Review Article

iMedPub Journals
www.imedpub.com

Journal of Eye and Vision

2019
Vol.2No.1:3

Burkholderia cepacia: A Cause of Post-Operative Endophthalmitis

Ogugua Ndubuisi Okonkwo[1,2]*, Adekunle Olubola Hassan[1,2] and Toyin Akanbi[2]

1 Eye Foundation Retina Institute, Lagos, Nigeria
2 Eye Foundation Hospital, Abuja, Nigeria

***Corresponding author:** Ogugua N Okonkwo

o_okonkwo@yahoo.com

Eye Foundation Retina Institute, Lagos, Nigeria

Tel: 234 8035027308

Citation: Okonkwo ON, Hassan AO, Akanbi T (2019) *Burkholderia cepacia*: A Cause of Post-Operative Endophthalmitis. J Eye Vis Vol.2No.1:3

Abstract

Background: Intraocular infection from *B. cepacia* can be persistent and devastating, yet it is rarely discussed. We reviewed reported cases of post operative endophthalmitis due to *B. cepacia* to determine the clinical course and outcome of treatment.

Method and findings: Search was done for reported cases of culture proven *Burkholderia cepacia* ocular infection. Cases in which *B. cepacia* alone was associated with post operative endophthalmitis were identified and used for this analysis and review. Trauma associated cases, mixed microbial infections and other non-intraocular infections were excluded from the analysis.

There were eight reports in literature over a 26 year period, including three case reports and five case series of post operative endophthalmitis secondary to *B. cepacia*, accounting for 34 cases in total. Majority of the cases (N=29 eyes, 85%) occurred post cataract extraction. Other cases were post filtering and cataract surgery 1 eye, post vitrectomy 3 eyes, post penetrating keratoplasty 1 eye and post intravitreal antiVEGF 1 eye. The visual outcome of treatment was 20/30 in two eyes (one each in post cataract surgery and post antiVEGF eyes). Several eyes had poor visual outcome. 14 eyes, 41% had a visual outcome of less than 6/60. Recurrence after initial treatment was a common clinical presentation, reported in 4 out of the 8 reports.

Conclusion: Though a rare cause of post-operative endophthalmitis, *Burkholderia cepacia* infection ought to be recognized as an important cause of gram negative infection occurring after intraocular surgery and results in considerable visual loss in several cases. Significant gaps still exist in the knowledge and best practice required to prevent recurrence and improve visual and anatomical outcome.

Keywords: Ocular infection; Post-operative endophthalmitis; Vision; Cystic fibrosis

Received: May 02, 2019; **Accepted:** June 06, 2019; **Published:** June 13, 2019

Introduction

Post-operative endophthalmitis is a devastating intraocular complication of ocular surgery [1]. It occurs at times as a result of exogenous inoculation of the infective microbe(s) into the eye during the peri operative or post-operative stages of surgery, but can also occur as a result of endogenous spread of the infective organism from foci of infection within the patient.

The more common causes of post operative infective endophthalmitis are gram-positive microbes, coagulase negative staphylococci such as *Staphylococcus epidermidis* accounting for most of the cases [2]. However, there are other rare causes of infection. Infection due to rare species also results in significant ocular disease. Several of the rare microbes are gram-negative organisms [3], including pseudomonas

species such as *Burkholderia cepacia* (previously known as *Pseudomonas cepacia*) [4-14].

Burkholderia cepacia is a rare gram-negative rod, oxidase-positive, non-fermenting bacillus. It is known to cause infection in cystic fibrosis, chronic granulomatous diseases and immuno-compromised patients. It can also be the cause of infection in healthy individuals, though it is less virulent in immuno competent hosts. Known to be a cause of nosocomial infection, it can colonize antiseptic including benzalkonium chloride and chlorhexidine [15,16].

There are currently several reports of *B. cepacia* causing post cataract surgery endophthalmitis, one case report of post intravitreal antiVEGF injection, one report of post penetrating keratoplasty infection and one case series of post vitrectomy endophthalmitis in which *B. cepacia* was isolated from 3 eyes. It has been isolated from a case of post traumatic endophthalmitis [17]. Lastly, there is a case report of *B. cepacia* keratitis post Lasik [18] and another report of *B. gladioli* causing keratitis and consecutive recurrent endophthalmitis post penetrating keratoplasty [19].

Infection with *B. cepacia* has been reported to be difficult to treat and may also be associated with recurrence, making it a unique infection and one to note. Mechanism of this intra ocular infection and resistance to antimicrobial include the fact that the organism has an unusually large genetic make up that accounts for its microbiological versatility. It also produces lipopolysaccharide and β lactamase that renders some antibiotics ineffective against it [20].

Magnitude of Problem

Gram negative endophthalmitis in general is less common than gram positive. However they constitute a more fatal disease with poorer prognosis following treatment. Irvine et al. [17] reported 52 patients (53 eyes) with culture-proven gram-negative endophthalmitis between January 1982 and December 1990 and noted that *Pseudomonas aeruginosa* which was isolated in 12 out of 53 and *Haemophilus influenzae* in 10 out of 53 were the most frequent isolates in this series.

In one report *Burkholderia cepacia* was the causative agent in 14 (1.8%) of 744 culture-positive cases seen in the endophthalmitis registry over a 5 years period [8].

Our search using popular search engines including Google scholar and Medline revealed eight reports including three case reports and five case series, of culture proven *B. cepacia* post-operative endophthalmitis between 1992 and 2018 (over a 26 year period). Majority of the cases (N=28 eyes, 82%) occurred following cataract extraction. Other cases were post filtering and cataract surgery 1 eye, post vitrectomy 3 eyes, post penetrating keratoplasty 1 eye and post intravitreal antiVEGF 1 eye. Within these reports, there were a total of 34 post operative endophthalmitis cases. This may not represent all the cases of post operative *B. cepacia* endophthalmitis that occurred during this period, since some cases may have gone un-reported and some may have been undiagnosed as culture was not sensitive to detect *B. cepacia* or culture was not done.

Predisposition

Aside from its contamination of know antiseptics, *B. cepacia* has also been known to contaminate ophthalmic solutions such as balanced salt solution, hyaluronic acid and trypan blue [14] phacoemulsification machine fluid units and hand piece. Also there has been a report of contamination of topical anesthetic eye drops resulting in a series of post-operative infections [7].

It is know that infection with *B. cepacia* is seen in cystic fibrosis and other debilitating chronic infection such as in the presence of granulomatous disease [21].

It is, however, not known if the presence of other systemic disease such as diabetes and use of insulin as previously reported [1], or if immunosuppression significantly increases the risk of post operative *B. cepacia* endophthalmits. In one report of a case having multiple recurrence and eventual poor outcome the patient was diabetic and had a poor glycemic control [10].

Clinical Features and Diagnosis

Often, infection with *B. cepacia* presents within days or few weeks after surgery. Most reported cases have presented, with an acute presentation after cataract surgery characterized by loss of vision and signs of intra ocular inflammation including pain. It can rarely present as a delayed-onset postoperative endophthalmitis [8].

The clinical signs vary considerably. There may be only a mild cellular reaction and flare initially which may progress to severe anterior chamber reaction (associated with severe pain), despite treatment. Hypopyon may be a feature and has been reported in several of the cases. The cornea may show a significant degree of involvement or only mild haze. In some cases keratitis and cornea abscess has been reported.

Rarely the patient may present in an unusual pattern too, with only a blur in vision [4]. Recurrence and persistent inflammation despite treatment is common and has been reported by several authors. This is related to its multidrug resistance.

Microbiological diagnosis is made by identification of the microbe after vitreous culture using standard biochemical techniques.

B. cepacia infection can co exist with other organisms such as *Pseudomonas aeruginosa* [5,13,14]. The behavior of the microbe in this polymicrobial situation may defer from what is already known in relation to its virulence and clinical presentation.

Microbial Sensitivity

Often *B. cepacia* shows multi drug resistance to a number of commonly used antibiotics. The multi-drug resistance of *B. cepacia* is due to rough lipopolysaccharide encasing the organism. The organism produces lipopolysaccharide and beta lactamase that renders the antibiotics ineffective against it [22].

Resistance has been reported to a wide range of anti microbial

including quinolones (e.g. ciprofloxacin, levofloxacin, moxifloxacin), ceftriaxone, cefoxitine, tobramycin, amikacin, gentamicin and vancomycin,

Several authors have reported sensitivity to ceftazidime. Also reported, is sensitivity to co-trimoxazole, cefotaxime and piperacillin/tazobactam.

Ceftazidime generally has demonstrated *in vitro* efficacy for a good number of gram-negative organisms causing endophthalmitis and should be used when this group of organisms are suspected or isolated. It has also been recommended for use by the endophthalmitis vitrectomy study (EVS) [23].

Treatment

Strategies that have been used for treatment of cases of post operative *B. cepacia* endophthalmitis is shown in **Table 1**. This consists of topical antibiotics (fortified in some cases) and steroids, subconjunctival injection of antibiotics, intravitreal antibiotics (administered in a tap and inject fashion), pars plana vitrectomy, explantation of intraocular lens, systemic antibiotics, as well as topical cycloplegics.

The treatment is tailored according to the microbial sensitivity pattern after culture and microscopy evaluation of vitreous samples.

Generally, it is a rare cause of intra ocular infection and may be difficult to treat. As is the general trend in post operative infections, treatment commences as soon as the patient presents and usual consists of topical preparations as well as initiating intravitreal injection of antibiotics, with or without steroids. In several case reports of *B. cepacia* endophthalmitis, multiple intravitreal injections have been required either on its own or at the conclusion of vitrectomy. Systemic i.e., oral or intravenous antibiotics were used in some cases. There is absence of specific evidence relating to treatment for *B. cepacia* endophthalmitis, except as is provided by the general knowledge and guidance of the EVS [23]. The several treatment approaches listed in **Table 1** point to the fact that knowledge and treatment strategy for *B. cepacia* post operative endophthalmitis is lacking. This is a significant gap and need to be met. However reports on gram-negative organisms such as by Duan et al. [3] and Irvine et al. [17] provide useful information on antimicrobial sensitivity and treatment.

Table 1 Summary of the 9 case reports and series from 1985-2018 in literature.

Year Reported	No of Cases	Surgery	Post op. Presentation	Treatment	Visual Outcome	Recurrence After Initial Response to Treatment	Remark
2018[4]	3	CE	2 to 3 weeks	T, IVI, PPV first 2 pts.	20/30 in 3rd patient	Recurrence in 2.	Phthisis bulbi X 1
				T, IVI 3rd patient.			Evisceration X 1
2018[5]	3	Vitrectomy with silicone oil	1week,	T, IVI, PPV all 3	HM, LP, HM	Recurrence in 3.	Phthisis bulbi X 1
2014[6]	1	Anti-VEGF (Ranibizumab)	2 weeks	PPV, IVI	20/30	None	Primary diagnosis was ARMD.
2013[7]	13	CE	Acute onset		6/60 or better X 9		Infection from contaminated anesthetic drops
					1/60 X 1		
					LP X 3		
2011[8]	10	CE (9)		Oral, IVI	6/60 or better in 6	Recurrence	
		PKP (1)					
2006[9]	2	CE	2 weeks	T, IVI,IV, PPV	20/63	None	
				T, IVI, PPV			
					20/50		
2005[10]	1	CE	4 weeks	PPV, IOL explanation, IVI, T , Oral	NLP	Severe Recurrence	Phthisis bulbi
							(known diabetic with poor glycaemic control).
1985[11]	1	Trabeculectomy +	Chronic Iridocyclitis for 8 months.	SC, IVI, IV			First documented case of *P. cepacia* endophthalmitis
		CE	Then acute hypopyon and vitritis.				

Abbreviations: CE: Cataract Extraction; PKP: Penetrating Kerato Plasty; T: Topical; IVI: Intravitreal Injection; IV: Intravenous; SC: Sub Conjunctival; IOL: Intraocular Lens; PPV: Pars Plana Vitrectomy; NLP: No Light Perception; LP: Light Perception; HM: Hand Motion

Outcome of Treatment

Post treatment visual outcome in eyes with post operative endophthalmitis is usually guarded. Poor vision could arise from toxins within the vitreous cavity, direct effect on the retina of the infecting microbe, toxicity from the intravitreal antibiotics and intra ocular inflammation.

In several reported cases the visual outcome following treatment of post operative *B. cepacia* endophthalmitis is poor **(Table 1)**. There were 14/34 (41%) eyes in which the vision after treatment was less than 6/60. Also there was phthisis bulbi reported in three out of the 8 reports.

Prognosis

The prognosis following *B. cepacia* post operative endophthalmitis varies significantly. Though some of the reports have reported remarkably good vision after management [4,6,9] there are 4 reports out of the 8 presented that have suggested recurrence as an important feature of the presentation. The recurrence of diseases tends to occur within days or weeks and is associated with poorer anatomical and visual outcome, as 3 out of the 4 reports of recurrence also reported occurrence of phthisis bulbi or evisceration **(Table 1)**. Therefore mechanisms to overcome this recurrence are desirable. Some known factors that could be responsible for recurrence include insensitive antibiotics given at the initial treatment, Gram-negative bacillus multidrug resistance and inadequate exposure time to antibiotics [24].

Conclusion

Post operative endophthalmitis due to *B. cepacia* is rare and appears to be more difficult to treat. Since the initial reports over 3 decades ago, there are presently several more reports implicating this opportunistic infection, mostly thought to be of significance in cystic fibrosis patients. It is responsible for poor visual outcome after intra ocular surgery. Going by the current trend, it is likely that the numbers of *B. cepacia* post operative endophthalmitis will continue to increase. It should be recognized as an important cause of gram-negative post operative infection. Since the visual outcome of therapy in 41% of eyes in this review is less than 6/60, strategies for early detection and optimum treatment should be investigated. There is still significant gap in knowledge to improve current outcomes including the treatment of possible ceftazidime resistant strains [25].

References

1 Silpa-Archa S, Papirachnart A, Singhanetr P, Preble JM (2019) Risk factors for endophthalmitis after cataract surgery in diabetic patients: A case control study. Int J Ophthalmol 12: 417-423.

2 Mollan SP, Gao A, Lockwood A, Durrani OM, Butler L (2007) Postcataract endophthalmitis: Incidence and microbial isolates in a United Kingdom region from 1996 through 2004. J Cataract Refract Surg 33: 265-268.

3 Duan F, Wu K, Liao J, Zheng Y, Yuan Z, et al. (2016) Causative microorganisms of infectious endophthalmitis: A 5-year retrospective study. J Ophthalmol 2016: 6764192.

4 Deka A, Siddique MA, Saikia SP (2018) Burkholderia cepacia endophthalmitis: An unusual presentation. J Ophthalmic Vis Res 13: 504-507.

5 Okonkwo ON, Hassan AO, Oderinlo O, Gyasi ME (2018) Burkholderia cepacia, a cause of post pars plana vitrectomy silicone oil related endophthalmitis: Clinico-pathological presentation and outcome of management. Int J Retina Vitreous 4: 35.

6 Saffra N, Moriarty E (2014) Burkholderia cepacia endophthalmitis, in a penicillin allergic patient, following a ranibizumab injection. BMJ Case Rep pii: bcr2013202075.

7 Lalitha P, Das M, Purva PS, Karpagam R, Geetha M, et al. (2014) Postoperative endophthalmitis due to Burkholderia cepacia complex from contaminated anesthetic eye drops. Br J Ophthalmol 98: 1498-1502.

8 Sachdeva V, Pathengay A, Joseph J, Sharma S, Das T (2011) Burkholderia cepacia endophthalmitis: Clinico-microbiologic profile and outcomes. Retina 31: 1801-1805.

9 Eser I, Altan T, Stahl JE, Aydin MD, Inan N, et al. (2006) Two cases of Burkholderia cepacia endophthalmitis. Br J Ophthalmol 90: 1211.

10 Pathengay A, Raju B, Sharma S, Das T (2005) Recurrent endophthalmitis caused by Burkholderia cepacia. Eye 19: 358-359.

11 Del Piero E, Pennett M, Leopold I (1985) Pseudomonas cepacia endophthalmitis. Ann Ophthalmol 17: 753-756.

12 Ornek K, Ozdemir M, Ergin A (2009) Burkholderia cepacia keratitis with endophthalmitis. J Med Microbiol 58: 1517-1518.

13 Mitra S, Padhi TR, Basu S, Priyadarshini SR, Sharma S (2018) Unusual microbiological presentations in polymicrobial post-operative endophthalmitis and their clinical correlations. Int Ophthalmol Pp: 1-6.

14 Sunenshine R, Schultz M, Lawrence MG, Shin S, Jensen B, et al. (2009) An outbreak of postoperative gram-negative bacterial endophthalmitis associated with contaminated trypan blue ophthalmic solution. Clin Infect Dis 48: 1580-1583.

15 Craven DE, Moody B, Connolly MG, Kollisch NR, Stottmeier KD, et al. (1981) Pseudobacteremia caused by povidone-iodine solution contaminated with Pseudomonas cepacia. N Engl J Med 305: 621-623.

16 Sobel JD, Hashman N, Reinherz G, Merzbach D (1982) Nosocomial Pseudomonas cepacia infection associated with chlorhexidine contamination. Am J Med 73: 183-186.

17 Irvine WD, Flynn HW, Miller D, Pflugfelder SC (1992) Endophthalmitis caused by gram negative organisms. Arch Ophthalmol 110: 1450-1454.

18 Reddy JC, Tibbetts MD, Hammersmith KM, Nagra PK, Rapuano CJ (2013) Successful management of Burkholderia cepacia keratitis after LASIK. J Refract Surg 29: 8-9.

19 Ritterband D, Shah M, Cohen K, Lawrence J, Seedor J (2002) Burkholderia gladioli keratitis associated with consecutive recurrent endophthalmitis. Cornea 21: 602-603.

20 Joklik WK, Willet HP, Amos DB, Wilfert CM (1988) Zinsser microbiology,

19th Edition. East Norwalk, Conn: Appleton & Lange Pp: 488-489.

21 Middleton PG, Kidd TJ, Williams B (2005) Combination aerosol therapy to treat Burkholderia cepacia complex. Eur Respir J 26: 305-308.

22 Simpson IN, Finlay J, Winstanley DJ, Dewhurst N, Nelson JW, et al. (1994) Multi-resistance isolates possessing characteristics of both Burkholderia (Pseudomonas) cepacia and Burkholderia gladioli from patients with cystic fibrosis. J Antimicrob Chemother 34: 353-361.

23 Han DP, Wisniewski SR, Wilson LA, Barza M, Vine AK, et al. (1996) Spectrum and susceptibilities of microbiologic isolates in the Endophthalmitis Vitrectomy Study. Am J Ophthalmol 122: 1-17.

24 Stern GA, Engel HM, Driebe WT (1990) Recurrent postoperative endophthalmitis. Cornea 9: 102-107.

25 Dave VP, Pathengay A, Nishant K, Pappuru RR, Sharma S, et al. (2017) Clinical presentations, risk factors and outcomes of ceftazidime-resistant Gram-negative endophthalmitis. Clin Exp Ophthalmol. 45: 254-260.