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Surgical Management of Corneal Perforation Secondary to Gonococcal Keratoconjunctivitis

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Abstract

Aims: To report 5 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 analyzed 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 5 cases, three patients showed resistance to ofloxacin. Intensive medical treatment using penicillins and/or cepheems 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.

Introduction

Neisseria gonorrhoeae is one of the most common causes of sexually transmitted disease. Due to public health intervention, the incidence of gonococcal infection showed a decline from the mid-1970s onward. Recently, however, it has shown an increase in various areas around the world, including Japan, especially among young people.¹⁻⁵ *Neisseria 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, *Neisseria 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 5 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.

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 4 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 *Neisseria gonorrhoeae* from ocular discharge, using either culture (4 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 elsewhere 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. Post-surgical follow-up was carried out for 13-61 months (mean 34.9 months).

Results

All adult cases were originally diagnosed as epidemic keratoconjunctivitis by elsewhere, 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 *Neisseria gonorrhoeae*

In all cases, *Neisseria 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 3 (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 elsewhere, 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 cepheems, 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 4 of 5 cases (Cases 1-4), emergency therapeutic keratoplasty was performed using cryopreserved corneas due to extensive corneal destruction with stromal melting. All these cases were subjected to lamellar keratoplasty using cryo-preserved 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) (Fig1A, B). Eight months later, the last case also had regrafting using a fresh cornea for visual rehabilitation (Fig1C).

In Case 5, the iris was incarcerated in the perforation wound, and there was no obvious leakage of aqueous humor. 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 chamber caused progressive corneal ectasia, we decided to perform penetrating keratoplasty using a fresh graft for both therapeutic and visual rehabilitation (Fig 1D, 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 5 patients without recurrence of gonococcal infection. No major complications such as graft failure were noted. In 2 eyes, secondary glaucoma developed, but intraocular pressure remained within the normal range due to application of anti-glaucoma tous 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.¹³⁻¹⁵ 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.¹⁶

Gonococcal keratoconjunctivitis is a potentially devastating infection because of the ability of *Neisseria 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 4 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 weeks¹⁰ 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 conjunctivitis.^{13,17,18} However, in the last few years, a high prevalence of fluoroquinolone-resistant *Neisseria gonorrhoeae* isolates has been reported in Japan.^{1,2,4,9} In addition, *Neisseria gonorrhoeae* isolates have evolved in acquiring multi-drug resistance not only to fluoroquinolone, but also to penicillin and tetracycline.^{9,11} With this rising incidence of drug-resistant *Neisseria gonorrhoeae* strains in mind, antibiotics should be chosen carefully and confirmatory sensitivity tests are ought to be performed. Among the 5 cases in this study, 4 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.¹⁹⁻²¹ 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.²²⁻²⁴

We believe 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 reestablish the structural integrity of the globe.

Faced with such an emergency, lamellar keratoplasty was our first choice to reduce risk of immunological rejection, endophthalmitis, and secondary glaucoma. (Cases 1-3)^{12, 25} With recent improvements in the surgical techniques of keratoplasty, therapeutic keratoplasty has been increasingly successful in managing corneal perforation and refractory corneal inflammation.^{22, 24, 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 can not

be achieved following initial therapeutic keratoplasty in such severe stromal involvement. Secondary regrafting with intensive postoperative management, including immunosuppression, can result in favorable visual rehabilitation, as in Case 4.

In summary, we reported 5 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.

Figure legends

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.
- 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.

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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

M = male, F = female, CVA= corrected visual acuity, NA= Not Applicable, LP=light perception, EKC=epidemic keratoconjunctivitis

Table 2 Medical treatment, surgical procedures and outcomes

Case No	Medical treatment							Surgical procedures and Outcomes				
	Initial management		Microbial sensitivity	Post-perforation and post-operative medical management				Perforation position, size	Surgical procedure (donor status)	Follow-up period (M)	Post operative CVA	Complications
	topical	systemic		antibiotics		steroid						
			topical	systemic	topical	systemic						
1	LVFX 3x	CFDN 300mg	OFLX resistance	SBPC+CMX per 30min	4g of PIPC	B 5x (7D~)	B (3~20D)	Peripheral, 3.5x1.5mm	LKP (cryopreserved)	23	20/16	none
2	LVFX 3x	CFDN 300mg	OFLX resistance	SBPC+CMX per 30min	80million U of PCG	B 5x (2D~)	B (2~22D)	Peripheral, 3.5x1.0mm	LKP (cryopreserved)	61	20/16	none
3	LVFX+ CP CL 4x	none	VCM resistance LVFX immediate	SBPC+CMX per30min	2g of FMOX	B 2x (3D~)	none	Paracentral, 2.5x2.0mm	DLKP (cryopreserved)	60	20/40*	glaucoma
4	LVFX 3x	none	OFLX resistance	LVFX+CMX per 2hours	2g of FMOX	F 5x (7D~)	B (6~26D)	Paracentral, 4.0x2.0mm	PKP ^S (cryopreserved)	14	20/16	none
5	SBPC 3x	none	NA	SBPC+CMX per 2hours	80mg/kg of CTRX	B 5x (1D~)	P (1~14D)	Central 1.0x1.0mm	PKP(fresh) [#]	17	20/60	glaucoma, cataract

LVFX=levofloxacin, CP CL=Chloramphenicol - colistin sodium methanesulfonate combination CFDN= cefdinir, OFLX=ofloxacin, VCM=vancomycin, PIPC=piperacillin sodium, SBPC= sulbenicillin sodium, CMX=Cefmenoxime hydrochloride, PCG= Benzylpenicillin Potassium, FMOX= Flomoxef, CTRX= ceftriaxone, LKP=lamellar keratoplasty, DLKP=deep lamellar keratoplasty, CVA=corrected visual acuity, B=betamethason (The dose of betamethason was tapered from 6mg (case1), 10mg (case2), 2mg(case4)), P=prednis olone (The dose of prednisolone was tapered from 10mg.), F= fluorometholone eye drop

* Case 3: Visual acuity was 20/40 due to stromal opacity.

\$ Case 4: Eye was regrafted using fresh donor for visual rehabilitation after 8 months.

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

M=months, D=days

