

## A CASE SERIES OF ACUTE POSTOPERATIVE ENDOPHTHALMITIS: MANAGEMENT AND OUTCOMES

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### ABSTRACT

#### Background:

Endophthalmitis is one of the rare and most devastating complications of intraocular surgery. Although the prevalence of post-cataract surgery endophthalmitis is very small, it has become an important eye health problem.

#### Case Presentation:

Six patients, 5 male and 1 female, were diagnosed with post-phacoemulsification endophthalmitis on the same day. Four patients had a visual acuity of 1/300, and two patients had 6/60. All patients underwent intravitreal injection of vancomycin-ceftazidime, and culture samples were taken from the vitreous tap and AC tap. Five patients were planned to undergo pars plana vitrectomy. Intravitreal injection of triamcinolone acetonide was performed on 1 patient, due to macular oedem. *Brevundimonas diminuta* was found from 1 patient and *Stenotrophomonas maltophilia* from 1 patient. Final visual acuity in 4 patients was > 6/30, and 3/60 in 1 patient.

#### Discussion:

Management must be carried out immediately, once there is a suspicion of acute postoperative endophthalmitis. All patients had intravitreal injection of vancomycin-ceftazidime. Pars plana vitrectomy was performed on 5 patients with 80% having final visual acuity > 6/30. Intravitreal injection of antibiotics followed by pars plana vitrectomy can provide a good prognosis for final visual acuity, although various factors predispose to poorer prognosis.

#### Conclusion:

Intravitreal injection of antibiotics and pars plana vitrectomy is a treatment for acute postoperative endophthalmitis, where this action will provide a good prognosis for the patient's final visual acuity if done immediately.

**Keyword:** acute endophthalmitis, management, outcome, post-operative.

### BACKGROUND

Endophthalmitis is one of the complications following an intraocular surgery which rarely happens but can be fatal to visualization. A common intraocular surgery, which is often carried out, is cataract surgery. Although its prevalence is very low, the occurrence of endophthalmitis can create a huge problem to the public health.<sup>1</sup> The cataract surgery's technique has transformed from an extraction of the intracapsular to a technique assisted by femtosecond laser. The aims of this transformation were enhancing the visualization and decreasing the risks of complications. Its occurrence must be avoided by all ophthalmologists. Whilst

proper patient selection, careful surgery, and strict adherence to asepsis may help prevent this complication, clinicians also use various antiseptic protocols and administration of antibiotics to prevent or combat intraocular contamination.<sup>2</sup>

According to the study published on ophthalmology literature, the incidence of endophthalmitis was quite various, ranging from 0.03% to 0.2% worldwide,<sup>3</sup> while in Indonesia its number reached 0.18%.<sup>4</sup> Based on the research which was held at six hospitals in Indonesia, including two private hospitals in Bali, the results showed that the complication rate of post-cataract endophthalmitis was 1.2%.<sup>5</sup> Several risk factors contributing to the incidence were

senescence (80 years old and above), immunocompromised condition due to systemic illness, focal infection inside and around the eyes, posterior capsule tear, and wound leakage. Lundstrom *et al.* (2015) analyzed the national data register of cataract in Sweden and found that not giving intracameral antibiotics, vitreous association, and age over 85 years as the three most common risk factors.<sup>6</sup> In another large epidemiological research by Jabbarvand *et al.* (2016), diabetes mellitus, age over 80 years, large conventional incision during the extraction of extracapsular cataract, and the perioperative association with vitreous were all linked to higher risk to contract endophthalmitis. The authors also report that no prophylaxis compared to preoperative antibiotic and subconjunctiva injection at the end of the procedure are associated with 40%-50% decreasing risks of endophthalmitis ( $p = 0.2$ ) and no case of endophthalmitis was found in the group which received intracameral cefuroxime.<sup>1</sup>

### CASE PRESENTATION

Six patients consisting of 5 males and 1 female, ranging in age from 58 to 84 years, came to Sanglah General Hospital with chief complaint of blurred vision after undergoing cataract surgery at a private hospital in Denpasar. All patients underwent cataract surgery on September 4<sup>th</sup>, 2020. On average, patients came 7-10 days after cataract surgery. The patients felt the blurred vision about 2-3 days after the surgery. All of them received oral cefixime, oral methylprednisolone, topical antibiotics such as levofloxacin or ofloxacin, topical anti-inflammatory prednisolone with some of them received intraocular pressure (IOP)-lowering drug such as acetazolamide, KSR, and timolol 0.5% eye drops.

#### Case 1

A 63-year-old male was with visual acuity (VA) 6/60 pinhole not improved (PHNI), which had improved after cataract surgery, from 1/60 to 6/12 on the first postoperative day. Clinical finding shows palpebral spasm, conjunctival and pericorneal injection, corneal edema and descemet fold, deep anterior chamber, fibrin, pupillary mid-dilation, intraocular lens (IOL) (+), and fundal reflex (FR) (+) but the details were difficult to evaluate. Ultrasound examination found moderate-severe vitreous opacity that show an endophthalmitis. His IOP was 7 mmHg and the patient denied any systemic disease. The patient received an intravitreal injection of vancomycin-ceftazidime 8 days after the surgery. Culture sample were taken from the anterior chamber (AC) tap, and no bacterial growth was found. He underwent pars plana vitrectomy (PPV), endo laser (EL), washing AC, and intracameral cefazolin injection 2 days after the intravitreal injection of antibiotics was administered. Visual acuity the day after the PPV procedure was 6/60 and 3 weeks after was 6/30 PH 6/12.

#### Case 2

A 72-year-old male with VA 1/300, which had improved after cataract surgery, from 4/60 to 6/15 on the first day. Clinical finding shows palpebral spasm, conjunctival and pericorneal injection, corneal edema and desc fold, shallow AC fibrin, synechia and pupil reflexes (-), IOL (+), FR (-), with ultrasound examination found severe vitreous opacity. His IOP was 14 mmHg and he denied any systemic disease. He received an intravitreal vancomycin-ceftazidime 8 days after. Culture sample was taken from the AC tap and no microbial colonization was found. He underwent PPV, EL, washing AC, intracameral injection of cefazoline 2 days after the intravitreal injection. The visual acuity after PPV was 2/60 and 1 month after was 6/24 PH 6/18.

**Case 3**

A 58-year-old male with visual acuity 1/300 on the right eye and it got worse after the cataract surgery, from 6/18 to 6/30. Clinical finding shows palpebral spasm, conjunctival and pericorneal injection, subconjunctival bleeding (SCB), shallow AC, fibrin, pupil reflex (-), IOL (+), FR (-), with ultrasound examination found severe vitreous opacity. His IOP was 8 mmHg and he had a history of hypertension. The patient had intravitreal antibiotic injection 6 days after the procedure. No culture sample was taken. He underwent PPV, EL, intracameral Cefazoline injection 8 days after the intravitreal antibiotic injection. The VA after PPV was 2/60 and 1 week after was 6/30 PH 6/21.

**Case 4**

A 64-year-old female with VA 6/60 PH 6/45 on the right eye and it got better from a light perception to 6/45 one day post operation. Clinical finding shows palpebral spasm, conjunctiva and pericorneal injection, edema and desc fold on cornea, shallow AC, hipopion (+), fibrin, pupil reflex (-), IOL (+), FR (+) with details hardly assessed, with ultrasound examination found moderate-severe vitreous opacity. Her IOP was 9 mmHg and the patient had a history of diabetes mellitus (DM) for more than 10 years and regularly used insulin. She had intravitreal antibiotic injection 9 days after the surgery. Culture sample were taken from the AC tap and no bacterial colonization was found. She underwent PPV, EL, intravitreal triamcinolone acetonide (IVTA) injection, intracameral Cefazoline injection 9 days after the intravitreal injection. A steroid intravitreal injection was done because of an inflammation found on the macula during the surgery. The VA one day after PPV was 6/30 and 1 week after was 6/18 PH 6/15.

**Case 5**

An 84-year-old male, whose left eye VA was 1/300, with VA before was 2/60 to 1/300 on the first postoperative day. Clinical finding shows palpebral spasm, conjunctival and pericorneal injection, SCB, corneal edema and desc fold, deep AC, with cells (2+), flare (2+), fibrin, pupillary reflex (-) and posterior synechia, IOL (+), FR (-), with ultrasound examination found severe vitreous opacity. His IOP was 15 mmHg and the patient denied any history of systemic disease. The patient received an intravitreal injection of vancomycin-ceftazidime antibiotic 10 days after surgery. Culture sample were taken from the vitreous tap, and found *Stenotrophomonas maltophilia* that resistant to cefotaxime, levofloxacin, cefuroxime, cefoperazone, and trimethoprim/sulfamethoxazole. He underwent PPV, EL, washing AC, intracameral injection of Cefazoline 4 days after intravitreal injection of antibiotics. Visual acuity the day after the PPV procedure was 1/300, with VA 2 weeks after was 3/60.

**Case 6**

A 63-year-old male, whose right eye VA was 1/300. Clinical finding shows in the form of palpebral spasm, conjunctival injection, clear cornea, deep AC, with cells (+2), flare (+2), pupillary reflex (+), IOL (+), RF (+) and details difficult to evaluate, with ultrasound examination found severe vitreous opacity. The patient's IOP was 10 mmHg and the patient denied any history of systemic disease. The patient underwent an intravitreal injection of vancomycin-ceftazidime antibiotic 11 days after surgery. Culture sample were taken from the AC tap, and found *Brevundimonas diminuta* that resistant to ceftriaxone, cefepime, gentamicin, ciprofloxacin, levofloxacin, amikacine, trimethoprim/sulfamethoxazole, and cefazolin. The patient was planned for vitrectomy surgery, but he refused the

action and forced to go home. Until the end of hospitalization, the patient had a visual

acuity of 1/300 and never returned to Sanglah General Hospital.

**Table 1. Overall Patients Summary**

Case	Gender/ Age	Laterality	Visual acuity	IOP (mm Hg)	Systemic ds	Intra- vitreous- AB ( <del>vanco- cefta</del> )	Time of inj. after surgery (day)	VA after injection	Culture		Culture result	PPV (days after the injection)	VA post PPV	IOP (mmHg)	Last VA
									AC tap	Vit. tap					
1	M / 63 <del>yo</del>	Right	6/60 PHNI	7	-	+	8		+		Negative	+ (2)	6/60	9	6/30 PH 6/12
2	M / 72 <del>yo</del>	Left	1/300	14	-	+	8	6/60	+		Negative	+ (2)	2/60	14	6/24 PH 6/18
3	M / 58 <del>yo</del>	Right	1/300	8	Hyper- tension (+)	+	6	1/300		Undone	Undone		2/60	18	
4	F / 64 <del>yo</del>	Right	6/60 PH 6/45	9	DM (+)	+	9	1/300	+		Negative	+ (+ IVTA) (9)	6/30	13	6/18 PH 6/15
5	M / 84 <del>yo</del>	Left	1/300	15	-	+	10	6/60 PH 6/48		+	<del>Stenotro- phaerococ- melliphilia</del>	+ (4)	1/300	19	3/60
6	M / 63 <del>yo</del>	Right	1/300	10	-	+	11	1/300	+		<del>Brevibac- terium diploide</del>	Reject	-	-	No data

**DISCUSSION**

Endophthalmitis is one of the complications following an intraocular surgery which rarely happens but can be fatal to visual acuity Six patients consisting of 5 males and 1 female, ranging in age from 58 to 84 years, came with chief complaint of blurred vision after undergoing cataract surgery on the same day. A cohort study in the United States stated that male patients had a greater risk (Relative Risk = 1.23) for endophthalmitis after cataract surgery.<sup>7</sup> Another study in the same country in 2006-2011 also stated male sex as a risk factor for this illness after the same procedure

(1.26x higher risk).<sup>8</sup> The opposite results were obtained from several other studies such as a study based on the Swedish National Study which recorded post-cataract endophthalmitis patients from 2005-2010, where there were more female patients than males (86 vs 49 people).<sup>9</sup> Another study in Iran (2006-2014), found more females, as many as 53.6%.<sup>1</sup> However, there is no specific theory regarding gender as a risk factor for endophthalmitis after cataract surgery.<sup>9</sup>

On average, patients came 7-10 days after cataract surgery. The patients

felt blurred vision about 2-3 days after cataract surgery. Four patients (case 2, 3, 5, 6) had VA 1/300, while the rest had 6/60 PHNI (case 1) and 6/60 PH 6/48 (case 4). A study in 2011 showed that from 118 patients which enrolled in it, 22% suffered endophthalmitis with a late onset post operation and 78% suffered endophthalmitis with acute onset. According to Endophthalmitis Vitrectomy Study (EVS), an acute onset is defined as an infection within 6 weeks after operation, while the late onset happened more than 6 weeks after the procedure. In the same study, most of the subjects (89%) had ≤ 5/200 visual acuity during admission.<sup>10</sup>

All patients had an intravitreal injection of vancomycin-ceftazidime. Vancomycin retains good coverage for Gram-positive in most areas, although some resistance has been reported. A previous report by Yanuzzi *et al* (2017), which analyzed the isolation of microbes from endophthalmitis cases in Miami between 1996-2005 and found no Gram-positives resistant to vancomycin.<sup>11</sup> The Gentile group (2014) reported 25 years of data from New York, of 727 Gram-positive organisms, only 2 showed resistance to vancomycin.<sup>12</sup> Khera *et al* (2013), more recently presented data from India and the United States, where of the 448 Gram-

positive isolated, 4 showed definite resistance and 3 with intermediate resistance.<sup>13</sup>

Ceftazidime has come as second line agent which is quite popular because of the Gram-negative scope and the low side effects compared to aminoglycoside. Meanwhile, the general scope is not as wide as vancomycin. Reddy *et al* (2015) reported data from Hyderabad, India, where Gram-negative bacteria dominated as much as 64.4% from the isolated and from these, as many as 18% showed resistance to ceftazidime, while 13% showed resistance to amikacin. They concluded that ceftazidime is still a reasonable choice as a first-line Gram-negative antibiotic in which the risk of macular infarction is associated with amikacin administration. The disadvantage of substituting aminoglycoside antibiotics with ceftazidime, is that they have been shown to have a synergistic effect on Gram-negative organisms when used in combination with vancomycin. Thus, in centers with lower rates of Gram-negative infection, ceftazidime remains the safest choice, where statistically the probability of resistance is low and coverage for Gram-positive can be increased, while centers with Gram-negative rates higher grades should consider various other antibiotics with appropriate Gram-negative coverage based on local microbiology.<sup>14</sup>

Third- and fourth-generation fluoroquinolones have been shown to be superior to ciprofloxacin in maintaining Gram-negative coverage.<sup>15</sup> In particular, Moxifloxacin has been shown to have the strongest in vitro activity against Gram-positive and Gram-negative isolates of endophthalmitis bacteria when compared to other fluoroquinolones.<sup>16</sup> This drug has been shown to have good effect as intracameral prophylaxis in cataract surgery, and Haripya *et al* (2017), recently reported a threefold reduction in cases of

endophthalmitis with its use in phacoemulsification.<sup>17</sup>

During intravitreal injection, culture sample is also taken to determine the organism which is responsible to cause endophthalmitis. Four out of five patient's samples (case 1, 2, 4, 6) were taken from the aqueous humor, and one of them (case 5) from the vitreous. Of the 5 patients, 3 of them (case 1, 2, 4) showed no pathogen in the culture results. The other 2 cases showed *Brevundimonas diminuta* (aqueous humor) and *Stenotrophomonas maltophilia* (vitreous).

Ocular fluid sampling was the method for establishing the primary microbial diagnosis at the time of EVS and this has not changed since then. However, the technique of analyzing such fluid samples has evolved over time and can now provide more information and with faster results. The vitreous tap technique with or without an anterior chamber tap is the technique commonly used. The AC tap is procedurally more complex, because it is not expected to cause damage to the iris and lens. The vitreous tap can be done with the naked eye, while the AC tap is recommended to use a slit lamp or microscope, and many technical difficulties may be encountered during its collection. Rates of positive vitreous culture ranging between 48% and 75% using gram stain and culture methods. These findings are primarily based on the results of a vitreous tap or biopsy, which can be difficult to obtain in the acute setting because of the possibility of a dry tap, whereas delays in access to operating room hinder a timely diagnostic and therapeutic vitrectomy. Viscosity of the vitreous may decrease the operator's ability to draw sufficient samples for appropriate laboratory processing. In addition, scleral rigidity, increased intraocular pressure and local inflammation/severe pain may decrease the likelihood of test success.<sup>18,19</sup> Therefore

AC tap has been proposed as an alternative for diagnosis, mainly because of the good accessibility of the anterior chamber and the higher probability of success from adequate sampling.<sup>19</sup> In clinical and preclinical studies by Koul *et al* (1990) and Barza *et al* (1997), microbiological analysis of aqueous humor samples has not been shown to be a reliable test for making therapeutic decisions such as choosing the type of antibiotic to be given,<sup>18,19</sup> and according to Liano *et al* (2017), AC tap had low sensitivity and specificity in all types of endophthalmitis, except in the case of postoperative endophthalmitis where the test had moderate to low sensitivity (37.73%) and high specificity (93%). The high false-negative rate precludes its use as a screening test. However, in the absence of disease, the test has a 93% chance of being negative due to its high specificity ( $p < 0.04$ ) and can be used as a confirmatory test. Moreover, in the case of symptomatic patients (high prevalence), and in the absence of a standard (vitreous sample), a positive AC tap can be used to make therapeutic decisions, due to its high positive predictive value (94%). In other cases, the results of an AC tap are not helpful in predicting the outcome of a vitreous sample and should not replace a vitreous tap or biopsy in establishing the diagnosis of bacterial endophthalmitis.<sup>20</sup>

Difficulties in sample collection techniques and use of antibiotics before vitreous tap, may have contributed to the low rate of positive culture results. The low rate of positive results from vitreous culture is a significant drawback, because even tests considered the standard for screening have low sensitivity and should not be used as the sole reference for making therapeutic decisions. On the other hand and to compensate for the lack of sensitivity, clinicians should consider the medical history, clinical features and

outcomes of the vitreous tap and AC tap as a whole to increase the likelihood of a correct diagnosis and better information in individual therapeutic decision making.

A better alternative is to use a biopsy of the vitreous as opposed to a vitreous tap. This will ensure a sufficient number of vitreous samples for microbiological analysis, and increase the chances of a positive culture result. Another alternative is to use molecular laboratory tests such as polymerase chain reaction (PCR) and immunohistochemistry.<sup>21</sup> Although this test has potentially better sensitivity and specificity for bacterial endophthalmitis, regardless of the vitreous tap or AC tap sample; they are more expensive, require more time to process, as well as specialized equipment and trained personnel.

Six patients, 4 (cases 2,3,5,6) with initial visual acuity of 1/300 and 2 (cases 1 and 4) with initial visual acuity of 6/60. There is one person (case 6) with a visual acuity of 1/300 who forced to go home and his last condition is not yet known. Of the 5 people who underwent vitrectomy surgery, 4 patients (cases 1,2,3,4) had visual acuity better than 6/30. The EVS concluded that early vitrectomy in endophthalmitis was only beneficial to patients with vision of light perception or worse, but this was a secondary finding, and the study had not been designed for such subgroup analysis. Delayed vitrectomy is common practice to improve vitreous clarity and remove visual floaters after an episode of endophthalmitis, but is rarely performed in the acute setting. Once intravitreal antibiotics have been given, 'advanced' presentation patients (LP vision or worse) should be scheduled for immediate vitrectomy as per the EVS protocol.<sup>22</sup>

Three patients took microbiological samples from the anterior chamber, and 1 patient did not undergo culture examination

because he had an intravitreal injection of antibiotics outside. Of these 3 patients, no pathogenic bacteria were found in the samples collected. Of the 5 people who underwent vitrectomy surgery, 1 person (case 5) had a visual acuity of 1/300 and after surgery, it increased to 3/60. This patient was 84 years old and said to have no previous history of systemic disease such as diabetes or high blood pressure. From the vitreous culture results, it was found the presence of *Stenotrophomonas maltophilia*. Based on the EVS, anatomical and functional prognoses have been reported to be related to several basic predisposing factors such as initial visual acuity, absence of fundal red reflex, patients with diabetes mellitus and glaucoma, and bacteria found in the samples.<sup>10,23</sup> There is a prospective study by Lambert *et al* (2013), which looks for predisposing factors to the prognosis of visual acuity in patients with cases of endophthalmitis. This study analyzes microbiological and clinical factors as basic prognostic factors, where this study shows that bacterial virulence is the main independent factor on visual acuity outcome after acute endophthalmitis surgery. One additional independent factor for good visual acuity is the absence of complications during cataract surgery. Diabetes mellitus is a systemic condition that has the potential to impact the severity of endophthalmitis, especially with higher rates of identification of Gram-positive and coagulase-negative *Staphylococcus* species (CNSP) infections.<sup>24</sup> The frequency of diabetes mellitus in this study was 13%, almost identical to the study in the EVS group (14%).<sup>10</sup> Gram-positive microorganisms were always identified in these situations, and in more than half of the cases (7 out of 13), the microorganisms found were *Streptococcus* species. The investigators found a trend towards a

higher frequency of diabetes mellitus in the group with poor visual acuity.<sup>24</sup>

Season can also play a role in the severity of infection and therefore also plays a role in the patient's visual acuity prognosis. Variations in the bacterial spectrum and virulence may explain the seasonal variation with the severity of postoperative endophthalmitis. A retrospective study in Australia showed a tendency to isolate bacteria in wet winters.<sup>24</sup>

*Stenotrophomonas maltophilia* is a Gram-negative bacillus that causes many opportunistic infections.<sup>25</sup> Previously this bacillus was identified as *Pseudomonas maltophilia* or *Xanthomonas maltophilia*, which have been reported to cause sepsis, pneumonia, urinary tract infections, meningitis, endocarditis, septic arthritis, and peritonitis. According to several studies, bacillus has also been noted as a pathogen in various eye infections, such as conjunctivitis, keratitis, dacryocystitis, cellulitis, infected scleral buckles, and endophthalmitis. Researchers have shown that, in some cases, these organisms are less malignant than other organisms causing endophthalmitis, and may be responsible for acute or chronic endophthalmitis. In this study, it was also concluded that all study samples were sensitive to the administration of ceftazidime.<sup>26</sup> Several investigators have found resistance of these bacilli to the ceftazidime, and found that these bacilli are sensitive to chloramphenicol, ciprofloxacin, and gatifloxacin, so the administration of intravitreal antibiotics chloramphenicol and oral ciprofloxacin can be considered as the treatment of choice given the level of safety as intravitreal therapy.<sup>25</sup> Some of the reasons for this difference in sensitivity may be related to selective restriction of antibiotic use in different geographic areas or in different study time periods. Likewise, methodologies, resistance criteria, and

media used for antibiotic susceptibility may differ. Ceftazidime is often the intravitreal antibiotic agent of first choice and is chosen because of its wide scope and low intraocular toxicity.<sup>26</sup>

## SUMMARY

Case reports of 6 patients which experienced endophthalmitis post cataract surgery on the same day show significant improvement of visual acuity. Intravitreal antibiotic injection followed by plana pars vitrectomy may provide a good results of final visual acuity and good prognosis in patients with acute postoperative endophthalmitis. Only one in five people who underwent vitrectomy therapy, had a final vision no more than 3/60. This patient was an 84-year-old male which had *Stenotrophomonas maltophilia* bacteria in the result of his vitreous culture. Various predisposing factors can influence the prognosis of visual acuity of the postoperative endophthalmitis patients.

## CONFLICT OF INTEREST

The authors declared no potential conflicts of interest concerning the research, authorship, and/ or publication of this article.

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