Endophthalmitis in Oman: A descriptive retrospective multi-center study

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Abstract:

PURPOSE: The aim of this study is to report the anatomical and functional outcome, microbiology profile and treatment used for endophthalmitis in Oman.

DESIGN: The study design involves retrospective descriptive multicenter study.

METHODS: Demographic and clinical data of patients diagnosed with endophthalmitis over a period of 9 years were collected in three tertiary hospitals in Oman.

RESULTS: A total of 50 endophthalmitis cases were included in the study. Exogenous endophthalmitis was diagnosed in 48 cases, whereas 2 cases were endogenous endophthalmitis. Culture-positive cases constituted 16 cases (32%) out of these, 12 cases were Gram-positive, 3 cases were Gram-negative and one case had a positive fungal culture. Immediate first-line treatment was vitreous tap and inject in 33 eyes and vitrectomy in 13 eyes. In 45 eyes in which the visual acuity (VA) was recorded; VA after treatment improved in 22 eyes (49%), remained the same in 16 eyes (36%) and worsened in 7 eyes (16%).

CONCLUSION: Although endophthalmitis is rare, it is a devastating ocular emergency. Early diagnosis and prompt intervention are crucial in management. Awareness among the patients undergoing intraocular surgeries about this rare condition is very crucial. Moreover, frontline health-care providers must be aware and critical if they encounter patients with suspicion of endophthalmitis as early recognition, prompt referral, and timely treatment are the key for better visual prognosis. Finally, establishing a National Endophthalmitis Registry is recommended as it will help analyze the incidence, treatment instituted and the outcome of this condition across Oman.

Keywords: Endophthalmitis, Oman, outcome, treatment

Introduction

Endophthalmitis is a rare but potentially sight-threatening ophthalmic condition characterized by marked inflammation of intraocular tissues and fluids.[¹] This ocular pathology can be divided into two broad categories of exogenous and endogenous endophthalmitis. Exogenous endophthalmitis is caused by inoculation of the eye by either bacterial or fungal microorganisms from an external environment and most commonly occurs as a complication of ocular surgery, traumatic open globe injuries, or intravitreal injections.[²] Blurred vision and pain are the main symptoms, and Gram-positive coagulase-negative organisms are the main etiology of exogenous endophthalmitis.[³] Endogenous endophthalmitis is caused by hematogenous spread of infectious organisms from distant sites of the body. Both categories of endophthalmitis lead to subsequent intraocular inflammation and potentially severe visual loss.[²] In addition, they have different risk factors and causative pathogens and thus require different diagnostic, prevention, and treatment strategies.[⁴]

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To the best of our knowledge, there are no previously reported studies on endophthalmitis in Oman. We believe this work will shed the light on such a devastating ophthalmic condition and we hope to raise awareness on the preventive aspects and treatment measures.

**Methods**

A retrospective study review of electronic medical records of all patients with the diagnosis of endophthalmitis over a period of 9 years between January 2008 and December 2016 was conducted in three referral tertiary hospitals in Oman; Al-Nahdha Hospital, Sultan Qaboos University Hospital (SQUH), and Armed Forces Hospital. Ethical approval was obtained from the respective institutional Ethical Committees.

Demographic details such as age, gender, preexisting medical illnesses, predisposing risk factors (e.g., trauma, surgeries), presenting complaints, duration of the symptoms, visual acuity (VA), ophthalmologic examination, microbiology profiles, treatment modalities, and final visual outcomes were collected. Acute-onset endophthalmitis is generally defined when the symptoms and signs are encountered within 6 weeks from the ocular surgery or trauma and delayed-onset (chronic) endophthalmitis if presents beyond 6 weeks.[10] Data were collected using Epi-data v4.6.0 (non-profit organization "The EpiData Association", Enghavevej 34, DK5230 Odense M, Denmark, Europe) and analyzed using the Statistical Package for Social Science software version 25.0 ((International Business Machines Corporation (IBM), Chicago, US)). Descriptive data were expressed as mean ± standard deviation for numerical data, and categorical variables were presented in frequencies and percentages.

**Results**

A total of 50 eyes of 50 patients were included in this study. Most of the patients received treatment in Al-Nahda Hospital 34 (68%), followed by SQUH 10 (20%), and Armed Forced Hospital 6 (12%). The age of patients ranged from 2 to 76 years and the mean age at presentation was 48 ± 22.1 years. The age distribution is as follows; 24% <30 years, 42% between 30 and 60 years and 34% >60. There was a female predominance (n = 27, 54%) compared to males (n = 23, 46%) as shown in Table 1.

Moreover, 39 eyes (78%) had acute endophthalmitis and 11 patients (22%) had chronic endophthalmitis. At presentation, 47 eyes (94%) had anterior chamber reaction in the form of cells and flare, 37 eyes (74%) had a hypopyon and no view of the posterior segment in 45 eyes (90%). Looking at the categories of endophthalmitis in this study, only 2 eyes (4%) had endogenous endophthalmitis, both were of patients who had an underlying renal failure on dialysis and the remaining 48 eyes (96%) had exogenous endophthalmitis. For the exogenous category, the following predisposing factors were identified; previous intraocular procedures in 34 eyes (70.8%) and ocular trauma in 14 eyes (29.2%). Further subcategories of predisposing factors are illustrated in Table 2.

Out of 16 eyes (32%) which were documented as culture-positive; Gram-positive organisms were the most common (12 eyes, 75%) followed by Gram-negative organisms (3 eyes, 19%) and fungal organism in one eye (6%). The remaining 34 eyes (68%) either they were culture-negative or positive gram staining without specific microbial isolates. The causative organisms cultured from vitreous and/or aqueous humor samples are summarized in Table 3.

In this study, 33 eyes (66%) underwent a vitreous tablet and intravitreal injections of antibiotics as the initial treatment for endophthalmitis and of these, 14 eyes (28%) ended up needing a pars plana vitrectomy (PPV). Moreover, 13 eyes (26%) underwent immediate PPV with intravitreal injections of antibiotics as initial treatment. However, four patients (4 eyes, 8%) had either systemic antibiotics (as 2 eyes in the study had endogenous endophthalmitis), enucleation or refused treatment and left against medical advice. Furthermore, 37 eyes (74%)
included in this study had a follow-up duration of >3 months in the tertiary centers. The remaining 13 eyes (26%) were followed up for <3 months, as they were referred to their referring hospitals for follow-up after definitive management.

The following anatomical outcomes were observed in this study; 30 eyes (60%) had favorable anatomical outcome; however, 6 eyes (12%) had retinal detachment, 2 eyes (4%) had choroidal detachment, recurrent endophthalmitis was documented in one eye (2%), 8 eyes (16%) had phthisis bulbi, and 3 eyes (6%) underwent enucleation.

In this study, the presenting VA was documented in 47 eyes. It was 6/12 in one eye (2%), counting fingers in 10 eyes (21%), and hand motion in 13 eyes (28%), light perception in 14 eyes (30%) and no light perception (NLP) in 9 eyes (19%). In 45 eyes in which the post-operative VA was available; VA after treatment improved in 22 eyes (49%), remained unchanged in 16 eyes (36%), and worsened in 7 eyes (16%).

Further sub-analysis of visual outcome based on the type of intervention is summarized in Figure 1.

### Table 3: Microbial isolates from vitreous and/or aqueous humorous samples

| Number of eyes (%) | Total culture-positive with isolates | Gram-positive | Staphylococcus epidermidis | Staphylococcus aureus | Staphylococcus lugdunensis | Streptococcus pneumoniae | Streptococcus spp. | Gram-negative | Pseudomonas aeruginosa | Salmonella spp. | Haemophilus influenzae | Fungal | Scedosporium apiospermum |
|--------------------|-------------------------------------|---------------|----------------------------|----------------------|--------------------------|------------------------|-------------------|---------------|----------------------|----------------|-----------------------|--------|-------------------------|
|                    | 16 (32)                             | 12 (75)       | 3 (18.75)                  | 1 (6.25)             | 1 (6.25)                 | 1 (6.25)               | 6 (37.5)         | 3 (18.75)     | 1 (6.25)             | 1 (6.25)        | 1 (6.25)               | 1 (6.25) | 1 (6.25)                |

### Discussion

In this multicenter study, we retrospectively investigated the cases of endophthalmitis referred and diagnosed in three tertiary referral centers in Oman over a period of 9 years. We present the anatomical and functional outcomes in addition to the microbiology profile of the causative agents and the therapeutic options used in these cases.

In this study, hypopyon and anterior chamber reaction were very common findings at presentation (74% and 94%, respectively). In addition, exogenous endophthalmitis was diagnosed in 48 cases (96%), while two cases (2%) were endogenous endophthalmitis. The latter usually occurs when microorganisms in the bloodstream cross the blood-retina barrier and infect the ocular tissue, especially in immunocompromised patients and chronic systemic diseases.[6,7] It is comparable to what is reported in the literature for the endogenous endophthalmitis, which accounts for approximately 5%–10% of all endophthalmitis cases.[8-11]

Many studies have reported that approximately 90% of postoperative endophthalmitis cases develop after cataract extraction.[3,7,12,13] In our study, we found that endophthalmitis after cataract surgery is the most common type of postoperative endophthalmitis which accounts for 70.5% as cataract surgery is the most frequently performed intraocular surgery in Oman and rest of the world.[14]

About 29% of endophthalmitis cases in our study were a result of open globe injuries. It is comparable to what is reported in the literature, which is about 25%.[15] It is well known that traumatic endophthalmitis is more often associated with a worse visual outcome. The following risk factors carry poor prognosis in the setting of open globe injuries; poor initial VA, contaminated wound, lens capsule rupture, older age, initial presentation for >24 h, the presence of intraocular foreign bodies, afferent papillary defect, rubeosis iridis, and the absence of the red fundus reflex.[15,16]

Bacterial infections are the most common cause of postoperative endophthalmitis, where Gram-positive isolates account for most cases. According to endophthalmitis vitrectomy study (EVS), 94.2% of culture-positive endophthalmitis cases had Gram-positive bacteria, and Gram-negative species were found in only 5.9% of cases.[3,12,17,18] In our study; 32% of studied eyes were culture-positive, in which 75% were Gram-positive and 19% were Gram-negative bacteria. In addition, positive fungal culture was found in one eye only.
Depending on the infecting organism, a correlation is thought to exist between clinical presentation and microbiologic spectrum. Gram-positive, coagulase-negative microorganism seems to cause less severe infection compared to more virulent Gram-negative and other Gram-positive microorganisms. Streptococcal endophthalmitis often results in earlier onset and notably worse outcomes than infections by staphylococcal species. Endophthalmitis cases which are reported as culture-negative tend to have a later onset and a better visual outcome.

For the treatment of endophthalmitis, an effective way to achieve a therapeutic intraocular concentration of an antimicrobial agent if given intravitreally. Therefore, intravitreal injection of antibiotics has become the standard of care in the treatment of exogenous endophthalmitis. Current antibiotic standard protocols for intravitreal application are empirically-based and include vancomycin (1.0 mg/0.1 mL) for Gram-positive coverage in combination with the ceftazidime (2.25 mg/0.1 mL) for Gram-negative coverage. It has been reported that Gram-positive organisms have a 99% susceptibility to vancomycin. However, only 89.5% of Gram-negative isolates were sensitive to amikacin or ceftazidime. In fungal endophthalmitis, vitrectomy and intravitreal amphotericin B are indicated in case of severe vitreous involvement.

Vitrectomy provides several substantial benefits in the treatment of endophthalmitis such as obtaining adequate vitreous sample, debulking the vitreous thereby reducing the infectious agent load, decreasing the concentration of toxins and theoretically increasing the effectiveness of the intravitreal antibiotics. In this study, 33 eyes (66%) had vitreous tablet and intravitreal injections of antibiotics as initial treatment for endophthalmitis, and out of these, 14 eyes (28%) ended up with vitrectomy. Moreover, 13 eyes (26%) required immediate vitrectomy with intravitreal injections of antibiotics as initial treatment.

In this study, 45 eyes in which the postoperative VA was available; VA after treatment improved in 22 eyes (49%), remained unchanged in 16 eyes (36%), and worsened in 7 eyes (16%). In EVS, patients whose initial VA was hand motions or better, there was no difference in visual outcome whether an immediate PPV was performed or not. However, in the subgroup of patients with light perception or worse, immediate PPV resulted in a threefold increase in the frequency of achieving 20/40 or better acuity (33% vs. 11%), approximately a two-fold chance of achieving 20/100 or better acuity (56% vs. 30%), and a 50% decrease in the frequency of severe visual loss (20% vs. 47%) over the vitreous tap and intravitreal antibiotics. The incidence of retinal detachment in EVS was 8.3% after treatment of endophthalmitis, with no difference in frequency based on whether initial management was vitrectomy or tap biopsy.

In a small case series of 33 eyes with endophthalmitis; Negretti et al. reported that 12% had final VA of 6/12 or better and 28% final VA of 6/36 or better. Vitrectomy within 7 days resulted in improved final VA outcomes (1.49 vs. 2.16 Log MAR, P = 0.032). Complications reported were retinal detachment (24.2%), macular hole (3%), hypotony (6%), suprachoroidal hemorrhage (3%), and enucleation/evicretion (6%).

In a postfiltering surgery endophthalmitis study, friends group reported that vitrectomy in 123 patients resulted with 40% had VA >20/40; 32% had VA <20/400; 8% had NLP, and 13% of patients developed retinal detachment postvitrectomy.

In this study, nine patients (9 eyes) presented late with a VA of NLP. This could have contributed to the rates of phthisis bulbi and enucleation of 16% and 6%, respectively. This delay in seeking urgent medical consultation is possibly attributed to the lack of awareness among some patients regarding the red flag symptoms of possible endophthalmitis after intraocular surgeries.

It is worthwhile mentioning that vitrectomy surgery has improved significantly in the past two decades with the introduction and improvement of small gauge instrumentation, wide-field viewing systems and increase in the cut-rate as well as the design of vitrectomy probes which was not the case when EVS was conducted. Therefore, the results and recommendations of EVS should be applied cautiously and early vitrectomy in endophthalmitis cases whenever possible, may lead to a better outcome. However, vitreous tap and intravitreal antibiotics injections remain a valid option in selected cases and when a delay in performing vitrectomy is anticipated.

The limitations of this study are those inherent in retrospective studies, including missing data resulted in relatively small sample size, cases managed at secondary care level and did not require referral to tertiary centers were not included and lack of controls. However, randomized control trial for this rare condition is not practical; reporting larger observational case series from all ophthalmology services in Oman will be an important source for addressing such condition in more details.

**Conclusion and Recommendations**

Although endophthalmitis is rare, it is a devastating ocular emergency. Early diagnosis and prompt
intervention are crucial in the management. Awareness among the patients undergoing intraocular surgeries about this rare condition as well as the potential risk of severe complications with or without treatment is very crucial. Moreover, frontline health care providers must be aware and critical if they encounter patients with suspicion of endophthalmitis as early recognition, prompt referral, and timely treatment are the key for better visual prognosis. Finally, establishing a National Endophthalmitis Registry is recommended as it will help analyze the incidence, treatment instituted and the outcome of this condition across Oman.

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Conflicts of interest
There are no conflicts of interest.

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