflammation. When corneal phlyctens were present topical dexamethasone 0.1% was used two to four times daily for up to 2 months before decreasing the strength and frequency. These patients were examined at 2 and 4 weeks after presentation, then at 4–8 weekly intervals. Intraocular pressures were assessed in all cases.

Statistical methods

The distribution of clinical signs among the ethnic groups were evaluated by Pearson's χ^2 test for association and the Fisher's exact test for small numbers, using the software package SPSS 11.5.1 for Windows.

RESULTS

During the 11 year study period, 44 children were identified with BKC. Patient demographics are shown in table 2. All children were born in the United Kingdom. In the final year of the study, 65 children attended the clinic, of whom 26 (40%) had recurrent BKC, 23 (35.4%) allergic conjunctivitis (perennial allergic conjunctivitis or vernal keratoconjunctivitis), and 16 (24.6%) had a variety of other disorders. The median age at presentation was 5.4 (range 1–14) years, but the age of symptom onset antedated presentation by 5–18 months (median age 4.1 (range 1–14) years) (fig 2). This delay was attributable to previous treatment trials by referring general practitioners or local hospitals. The children were reviewed for a median of 7 years (range 7 months–12 years), and the median age at discharge was 9.5 (6–15)

Table 2 Patient demographics

Total number of patients	44
Sex (male: female)	20:24
Age (median (range) years)	
at onset	4.1 (1–14)
at presentation	5.4 (1–14)
at discharge	9.5 (6–15)
Ethnic origin (n)	
White	20
Asian*	22
Middle Eastern	2
African-Caribbean	0
Follow up (median (range) (years))	7 (0.58–12)

*Non-oriental children of Indian and Sri Lankan origin. There were no children from Pakistan or Bangladesh.

years. BKC was more common in the Asian (Indian and Sri Lankan) population (22 (50%)); this is a substantial over-representation of Asians as only 29% of the London population comprised ethnic minorities in the 2001 census. All children had bilateral disease although there was marked asymmetry of symptoms and signs. The main symptoms are shown in table 3.

The most severe disease was seen in the Asian and Middle Eastern children ($p < 0.001$) while the white group had significantly milder disease ($p < 0.001$) (table 4). The most common corneal features found in all ethnic groups were epithelial punctate keratitis and marginal infiltrates. Although subepithelial punctate keratitis was also seen in 28 (63.6%) patients, this was principally associated with the Asian and Middle Eastern groups ($p = 0.008$). Asian and Middle Eastern children were more likely to develop corneal vascularisation ($p < 0.001$), often involving all clock hours of the limbus ($p = 0.008$). These children were also more susceptible to marginal corneal ulceration ($p = 0.003$). Punctate erosions and corneal phlyctenules were restricted to the Asian subpopulation.

Table 3 Clinical symptoms and signs

	No (%)
Symptoms	
Redness	21 (47.7)
Watering	22 (50)
Itching	10 (22.7)
Grittiness	24 (54.5)
Discharge	29 (65.9)
Photophobia	28 (63.6)
Pain	3 (6.8)
Signs	
Lids/conjunctiva	
Blepharitis	29 (65.9)
Chalazia	7 (15.9)
Folliculitis	6 (13.6)
Meibomianitis	3 (6.8)
Styes	3 (6.8)
Hyperaemia	21 (47.7)
Bulbar conjunctival phlyctenules	9 (20.5)
Papillary hyperplasia	22 (50)
Follicular hyperplasia	20 (45.5)
Cornea	
Punctate erosions	4 (9.1)
Epithelial punctate keratitis	26 (59.1)
Subepithelial punctate keratitis	28 (63.6)
Marginal infiltrates	28 (63.6)
Corneal phlyctenule	2 (4.6)
Sectoral vascularisation	15 (34.1)
Circumcorneal vascularisation	12 (27.3)

Figure 1 Clinical signs seen in staphylococcal blepharokeratoconjunctivitis. (A) Blepharitis; (B) ulcerative blepharitis with marked collarettes; (C) sectoral marginal vascularisation and keratitis; (D) severe corneal vascularisation and keratitis; (E) subepithelial keratitis; (F) central corneal scar; (G) conjunctival phlyctenule; (H) resolved corneal phlyctenule with residual scarring and corneal vascularisation (I) upper tarsus (mild to moderate inflammation); and (J) upper tarsus (severe inflammation).

Fifteen (34.1%) children had culture positive lid margin and conjunctival swabs. Of these, 12 had a moderate or heavy growth of *Staphylococcus aureus*, one *S epidermidis*, and two mixed *S aureus/S epidermidis*. All bacterial loads were sensitive to chloramphenicol and erythromycin. Clinically, these children had moderate or severe disease and were predominantly Asian.

With treatment, the children had a reduction in symptoms and signs, and continuation of the disease after the age of 8

was uncommon (fig 2). In the most severe cases, long term, low dose topical corticosteroid therapy was used to prevent active inflammatory disease or corneal scarring.

DISCUSSION

Our data have shown that the clinical syndrome of BKC is an identifiable inflammatory external disease in children, in which the symptoms and signs are similar to those found in adults although the disease course differs. Children presented

Table 4 Distribution of corneal signs within the ethnic groups

	All patients No (%)	White No (%)	Asian No (%)	Middle East No (%)	p Value*
Number of patients	44	20	22	2	–
Severity of disease					
Mild	21 (47.7)	18 (90.0)	3 (13.6)	0 (0)	<0.001
Moderate	11 (25.0)	2 (10.0)	9 (40.9)	0 (0)	0.03
Severe	12 (27.2)	0 (0)	10 (45.5)	2 (100)	<0.001
Punctate erosions	4 (9.1)	0 (0)	4 (18.2)	0 (0)	NS
Epithelial punctate keratitis	26 (59.1)	11 (55)	13 (59.1)	2 (100)	NS
Subepithelial punctate keratitis	28 (63.6)	8 (40)	18 (81.8)	2 (100)	0.008
Vascularisation	27 (61.4)	6 (30)	19 (86.4)	2 (100)	<0.001
Sectoral	15 (34.1)	6 (30)	9 (40.9)	0 (0)	NS
Circumcorneal	12 (27.2)	0 (0)	10 (45.5)	2 (100)	<0.001
Marginal infiltrates	28 (63.6)	12 (60)	14 (63.6)	2 (100)	NS
Marginal ulcers	4 (9.1)	0 (0)	2 (9.1)	2 (100)	0.003
Corneal ptyctenules	2 (4.6)	0 (0)	2 (9.1)	0 (0)	NS

*Fisher's exact test; NS, not statistically significant.

Figure 2 Distribution of the age at onset of symptoms and presentation. Open bars, age at onset of symptoms; solid bars, age at presentation; n = 44.

between the ages of 1 and 14 (median 5.4) years with chronic redness and irritation that resulted in constant eye rubbing and photophobia. During our follow up period of 7 (range 0.58–12) years, the symptoms and signs reduced with treatment, and progression after the age of 8 was rare. The most severe cases, however, required long term therapy. These findings were similar to those of Farpour *et al*⁵ who followed eight children with BKC for a shorter period of 8.3 (range 2–23) months. By contrast, their cohort was younger (3.2 years (range 0.5–8 years)), and relief of symptoms and signs occurred within 2 months of treatment; however, all had recurrences within the follow up period requiring repeat therapy and long term treatment was not used.

Asian and Middle Eastern children were most severely affected and often had *S aureus* growth on lid or conjunctival cultures. There is no clear explanation for this finding. Our treatment strategies were aimed at (i) reducing the stimulus for the disease by lowering the local population of staphylococci, (ii) improving meibomian gland dysfunction, and (iii) reducing the host's local immune response. This was achieved by the therapy described in the methods section above. The preferred systemic antibiotic was erythromycin. This is safe for use in children under the age of 8 years,^{5–7} and has previously been used in small case series of children with BKC.^{5,6} Like the tetracyclines in adults,^{8,9} macrolides, such as erythromycin, appear to penetrate and accumulate in the

meibomian glands affecting sebum composition, as well as inhibiting bacterial protein synthesis and lipase production. It is unclear if these antibiotics also alter the ocular flora or an antigenically stimulated immune response.

In summary, our data have characterised the syndrome of childhood BKC, and have found it to be a common disease in the children in our corneal and external diseases clinics at our tertiary referral centre. The most severe disease occurred in the Asian and Middle Eastern populations. Progression was rare after the age of 8 although long term treatment was needed until age 15 in a few children. Further studies to define the immunopathogenesis and genetic components of this disease would be appropriate.

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