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Delayed Versus Acute-Onset Endophthalmitis after Cataract Surgery

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Abstract

Purpose—To report a large consecutive case series of patients who developed delayed-onset and acute-onset endophthalmitis after cataract surgery.

Design—Retrospective consecutive case series.

Methods—The current study is a retrospective consecutive case series of patients treated between January 2000 and December 2009 for culture-proven endophthalmitis after cataract surgery. The study defined two groups after cataract surgery: acute-onset endophthalmitis (< 6 weeks after surgery) and delayed-onset endophthalmitis (> 6 weeks after surgery).

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Results—A total of 118 patients met study criteria and included 26 delayed-onset cases and 92 acute-onset cases. The following clinical features and outcomes occurred in delayed versus acute-onset cases: (1) the presenting visual acuity was 5/200 in 31% versus 89%, (2) hypopyon was found in 46% versus 80%, (3) the most frequent isolate was *Propionibacterium acnes* (11/26) versus coagulase-negative *Staphylococcus* (57/92), (4) patients with the most frequent isolate achieved a visual outcome of 20/100 in 91% versus 56%. In delayed-onset cases, the intraocular lens was removed or exchanged in 19/26 (73%). Of these 19 cases, 13 achieved a visual outcome of 20/100.

Conclusions—Patients with delayed-onset endophthalmitis generally presented with better initial visual acuities, had a lower frequency of hypopyon, and had better visual outcomes compared to acute-onset patients. *Propionibacterium acnes* and coagulase-negative *Staphylococcus* species were the most common organisms cultured in delayed and acute-onset categories, respectively, and were associated with the best visual acuity outcomes in each group.

INTRODUCTION

Endophthalmitis is a serious sight-threatening condition that can be classified into two broad categories: acute-onset and delayed-onset. As used in the Endophthalmitis Vitrectomy Study, acute-onset postoperative endophthalmitis was defined as infections within six weeks of surgery.¹ By contrast, delayed-onset postoperative endophthalmitis has been defined as greater than 6 weeks after the surgery.¹ These two categories may differ in their incidence, clinical features, microbiology and visual acuity outcomes.

The reported incidence of acute-onset endophthalmitis after cataract surgery ranges from 0.03%-0.15%.²⁻⁴ Since the mid-1990s, cataract surgical techniques have evolved to clear corneal, sutureless techniques. In spite of this change in technique, the nature of acute-onset endophthalmitis in both settings is virtually identical.⁵ Acute-onset postoperative endophthalmitis is characterized by a rapid onset of visual loss, marked intraocular inflammation, and is frequently caused by coagulase-negative *Staphylococcus*.¹

In one single-center, the reported rate of delayed-onset endophthalmitis following cataract surgery was 0.017%.⁶ In delayed-onset postoperative endophthalmitis, the onset is frequently insidious, the inflammation is often low grade, and is caused by less virulent bacteria and fungi. *Propionibacterium acnes* has been reported to be a common organism isolated in published series.^{6,7,8}

The purpose of the current study was to compare the clinical features, causative organisms, and visual acuity outcomes associated with delayed-onset versus acute-onset endophthalmitis after cataract surgery in a contemporary series from a university referral center.

METHODS

The clinical and microbiology records were reviewed for all patients treated at Bascom Palmer Eye Institute between January 1, 2000, and December 31, 2009, for clinically diagnosed, culture-positive endophthalmitis following cataract surgery. The study included patients who were operated elsewhere and referred for care, as well as patients who underwent cataract surgery at Bascom Palmer Eye Institute. Patients were excluded from the study if the endophthalmitis was not associated with cataract surgery or if consequent to combined procedures (glaucoma and cataract surgery). Patients with pre-existing macular degeneration, diabetic retinopathy, or glaucoma were not excluded from the study.

Intraocular fluid specimens were plated directly on chocolate agar, 5% sheep blood agar, CDC anaerobic blood agar, Sabouraud agar and in thioglycolate medium. Chocolate and blood agar plates and thioglycolate broth were incubated for up to two weeks at 35°C in 5% CO₂. Anaerobic plates were incubated in an anaerobic jar in non-CO₂ for up to two weeks. Sabouraud agar was incubated at 35°C for 72 hours and then at 25°C for up to two weeks. To be considered a positive culture, a specimen must have demonstrated growth of the same organism on two or more solid culture media or growth on a single medium after identification on an initial smear.

Because the current study was a retrospective case series, there was no rigid protocol for managing these patients, although the practice algorithm is fairly consistent for all investigators. Intravitreal antibiotics were injected at the time of initial treatment in all patients. The use of vitrectomy was at the discretion of the treating physician, although the guidelines of the Endophthalmitis Vitrectomy Study (EVS) were generally followed for acute-onset cases. Recorded data included clinical features, visual acuity at diagnosis, cultured organisms and visual acuity at follow-up.

RESULTS

Between January 1, 2000, and December 31, 2009, 118 patients met study criteria. Of these 118 patients, 26 (22%) had delayed-onset postoperative endophthalmitis and 92 (78%) had acute-onset postoperative endophthalmitis (see Tables 1 and 2). In this study, 71 (60%) cases were from male patients and 47 (40%) were from female patients. The mean age at presentation was 74 years (range 52 to 87, SD 9) in the delayed-onset group and 76 years (range 48 to 90, SD 9) in the acute-onset group.

Delayed-onset postoperative endophthalmitis

The mean time between surgery and the diagnosis of endophthalmitis was 343 days (range 48 to 1840, SD 379). Intraocular cultures became positive on days 2 to 7 after obtaining the specimen (mean time to culture positivity: 3.5 days). The average follow-up time after initial treatment was 804 days (range: 61 to 3069, SD: 774). A presenting visual acuity of 5/200 was noted in 8 (31%) of 26 patients. Hypopyon was present in 12 (46%) of 26 patients, and keratic precipitates were present in 19 (73%) of 26 patients (see example in Figure 1). A white plaque associated with the capsular bag was noted in 17 (68%) of 25 patients (see examples in Figures 2 and 3). In delayed-onset cases, the following organisms were isolated: *Propionibacterium acnes* in 11 (42%), fungal species in 7 (27%), gram-negative species in 3 (12%), gram-positive species in 3 (12%), and *Mycobacterium chelonae* in 2 (8%).

Initial treatment consisted of three different strategies: (1) Vitreous tap and injection of intraocular antibiotics, (2) Three-port pars plana vitrectomy (PPV) with injection of intraocular antibiotics, and (3) Three-port pars plana vitrectomy with partial posterior capsulectomy and injection of intraocular antibiotics. No patients underwent initial treatment with total capsulectomy, intraocular lens (IOL) exchange, or intraocular lens removal. However, 19 (73%) of 26 delayed-onset patients subsequently underwent combinations of these procedures due to recurrence of inflammation (Figure 4).

Of these 19 patients who underwent exchange or removal of the IOL, initial treatment included injection of intraocular antibiotics in two, PPV with intraocular antibiotics in eight, and PPV with partial capsulectomy and intraocular antibiotics in nine. Seventeen (89%) of 19 patients underwent PPV with total capsulectomy and IOL removal or exchange as a secondary procedure. Only 2 (11.7%) of these 17 patients developed recurrence, which was managed by PPV with IOL removal in one patient and penetrating keratoplasty for keratitis in the other patient. Two patients who underwent PPV as a secondary procedure developed

recurrence which was treated with PPV, total capsulectomy, and IOL removal. In patients without recurrence, removal or exchange of the IOL was often the last procedure utilized to eliminate the infection.

Seven (27%) of 26 patients did not undergo exchange or removal of the IOL. Initial treatment in these patients included injection of intraocular antibiotics in one, PPV with intraocular antibiotics in two, and PPV with partial capsulectomy and intraocular antibiotics in four. None of these patients had further recurrences or interventions after initial treatment.

Visual outcomes were 20/100 in 65% and 5/200 in 27% of delayed-onset patients. The distribution of visual outcomes according to the various isolates is displayed in Table 3. Clinical features, presenting visual acuity, and visual outcomes of delayed-onset patients classified by those who underwent IOL exchange or removal is shown in Table 4 and Figure 4.

Acute-onset postoperative endophthalmitis

The mean time between surgery and the diagnosis of endophthalmitis was 9 days (range: 1 to 39, SD: 8). The average follow-up time after initial treatment was 268 days (range: 7 to 3307, SD: 477). A presenting visual acuity of 5/200 was noted in 82 (89%) of 92 patients. Hypopyon was present in 74 (80%) of 92 patients. The culture isolates in acute-onset cases were the following: *Staphylococcus epidermidis* in 57 (62%) cases, *S. aureus* in 11 (12%), *Streptococcus* species in 8 (8.7%), and other organisms including gram-negative species in 16 (17.4%). A visual outcome of 20/100 was achieved in 41% of patients. An unfavorable visual outcome of 5/200 was present in 35%. The distribution of visual outcomes according to the various isolates is shown in Table 3.

DISCUSSION

Patients with delayed-onset postoperative endophthalmitis have several distinguishing clinical features. The signs and symptoms vary according to time to presentation and causative microorganism. The inflammation is often low grade and slowly progressive for delayed-onset postoperative endophthalmitis, since it is typically caused by less virulent bacteria and fungi. *P. acnes* was the most common organism isolated in the current series and other delayed-onset postoperative endophthalmitis series (Table 5).^{6,7,8} Other less virulent gram-positive organisms (coagulase-negative *Staphylococcus* species, *Corynebacterium* species), gram-negative organisms and fungi have also been reported in delayed-onset postoperative endophthalmitis.^{6,9,10,11,12}

The syndrome of delayed-onset postoperative endophthalmitis caused by *P. acnes*, manifesting with a white intracapsular plaque, moderate visual loss, and often granulomatous inflammation was originally described by Meisler and associates.¹³ In two previous published reports, a white intracapsular plaque was noted in 28.5%, 89%, and 100% of patients with *P. acnes*.^{6,7,8} Such plaques have been reported in association with other microorganisms as well.^{6,11,12} In the present series, 68% of delayed-onset patients were noted to have this clinical sign. Intracapsular white plaques were not noted in acute-onset patients in the current study. All patients demonstrated conjunctival congestion and varied amounts of vitreous inflammation. Hypopyon as a presenting feature was noted in 46% of delayed-onset patients in the current study, compared to 80% of acute-onset patients, which is similar to previous reports in the literature.^{1,6,7,8} *P. acnes* has been also been reported to present uncommonly as acute-onset postoperative endophthalmitis.¹⁴

The spectrum of microorganisms seen in delayed-onset postoperative endophthalmitis differs from those seen in acute-onset postoperative endophthalmitis. Even though

Staphylococcus species often occur in both categories, Streptococcus species and gram-negative organisms are more commonly noted in acute-onset postoperative endophthalmitis.

Anaerobic culture techniques are critical to microbiologically confirm *P. acnes*. In addition, it is important to monitor anaerobic cultures for a longer period of time due to the slow growth of these microorganisms; the time to culture positivity ranged from 2-7 days in the present case series. The findings of other aerobic bacteria and fungi underscore the importance of using both aerobic culture and Sabouraud agar in patients with delayed-onset postoperative endophthalmitis.

The ideal management of *P. acnes* endophthalmitis is controversial. In one report, resolution of inflammation in patients with *P. acnes* endophthalmitis occurred with systemic antibiotics alone.¹⁵ Other cases of resolution after intraocular antibiotics injected into the capsular bag or simultaneously into the aqueous and the vitreous have also been described.^{13,16,17,18,19} Recurrence of inflammation in these patients may warrant PPV with partial capsulectomy or total capsulectomy, with or without removal or exchange of the IOL. In the current series, recurrence of disease was noted in 73% of delayed-onset patients after the initial procedure. Similar recurrences of inflammation has also described in other published reports.^{6,7,8,17} Of the 19/26 delayed-onset patients in the current study who underwent PPV with total capsulectomy and IOL removal or exchange for recurrence of inflammation either as a secondary or a tertiary procedure, 17 (89.4%) showed resolution of inflammation. In the current series, intraocular vancomycin and ceftazidime was used for empiric coverage of gram-positive and gram-negative organisms in the primary procedure. Intraocular amikacin or amphotericin B was injected in cases of culture-proven Mycobacteria or fungal endophthalmitis, respectively. Although the study was not designed to prospectively compare the various treatment modalities in the management of delayed-onset postoperative endophthalmitis, the study data suggests that PPV with total capsulectomy and IOL removal or exchange may be the procedure of choice in cases of recurrent infection.

A potential distinction could be argued between the terms “delayed-onset” and “chronic” endophthalmitis. The term “delayed-onset” was used in the current study based on the onset of the signs and symptoms greater than six weeks after surgery. It is not possible to determine if the infecting organism was present from the time of cataract surgery, which would be more in keeping with the term “chronic” endophthalmitis. The significance of this case series is the delayed worsening of signs and symptoms leading to treatment beyond six weeks from cataract surgery.

The current study is a large contemporary series comparing clinical features and outcomes in delayed-onset and acute-onset postoperative endophthalmitis. This large series of delayed-onset patients helps to better define management options and outcomes. The study is limited by its small sample size, retrospective nature, and the variability between multiple physicians involved in the treatment of these patients. The current study from a large tertiary care center population demonstrated that patients with delayed-onset endophthalmitis generally presented with better initial acuities and visual outcomes, and with less frequent hypopyon than patients with acute-onset endophthalmitis. Recurrence of infection is more commonly observed in patients with delayed-onset postoperative endophthalmitis. Inflammation which recurs after initial IOL sparing treatment may warrant removal of the entire capsular bag including removal or exchange of the IOL.

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Biography

Biosketch for Anita Rajadhyaksha Shirodkar, MD (photo also uploaded)

Anita Rajadhyaksha Shirodkar, MD, received undergraduate double degrees in bioengineering and economics at Rice University in Houston, Texas. She then received her medical degree from Baylor College of Medicine in Houston, Texas, which was followed by a residency in ophthalmology at Bascom Palmer Eye Institute in Miami, Florida. She is currently a second year fellow in vitreoretinal diseases and surgery at Bascom Palmer Eye Institute, where she is also serving as Chief Resident.

Biosketch for Avinash Pathengay, MD (photo also uploaded)

Avinash Pathengay, MD, FRCS, completed his residency in ophthalmology at Regional Institute of Ophthalmology in Chennai, India. He went on to do a fellowship in vitreoretinal diseases and surgery at Sankara Nethralaya in Chennai, India. He is an associate ophthalmologist at L.V. Prasad Eye Institute in India, and is currently at Bascom Palmer Eye Institute as an international fellow with Dr. Harry Flynn, Jr. His main areas of research interest are endophthalmitis and vitreoretinal diseases.

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Figure 1. Hypopyon and granulomatous keratic precipitates associated with *Propionibacterium acnes* endophthalmitis.

Upper. Initial presentation of patient #2; visual acuity 5/200.

Lower. After pars plana vitrectomy with total capsulectomy and IOL removal; visual acuity was 20/20 with aphakic contact lens correction.

Figure 2.

White plaque within the capsular bag associated with *Propionibacterium acnes* endophthalmitis.

Upper. Initial presentation of patient #22; visual acuity was 20/40.

Lower. After pars plana vitrectomy with partial capsulectomy; visual acuity was 20/25.

Figure 3.
White plaque within the capsular bag associated with *Acremonium strictum* endophthalmitis.

Upper. Initial presentation of patient #12; visual acuity was 20/200.

Middle. Recurrence of infection with hypopyon after pars plana vitrectomy; visual acuity was hand motions.

Lower. After pars plana vitrectomy with total capsulectomy and IOL removal; visual acuity was 20/30 with aphakic contact lens correction.

Figure 4.

Surgical procedures in delayed-onset endophthalmitis patients who had intraocular lens implant (IOL) removal*.

*Of the 7 patients with delayed-onset endophthalmitis who did not undergo IOL removal, initial treatment was PPV/PC/IOAB (4 patients), PPV/IOAB (2 patients), and IOAB (1 patient). No patients had recurrences or further interventions.

Abbreviations: IOAB = intraocular antibiotics; PPV = pars plana vitrectomy; PC = partial capsulectomy; TC = total capsulectomy; noIOL = IOL removal; PKP = penetrating keratoplasty; IOLx = IOL exchange.

Table 1

Presenting clinical features of patients with endophthalmitis following cataract surgery.

Total n = 118	VA 5/200	Hypopyon	Mean Days to Diagnosis
Delayed-onset (n = 26)	8 (31%)	12 (46%)	343 (median: 230, range: 48-1840)
Acute-onset (n = 92)	82 (89%)	74 (80%)	9 (median: 7, range: 1-39)

Table 2

Visual acuity outcomes by category of endophthalmitis.

Total n = 118	20/40	20/100	5/200	NLP
Delayed-onset (n = 26)	50%	65%	27%	12%
Acute-onset (n = 92)	27%	41%	35%	4%

Table 3

Visual acuity outcomes by cultured organism in delayed-onset and acute-onset endophthalmitis.

DELAYED-ONSET ENDOPHTHALMITIS				
Total n = 26	20/40	20/100	5/200	NLP
<i>Propionibacterium acnes</i> (n = 11)	55%	91%	9%	0
Fungal species ^a (n = 7)	57%	57%	29%	0
<i>Mycobacterium chelonae</i> (n = 2)	50%	50%	50%	50%
Gram (–) species (n = 3)	0	0	67%	33%
Other Gram (+) species (n = 3)	67%	67%	33%	33%
ACUTE-ONSET ENDOPHTHALMITIS				
Total n = 92	20/40	20/100	5/200	NLP
Coagulase (–) <i>Staphylococcus</i> (n = 57)	38%	56%	13%	0
<i>S. aureus</i> (n = 11)	0	0	100%	0
<i>Streptococcus</i> species (n = 8)	0	0	67%	33%
Other ^b (n = 16)	11%	22%	67%	11%

^aFungal species include *Candida parapsilosis* (3), *Aspergillus fumigatus*, *Penicillium citrinum*, *Paecilomyces variotti*, *Acremonium strictum*.

^bOther cultured organisms include gram-negative species.

Table 4

Clinical and microbiologic features of delayed-onset endophthalmitis patients who had the intraocular lens implant (IOL) removal versus those who did not have IOL removal.

Patient	Eye	Days to Diagnosis	Organism	Visual Acuity at Diagnosis	Hypopyon	Keratic Precipitates	Visual Outcome
DELAYED ONSET ENDOPHTHALMITIS WITH IOL REMOVAL							
1 *	OD	278	<i>Propionibacterium acnes</i>	20/60	Y	Y	20/25
2	OD	256	<i>Propionibacterium acnes</i>	5/200	Y	Y	20/20
3 *	OD	476	<i>Propionibacterium acnes</i>	20/100	N	N	20/30
4	OD	735	<i>Propionibacterium acnes</i>	20/150	N	Y	20/80
5 *	OD	127	<i>Propionibacterium acnes</i>	20/30	N	Y	20/40
6 *	OS	808	<i>Propionibacterium acnes</i>	20/80	N	Y	20/60
7	OS	714	<i>Propionibacterium acnes</i>	20/40	N	Y	LP [†]
8 *	OD	210	<i>Propionibacterium acnes</i>	20/40	N	Y	20/70
9	OS	331	<i>Candida parapsilosis</i>	20/200	N	Y	20/400
10	OS	125	<i>Candida parapsilosis</i>	CF	N	Y	5/200
11	OD	133	<i>Candida parapsilosis</i>	20/200	N	Y	20/25
12	OD	250	<i>Acremonium strictum</i>	20/200	N	Y	20/30
13	OS	125	<i>Aspergillus fumigatus</i>	20/60	Y	Y	20/20
14	OD	716	<i>Paecilomyces variotti</i>	CF	Y	N	5/200
15 **	OD	154	<i>Mycobacterium chelonae</i>	20/30	Y	Y	20/25
16	OS	57	<i>Mycobacterium chelonae</i>	20/400	Y	Y	NLP ^{††}
17	OD	276	<i>Agrobacterium radiobacter</i>	HM	Y	Y	LP
18 *	OD	202	<i>Staphylococcus epidermidis</i>	5/200	Y	Y	20/15
19	OS	104	<i>Staphylococcus epidermidis</i>	2/200	Y	N	20/40
DELAYED ONSET ENDOPHTHALMITIS WITHOUT IOL REMOVAL							
20	OS	126	<i>Propionibacterium acnes</i>	20/50	N	Y	20/25
21	OD	111	<i>Propionibacterium acnes</i>	20/50	N	Y	20/100
22	OS	381	<i>Propionibacterium acnes</i>	20/40	N	N	20/25

Patient	Eye	Days to Diagnosis	Organism	Visual Acuity at Diagnosis	Hypopyon	Keratic Precipitates	Visual Outcome
23	OD	258	<i>Penicillium citrinum</i>	20/60	N	Y	20/30
24	OD	73	<i>Ewingella americana</i>	20/400	Y	N	20/300
25	OS	1840	<i>Haemophilus influenzae</i>	LP	Y	N	NLP
26	OD	48	<i>Streptococcus intermedius</i>	LP	Y	N	NLP

Abbreviations: CF = count fingers, HM = hand motions, LP = light perception, NLP = no light perception

* Patients who underwent IOL exchange

** Patient who underwent IOL exchange, and then subsequent IOL removal for recurrence

[†] Patient had a suprachoroidal hemorrhage in the first week after PPV/IOL removal

^{††} Patient had a retinal detachment three months after PPV/IOL removal

Table 5

Microbiologic comparison of delayed-onset pseudophakic endophthalmitis studies.

Study (dates of data collection)	Current study (2000-2009)	Al-Mezaine, et al. ⁵ (1997-2006)	Clark, et al. ⁶ (1974-1996)	Fox, et al. ⁷ (1979-1989)
Number of cases	26	17	36	19
<i>P. acnes</i>	11	7	36	12
Fungal species	7	3	0	3
Gram (+) species	3	3	0	4
Gram (–) species	3	1	0	0
Mycobacteria	2	0	0	0
Mixed	0	3	0	0