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Case Report

Postoperative Endophthalmitis Caused by *Cutibacterium* (Formerly *Propionibacterium*) Acnes: Case Series and Review

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Keywords
Cutibacterium acnes · *Propionibacterium acnes* · Postoperative endophthalmitis · Chronic endophthalmitis · Delayed endophthalmitis

Abstract
We report the clinical features, treatment strategies and outcomes in a series of patients with infectious endophthalmitis after cataract surgery caused by *Cutibacterium acnes (C. acnes)*, formerly known as *Propionibacterium acnes (P. acnes)*. This retrospective case series includes six eyes of six patients with chronic postoperative endophthalmitis caused by culture-proven *C. acnes* from December 2010 to July 2019 at a University referral center. All patients underwent prior cataract extraction with intraocular lens (CE/IOL) implantation. The mean time between cataract surgery and the microbiologic diagnosis of endophthalmitis was 7.4 ± 5.2 months (range 1.5–17 months). The average time from obtaining the specimen to culture positivity was 7.7 ± 4.4 days (range 3–15 days). Three eyes (50%) presented with hypopyon and

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three eyes (50%) presented with prominent keratic precipitates without hypopyon. Presenting visual acuity ranged from 20/25 to 2/200. Initial treatments included intravitreal antibiotics alone (*n* = 2), pars plana vitrectomy (PPV) with partial capsulectomy and intravitreal antibiotics (*n* = 3), and pars plana vitrectomy with IOL removal and intravitreal antibiotics (*n* = 1). Follow-up treatments included IOL removal (*n* = 2), intravitreal antibiotics (*n* = 1), and topical antibiotics (*n* = 1). The best-corrected visual acuity at last follow-up was 20/70 or better in all patients. In a literature review, the clinical features and treatment outcomes for all case series of delayed-onset postoperative endophthalmitis caused by *C. acnes* (*n* = 120) are listed. A definitive cure (the absence of recurrent inflammation) was achieved in 100% of patients that underwent IOL removal, in 77% of those that underwent PPV/partial capsulectomy and intravitreal antibiotics, and in 18% of cases treated with intravitreal antibiotics alone. Endophthalmitis after CE/IOL caused by *C. acnes* is characterized by slowly progressive intraocular inflammation and has a protracted course from surgery to microbiologic diagnosis. Visual outcomes are generally favorable, but IOL explantation may be necessary for definitive cure.

Introduction

Cutibacterium acnes (*C. acnes;* basonym *Propionibacterium acnes*) is a gram-positive anaerobic rod-shaped commensal bacterium that is present on human skin [1]. *C. acnes* is an uncommon cause of endophthalmitis after cataract surgery, typically presenting months after surgery as an indolent, smoldering inflammation [2–4]. The purpose of the current study is to examine the clinical and microbiological features, as well as treatment approaches and outcomes of chronic endophthalmitis caused by *C. acnes* in six patients after cataract surgery.

Case Report

Methods

The study and data accumulation were carried out with approval from an Institutional Review Board (IRB) at the University of Miami/Bascom Palmer Eye Institute. The study is in accordance with HIPAA regulations.

This study was a retrospective case series of 588 charts with ICD-10 codes H44.0-H44.029, in addition to microbiology laboratory database of *C. acnes*-positive cultures. Study period and location: December 2010 to July 2019, Bascom Palmer Eye Institute, Miami, FL, USA. Six eyes of six patients fit the inclusion criteria: diagnosis of endophthalmitis, presentation at least four weeks after cataract surgery, and culture positivity for *C. acnes*.

For the literature review, a Pubmed search was performed for "*Propionibacterium acnes*" OR *"P. acnes"* OR *"Cutibacterium acnes"* OR *"C. acnes"* AND "endophthalmitis." Studies with ≥ five cases were included, and cases that presented <4 weeks after cataract extraction were excluded. For calculation of average visual acuity, the Snellen value for each eye was converted to LogMAR value, the average was taken, and then the average LogMAR value was converted back to Snellen equivalent [5].

Findings

Clinical features, treatments and outcomes for the current study are summarized in Table 1 and Figure 1. The mean time between cataract surgery and the microbiologic diagnosis of endophthalmitis was 7.4 ± 5.2 months (range 1.5–17 months). Average time from obtaining the specimen to culture positivity was 7.7 ± 4.4 days (range 3–15 days). Three eyes (50%) presented with hypopyon and three eyes (50%) presented with keratic precipitates without hypopyon. Presenting visual acuity ranged from 20/25 to 2/200 and was 20/80 or better in five out of six patients.

The most common initial treatment was pars plana vitrectomy (PPV) with partial capsulectomy and intravitreal antibiotics (n = 3). The initial treatment for other patients was intravitreal antibiotics alone (n = 2), and PPV with intraocular lens (IOL) removal and intravitreal antibiotics (n = 1). Two out of 6 patients (33%) did not require further treatment after initial therapy, including one patient treated with PPV/partial capsulectomy and intravitreal antibiotics, and another initially treated with PPV/IOL removal and intravitreal antibiotics. Ultimately, three out of six patients (50%) underwent IOL removal.

The best-corrected visual acuity at last follow-up ranged from 20/20 to 20/70, with an average follow-up time after last treatment of 25 months (range: 2–59 months).

Discussion/Conclusion

The new nomenclature for *C. acnes* has been discussed in previous publications [1, 6]. Since the first case series of *P. acnes* was published in 1986 [3], some studies have proposed that milder cases may be managed initially with topical or intravitreal antibiotics alone, whereas advanced cases may be treated initially with PPV and capsulectomy [7]. In the current review, all case series of delayed-onset postoperative endophthalmitis caused by *C. acnes* are summarized in Table 2. In this review of the literature, IOL removal was the definitive treatment in 42/42 cases (100%). Partial capsulectomy/removal of the intracapsular plaque was slightly less effective: 44/57 (77%) of cases that underwent PPV/partial capsulectomy and intravitreal antibiotics did not have recurrence of inflammation. On the other hand, only 6/34 (18%) of cases treated initially with intravitreal antibiotics did not have recurrence of inflammation.

In the current series, removal of capsular bag and IOL was the initial treatment for one patient, and subsequent treatment for two patients with recurrent inflammation. Capsular bag and IOL removal was a definitive treatment in all three of these cases, consistent with findings from prior studies (Table 2) [8–11]. The other three cases in the current series did not require IOL explantation, including one patient who was managed with intravitreal and topical antibiotics alone. Importantly, visual outcomes for all patients in this series were generally favorable, regardless of initial treatment and in some cases in spite of a protracted treatment course. Therefore, neither IOL removal nor early surgical intervention was required for a good visual outcome.

The current case series supports an individualized approach in that there can be a role for initial non-surgical management of endophthalmitis caused by *C. acnes.* For example, Case 2 (initial intravitreal antibiotics) had a favorable outcome without any surgical intervention, whereas Case 1 (initial vitrectomy with capsulectomy and IOAB) avoided additional surgery and IOL removal after a treatment response to three post-surgical intravitreal injections of vancomycin. On the other hand, only one patient did not undergo any surgical management; thus, most patients initially managed with topical therapy/injection ultimately underwent surgical intervention to definitively treat *C. acnes* endophthalmitis [8, 9].

First-line antibiotic treatment for *C. acnes* endophthalmitis is intravitreal injection of vancomycin. A 1995 study of six *C. acnes* isolates from chronic postoperative endophthalmitis showed that all strains were sensitive to vancomycin, which was more bactericidal than penicillin and cefazolin [12]. *C. acnes* is typically susceptible to beta-lactams, weakly affected by aminoglycosides, and intrinsically resistant to metronidazole and fosfomycin [13]. Given the slow growth of *C. acnes* and the high sensitivity rate to antibiotics in older studies, antibiotic susceptibility testing was not performed in the current study and is not routinely performed in studies of *C. acnes* endophthalmitis*.* However, microbiologic data from the dermatology and prosthetic joint infection literature show the emergence of antibiotic-resistant strains of *C. acnes.*

In a 1977 study, nearly all 96 strains of *C. acnes* examined were susceptible to 14 different antibiotics, including penicillin G, cephalosporins, clindamycin, and vancomycin [14]. On the other hand, there was a very high resistance rate (91–100%) to the aminoglycosides gentamicin, tobramycin, and amikacin*.* Two other studies from 1972 (16 clinical isolates) and 1975 (six clinical isolates) also showed 100% susceptibility to clindamycin [15] and cephalosporins [15, 16].

More recent work has demonstrated the emergence of fluoroquinolone-, clindamycin-, and penicillin G-resistant *C. acnes* strains. In a 2016 study (106 samples from a variety of sterile body sites), none of the *C. acnes* strains were resistant to penicillin G, cephalothin and vancomycin, whereas 2.8 and 8.5% were resistant to ciprofloxacin and clindamycin, respectively [17]. In a 2013 study, all of the 33 clinical samples from prosthetic joint infections were susceptible to vancomycin, ciprofloxacin, moxifloxacin, cephalothin, and ceftriaxone; however, 4 and 7% of strains were resistant to penicillin G and clindamycin, respectively [18]. A much higher percentage clindamycin resistance (45%) was found in skin isolates from acne patients, particularly those with a history of topical or systemic antibiotic use [19]. Given the emergence of antibiotic-resistant strains, future work could focus on updating the antibiotic susceptibility profile for *C. acnes* in endophthalmitis.

The relative inefficacy of antibiotic treatment alone in *C. acnes* endophthalmitis could be explained by several unique mechanisms of resistance. For example, resistance genes (i.e., topoisomerase and DNA gyrase mutations) have been identified in *C. acnes* [6]; such mutations could potentially contribute to a poor response to standard antibiotics, including prophylactic intracameral fluoroquinolone use during cataract surgery [20]. Moreover, *C. acnes* resistance to fluoroquinolones develops in an anaerobic environment [6], and therefore may be promoted by its sequestration within an intracapsular plaque. In addition, biofilm formation by *C. acnes* confers resistance to antibiotics and promotes the production of virulence factors [21, 22]. Interestingly, the antibiotic rifampin is known to improve the penetration of vancomycin through biofilms [23], and oral rifampin has excellent intraocular penetration in humans [24]. Future work could investigate rifampin adjunct therapy to increase the clinical response rate of *C. acnes* endophthalmitis to intraocular antibiotics.

One patient in our study (Case 6) developed signs of endophthalmitis four days after Nd:YAG capsulotomy, which has been described as an inciting factor in four other cases of *C. acnes* endophthalmitis in the peer-reviewed literature (summarized in Table 3) [3, 25–27]. Other than the current study and the case series by Meisler et al. in 1986 [3], other case series (Table 2) did not evaluate Nd:YAG capsulotomy as a clinical feature of *C. acnes* endophthalmitis; therefore, it is possible that the number of these cases are underreported. Three cases of *C. acnes* endophthalmitis developed within the first week after Nd:YAG capsulotomy, whereas the other two cases presented later, at two weeks and one month. It is thought that the capsulotomy liberates sequestered bacteria and mobilizes their spread into the vitreous cavity. Endophthalmitis following Nd:YAG capsulotomy is not unique to *C. acnes*, and has been described for other bacteria, including *Staphylococcus epidermidis* [28] *and Corynebacterium* species [29].

The microbiologic diagnosis of *C. acnes* is particularly challenging for several reasons. First, the time to positive microbiology culture was an average of 8 days in our study and ranged from 5 to 10 days in other case series (Table 2). A study of bone and joint infections found that 21 and 9% of *C. acnes* cases were detected after day 7 or day 10 of culture, respectively, which highlights the importance of an extended culture time [30]. The microbiologic culture conditions are also important in the detection of *C. acnes*. The use of thioglycolate broth increases the sensitivity of microbiologic detection of *C. acnes* compared to anaerobic agar culture, which in turn is much more sensitive than aerobic agar culture. The low redox potential of thioglycolate broth supports the growth of *C. acnes,* and thioglycolate culture has been shown to yield a faster time to positive diagnosis when compared to agar plate culturing [30]. The optimization of culture conditions can increase the yield of *C. acnes* endophthalmitis. However, in cases of negative culture results, the detection of *C. acnes* by polymerase chain reaction may still be possible [31]. In one study of delayed-onset endophthalmitis after cataract surgery, 14/25 of culture-negative anterior chamber samples and 14/19 of culture-negative vitreous samples were PCR-positive for *C. acnes* [32]. It is likely that *C. acnes* endophthalmitis is underreported, given the challenges of microbiologic diagnosis and the fact that up to 30% of endophthalmitis cases are culture-negative [33].

Limitations to this study include a small sample size, a retrospective design, and short follow-up for some patients. In addition, there could have been treatment bias among the treating surgeons. Nevertheless, the findings of the current study are overall consistent with those of previous studies, as reviewed in Table 2.

In summary, chronic endophthalmitis caused by *C. acnes* is characterized by slowly progressive intraocular inflammation that is typically not diagnosed until months after cataract surgery [34]. Visual acuity outcomes are generally favorable. Microbiologic cultures may take up to two weeks for identification. Many patients diagnosed with endophthalmitis caused by

C. acnes eventually require PPV with capsulectomy or IOL removal. Nevertheless, a nonsurgical approach still remains a reasonable initial therapy, and visual acuity outcomes are generally favorable even in cases that require multiple treatments.

Statement of Ethics

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethics and consent were approved by IRB # 20120897 at the University of Miami/Bascom Palmer Eye Institute. The study is in accordance with HIPAA regulations.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

B.J.F., H.W.F., and N.A.Y. designed the research; B.J.F., H.W.F., N.A.Y., D.M., and X.Y. performed the research and analysis; B.J.F. and H.W.F. wrote the manuscript with assistance from X.Y. and N.A.Y.

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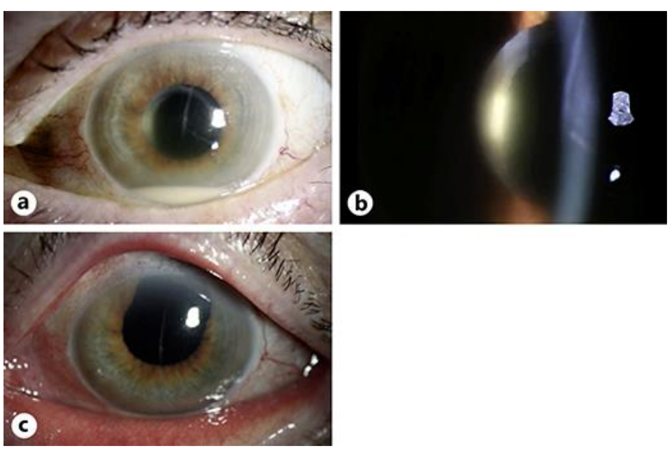

Fig. 1. External (**a**) and slit lamp (**b**, **c**) photographs of Case 6. **a** The patient presented with hypopyon, corneal edema, and conjunctival injection. The nasal aspect of the capsular bag has a white plaque, a characteristic finding in *C. acnes* endophthalmitis (seven months after cataract surgery, and prior to capsulectomy). **b** Corneal edema and white plaque in capsular bag (seven months after cataract surgery, and prior to capsulectomy). **c** Resolution of corneal edema and hypopyon (12 months after cataract surgery, and one month after IOL removal.

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Table 1. Clinical summary of patients with chronic endophthalmitis caused by *Cutibacterium* acnes

Case	Age/Sex/Eye	Time from cataract surgery to culture diagnosis, months	Initial BCVA	Last BCVA	Treatments	Follow-up time after last treatment, months
1	78/M/OD	11	20/25	20/20	**Initial:** PPV/capsulectomy/IOAB **Subsequent:** Intravitreal injection with vancomycin (×3)	59
2	50/F/OS	1.5	20/60	20/70	**Initial:** Intravitreal vancomycin (×1) **Subsequent:** Topical antibiotics (V/C)	2
3	69/F/OS	11	20/30	20/40	**Initial:** PPV/IOL removal and IOAB (V/C)	52
4	68/M/OS	17	20/80	20/60	**Initial:** Intravitreal injection with vancomycin **Subsequent:** Intravitreal injection with vancomycin (×5), STK (×1); PPV/IOL removal; secondary scleral sutured intraocular lens	31
5	80/M/OD	7	20/30	20/50	**Initial:** PPV/capsulectomy/IOAB (V/C)	3
6	71/M/OS	7	CF	20/40	**Initial:** PPV/capsulectomy/IOAB (V/C) **Subsequent:** PPV/IOL removal and IOAB (V)	6

V, vancomycin; C, ceftazadime; PPV, pars plana vitrectomy; IOAB, intraoperative antibiotics; IOL, intraocular lens; STK, sub-tenon's kenalog.

Table 2. Literature summary of clinical features and treatment outcomes of patients with chronic endophthalmitis[a] caused by *C. acnes*

Study	Meisler et al. [3]	Zambrano et al. [7]	Clark et al. [9]	Winward et al. [11]	Aldave et al. [8]	Fox et al. [34]	Shirodkar et al. [10]	Current study
Cases[a]	6	8	36	20c	21	12[e]	11	6
Average time from cataract surgery to culture diagnosis[#], presentation[@] or time to treatment[$], months	14[#]	13[#]	9[$]	N/A	5[$]	11[#]	13[#]	7[#]
Average time to culture growth, days	5	9	8	N/A	10	N/A	N/A	8
Average BCVA at presentation	20/30	20/800	See legend[c]	N/A	N/A	20/390	20/80	20/80
Average BCVA at last follow-up	20/40[f]	20/60	See legend[c]	20/80[g]	≥20/40[b]	20/50	20/50	20/40
Cases with recurrent inflammation after initial therapy with intravitreal antibiotics	N/A	2/5	12/12	7/8[h]	1/2	4/5	N/A	2/2
Cases with recurrent inflammation after PPV/partial capsulectomy, and intravitreal antibiotics	0/2	1/4	4/21	1/9[j]	4/9[i]	1/9	N/A	2/3
Cases with recurrent inflammation after PPV/IOL removal or exchange, and intravitreal antibiotics	0/2	0/2	0/12	0/8	0/13	0/2	N/A	0/3

N/A: Not available. [a] Number of cases excludes those that presented within 1 month of cataract surgery. [b] The average BCVA at last follow-up (6 months to 5 years after curative intervention) was equal to or better than 20/40 in all patient treatment groups. The authors excluded 6 patients with comorbid ocular pathology. [c] Mean change in BCVA was +3.8 Snellen lines. Final BCVA at last follow-up was equal or better than 20/40 in 50% of patients. [d] 14 of the patients in this series were described in other series [4, 7, 34]. [e] 4 of the patients in this report were described in other case series [7]. [f] 5 out of 6 patients had BCVA at last follow-up better than 20/40; 1 patient had 6/200 vision due to suprachoroidal hemorrhage/retinal detachment. [g] Average BCVA excludes 2 patients with final VA of NLP. [h] 3 out of 5 patients who failed initial treatment with intravitreal antibiotics were cured by PPV. The other 2 required further intervention. [i] Another 10 patients in this series were initially treated with PPV and IOAB; 5 out of these 10 did not require further therapeutic intervention. [j] Entirety of the white plaque was not removed in the 1 case of recurrent inflammation.

Table 3. Literature summary of clinical features of patients with endophthalmitis caused by *C. acnes* following Nd:YAG capsulotomy

	Patients, *n* (% of total in case series)	Days from Nd:YAG capsulotomy to onset of symptoms or clinical signs of endophthalmitis
Case series		
Current study	1 (17%)	4
Meisler et al. [3]	1 (17%)	30
Case report		
Carlson et al. [25]	1	7
Chaudhry et al. [26]	1	7
Tetz et al. [27]	1	11