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CLINICAL STUDY

Surgical management of corneal perforation secondary to gonococcal keratoconjunctivitis

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Abstract

Aims **To report five cases of gonococcal keratoconjunctivitis with severe corneal involvement treated with therapeutic keratoplasty.**

Design **Retrospective case series.**

Methods **Five consecutive cases of gonococcal keratoconjunctivitis treated with keratoplasty for corneal perforation, with a mean age of 21.2 years, were analysed by patient's history, surgical approaches, and clinical outcomes, corrected visual acuity at initial visit and last follow-up.**

Results **All adult cases were originally diagnosed as epidemic keratoconjunctivitis by elsewhere, and corneal perforation occurred with a mean duration of 11 days after development of conjunctivitis. While laboratory tests revealed *Neisseria gonorrhoeae* in all five cases, three patients showed resistance to ofloxacin. Intensive medical treatment using penicillins and/or cephems was initiated. Two patients had peripheral corneal perforations, one had a paracentral perforation, and another, a large corneal perforation with stromal melting. One case had a central microcorneal perforation. In all cases, the anterior chamber was flat. Corneal perforations were treated with lamellar or penetrating keratoplasty using cryopreserved or fresh corneal grafts. All grafts remained clear during the mean follow-up period of 34.9 months. Final best-corrected visual acuity ranged from 20/60 to 20/16.**

Conclusions **Severe gonococcal keratoconjunctivitis can benefit from intensive surgical and medical intervention resulting in satisfactory visual rehabilitation.**

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Keywords: keratoplasty; gonococcal keratoconjunctivitis; *Neisseria gonorrhoeae*; corneal perforation

Introduction

Neisseria gonorrhoeae is one of the most common causes of sexually transmitted disease. Owing to public health intervention, the incidence of gonococcal infection showed a decline from the mid-1970s onwards. Recently, however, it has shown an increase in various areas around the world, including Japan, especially among young people.[1–5] *N. gonorrhoeae* can cause vision-threatening corneal involvement, resulting in scarring and possible perforation. A proper diagnosis is vital if this is to be avoided, as the clinical outcome of gonococcal keratoconjunctivitis depends on its level of severity at the commencement of the appropriate therapy.[6–8]

Ocular gonococcal infection is relatively rare, and during its early stage of development, the resulting keratoconjunctivitis may be attributed to other pathogens, thus delaying a proper clinical diagnosis. Furthermore, *N. gonorrhoeae* has recently shown increased resistance to antimicrobial agents.[1,2,4,9–11] Such delays in attaining a correct diagnosis, and increased resistance can result in the development of keratitis with severe corneal involvement.

In this study, we report five cases of gonococcal keratoconjunctivitis with corneal perforation, which were managed by a combination of intensive medical and surgical intervention. The objective of the study was to report the clinical findings and efficacy of this approach.

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Patients and methods

Five consecutive cases of gonococcal keratoconjunctivitis with corneal perforation were treated at the Department of Ophthalmology, Tokyo Dental College, between 2001 and 2006. Patients consisted of four adult men and one female child with a mean age of 21.2 years (range: 5–29 years). Cases of gonococcal keratoconjunctivitis successfully treated by medical management alone were not included in this study. A demographic profile of the patients is shown in Table 1. All patients were diagnosed with gonococcal keratoconjunctivitis by detection of *N. gonorrhoeae* from ocular discharge, using either culture (four cases) or polymerase chain reaction (PCR) (1 case).

In all cases, severe corneal involvement and extensive destruction of the cornea and flat anterior chamber were observed at the initial visit to our hospital after medical management. Other strategies including pressure-bandaging and adhesives could not be applicable to reform the anterior chamber because of severe destruction of corneal stroma. Therefore, surgical management was scheduled to eradicate the infection and preserve the integrity of the globe. Postsurgical follow-up was carried out for 13–61 months (mean: 34.9 months).

Results

All adult cases were originally diagnosed as epidemic keratoconjunctivitis by local doctors, and corneal perforation occurred before referral within a mean period of 11 days following development of conjunctivitis. Four cases were presumably infected through sexual contact and the only child was infected by her mother.

Resistance of N. gonorrhoeae

In all cases, *N. gonorrhoeae* was detected from ocular discharge by laboratory tests. Data on sensitivity to antibiotics were not available in one case. All the other cases (cases 1–4) yielded resistant isolates, with three (cases 1, 2, and 4) showing ofloxacin-resistant isolates and one (case 3) showing vancomycin-resistant isolates.

Medical management

All the adult cases were originally diagnosed as epidemic keratoconjunctivitis, and were initially treated with topical application of levofloxacin eye drops (Cravit®, Santen Pharmaceutical Co., Osaka, Japan) before referral to us, but showed no clinical improvement (Table 2). After visiting our hospital, all were put on an intensive course of antibiotics consisting of topical penicillins and/or cephems, accompanied by intravenous penicillins/cephems chosen based on the results of a sensitivity test carried out at our laboratory (Table 2).

Postoperatively, topical antibiotics were tapered depending on clinical findings. To reduce postoperative inflammation, systemic and topical steroids were administered in all cases.

Surgical management

Clinical characteristics of the patients are summarized in Table 2, including the size and location of perforation. Corneal perforation occurred within a mean period of 11 days following development of conjunctivitis. In four of five cases (cases 1–4), emergency therapeutic keratoplasty was performed using cryopreserved corneas owing to extensive corneal destruction with stromal melting. All these cases were subjected to lamellar keratoplasty using cryopreserved grafts: lamellar (patch) keratoplasty in cases 1 and 2 (peripheral perforation), deep lamellar keratoplasty in case 3 (paracentral perforation), and corneoscleral keratoplasty in case 4 (large perforation) (Figure 1a and b). Eight months later, the last case also had regrafting using a fresh cornea for visual rehabilitation (Figure 1c).

In case 5, the iris was incarcerated in the perforation wound, and there was no obvious leakage of aqueous humour. Therefore, intensive medical treatment was initiated with hospitalization, and the infection was successfully managed. However, as severe corneal opacity and stromal thinning associated with flat anterior

Table 1 Patients' profiles

Case no.	*M/F*	*Age*	*CVA*	*Initial diagnosis*	*Duration between conjunctivitis and perforation (days)*	*Infection route*	*Systemic involvement*
1	M	29	20/2000	EKC	12	Sexual contact	Urodynia
2	M	25	NA	EKC	9	Sexual contact	—
3	M	25	20/400	EKC	11	Sexual contact	—
4	M	22	LP	EKC	10	Sexual contact	—
5	F	5	NA	Conjunctivitis	11	Mother	Pelvitis

CVA = corrected visual acuity; EKC = epidemic keratoconjunctivitis; F = female; LP = light perception; M = male; NA = not applicable.

Table 2 Medical treatment, surgical procedures, and outcomes

Case no.	*Medical treatment*							*Surgical procedures and Outcomes*				
	Initial management		*Microbial sensitivity*	*Postperforation and postoperative medical management*				*Perforation position, size*	*Surgical procedure (donor status)*	*Follow-up period (M)*	*Postoperative CVA*	*Complications*
				Antibiotics		*Steroid*						
	Topical	*Systemic*		*Topical*	*Systemic*	*Topical*	*Systemic*					
1	LVFX 3 ×	CFDN 300 mg	OFLX resistance	SBPC + CMX per 30 min	4 g of PIPC	B 5 × (7D–)	B (3–20 D)	Peripheral, 3.5 × 1.5 mm	LKP (cryopreserved)	23	20/16	None
2	LVFX 3 ×	CFDN 300 mg	OFLX resistance	SBPC + CMX per 30 min	80 million U of PCG	B5 × (2D–)	B (2–22 D)	Peripheral, 3.5 × 1.0 mm	LKP (cryopreserved)	61	20/16	None
3	LVFX + CP CL 4 ×	None	VCM resistance LVFX immediate	SBPC + CMX per30 min	2 g of FMOX	B 2 × (3D–)	None	Paracentral, 2.5 × 2.0 mm	DLKP (cryopreserved)	60	20/40[a]	Glaucoma
4	LVFX 3 ×	None	OFLX resistance	LVFX + CMX per 2 h	2 g of FMOX	F 5 × (7D–)	B (6–26 D)	Paracentral, 4.0 × 2.0 mm	PKP[b] (cryopreserved)	14	20/16	None
5	SBPC 3 ×	None	NA	SBPC + CMX per 2 h	80 mg/kg of CTRX	B5 × (1D–)	P (1–14 D)	Central 1.0 × 1.0 mm	PKP (fresh)[c]	17	20/60	Glaucoma, cataract

B = betamethason (the dose of betamethason was tapered from 6 mg (case 1), 10 mg (case 2), 2 mg(case 4)); CFDN = cefdinir; CMX = cefmenoxime hydrochloride; CP CL = Chloramphenicol–colistin sodium methanesulphonate combination; CTRX = ceftriaxone; CVA = corrected visual acuity; D = days; DLKP = deep lamellar keratoplasty; F = fluorometholone eye drop; FMOX = flomoxef; LKP = lamellar keratoplasty; LVFX = levofloxacin; M = months; OFLX = ofloxacin; P = prednisolone (the dose of prednisolone was tapered from 10 mg); PCG = benzylpenicillin potassium; PIPC = piperacillin sodium; SBPC = sulbenicillin sodium; VCM = vancomycin.

[a]Case 3: visual acuity was 20/40 due to stromal opacity.

[b]Case 4: eye was regrafted using fresh donor for visual rehabilitation after 8 months.

[c]Case 5: while infection was successfully managed by systemic and local antibiotic treatment, progressive corneal thinning required PKP using fresh graft.

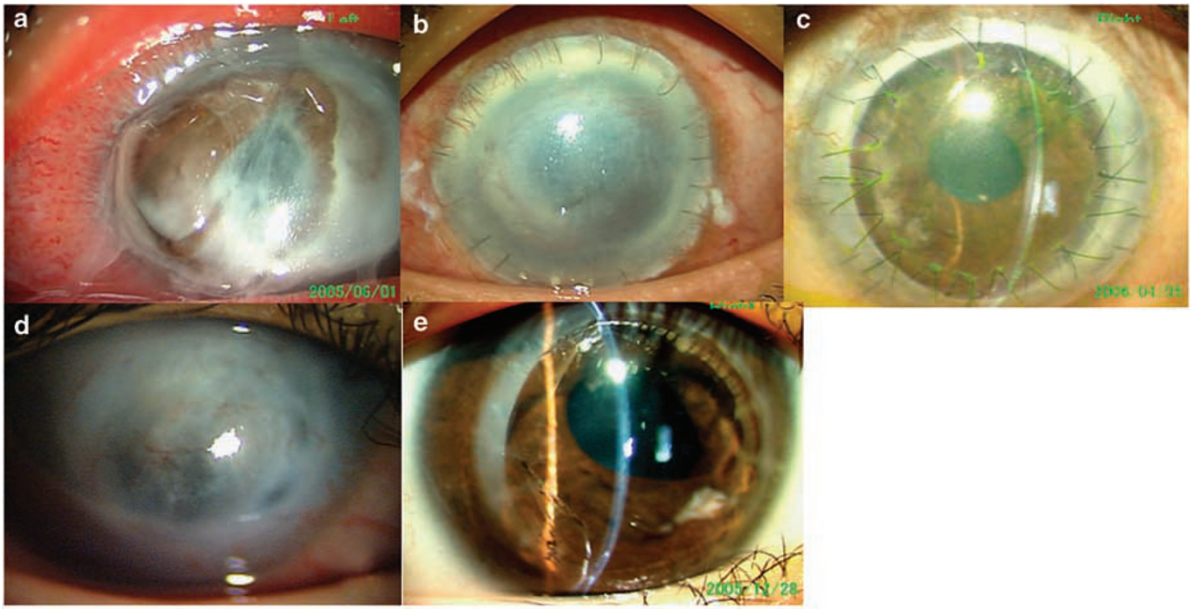

Figure 1 Case 4: (a) 22-year-old man with subtotal corneal abscess and corneal perforation; (b) therapeutic corneoscleral keratoplasty was performed, and no recurrence of infection was noted; and (c) after 8 months, optical keratoplasty was performed, and patient attained a best-corrected visual acuity of 20/16. Case 5: (d) 5-year-old girl with corneal opacity and progressive corneal thinning; (e) therapeutic and optical keratoplasty was performed, and graft remained clear.

chamber caused progressive corneal ectasia, we decided to perform penetrating keratoplasty using a fresh graft for both therapeutic and visual rehabilitation (Figure 1d and e).

Visual outcome and complications

All cases showed clear corneas at the final examination, with a mean follow-up period of 34.9 months (range: 16–61 months). Final visual acuity ranged from 20/60 to 20/16 (mean: 20/20). In case 3, visual acuity was limited to 20/40 due to paracentral corneal scar. In case 5, visual acuity was limited to 20/60 due to the development of a complicated posterior subcapsular cataract.

The postoperative course was uneventful in five patients without recurrence of gonococcal infection. No major complications such as graft failure were noted. In two eyes, secondary glaucoma developed, but intraocular pressure remained within the normal range due to the application of antiglaucomatous eyedrops.

Histopathological examination

Histopathologic examination revealed destruction of stromal structure with fibrosis and various degrees of neutrophil infiltration.

None of the cases showed positive staining for bacteria, which was later confirmed by negative bacterial and fungal culture on excised tissues.

Discussion

Despite effective antimicrobial agents, public health intervention, and efforts to improve health education, gonococcal infection has been on the increase in Japan, especially among young men.[12–14] Most cases of gonococcal keratoconjunctivitis occur in sexually active adults and are transmitted by contact with infected urine or genital secretions, and the increase in gonococcal keratoconjunctivitis seems to be associated with the increase of genital–oral sexual practice.[15]

Gonococcal keratoconjunctivitis is a potentially devastating infection because of the ability of *N. gonorrhoeae* to cause severe, ulcerative keratitis, which may rapidly progress to corneal perforation.[6–8] Therefore, it is necessary to obtain an accurate diagnosis and commence parenteral antibiotic treatment as early as possible. However, accurate clinical diagnosis may be delayed due to the relative low incidence of this disease. Indeed, all four adult cases in our series were originally misdiagnosed as epidemic keratoconjunctivitis. Urethral symptoms may precede the ocular symptoms by a period of one to several weeks,[10] and retrieval of relevant patient history may help in establishing a correct diagnosis. In

our experience, sexually active subjects with hyperacute purulent conjunctivitis or bacterial conjunctivitis refractory to primary antibiotic eyedrops should receive prompt confirmatory cultures for gonococcal organisms and for initiation of early specific antibiotic treatment. In Japan, the new quinolone eyedrops have been used widely. They occupy an approximately 90% market share in antibiotic eyedrops, and are considered to be the first choice for acute conjuncitivitis.[12,16,17] However, in the last few years, a high prevalence of fluoroquinolone-resistant *N. gonorrhoeae* isolates has been reported in Japan.[1,2,4,9] In addition, *N. gonorrhoeae* isolates have evolved in acquiring multidrug-resistance not only to fluoroquinolone, but also to penicillin and tetracycline.[9,11] With this rising incidence of -resistant *N. gonorrhoeae* strains in mind, antibiotics should be chosen carefully and confirmatory sensitivity tests ought to be performed. Among the five cases in this study, four of the isolates were fluoroquinolone-resistant, and initial use of fluoroquinolones may have been responsible for the ensuing rapid corneal involvement.

Corneal perforation constitutes an emergency situation that requires prompt attention in terms of both medical and surgical management if permanent blindness is to be prevented. When corneal perforation does not respond to appropriate medical treatment, other therapeutic approaches including conjunctival flap, amniotic membrane transplantation, and/or tissue adhesive may be considered.[18–20] However, such preservative therapies do not remove infectious pathogens, and cannot be applied to severe keratitis with stromal melting, as noted in our cases. Therefore, we believe that therapeutic keratoplasty is the most effective treatment in such cases.[21–23]

We believe that it is better to perform optical keratoplasty after achieving control of infection and inflammation, as severe ocular inflammation at the time of surgery has a negative impact on graft survival. However, most of the cases in this study needed surgical management as soon as possible to avoid secondary endophthalmitis or phthisis, and to control refractory infection and re-establish the structural integrity of the globe.

Faced with such an emergency, lamellar keratoplasty was our first choice to reduce the risk of immunological rejection, endophthalmitis, and secondary glaucoma (cases 1–3).[24,25] With recent improvements in the surgical techniques of keratoplasty, therapeutic keratoplasty has been increasingly successful in managing corneal perforation and refractory corneal inflammation.[21,23,26] In addition, fresh corneal grafts are not readily available in Japan. Thus, lamellar keratoplasty offers advantages over penetrating keratoplasty for optical purposes. It should be noted that clear grafts cannot be achieved following initial therapeutic keratoplasty in such severe stromal involvement. Secondary regrafting with intensive postoperative management, including immunosuppression, can result in favourable visual rehabilitation, as in case 4.

In summary, we reported five cases of severe corneal perforation secondary to gonococcal keratoconjunctivitis treated by intensive medical and surgical management. Proper diagnosis and intensive antibiotic treatment at an early stage are vital in avoiding irreversible corneal involvement. Therapeutic keratoplasty, especially lamellar keratoplasty when available, appears to be effective in cases with corneal perforation and stromal melting.

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Conflict of interest

None.

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