Recurrent bleb infections

Samra Waheed, Jeffrey M Liebmann, David S Greenfield, David C Ritterband, John A Seedor, Mahendra Shah, Robert Ritch

Abstract

Aim—To report the patient characteristics, causative organisms, and clinical outcomes in patients with recurrent bleb related ocular infections.

Methods—The medical records of all patients diagnosed with bleb related ocular infection at the New York Eye and Ear Infirmary over a 10 year period were reviewed. Recurrent bleb infection was defined as at least two episodes of bleb purulence with or without associated intraocular inflammation separated by a quiescent period of at least 3 months.

Results—Recurrent bleb infections developed in 12 eyes of 12 patients (10 men, two women) a mean of 16.3 (SD 17.9) months (range 3–51 months) after the initial infection. Two patients developed a third episode 3 and 20 months, respectively, after the second infection, yielding a total of 14 recurrent infection episodes. Recurrent infection developed after trabeculectomy in 11 eyes (adjunctive 5-fluorouracil, nine eyes; mitomycin C, one eye; no antifibrosis agent, one eye) and following cataract extraction with inadvertent bleb formation in one eye. Four (36.4%) of the filtered eyes had undergone trabeculectomy at the inferior limbus. The mean follow up time from filtering surgery to the first bleb related infection was 28 months for the nine patients treated with 5-fluorouracil and 14 months for the single patient treated with mitomycin C. 11 (78.6%) cases had a documented bleb leak in the 4 week period before or at the time of recurrent infection. Topical, prophylactic antibiotics had been used in 7/14 (50%) cases. The same organism was cultured from the initial and recurrent infections in 2/14 (14.3%) cases.

Conclusion—Eyes that have been successfully treated for bleb related infection remain at risk for recurrent infection. No apparent correlation exists between organisms responsible for the initial and recurrent infections. The increased rate of recurrent bleb related infection in patients receiving adjunctive 5-fluorouracil compared to mitomycin C may have been related to the longer follow up of the 5-fluorouracil eyes.

(Br J Ophthalmol 1998;82:926-929)

Bleb related ocular infection is a potentially devastating late complication of glaucoma filtering surgery. In contrast with early postoperative endophthalmitis, which results from introduction of the infectious agent at the time

of surgery, the route of infection in late onset, bleb related infection is thought to involve transconjunctival migration of bacteria from the ocular surface into the eye. The spectrum of disease severity ranges from bleb limited infection to endophthalmitis.

The widespread use of adjunctive antifibrosis chemotherapy in glaucoma surgery and the resultant thin walled, avascular conjunctival filtration blebs have led to increased frequency of bleb related ocular infection and bleb related endophthalmitis.¹⁻⁴ Despite the potentially severe nature of infection, early, aggressive antimicrobial therapy often permits retention of functional vision and successful filtration.¹ However, many of these eyes remain at risk for recurrent infection. We investigated the patient characteristics, causative organisms, and clinical outcomes associated with recurrent bleb related infections.

Patients and methods

We reviewed the clinical and laboratory records of all patients diagnosed with bleb related ocular infection at the New York Eye and Ear Infirmary between January 1987 and July 1996. Recurrent bleb related infection was defined as at least two episodes of bleb purulence with or without associated intraocular inflammation after a quiescent period of at least 3 months following the original infection.

Data abstracted from medical records included patient demographics, time interval between episodes of bleb infection, location of the bleb, bleb leak, history of bleb manipulation, refractive or therapeutic contact lens use, ocular trauma, recent conjunctivitis, topical antibiotic prophylaxis, ocular findings at the time of presentation, and treatment. Conjunctival surface cultures and/or intraocular cultures were obtained in all cases as clinically indicated. Ocular cultures were considered positive if there was growth of the same organism on two or more media (chocolate agar, blood agar, Sabouraud's agar, anaerobic agar, or thioglycolate) or growth at inoculation on one medium confirmed by organisms seen on Gram or Giemsa stain.

There was no standard treatment protocol. Medical and surgical treatment varied at the discretion of the treating physician. Medical treatment consisted of topical, subconjunctival, intravitreal, oral and/or intravenous antibiotics, and topical or intravitreal corticosteroids. Surgical treatment included anterior chamber or vitreous biopsy and/or pars plana vitrectomy.

Snellen visual acuity data and intraocular pressures (IOP) were recorded for all patients 6 months before infection, following the initial

Department of Ophthalmology, The New York Eye and Ear Infirmary, New York, USA

S Waheed
J M Liebmann
D S Greenfield
D C Ritterband
J A Seedor
M Shah
R Ritch

Department of Neurology, New York Medical College, Valhalla, New York, USA
D S Greenfield

Correspondence to:
Robert Ritch, MD,
Glaucoma Service, The New York Eye and Ear Infirmary,
310 East 14th Street, New York, NY 10003, USA.

Accepted for publication
4 March 1998

Table 1 Patient data

No (recurrent infections)	14
Age (years) ((SD) range)	62.3 (17.6) (31–87)
Sex	
Male	10
Female	2
Surgery	
Glaucoma filtering surgery	11 (91.6%)
Superior trabeculectomy	7 (63.6%)
Inferior trabeculectomy	4 (36.4%)
Inadvertent filtering bleb	1 (8.3)
Filtering surgery with antifibrosis agents	10 (90.9)
5-FU	9 (90.0)
MMC	1 (10.0)
Filtering surgery without antifibrosis agents	1 (9.1)
Time between recurrent infections (months) ((SD) range)	16.3 (17.9) (3–51)

Table 2 Associated clinical findings

Clinical findings	No
Bleb leak	11/14 (78.6%) infection episodes
Inferior location of bleb	4/11 (36.4%) filtered eyes
Bleb manipulation	3/14 (21.4%) infection episodes
Use of refractive contact lens	2/14 (14.3%) infection episodes
Conjunctivitis	2/14 (14.3%) infection episodes
Ocular trauma	0 infection episodes

episode of infection and 6 months following treatment of the recurrent infection.

Results

Recurrent bleb related ocular infection developed in 12 eyes of 12 patients an average of 16.3 (SD 17.9) months (range 3–51 months) after the initial episode. Two patients developed a third episode of bleb related infection, 3 and 20 months, respectively, after the second infection, yielding a total of 14 recurrent infection episodes. Recurrent infection developed in 11 (91.6%) eyes following glaucoma filtering surgery (adjunctive 5-fluorouracil, nine eyes; mitomycin C, one eye; no antifibrosis agent, one eye) and in one eye with an inadvertent bleb following cataract surgery. In four (36.4%) cases, the filtering bleb was at the inferior limbus (Table 1). The mean follow up time from filtering surgery to the first bleb

related infection was 28 months for the nine patients treated with adjunctive 5-fluorouracil, 14 months for the single patient treated with mitomycin C, and 20 months for the patient with the inadvertent filtering bleb following cataract surgery.

Presenting complaints included ocular pain (10 cases (71.4%)) and redness (11 cases (78.6%)) of recent (0–3 days) onset. Additional complaints included blurred vision (three cases (21.4%)), tearing (three cases (21.4%)), purulent discharge (three cases (21.4%)), and photophobia (two cases (14.3%)). Clinical findings included anterior chamber inflammation in all 14 cases, and vitritis in eight (57.1%). Topical antibiotics for prophylaxis were being used at the time of infection in seven (50%) cases.

Eleven (78.6%) cases had a documented bleb leak in the 4 week period before or at the time of recurrent infection (Table 2). In three (21.4%) cases, there was a history of bleb manipulation (collagen shield placement to treat a known leak, two eyes; bleb needling, one eye) within 2 weeks before presentation. A preceding episode of mucopurulent conjunctivitis which could be temporally separated from the redness and discharge accompanying the episode of bleb infection, was documented in 2/14 (14.3%) cases within 2 weeks of the bleb infection. Refractive contact lenses were being used at the time of presentation in 2/14 (14.3%) cases. Ocular trauma did not precede any of the recurrent episodes.

Cultured pathogens from the recurrent infections were diverse (Table 3). Staphylococcal species were isolated in five (35.7%) cases (*Staphylococcus aureus*, three cases; coagulase negative staphylococcus, two cases). *Haemophilus influenzae* was isolated in three (21.4%) cases, and *Streptococcus pneumoniae*, lactobacillus, and acinetobacter in one (7.1%) each. Cultures were negative in two (14.3%) recurrent infection episodes. In one case, cultures were not obtained. The infecting organism

Table 3 Microbiological data

Patient	Infection episode	Culture source	Bleb site adjunctive agent	Organism	Antibiotic prophylaxis	Intraocular antibiotics	Intraocular steroids	PPV
1	1st	Vitreous	Superior	<i>S aureus</i>	bacitracin	+	–	–
	2nd	Vitreous	5-FU	Coag (–) <i>Staph</i>	bacitracin	+	–	–
2	1st	Vitreous	Superior	<i>S pneumoniae</i>	tobramycin	+	+	–
	2nd	Vitreous	no agent	Coag (–) <i>Staph</i>	tobramycin	+	+	+
3*	1st	Vitreous	Inferior	no growth	tobramycin	+	–	–
	2nd	Vitreous	5-FU	<i>S aureus</i>	–	+	–	+
	3rd	Vitreous		<i>S aureus</i>	–	+	+	+
4	1st	Vitreous	Superior	<i>Acinetobacter</i>	–	+	+	–
	2nd	Vitreous	5-FU	<i>Acinetobacter</i>	–	+	+	+
5	1st	Vitreous	Inferior	no growth	–	+	+	–
	2nd	Vitreous	5-FU	no growth	–	+	–	+
6	1st	Vitreous	Superior	Coag (–) <i>Staph</i>	–	+	–	–
	2nd	Vitreous	inadvertent bleb	<i>Lactobacillus</i>	–	+	+	–
7	1st	Bleb†	Superior	<i>S aureus</i>	–	–	–	–
	2nd	Vitreous	MMC	<i>S pneumoniae</i>	–	+	+	+
8	1st	Bleb†	Inferior	<i>S aureus</i>	tobramycin	–	–	–
	2nd	Bleb†	5-FU	<i>H influenzae</i>	tobramycin	–	–	–
9	1st	Bleb†	Superior	no growth	–	–	–	–
	2nd	Bleb†	5-FU	<i>S aureus</i>	–	–	–	–
10	1st	Not Done	Superior	–	–	–	–	–
	2nd	Bleb†	5-FU	<i>H influenzae</i>	sulfacetamide	–	–	–
11	1st	Bleb†	Inferior	<i>Serratia</i>	–	–	–	–
	2nd	Not Done	5-FU	–	tobramycin	–	–	–
12*	1st	Bleb†	Superior	<i>S aureus</i>	sulfacetamide	–	–	–
	2nd	Bleb†	5-FU	no growth	tobramycin	–	–	–
	3rd	Bleb†		<i>H influenzae</i>	tobramycin	–	–	–

*Eyes with three infection episodes; †bleb surface cultures.

5-FU = 5-fluorouracil; MMC = mitomycin C; PPV = pars plana vitrectomy.

Table 4 Visual outcomes and IOP control

Patient	VA-1	VA-2	VA-3	VA-4	IOP-1	IOP-2	IOP-3	IOP-4
1*	20/40	20/50	20/50	—	5	7	28	—
2*	20/400	20/800	CF	—	14	24	3	—
3*	20/40	20/60	20/200	CF	10	12	8	17
4*	20/60	20/70	20/60	—	8	14	13	—
5*	20/200	20/400	CF	—	3	43	19	—
6*	20/30	20/30	20/30	—	20	12	13	—
7*	20/25	20/200	20/200	—	10	7	8	—
8	20/30	20/30	20/30	—	18	18	12	—
9	20/40	20/50	20/50	—	10	8	8	—
10	20/30	20/30	20/30	—	9	15	16	—
11	20/50	20/50	20/40	—	10	12	3	—
12	20/100	20/200	20/200	20/200	10	14	12	12

*Endophthalmitis.

VA-1 = visual acuity before infection; VA-2 = visual acuity following initial infection; VA-3 = visual acuity 6 months following second episode; VA-4 = visual acuity following third episode; IOP-1 = IOP before infection; IOP-2 = IOP following initial infection; IOP-3 = IOP following second episode; IOP-4 = IOP following third infection.

isolated at the time of the recurrent infection was the same as the one isolated in the preceding infection in two (14.3%) cases.

All patients were treated with topical antibiotics. Intraocular antibiotics were administered in the eight (57.1%) cases presenting with vitritis or hypopyon. Four eyes underwent vitreous biopsy and four underwent pars plana vitrectomy. Concomitant intraocular steroids were administered in six (42.9%) of these cases (Table 3).

A visual acuity of 20/400 or better was achieved in 9/12 (75%) eyes following treatment of the recurrent bleb infection (Table 4). Two (16.7%) eyes lost more than two lines of visual acuity. The mean IOP before development of bleb related infection was 10.6 (7.3) mm Hg (range 3–20 mm Hg) on a mean of 0.8 (1.1) antiglaucoma medications (range 0–3 medications). The mean IOP 6 months following the resolution of recurrent infection was 11.9 (7.0) mm Hg (range 3–28 mm Hg) on a mean of 0.7 (1.2) antiglaucoma medications (range 0–3 medications).

Discussion

Bleb related endophthalmitis is a well described late complication of glaucoma filtering surgery.^{1–13} Reported risk factors have included location of the bleb below the horizontal meridian,^{1–3 9 14} blepharoconjunctivitis,^{2 6 8–10 15–18} contact lens use,^{5–8 15 16 18–20} chronic bleb leak,^{1 5 6 16} nasolacrimal duct obstruction,^{8 21} male sex,¹ and young age.¹ Eyes which have been successfully treated for bleb related infection remain at risk for recurrent infection. To our knowledge, however, there have been no reports of recurrent episodes of bleb related infection.

We identified 12 eyes which developed recurrent bleb infection. Many blebs (78.6%) had leaks either before or at the time of presentation. Although bleb leaks have been suggested as a risk factor in the development of delayed infection, a clear causative relation between them has not yet been established. A leaking bleb may predispose to intraocular infection by providing a direct route for the migration of bacteria into the eye.

Trabeculectomy performed at the inferior limbus has been associated with an increased risk of late endophthalmitis.^{1–3 9 14} Filtering

blebs at this position are thought to be less protected by the upper lid, more susceptible to mechanical irritation from the lower lid, and are immersed in the lacrimal lake and its endogenous flora.^{1 2 14} In the current series, more than one third of the eyes had inferiorly located blebs.

It is interesting that of the 10 eyes in which adjunctive antifibrosis therapy had been administered at the time of filtering surgery, the overwhelming majority had received 5-fluorouracil rather than mitomycin C. Although this may suggest a causal relation, it is more likely that the longer follow up for eyes treated with 5-fluorouracil contributed to the increased infection rate. The inferior quadrant position of four of these surgeries, each performed in the 1980s, also predisposed to infection.

There was little uniformity in the microbiological spectrum of the cultured organisms. Staphylococcal species were the most common isolates recovered. The infrequent identification of the same infecting organism at the time of the initial and recurrent infections does not permit conclusions to be drawn about antibiotic choice at the time of the recurrent infection presentation. This supports a previously described hypothesis that bleb related ocular infection is caused by transient rather than permanent ocular surface flora.^{1 9 22}

Long term antibiotic prophylaxis did not protect against development of recurrent infection. Interestingly, two patients infected by *H influenzae* were on chronic tobramycin prophylaxis at the time of recurrent infection. Yet every *H influenzae* isolate in our microbiology laboratory during the past 5 years, including these two cases, has been sensitive to aminoglycosides (M Shah, unpublished data). This supports our belief that long term prophylaxis neither sterilises the external ocular surface or prevents bleb related ocular infection.

Visual outcomes were unexpectedly good, with most patients recovering to the level of visual acuity before the initial bleb infection. We attribute this to the limited extent of infection in many of our eyes at the time of presentation, as early intervention may prevent progression to fulminant endophthalmitis.^{1 7 17} Alternatively, a delay in diagnosis can lead to a rapid spread of the infection, inflammation, and permanent loss of vision. Better visual outcomes have also been attributed to infecting micro-organisms of lower virulence,¹³ which may have played a role in this series. The good post infection IOP control in our patients suggests that filtering blebs may survive repeated episodes of bleb purulence and intense inflammatory reaction, and continue to function satisfactorily.

In summary, this series demonstrates that eyes which have been successfully treated for bleb related infection remain at risk for recurrent infections. Leaking or inferiorly located blebs may be particularly vulnerable to recurrent bleb infection, which does not appear to be preventable by long term antibiotic prophylaxis. No apparent correlation exists between organisms responsible for the

initial and recurrent infections. The optimal management of blebs with repeat bouts of infection remains unclear and includes observation or bleb closure with implantation of a glaucoma drainage device. Eyes with recurrent bleb related infections may retain good visual function provided they are monitored closely and treated aggressively with intravitreal antibiotics if spread of intraocular inflammation is noted. Our current practice is to treat empirically any patient with a bleb abscess, a clear vitreous, and occasional cells in the anterior chamber with high dose, frequent, fortified, topical antibiotics along with close inpatient or outpatient observation. If, over the following 24–48 hours, there is no improvement in the external disease no decrease in the anterior chamber reaction, or if cells are noted in the vitreous at any time, intraocular antibiotics are administered immediately. It has become our policy to lower the threshold for surgical intervention to 24 hours in patients with a history of a previous bleb infection and patients who are not improving on topical therapy.

Supported in part by the New York Glaucoma Research Institute, New York, NY, USA.

Presented in part at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Ft Lauderdale, FL, 15 May, 1997.

- 1 Wolner B, Liebmann JM, Sassani JW, *et al.* Late bleb-related endophthalmitis after trabeculectomy with adjunctive 5-fluorouracil. *Ophthalmology* 1991;**98**:1053–60.
- 2 Greenfield DS, Suner IJ, Miller MP, *et al.* Endophthalmitis after filtering surgery with mitomycin C. *Arch Ophthalmol* 1996;**114**:943–9.
- 3 Higginbotham EJ, Stevens RK, Musch DC, *et al.* Bleb-related endophthalmitis after trabeculectomy with mitomycin C. *Ophthalmology* 1996;**103**:650–6.
- 4 Parrish RK, II, Minckler D. Late endophthalmitis—filtering surgery time bomb? (editorial). *Ophthalmology* 1996;**103**:1167–8.
- 5 Sugar HS, Zekman T. Late infection of filtering conjunctival scars. *Am J Ophthalmol* 1958;**46**:155–70.
- 6 Hattenhauer JM, Lipsich MP. Late endophthalmitis after filtering surgery. *Am J Ophthalmol* 1971;**72**:1097–101.
- 7 Kanski JJ. Treatment of late endophthalmitis associated with filtering blebs. *Arch Ophthalmol* 1974;**91**:339–43.
- 8 Tabbara KF. Late infections following filtering procedures. *Ann Ophthalmol* 1976;**8**:1228–31.
- 9 Mandelbaum S, Forster RK, Gelende H, *et al.* Late onset endophthalmitis associated with filtering blebs. *Ophthalmology* 1985;**92**:964–72.
- 10 Elliot RH. *A treatise on glaucoma*. Oxford: Oxford Medical Publications, 1921.
- 11 Waheed S, Ritterband DC, Greenfield DS, *et al.* Bleb-related ocular infection in children after trabeculectomy with mitomycin C. *Ophthalmology* 1997;**104**:2117–19.
- 12 Kangas TA, Greenfield DS, Flynn HW Jr, *et al.* Delayed-onset endophthalmitis associated with conjunctival filtering blebs. *Ophthalmology* 1997;**104**:746–52.
- 13 Phillips WB, Wong TP, Berger RL, *et al.* Late-onset endophthalmitis associated with filtering blebs. *Ophthalmic Surg* 1994;**25**:88–91.
- 14 Caronia RM, Liebmann JM, Friedman R, *et al.* Trabeculectomy at the inferior limbus. *Arch Ophthalmol* 1996;**114**:387–91.
- 15 Bellows AR, McCulley JP. Endophthalmitis in aphakic patients with unplanned filtering blebs wearing contact lenses. *Ophthalmology* 1981;**88**:839–43.
- 16 Aschkenazi I, Melamed S, Avni I, *et al.* Risk factors associated with late infection of filtering blebs and endophthalmitis. *Ophthalmic Surg* 1991;**22**:570–4.
- 17 Brown RH, Yang LH, Walker SD, *et al.* Treatment of bleb infection after glaucoma surgery. *Arch Ophthalmol* 1994;**112**:57–61.
- 18 Forster RK. Endophthalmitis. In: Tasman W, Jaeger EA, ed. *Duane's clinical ophthalmology*. Philadelphia: JB Lippincott, 1990: vol 4.
- 19 Ashline JW, Ellis PP. Endophthalmitis and contact lenses. *Am J Ophthalmol* 1968;**66**:960–1.
- 20 Wild FF. Endophthalmitis in a contact lens wearer. *Am J Ophthalmol* 1962;**54**:847–8.
- 21 Sidoti PA, Lopez PF, Michon J, *et al.* Delayed-onset pneumococcal endophthalmitis after mitomycin-C trabeculectomy: association with cryptic nasolacrimal obstruction. *J Glaucoma* 1995;**4**:11–5.
- 22 Greenfield DS, Suner IJ, Miller MP, *et al.* Endophthalmitis after filtering surgery with mitomycin. *Arch Ophthalmol* 1996;**114**:943–9.