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Early and late endophthalmitis following trabeculectomy in a Chinese population

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PURPOSE. *To investigate the rate of bleb-related endophthalmitis over 5 years in a Chinese population.*
METHODS. *Retrospective chart review.*
RESULTS. *Of 988 trabeculectomies performed over 5 years, one case (0.1%) developed early endophthalmitis caused by Morganella morganii, which was rarely reported in the literature. Six cases (0.6%) developed late-onset endophthalmitis. Mitomycin C significantly increased the risk of late-onset endophthalmitis (p=0.0002).*
CONCLUSIONS. *Physicians should weigh the benefits against the risks of mitomycin C application in performing trabeculectomies. (Eur J Ophthalmol 2008; 18: 66-70)*

KEY WORDS. *Endophthalmitis, Trabeculectomy, Bleb, Mitomycin C, Morganella morganii*

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INTRODUCTION

Despite the development of many nonpenetrating glaucoma filtering procedures, trabeculectomy remains the mainstream of treatment for lowering intraocular pressure (IOP) and is still the procedure of choice for many surgeons. The learning curve of conventional trabeculectomy is less steep, the result is more predictable, and the technique is more familiar to most surgeons.

However, complications related to trabeculectomy may be devastating. Endophthalmitis after trabeculectomy is an ocular infection that can be destructive with a reported incidence of 0.2 to 9.6% (1-4). Typically, late endophthalmitis has a sudden onset in a post-trabeculectomy eye which has been quiet for months or years. Early bacterial endophthalmitis has been rarely reported and a different mode of pathogenesis was suggested (3). This type of endophthalmitis follows a relentless course and has poor prognosis. The rate of bleb-related endophthalmitis in Asian countries was rarely reported. In this study, the clinical course and visual outcome of early as well as late endophthalmitis was investigated.

MATERIALS AND METHODS

The study was conducted retrospectively with chart review of patients receiving trabeculectomy at Taipei Veterans General Hospital between January 1998 and September 2002.

Data collected included patients' age, sex, glaucoma type, concomitant ocular and underlying systemic disease, best-corrected Snellen visual acuity and IOP at each visit, dosage and duration of mitomycin C used, lens status, blebitis history, and time interval between trabeculotomy and onset of endophthalmitis. Culture results including conjunctival swab and aqueous and vitreous samples were also recorded. The management at first visit and at each consecutive follow-up was also noted. All patients had a minimal follow-up period of 3 months.

In this study, blebitis is defined as bleb infection without vitreous involvement (5). Bleb-associated endophthalmitis denotes an ocular infection with involvement of the vitreous (6-8).

Fisher exact test was used to detect any statistically significant difference on the occurrence of endophthalmitis

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with and without use of mitomycin C. Statistical analysis was performed with commercial software (SAS v 6.12; SAS Institute Inc., Cary, NC).

RESULTS

Of 988 consecutive trabeculectomies (828 patients) performed over 5 years, 185 procedures were performed with intraoperative use of mitomycin C. The concentration and duration of mitomycin C application (0.01% or 0.02% mitomycin soaked in cellulose sponge was placed over the area of the scleral flap with duration of 2 or 3 minutes, with one case applied for 8 minutes) was at the operator's discretion and depended on the patient's ocular condition. Over the study period, there were seven cases of infectious endophthalmitis. One patient developed early endophthalmitis (5-year incidence: 0.1%) and the other six (5-year incidence: 0.6%) belonged to the late type.

Early endophthalmitis

A 74-year-old-man presented with eyeball rupture of left eye on January 8, 2000. His right eye was eviscerated in 1968 because of absolute glaucoma. He had a history of pulmonary tuberculosis, gastric ulcer, and hyperthyroidism. After wound repair and vitrectomy due to retinal detachment for his left eye, he was regularly followed up at our clinic for his glaucomatous condition. Best-corrected visual acuity of his left eye was 3/60 after operation. He was in aphakic state with iridodialysis of nasal half of iris. Because of uncontrollable IOP under maximal antiglaucomatous medication, he was admitted for trabeculectomy without any antifibrotic agent on April 27, 2001. The trabeculectomy was performed uneventfully. There was minimal reaction in anterior chamber with an IOP of 8 mmHg on the next day. At midnight on the next day, severe pain of left eye was experienced. Lid edema was noted and diffuse whitish exudates in anterior chamber with purulent bleb of left eye was observed, and acute endophthalmitis was diagnosed. IOP rose to 55 mmHg, hence, intravenous mannitol infusion and oral Diamox in addition to topical antiglaucomatous medication was given. Five percent ceftazidime and 5% vancomycin eyedrop was given alternatively every hour together with intravenous broad-spectrum antibiotics (amikacin 400 mg q8h and 1g cefazolin q8h). Subconjunctival injection of cefazolin (100 mg/0.2 cc) and amikacin (50 mg/0.5cc) was performed once. However, vitreal cavity extension of infection was documented on B-mode ultrasound. Intravitreous antibiotics of ceftazidime (2 mg/0.1 cc) and vancomycin (1 mg/0.1 cc) were given. Eye swab and vitreous culture revealed *Morganella morganii*. Cornea was edematous and anterior chamber was nearly filled with total hypopyon. Cornea melted rapidly and anterior chamber could not be observed on the third day. The patient was then returned to the operating room where wound debridement was performed. The scleral flap was noted to

TABLE I - OCULAR HISTORY AND INFORMATION OF LESION EYE

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age/Sex/eye	37/F/OS	76/F/OS	72/M/OD	47/M/OS	71/M/OD	62/M/OD
Type of Glaucoma	Angle recession	Angle closure	Open angle	Angle closure	Angle closure	Angle recession
Ocular History	Blunt trauma	-	-	Chemical burn	Flame burn	Blunt trauma
Preinfection VA	4/60	1/60	6/6	1/60	6/20	6/10
Mitomycin C	0.01%, 3min.	ECCE+Trab (0.02%, 3min.)	0.02%, 2.5 min.	1. ECCE+Trab† 2. 0.01%, 8 min.	0.02%, 3 min.	0.02%, 3 min.
Blebitis /Time*	-	-	once /1 year	once /1 year	-	-
Time ‡	1 year	5 year	3 year	6 year	6 year	3 year
Bleb culture	NBG	NBG	Coag(-) *Staphy*	*Staphy aureus*	*Staphy aureus*	*Strept viridans*
Aqueous culture	NBG	NBG	NBG	NBG	*Staphy aureus*	NBG
Vitreous culture	NBG	NBG	Coag (-) *Staphy*	NBG	*Staphy aureus*	*Strept viridans*
Final VA	1/60	NLP	NLP	NLP	2/60	LP

*Triple procedure was performed without mitomycin C at the first time, mitomycin C was used at the second time for trabeculectomy.
†Time interval between blebitis and onset of endophthalmitis.
‡Time interval between trabeculectomy and onset of endophthalmitis.
VA = Visual acuity; ECCE = Extracapsular cataract extraction + intraocular lens implantation; Trab = Trabeculectomy; NBG = No bacterial growth; Coag (–) = Coagulase negative; NLP = No light perception; LP = Light perception; Staphy = Staphylococcus; Strept = Streptococcus

be covered with purulent material and melting. Vitrectomy was unable to be performed and anterior chamber was flushed using balanced salt solution with low concentration of antibiotics (amikacin 10 µg/mL balanced salt solution). After intensive antibiotics treatment, the infection was under control. However, visual acuity of left eye deteriorated to no light perception. Due to intolerable pain, evisceration of left eye was performed.

Late endophthalmitis

The average age of the six patients with late endophthalmitis was 60.8±15.6 years (Tab. I). Two patients (Cases 1 and 6) had history of ocular trauma; no abnormality of eyelid or ocular surface was noted in these two cases. Case 4 had chemical burn after xerograft treatment. Lagophthalmos was present in both eyes and he had received penetrating keratoplasty for his left eye. Corneal graft was clear before the onset of endophthalmitis. Case 5 had facial flame burn involving both eyes resulting in cicatricial entropion after operation and had lagophthalmos. Limbal deficiency of both eyes was noted in this patient. Case 3 had a history of Henoch-Schönlein purpura. Endophthalmitis developed within 1 to 6 years with a mean of 4.0±2.0 years after trabeculectomy. Two cases (1 and 6) were phakic at the onset of endophthalmitis. Four cases were noted to have very thin cystic avascular bleb, however, none of the cases was noted to have bleb leak before the onset of endophthalmitis. Two of the cases experienced blebitis caused by *Staphylococcus* about 1 year before endophthalmitis. Culture results of endophthalmitis and initial visual acuity are shown in Table I. At last follow-up, none of the lesion eyes was able to maintain stable vision. Three lesion eyes deteriorated to no light perception despite intensive treatment with intravitreous and intravenous antibiotics as well as pars plana vitrectomy.

Analysis of our cases over the past 5 years demonstrated that mitomycin C use was significantly associated with a higher incidence of endophthalmitis (Fisher exact test; p=0.0002).

DISCUSSION

Katz et al reported a 10-year incidence of 0.1% for early endophthalmitis (3). One patient each from Sugar and Zekman's (9) and Wilson's (10) series exhibited an early onset endophthalmitis at 3 days after surgery. In Ciulla et al 33 cases, 6 were early type and 27 were of late onset (16 received trabeculectomy, 8 received mitomycin-treated trabeculectomy) (11). Other studies have reported an incidence of 0.2–9.6% for late endophthalmitis (1-4). This is in accordance with our findings. Our 5-year rate of endophthalmitis using mitomycin C was 3.2% (6/185) and this was comparable to Higginbotham et al's 2.6% with 232 consecutive trabeculectomies with adjunctive use of mitomycin C (2) and Greenfield et al's 2.1% (13 of 609 eyes with adjunctive mitomycin) (12).

Early endophthalmitis by *M morganii* after filtering surgery has rarely been reported in the literature. *M morganii* is not part of the normal ocular flora. Sources from which this organism has been isolated included soil, urine, and respiratory samples. *M morganii* is an opportunistic secondary invader and case reports implicating this organism as a cause of disease were rare (13). Perioperative introduction of host flora through instruments, irrigating solutions, surgeons, or the patient are possible sources of inoculum (3).

It was suggested that late bleb-associated endophthalmitis has a different mechanism of infection; it is likely caused by transconjunctival migration of transiently present bacteria, especially through thin-walled blebs and through bleb leaks (4, 7-8). Ciulla et al documented the progression of blebitis to endophthalmitis, suggesting that blebitis may be prodromal to endophthalmitis and may not truly represent a distinct entity as previously reported. In their series, one case of blebitis progressed to endophthalmitis in 8 days despite treatment (11). Lehmann et al also found that the odds of endophthalmitis are increased approximately 12-fold in a patient in whom blebitis has occurred (14). In our six cases, two had a history of blebitis after successful treatment 1 year prior to onset of endophthalmitis. Patients with histories of blebitis should be educated about personal and lid hygiene and awareness of early symptoms and signs of ocular infection, and should promptly seek medical consultation if such signs occur. In contrast to many studies indicating that *Streptococcus* species was the most common causal agent of late onset endophthalmitis (11, 12, 15, 16), our predominant species was *Staphylococcus,* and this may be due to geographic or racial differences.

Since the introduction of mitomycin C for trabeculectomy in the early 1990s, the success of long-term IOP control has improved and the chance of bleb failure has been reduced. Studies report better IOP control with higher mito-

mycin C concentrations and longer exposure times, but they also report higher complication rates. Controversy exists with regard to optimum mitomycin concentration, exposure time, and delivery vehicle.

Mitomycin not only inhibits fibroblast proliferation but also alters conjunctival vascular endothelium; filtering blebs have thinner epithelium and more atrophic stroma and are more avascular (17). Hence, this may compromise immune function against invading organisms.

Our results supported that intraoperative use of mitomycin C in a specific way (0.01% or 0.02% mitomycin soaked in cellulose sponge placed over the area of the scleral flap with duration of 2 or 3 minutes) is a predisposing factor for endophthalmitis (p=0.0002). In Greenfield et al's study, adjunctive use of mitomycin is associated with a higher rate of endophthalmitis than without antifibrotic agent (12). Lehmann et al reported the odds of endophthalmitis to be three times higher in patients who receive antiproliferatives versus those who do not (14). It was how the mitomycin was used and not the mitomycin per se that caused the problem and our study provided evidence that mitomycin C (0.01% or 0.02% mitomycin soaked in cellulose sponge placed over the area of the scleral flap with duration of 2 or 3 minutes) was significantly associated with late-onset endophthalmitis.

The visual outcome of endophthalmitis was poor (4,11,16), with the majority of cases losing substantial vision. Three of our six cases deteriorated to no light perception despite intensive treatment. The virulence of organisms may partially explain why these cases have poor outcomes despite appropriate intravitreous, systemic, and topical antibiotic therapy (18-21). In two of our cases, one with chemical burn and one with flame burn, the eyelid structure had compromised the blinking mechanism and hence the protective effect of tear film, which might have further predisposed the ocular condition to infection. Jett et al (22) have shown the importance of bacterial toxins in ophthalmic infections and their role in treatment failure.

While the higher success rate of trabeculectomy with mitomycin C is important, the ophthalmologist should be aware of the possibility of endophthalmitis even many years after operation. Physicians should weigh the benefits against the risks of mitomycin C application in performing trabeculectomies.

The authors have no proprietary interest in any aspect of this study.

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