

Delayed-onset bleb-associated endophthalmitis: presentation and outcome by culture result

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Purpose: To determine how culture results are associated with clinical presentations and outcomes in delayed-onset bleb-associated endophthalmitis (BAE).

Methods: Retrospective consecutive case series of BAE at Bascom Palmer Eye Institute between January 1, 1996 and December 31, 2009. All patients had prior glaucoma filtering surgery. BAE was defined as intraocular infection with vitreous involvement receiving treatment with intravitreal antibiotics. Visual acuity (VA) outcomes and other clinical data were grouped by culture result and compared using the 2-sided Student's *t*-test.

Main outcome measure: Mean logMAR change at 3 months after treatment (3-month logMAR Δ).

Results: Eighty-six eyes of 85 patients were identified. Two eyes were primarily eviscerated. Fifty-three (63%) eyes were culture-positive with the following organisms: *Streptococcus*, 21 (25%); coagulase-negative *Staphylococcus*, 9 (11%); *Enterococcus*, 6 (7%); Gram-negative, 15 (18%); *Moraxella*, 8 (10%); *Pseudomonas*, 3 (4%); and *Serratia*, 3 (4%). Presenting logMAR VA: culture-positive worse than culture-negative cases (2.45 vs 2.19, $P = 0.05$). Presenting intraocular pressure (IOP): culture-positive higher than culture-negative cases (24 mmHg vs 14 mmHg, $P = 0.002$). Poor presenting view of the fundus: *Streptococcus* worse than coagulase-negative *Staphylococcus* cases (90% vs 44%, $P = 0.006$), *Pseudomonas* and *Serratia* worse than *Moraxella* cases (100% vs 50%, $P = 0.04$). Three month logMAR Δ : culture-positive worse than culture-negative cases (1.03 vs 0.43, $P = 0.02$), *Streptococcus* worse than coagulase-negative *Staphylococcus* cases (1.44 vs 0.31, $P = 0.004$), *Pseudomonas* and *Serratia* worse than coagulase-negative *Staphylococcus* cases (2.41 vs 0.31, $P = 0.001$), *Pseudomonas* and *Serratia* worse than *Moraxella* cases (2.41 vs 0.04, $P = 0.001$). A culture result of *Streptococcus* or *Serratia* was present in 6 of 7 eyes that received an additional treatment of enucleation or evisceration ($P = 0.01$).

Conclusion: Culture-positive cases were associated with worse presenting VA, higher presenting IOP, and worse VA outcomes than culture-negative cases. *Streptococcus*, *Pseudomonas*, and *Serratia* cases were associated with poor presenting view of the fundus and worse VA outcomes than coagulase-negative *Staphylococcus* and *Moraxella* cases.

Keywords: endophthalmitis, bleb-associated endophthalmitis, trabeculectomy, culture results

Introduction

Visual acuity (VA) outcomes after treatment of delayed-onset bleb-associated endophthalmitis (BAE) are poor.¹⁻¹⁰ Only 22%–67% of eyes with BAE achieve a VA outcome of 20/400 or better. The most frequent causative organisms isolated include *Streptococcus* sp. and Gram-negative organisms in 31%–57% and 15%–32% of cases, respectively.¹⁻⁶

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The association between culture results and VA outcomes has been addressed in small case series.¹⁻⁶ In one study there was no significant difference between VA outcomes of eyes with *Streptococcus* sp., non-*Streptococcus* Gram-positive organisms, and Gram-negative organisms.² Another study showed no significant difference between VA outcomes of eyes with *Streptococcus* and *Staphylococcus* sp.³ Others reported VA outcomes for eyes with *Streptococcus* sp. and non-*Streptococcus* organisms but did not perform a comparative analysis.⁴⁻⁶ The inability to identify a significant association between VA outcomes and culture result may be due to the relatively small number of reported BAE cases and the pre-existing ocular disease in these patients.

It is also unclear if the clinical presentation of BAE differs by culture result. Presently no studies have reported presenting clinical information (eg, intraocular pressure, presence of hypopyon, view of the fundus) by culture result. The purpose of the current study is to determine how culture results are associated with clinical presentations and outcomes in BAE by performing a comparative analysis within a large case series.

Methods

The study protocol was approved by the Institutional Review Board of the University of Miami Miller School of Medicine Subcommittee for the Protection of Human Subjects in Research. The medical records and microbiologic records of all patients treated for BAE at Bascom Palmer Eye Institute (BPEI) between January 1, 1996 and December 31, 2009 were reviewed. All patients had prior glaucoma filtering surgery. BAE was defined as intraocular infection with vitreous involvement receiving treatment with intravitreal antibiotics. Patients with tube shunts as the filtering mechanism, bleb infection only (no posterior inflammation), onset within 1 month of glaucoma surgery, and inadvertent filtering blebs after cataract surgery were excluded. Clinical history and presentation, treatment, intraocular culture data, VA outcomes, and factors affecting VA were recorded. The current study included clinical information from the series of 71 eyes treated at BPEI between January 1, 1996 and July 1, 2008, which has been reported previously.¹

Snellen VAs were converted to logMAR equivalents for statistical analysis; VAs of hand motion, light perception, and no light perception were assigned logMAR values of 2.6, 3, and 4 respectively. Change in VA was determined by comparing the last recorded VA before the onset of endophthalmitis with VA at 3 months. The mean logMAR change at 3 months after presentation (3-month logMAR Δ) and other clinical

data were grouped by culture result and compared using the 2-sided Student's *t*-test. A *P*-value of ≤ 0.05 was considered statistically significant.

Results

Eighty-six eyes of 85 patients were identified. Two eyes were primarily eviscerated. Intraocular culture results were positive in 53 of 84 eyes, 63% *Streptococcus* sp. and Gram-negative organisms were the most frequent isolates, accounting for 25% and 18% of cases respectively. In five eyes, two organisms were isolated. All isolated organisms were sensitive to the intravitreal antibiotics clinically administered which included Vancomycin and Ceftazidime in 77 eyes, 92%, Vancomycin and Amikacin in two eyes, Vancomycin and Gentamicin in one eye, Vancomycin alone in two eyes, Ceftazidime and Amikacin in one eye, and Cefazolin and Gentamicin in one eye. Intravitreal Dexamethasone injections were given to 69 eyes, 82%. All eyes received topical antibiotics and steroids.

A comparison of culture-positive and culture-negative cases showed no significant difference in baseline demographics (Table 1). A greater number of culture-positive cases presented with a poor view of the fundus. The mean presenting intraocular pressure (IOP) was higher in culture-positive cases with no significant difference in final IOP. The mean pre-endophthalmitis VA showed no significant difference between groups, however mean presenting VA and 3-month logMAR Δ were worse in culture-positive cases (Figures 1 and 2).

Comparing *Streptococcus* cases with non-*Streptococcus* Gram-positive and coagulase-negative *Staphylococcus* cases showed no significant difference in baseline demographics (Table 2). The *Streptococcus* cases presented with a higher mean IOP and greater number of cases with a poor view of the fundus. A higher number of coagulase-negative *Staphylococcus* cases received tap and injection as the initial treatment. There was no significant difference in mean pre-endophthalmitis VA or presenting VA, however 3-month logMAR Δ was significantly worse in *Streptococcus* cases (Figure 3).

A comparison of Gram-negative cases with coagulase-negative *Staphylococcus* cases showed that fewer Gram-negative cases achieved VA $\geq 20/400$ at 3 months (Table 3). *Pseudomonas* and *Serratia* cases were associated with a poor view of the fundus, higher mean presenting IOP, and a worse 3-month logMAR Δ compared with coagulase-negative *Staphylococcus* cases. *Pseudomonas* and *Serratia* cases were also associated with a poor view of the fundus and worse 3-month logMAR Δ compared to *Moraxella* cases (Figure 4).

Table 1 Culture-positive and culture-negative cases

	Culture-positive 53/84 (63%)	Culture-negative 31/84 (37%)
Age		
Mean, SD	75 (12)	71 (13)
Gender		
Female	26 (50%)	15 (48%)
Male	26 (50%)	16 (52%)
Diabetes mellitus		
Present	6 (12%)	5 (17%)
Absent	46 (88%)	25 (83%)
Antimetabolites		
Used	33 (64%)	20 (69%)
Not used	19 (36%)	9 (31%)
Bleb leak		
Present	10 (19%)	11 (35%)
Absent	43 (81%)	20 (65%)
Mean time of onset of endophthalmitis, SD	64 months (46)	49 months (42)
Anterior chamber Hypopyon	36 (68%)	23 (74%)
View to fundus		
Hazy	15 (28%)	15 (48%)
Poor/none	38 (72%)	16 (52%)
Intraocular pressure		
Presentation, SD	24 (15)	14 (9)*
Treatment, initial		
Tap and injection	30 (57%)	24 (77%)
Pars plana vitrectomy	23 (43%)	7 (23%)
Treatment, additional		
Filtering procedure	7 (13%)	6 (19%)
Pars plana vitrectomy	19 (36%)	5 (16%)*
VA before endophthalmitis	n = 50	n = 31
Mean	20/81	20/95
Range	20/20-LP	20/25-CF
Presenting VA	n = 53	n = 31
Mean	0.7/200	1.6/200*
Range	20/40-NLP	20/50-LP
VA 3 months posttreatment	n = 47	n = 19
Mean	4.1/200	20/209*
Range	20/25-NLP	20/25-LP
20/400 or better	26 (55%)	14 (74%)
LogMAR Δ	1.03	0.43*

Note: * $P \leq 0.05$, culture-positive compared to culture-negative cases.

Abbreviations: CF, counting fingers; LP, light perception; NLP, no light perception; SD, standard deviation; VA, visual acuity.

Streptococcus and *Serratia* cases were associated with enucleation or evisceration (Table 4). Six of seven eyes that received an additional treatment of enucleation or evisceration had a culture result of *Streptococcus* or *Serratia* sp.

Discussion

The current study reports associations between culture results and clinical presentations and outcomes not clearly demonstrated in previous BAE series. The inability to detect these associations in past studies may have been due to the

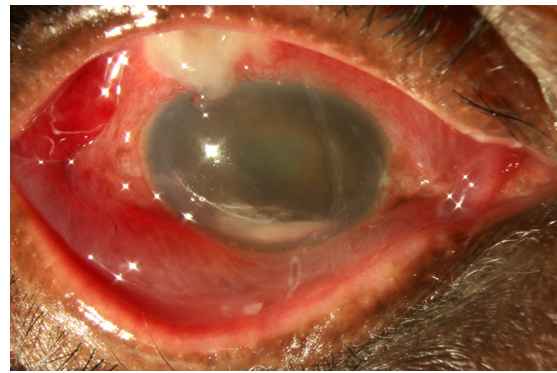


Figure 1 Photograph of right eye of 66-year-old male presenting with BAE from *Streptococcus* sp. Presenting VA: HM, IOP: 28 mmHg. Treatment: tap and injection. Final VA: HM, IOP: 12 mmHg. Culture-positive cases were associated with worse presenting VA and higher presenting IOP than culture-negative cases.
Abbreviations: BAE, bleb-associated endophthalmitis; HM, hand motion; IOP, intraocular pressure; VA, visual acuity.

limited power inherent in smaller case series and the manner in which VA outcomes were analyzed. Previous BAE studies reported the percentage of eyes $\geq 20/400$ or the loss of ≥ 5 Snellen lines.¹⁻⁶ While this information is clinically descriptive, it may be limited for comparative purposes by the poor baseline VA of many glaucomatous eyes. Mean logMAR Δ more precisely measures VA outcomes in low vision eyes.

The broad groups of causative organisms used in past BAE case series may also have limited the ability to detect associations with VA outcomes. A previous BAE case series used the classification of non-*Streptococcus* Gram-positive organisms.² Non-*Streptococcus* Gram-positive organisms include a wide range of organisms such as *Staphylococcus aureus*, *Enterococcus*, and coagulase-negative

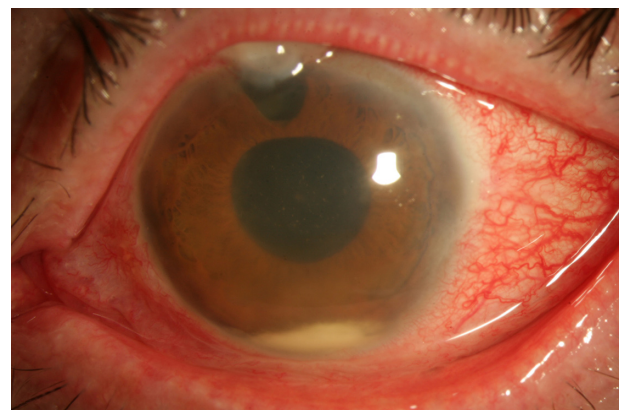


Figure 2 Photograph of left eye of 67-year-old male presenting with culture-negative BAE. Presenting VA: 20/200, IOP: 10 mmHg. Treatment: tap and injection. Final VA 20/200, IOP 16 mmHg. Culture-negative cases were associated with better VA outcomes than culture-positive cases.
Abbreviations: BAE, bleb-associated endophthalmitis; IOP, intraocular pressure; VA, visual acuity.

Table 2 Gram-positive cases

	Streptococcus	Non-Streptococcus Gram-positive	Coagulase-negative Staphylococcus	Enterococcus
	21/84 (25%)	17/84 (20%)	9/84 (11%)	6/84 (7%)
Age				
Mean, SD	72 (14)	77 (8)	77 (9)	76 (9)
Gender				
Female	9 (45%)	7 (41%)	3 (33%)	3 (50%)
Male	11 (55%)	10 (59%)	6 (67%)	3 (50%)
Diabetes mellitus				
Present	2 (10%)	1 (6%)	1 (11%)	0 (0%)
Absent	18 (90%)	16 (94%)	8 (89%)	6 (100%)
Antimetabolites				
Used	11 (55%)	14 (82%)	9 (100%)	3 (50%)
Not used	9 (45%)	3 (18%)	0 (0%)	3 (50%)
Bleb leak				
Present	4 (19%)	4 (24%)	3 (33%)	1 (17%)
Absent	17 (81%)	13 (76%)	6 (67%)	4 (67%)
Anterior chamber				
Hypopyon	11 (52%)	13 (77%)	7 (78%)	4 (67%)
View to fundus				
Hazy	2 (10%)	9 (53%)	5 (56%)	2 (33%)
Poor/none	19 (90%)	8 (47%)*	4 (44%) [†]	4 (67%)
Mean time of onset of endophthalmitis, SD	71 months (40)	64 months (57)	57 months (58)	77 months (72)
Intraocular pressure				
Presentation, SD	29 (16)	18 (15)*	11 (8) [†]	30 (17)
Treatment, initial				
Tap and injection	9 (43%)	12 (71%)	8 (89%) [†]	3 (50%)
Pars plana vitrectomy	12 (57%)	5 (29%)	1 (11%)	3 (50%)
Treatment, additional				
Filtering procedure	2 (10%)	5 (29%)	4 (44%) [†]	0 (0%)
Pars plana vitrectomy	10 (48%)	3 (18%)*	1 (11%) [†]	2 (33%)
VA before endophthalmitis	n = 19	n = 17	n = 9	n = 6
Mean	20/62	20/73	20/54	20/167
Range	20/20-4/200	20/20-LP	20/25-20/200	20/25-LP
Presenting VA	n = 21	n = 17	n = 9	n = 6
Mean	0.5/200	0.8/200	1/200	0.5/200
Range	20/40-LP	20/80-NLP	20/200-LP	20/80-NLP
VA 3 months posttreatment	n = 20	n = 14	n = 9	n = 4
Mean	1.9/200	20/209*	20/110 [†]	3/200
Range	20/30-NLP	20/25-LP	20/25-HM	20/100-LP
20/400 or better	9 (45%)	11 (79%)*	8 (89%) [†]	2 (50%)
LogMAR Δ	1.44	0.46*	0.31 [†]	0.89

Notes: * $P \leq 0.05$, *Streptococcus* compared to non-*Streptococcus* Gram-positive cases; [†] $P \leq 0.05$, *Streptococcus* compared to coagulase-negative *Staphylococcus* cases.

Abbreviations: HM, hand motion; LP, light perception; NLP, no light perception; SD, standard deviation; VA, visual acuity.

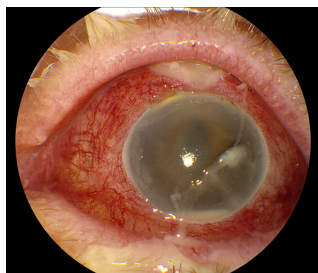


Figure 3 Photograph of left eye of 79-year-old female presenting with BAE from *Streptococcus* sp. Presenting VA: LP, IOP: 40 mmHg. Treatment: pars plana vitrectomy. Final VA: LP, IOP: 0 mmHg. Only 45% of *Streptococcus* cases had VA outcomes $\geq 20/400$.

Abbreviations: BAE, bleb-associated endophthalmitis; IOP, intraocular pressure; LP, light perception; VA, visual acuity.

Staphylococcus cases that have varying VA outcomes. The current study narrowed the analysis to individual causative organisms, strengthening associations with VA outcomes.

An analysis of Gram-negative cases by individual organism showed that *Pseudomonas* and *Serratia* cases had worse mean VA outcomes than *Moraxella* cases. The relatively good VA outcomes of *Moraxella* cases, 71% $\geq 20/400$, confirms the previous report by Berrocal et al of favorable outcomes with *Moraxella* cases.¹¹

The current study also provides insight into the clinical presentation of causative organisms in BAE. *Streptococcus*, *Pseudomonas*, and *Serratia* cases were associated with

Table 3 Gram-negative cases

	Gram-negative	<i>Moraxella</i>	<i>Pseudomonas</i>	<i>Serratia</i>
	15/84 (18%)	8/84 (10%)	3/84 (4%)	3/84 (4%)
Age				
Mean, SD	78 (14)	72 (11)	82 (18)	89 (12)
Gender				
Female	10 (67%)	4 (50%)	3 (100%)	2 (67%)
Male	5 (33%)	4 (50%)	0 (0%)	1 (33%)
Diabetes mellitus				
Present	3 (20%)	2 (25%)	1 (33%)	0 (0%)
Absent	12 (80%)	6 (75%)	2 (67%)	3 (100%)
Antimetabolites				
Used	8 (53%)	5 (63%)	1 (33%)	2 (67%)
Not used	7 (47%)	3 (37%)	2 (67%)	1 (33%)
Bleb leak				
Present	2 (13%)	2 (75%)	0 (0%)	0 (0%)
Absent	13 (87%)	6 (75%)	3 (100%)	3 (100%)
Anterior chamber				
Hypopyon	12 (80%)	6 (75%)	2 (67%)	3 (100%)
View to fundus				
Hazy	4 (27%)	4 (50%)	0 (0%)	0 (0%)
Poor/none	11 (73%)	4 (50%) [†]	3 (100%)	3 (100%) [‡]
Mean time of onset of endophthalmitis, SD	51 months (36)	56 months (32)	57 months (77)	34 months (38)
Intraocular pressure				
Presentation, SD	22 (12)*	23 (15)	26 (12)	18 (4) [‡]
Treatment, initial				
Tap and injection	9 (60%)	5 (63%)	1 (33%)	2 (67%)
Pars plana vitrectomy	6 (40%)	3 (37%)	2 (67%)	1 (33%)
Treatment, additional				
Filtering procedure	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pars plana vitrectomy	6 (40%)*	4 (50%) [†]	0 (0%)	1 (33%)
VA before endophthalmitis	n = 14	n = 7	n = 3	n = 3
Mean	20/131	20/194	20/141	20/74
Range	20/25-HM	20/25-HM	20/40-4/200	20/50-20/100
Presenting VA	n = 15	n = 8	n = 3	n = 3
Mean	0.9/200	1.4/200	1.6/200	LP
Range	20/80-LP	20/80-LP	20/100-LP	HM-LP
VA 3 months posttreatment	n = 13	n = 7	n = 2	n = 3
Mean	2.5/200*	20/264 [†]	LP	LP [‡]
Range	20/40-NLP	20/40-HM	LP-LP	LP-NLP
20/400 or better	6 (46%)*	5 (71%) [†]	0 (0%)	0 (0%) [‡]
LogMAR Δ	1.08	0.04 [†]	1.88	2.77 [‡]

Note: * $P \leq 0.05$, Gram-negative compared to coagulase-negative *Staphylococcus* cases. [†] $P \leq 0.05$, *Pseudomonas* and *Serratia* compared to *Moraxella* cases. [‡] $P \leq 0.05$, *Pseudomonas* and *Serratia* compared to coagulase-negative *Staphylococcus* cases.

Abbreviations: HM, hand motion; LP, light perception; NLP, no light perception; SD, standard deviation; VA, visual acuity.



Figure 4 Photograph of left eye of 72-year-old female with BAE from *Moraxella* sp. Presenting VA: 1/200, IOP: 35 mmHg. Treatment: tap and injection. Final VA: 20/25, IOP: 11 mmHg. *Moraxella* cases were associated with a better presenting view of the fundus and better VA outcomes than *Pseudomonas* and *Serratia* cases.

Abbreviations: BAE, bleb-associated endophthalmitis; IOP, intraocular pressure; VA, visual acuity.

a higher mean IOP and worse view of the fundus than coagulase-negative *Staphylococcus* cases. Similarly culture positive cases were associated with a worse presenting VA and higher presenting IOP than culture negative cases. The clinician can consider the increased likelihood of a more virulent organism and worse visual prognosis when the patient presents with poor VA, high IOP, and poor view of the fundus.

The VA outcome analysis provided in this study confirms what clinicians have suspected for decades. Worse VA outcomes in BAE are associated with the most frequent isolates, *Streptococcus* sp. and Gram-negative organisms such as

Table 4 Enucleation or evisceration in nine eyes (10%)

Case #	Culture result	Initial treatment	Additional treatment
5	<i>Serratia</i> and <i>Streptococcus</i>	T&I	Enucleation
17	<i>Serratia</i>	T&I	Enucleation
33	<i>Serratia</i>	PPV	Evisceration
26	<i>Streptococcus</i>	T&I	Evisceration
37	<i>Streptococcus</i>	PPV	Enucleation
43	<i>Streptococcus</i>	PPV	Enucleation
46	No growth	PPV	Evisceration
25	Not done	Evisceration	
70	Not done	Evisceration	

Note: $P = 0.01$, Enucleation or evisceration for *Streptococcus* or *Serratia* compared with other culture results.

Abbreviations: PPV, Pars planavitrectomy; T&I, tap and injection.

Pseudomonas and *Serratia* sp. When discussing prognosis, clinicians may consider that eyes with *Streptococcus* sp. and Gram-negative organisms had VA outcomes $\geq 20/400$ in only 45% and 46% of cases respectively while eyes with coagulase-negative *Staphylococcus* sp. Achieved $\geq 20/400$ in 89% of cases.

Interestingly coagulase-negative *Staphylococcus* cases achieved better VA outcomes despite less aggressive treatment. Only 11% of the coagulase-negative *Staphylococcus* cases received pars plana vitrectomy compared with 57% of the *Streptococcus* cases. The higher mean IOP and worse view of the fundus in the *Streptococcus* cases likely compelled the treating clinician to more frequently favor pars plana vitrectomy. The role pars plana vitrectomy plays in BAE can only be determined by a sufficiently powered prospective randomized control trial. Unfortunately this may not be feasible due to the limited number of BAE cases.

The current study was not designed to determine the best management for BAE, but it does provide insight into the key role causative organisms play in the clinical presentation and prognosis of BAE. Culture-positive cases were associated with worse presenting VA, higher presenting IOP, and worse VA outcomes than culture-negative cases. *Streptococcus*, *Pseudomonas*, and *Serratia* cases were associated with poor presenting view of the fundus and worse VA outcomes than coagulase-negative *Staphylococcus* and *Moraxella* cases.

Disclosure

No conflicts of interest were declared in relation to this paper.

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