

# Endogenous endophthalmitis in a tertiary centre of northern Malaysia: a case series and literature review

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## Abstract

**Background:** Endogenous endophthalmitis is an uncommon ophthalmological emergency caused by hematogenous spread of infection from a distant focus. It can lead to permanent blindness, panophthalmitis, enucleation, or evisceration. Difficulties are often encountered in making a diagnosis, yielding cultures of causative pathogens and selecting appropriate antibiotics.

**Case series:** We describe 4 cases treated in Hospital Sultanah Bahiyah from 2021 to 2022. The studied cases belonged to a high-risk group in common with at least 1 predisposing medical condition. Endogenous endophthalmitis was caused by different etiologies and demonstrated various clinical manifestations. Two patients were initially misdiagnosed and later referred to our centre. The identified pathogens were predominantly Gram-negative bacteria, *i.e.*, *Klebsiella variicola* and *Pseudomonas aeruginosa*. Magnetic resonance imaging was utilized in 1 patient to help distinguish an infection from a metastatic carcinoma. All patients received intravitreal antibiotics. Two patients underwent vitreoretinal surgery and were able to achieve 2/60 or better postoperatively. One patient required evisceration and another developed phthisis bulbi.

**Conclusion:** Aggressive screening for occult infection is important to identify the source of infection and guide appropriate antibiotic treatment. Early diagnosis and prompt antimicrobial treatment are crucial to prevent devastating complications.

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*Keywords:* endogenous endophthalmitis, Gram-negative bacteria, panophthalmitis

## Endogenous endophthalmitis di pusat tertiar bahagian utara Semenanjung Malaysia: siri kes dan semakan kajian terkini

### Abstrak

*Latar belakang:* *Endogenous endophthalmitis* merupakan satu kecemasan oftalmologi yang jarang

berlaku disebabkan oleh penyebaran kuman di dalam darah dari bahagian lain badan ke mata. Ia boleh mengakibatkan kebutaan kekal, infeksi dalam semua lapisan mata atau kehilangan bola mata. Cabaran yang sering dihadapi adalah untuk menghasilkan diagnosis, mengkultur mikroorganisma yang berkenaan dan memilih antibiotik yang tepat dan sesuai.

*Siri kes:* Kami melaporkan empat kes di Hospital Sultanah Bahiyah dari tahun 2021 sehingga 2022. Kes-kes tersebut adalah daripada kumpulan berisiko tinggi dengan sekurang-kurangnya satu penyakit kronik. *Endogenous endophthalmitis* disebabkan oleh pelbagai punca dan mempunyai pelbagai manifestasi klinikal. Dua pesakit telah tersalah diagnosa sebelum dirujuk ke pusat kami. Kebanyakan mikroorganisma yang dipastikan adalah bakteria Gram negatif seperti *Klebsiella variicola* dan *Pseudomonas aeruginosa*. Satu kes memerlukan pengimejan MRI untuk membezakan jangkitan daripada kanser metastatik. Semua pesakit menerima antibiotik secara intravitreal. Dua pesakit telah menjalani pembedahan vitreoretina dan mereka mencapai ketajaman penglihatan 2/60 atau lebih baik selepas pembedahan. Malangnya, seorang pesakit memerlukan bola mata dibedah keluar manakala seorang lagi mengalami pengecutan bola mata.

*Kesimpulan:* Saringan awal yang agresif untuk kes endogenous endophthalmitis adalah penting dalam mengenal pasti punca jangkitan dan mikroorganisma yang terlibat supaya rawatan antibiotik yang berkesan dapat diberikan. Diagnosis awal dan rawatan segera adalah mustahak untuk mencegah komplikasi serius.

*Kata kunci:* bakteria Gram-negatif, endoftalmitis dalaman, panoftalmitis

## Introduction

Endophthalmitis is a debilitating intraocular infection that can be classified as exogenous or endogenous. Exogenous endophthalmitis occurs after an eye procedure or surgery, a penetrating ocular injury, or as an extension of periocular infection. On the other hand, endogenous endophthalmitis is caused by blood-borne spread from a distant focus of infection. Endogenous endophthalmitis, also known as metastatic endophthalmitis, accounts for 2–8% of all endophthalmitis cases.<sup>1-3</sup> Most cases are unilateral, occurring bilaterally in 12–29% of cases.<sup>1,4,5</sup> In this study, we describe 4 cases of endogenous endophthalmitis varying clinical manifestations and caused by different aetiologies (Table 1).

## Case presentation

### Case 1

A 42-year-old woman with renal failure secondary to hypertension (HPT), presented with chills, rigors, and pus in the internal jugular catheter. She had painless blurred vision in the right eye associated with eye redness and floaters. Vision was 6/60 in the right eye and 6/12 in the left eye. The anterior segment examination was unremarkable except for conjunctival hyperaemia. Fundus examination revealed vitritis and a subretinal whitish lesion measuring 3 disc diameters, located nasal to the optic disc. There was no vasculitis or fungal ball. The left eye was normal.

C-reactive protein was markedly raised at 156 mg/L, but with no leucocytosis. Pus culture grew *Klebsiella variicola*, while vitreous and blood cultures were negative. Other possible sources of infection were investigated. Ultrasound of the kidney, ureter, and bladder (KUB) was unremarkable, and echocardiography did not show any vegetation.

She was commenced on ceftriaxone and linezolid. She received 3 intravitreal injections of ceftazidime and vancomycin. Topical moxifloxacin, dexamethasone, and cycloplegics were instilled. The topical antibiotics were replaced by fortified gentamicin and cefuroxime to target *Klebsiella* sp.

Her symptoms ameliorated with resolving vitritis while the choroidal abscess became more confined. Vision improved to 6/60. On day 10 of treatment, the retina overlying the contracting choroidal abscess became atrophied, resulting in a retinal break and rhegmatogenous retinal detachment nasally at 1–7 o'clock with macular involvement (Fig. 1). She underwent vitrectomy, endolaser, and tamponade with silicone oil. Subsequently, her general and ocular condition improved. Upon discharge, vision in the right eye was 2/60 pinhole 6/60.

Table 1. Summary of clinical profiles of studied cases.

Case, age	UC	Organism	Location	Vitreous culture	Blood culture	IVT	Vitr	Initial VA	Outcome
1, 42	Renal failure, HPT	K. variicola	Posterior	Negative	S. aureus	+	+	6/60	2/60 PH 6/60
2, 48	DM, HPT, breast cancer	P. aeruginosa	Anterior, later PO	P. aeruginosa	Negative	+	-	HM	PL
3, 61	DM, IHD	Mixed	Posterior	Mixed growth (3 organisms)	Negative	+	+	HM	1/60 PH 2/60
4, 45	DM, CKD	E. coli	PO	E. coli	Negative	+	-	PL	Evisceration

UC: underlying condition; DM: diabetes mellitus, HPT: hypertension, IHD: ischaemic heart disease

HM: hand movement; PL: perception of light; PH: pinhole; PO: panophthalmitis; IVT: intravitreal culture; Vitr: vitrectomy; VA: visual acuity

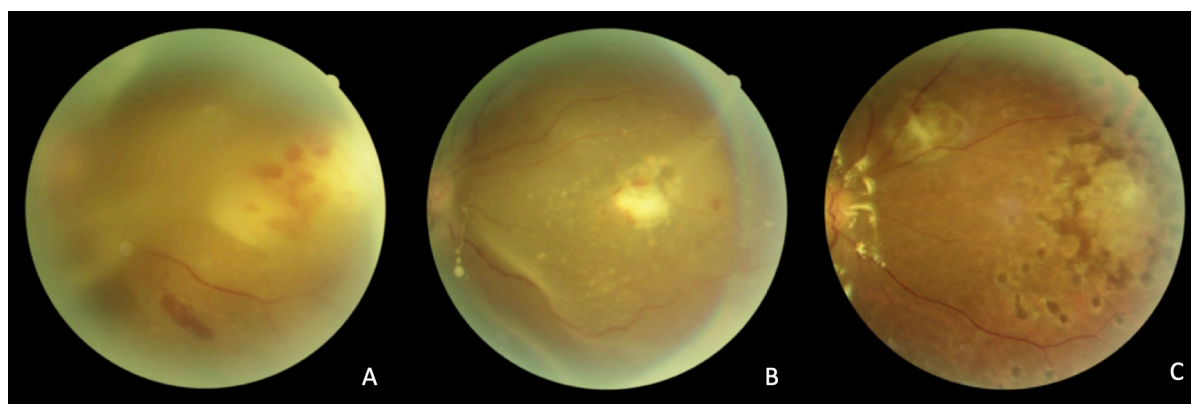


Fig. 1. (A, B) Case 1. Fundus photographs of a choroidal abscess that contracted during the course of antibiotics but complicated with retinal detachment. (C) Fundus photography after vitrectomy.

**Case 2**

A 48-year-old Malay woman with diabetes mellitus (DM), HPT, Stage IV carcinoma in the left breast, and necrotising fasciitis on the left side of the chest was in sepsis. She had been initially managed for conjunctivitis with painless redness and blurred vision in the left eye for 2 days.

In the left eye, vision was hand movement, eyelid was oedematous, conjunctiva was chemosed, a subconjunctival mass was noted superonasally (Fig. 2), intraocular pressure (IOP) was 56 mmHg, and the fundus could not be visualized. Examination of the right eye showed severe non-proliferative diabetic retinopathy features with vision 6/21.

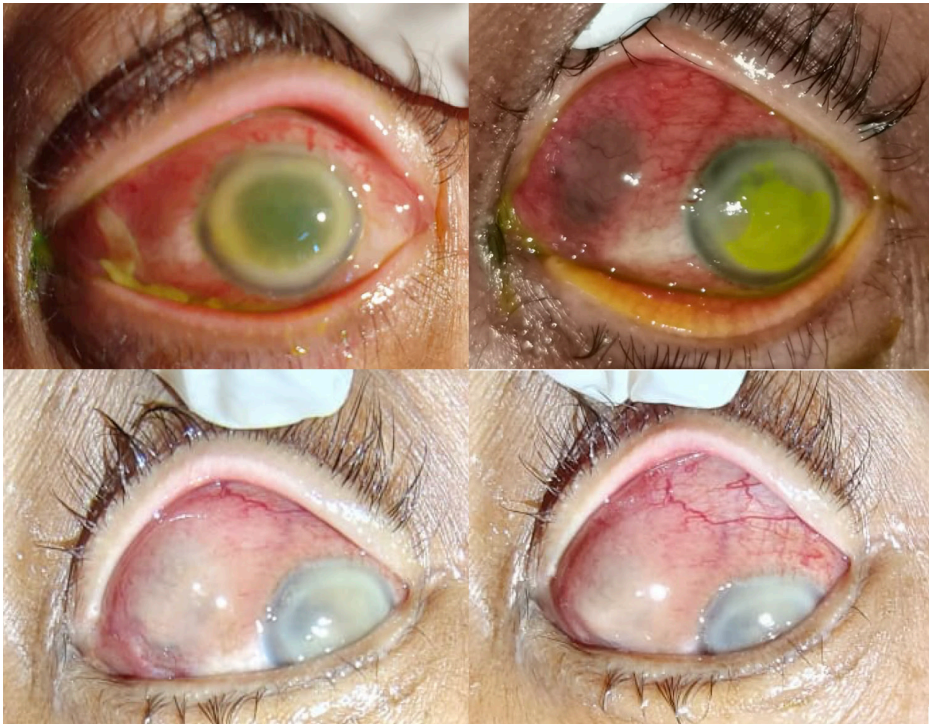


Fig. 2. Case 2. Anterior segment photographs of worsening subconjunctival abscess despite systemic and intravitreal antibiotics.

She had leucocytosis, with a white cell count of  $31.6 \times 10^9/L$  and markedly raised C-reactive protein of 175 mg/L. A vitreous sample of the left eye grew *Pseudomonas aeruginosa*. Tissue and pus culture from the breast wound showed mixed growth of microorganisms. Blood and urine cultures were insignificant. Vitreous cytology was performed for malignancy but revealed only inflammatory debris. No evidence



Fig. 3. Case 2. Axial cut of MRI imaging depicts panophthalmitis in the left eye. T1 FSE; T2 FLAIR.

of infection was seen on echocardiography or ultrasound of the abdomen or KUB. Computed tomography and magnetic resonance imaging showed panophthalmitis with subretinal and conjunctival abscesses (Fig. 3).

She received intravenous ceftazidime for 3 weeks, followed by oral ciprofloxacin 750 mg BD for a month. Intravitreal vancomycin and ceftazidime were given thrice within 14 days. She was on topical gentamicin, ceftazidime, homatropine, dexamethasone, and timolol. The left eye became phthisical upon completion of treatments.

### Case 3

A 61-year-old Malay man presented with decreased vision in his right eye, associated with ocular pain and redness for a week. He was initially managed as uveitis. He had underlying uncontrolled DM, ischaemic heart disease, and a recently partially treated perianal abscess.

Upon ophthalmological evaluation, the right eye had vision of hand movement, injected conjunctiva, hypopyon and dense fibrinous exudates in the anterior chamber, IOP of 18 mmHg, and the fundus could not be visualised. B-scan ultrasonography indicated dense vitritis with loculation and subretinal collections suggestive of abscesses. The left eye was unremarkable with vision of 6/9. The patient had mild leucocytosis with a white cell count of  $13.94 \times 10^9/L$ . C-reactive protein was raised at 10.01 mg/L. Cultures from blood, urine, aqueous humour, and vitreous from tapping were negative. Ultrasound of the abdomen was normal.

Intravenous ceftriaxone and vancomycin were administered for a month. He was prescribed topical moxifloxacin, dexamethasone, and homatropine. He also received intravitreal vancomycin and ceftazidime twice in the right eye before pars plana vitrectomy and subretinal abscess drainage. Vitreous culture from vitrectomy grew mixed organisms.

Clinical improvement continued over 2 months, with vision of 2/60 attained in the affected eye. Fundus showed minimal subretinal fibrosis superiorly and inferiorly (Fig. 4). He subsequently developed inferior retinal detachment involving the macula secondary to proliferative vitreoretinopathy.



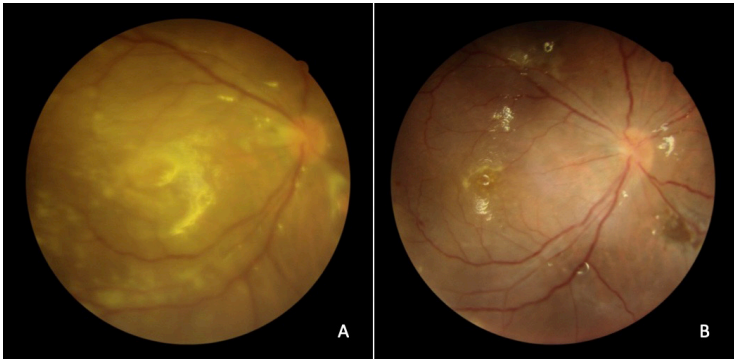


Fig. 4. Case 3. Fundus photographs of the right eye: (A) 6 days after vitrectomy and (B) 1 month after vitrectomy.

#### Case 4

A 45-year-old woman with underlying uncontrolled DM and chronic kidney disease (CKD), was diagnosed with acute bilateral pyelonephritis one day before her referral to our centre with sudden painless blurred vision in the right eye. On examination, vision in the right eye was limited to light perception in the temporal quadrant and no light perception elsewhere. The affected eye had severe anterior chamber inflammation, hypopyon, and elevated IOP. There was no fundal view. B-scan ultrasonography showed thickened posterior hyaloid with dense vitritis and loculations. The contralateral eye revealed advanced diabetic eye disease findings with vision of 1/60. The patient had leucocytosis and markedly raised C-reactive protein of 403 mg/L. The blood culture was negative, whereas the vitreous sample grew *Escherichia coli*. Ultrasound and echocardiography were unremarkable.

She was immediately prescribed intravitreal tapping and antibiotics for the right eye (vancomycin/ceftazidime) along with gentamicin and cefuroxime eye drops hourly, topical steroids, cycloplegics, and IOP-lowering agents. She was given intravenous moxifloxacin for 2 weeks.



Fig. 5. Case 5. Complete ophthalmoplegia in panophthalmitis.

Even though she showed improvement systemically, her ocular condition deteriorated in the following 2 days. The affected eye became chemosed, with worsening inflammation and total ophthalmoplegia (Fig. 5). With the development of panophthalmitis and orbital cellulitis, the patient underwent evisceration.

## Discussion

### Mechanism

Endogenous endophthalmitis typically occurs when a microbial load crosses the blood-ocular barrier to enter the intraocular space as a chorioretinitis. During early infection, the microbial load is more concentrated in the posterior vitreous compared with the anterior vitreous. Hence, a vitreous culture from vitreous tapping can be falsely negative. In addition, tapping provides a relatively smaller yield, and therefore it is less sensitive than a vitrectomy sample.<sup>6</sup> On the other hand, inoculation of pathogenic microorganisms can occasionally occur in the anterior ocular structures via uveal circulation.<sup>7</sup> In such an entity, significant evidence of inflammation is in the anterior segment of the eye while the posterior segment may or may not be involved.

### Comorbidities

Most cases are reported to occur in patients who have an underlying medical condition or are immunocompromised.<sup>1,6</sup> The immunocompromised state is often attributable to DM, malignancy, and renal disease. The most common medical condition is DM, accounting for 40–79% of total cases.<sup>2,7-9</sup> Of our patients, 3 had poorly controlled DM and 1 had malignancy, which may have increased their vulnerability to infection.

### Aetiology

Patients with endogenous endophthalmitis have a remote focus of infection. Systemic examinations and extensive investigations such as echocardiography, ultrasound of the abdomen, and urine culture are essential to identify the source of infection. Common aetiologies include infected wounds, urinary tract infection, and meningitis. Less common is endocarditis, which should be considered and investigated in all cases.<sup>7</sup>

### Causative organisms

Aetiologic pathogens can be identified from cultures of ocular and non-ocular specimens. Yielded results guide for a more targeted treatment. Most cases in the literature review reported bacteria, with fungal infections being rarer.<sup>8</sup> Common causative pathogens in East Asia are Gram-negative bacteria, such as *Klebsiella* sp., accounting for 50–90% of patients.<sup>1,8</sup> Our findings correspond to the studies.



In contrast, Gram-positive microbes emerged more commonly in non-East Asian populations.<sup>1</sup>

### **Presentation**

Interestingly, Greenwald *et al.* further classified endogenous endophthalmitis into 4 groups, namely focal, anterior diffuse, posterior diffuse, and panophthalmitis.<sup>7</sup> In our reported cases, 2 were posterior diffuse while the others were panophthalmitis. Panophthalmitis cases eventually resulted in phthisis or evisceration, which is consistent with Greenwald *et al.*'s observations. Bilateral eye involvement has been reported in one-quarter of cases with different severity. Delayed involvement of the fellow eye despite systemic therapy has also been reported.<sup>7</sup> Hence, a thorough periodical examination of fellow eyes is advised.

Initial diagnostic error is commonly encountered in 16–63% of cases<sup>1,7</sup>. Misdiagnoses include conjunctivitis, uveitis, and acute glaucoma. There were 2 cases in our observation that were managed inappropriately before a correct diagnosis.

### **Management**

Medical management includes immediate control of both systemic and local infections. Liaison with an infectious disease team is recommended for the selection of systemic antibiotics. Broad-spectrum antibiotics with good ocular penetration should be initiated and can be further tailored based on the results of cultures. Frequency and dosage of intravenous antibiotics for serious infection are suggested for at least 2 to 3 weeks or longer depending on clinical response.<sup>7</sup> Common systemic antibiotics administered include third-generation cephalosporins and fluoroquinolones.<sup>10</sup> Locally, better outcomes were achieved when patients receive intravitreal antibiotics within 48 hours of diagnosis.<sup>11</sup> Vancomycin is commonly chosen to target Gram-positive bacteria while ceftazidime is for Gram-negative bacteria.<sup>5</sup>

Vitrectomy clears microorganisms and toxins in the vitreous to avoid further destruction of ocular tissues. Vitrectomy has been increasingly employed in recent years.<sup>10,12</sup> Lee *et al.* reported that 60% of cases in Korea received pars planar vitrectomy.<sup>12</sup> Early vitrectomy for eyes with counting fingers or better is associated with a better outcome with vision counting fingers or better.<sup>12</sup> Our study is consistent with their findings, as both cases who had early vitrectomy achieved vision better than counting fingers.

### **Outcomes**

The visual outcome of endogenous endophthalmitis is guarded, with almost half of the cases ending with vision poorer than 6/60 and one-quarter of the cases requiring evisceration or enucleation.<sup>8</sup> The outcome of endogenous endophthalmitis has been reported as poor. Okada described that one-third of cases resulted in outcomes of no light perception, evisceration, or enucleation.<sup>2</sup> Other studies have reported that 73% of cases achieved a vision of counting fingers or better after

treatment.<sup>9</sup> Late complications include retinal detachment, cataract formation, and macular oedema. A relatively high mortality of 29% was reported to be due to disseminated fungemia.<sup>4</sup> No mortality was reported in this series.

## Conclusion

In summary, endogenous endophthalmitis is an ophthalmological emergency that can manifest variably. Misdiagnosis often delays treatment and therefore a high clinical suspicion is essential. Prompt treatment for early diagnosis improves the outcome.

## Declarations

### Informed consent for publication

The patients and/or their guardian have provided written informed consent for the publication of the clinical data and images contained in this report.

### Competing interests

None to declare.

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