

CASE REPORT

Severe Endogenous Endophthalmitis with Panophthalmitis-Lessons to Learn

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ABSTRAK

*Endophthalmitis endogenous merupakan sejenis jangkitan mata serius yang biasanya berpunca daripada penyebaran kuman dari anggota badan lain ke dalam mata melalui darah pesakit. Usaha untuk mencari punca utama jangkitan dan memulakan rawatan serta-merta adalah sangat penting untuk menyelamatkan nyawa dan penglihatan pesakit. Laporan kes ini adalah berkenaan seorang lelaki yang berumur 47 tahun yang kedua-dua matanya mengalami kehilangan penglihatan secara progresif dan kemerahan mata kiri sejak dua minggu lepas. Mata kiri adalah mata yang lebih teruk dan penglihatan mata kiri hanya dapat melihat pergerakan tangan. Pemeriksaan mata kiri menunjukkan koleksi nanah yang besar dalam lapisan koroid di bahagian makula. Diagnosis endogenous endophthalmitis telah dibuat berdasarkan sejarah yang diberi oleh pesakit berkenaan, bersama penyiasatan darah pesakit dan pengimejan mata seperti *Enterobacter sp.* yang diisolasikan dari kultur darah, ultrasound B-scan dan contrasted enhanced computerized tomography (CECT) untuk mata dan kepala. Keadaan pesakit bertambah baik dari segi kehilangan demam, keputusan darah, dan ultrasound B-scan, selepas rawatan antibiotik yang diberikan secara intravitreal dan sistemik. Tetapi keradangan mata yang berlarutan telah mengaburkan butiran fundus mata kiri. Malangnya, pesakit mengalami glaukoma rubeotik dan dirawat secara konservatif. Kesimpulannya, endogenous endophthalmitis dapat menyebabkan panophthalmitis dan sukar untuk dirawat. Laporan kes ini ingin menitik-beratkan cabaran-cabaran yang dihadapi sepanjang perawatan pesakit yang mengalami endophthalmitis.*

Kata kunci: endophthalmitis, koroid, nanah, panophthalmitis

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ABSTRACT

Endogenous endophthalmitis is a devastating intraocular infection. Finding the primary infection and directed treatment is life-saving. We describe a 47-year-old man, with uncontrolled diabetes mellitus, who presented with two weeks history of progressive reduced vision and redness of the left eye (LE). He was generally unwell since a month, previously. Examination showed relative afferent pupillary defect (RAPD) in the affected eye and visual acuity was hand movement. There was moderate anterior chamber and vitreous reaction. Fundus examination showed a huge dome-shaped choroidal mass covering the entire macula. Diagnosis of severe endogenous endophthalmitis was made, with isolation of *Enterobacter sp.* from his blood culture. Meanwhile, he also had elevated inflammatory markers with presence of leucocytosis, neutrophilia and elevated erythrocyte sedimentation rate (ESR) as well as C-reactive protein (CRP). Vitreous tap and aqueous tap had no growth. He improved with combination of intravitreal and systemic antibiotic, as shown by the resolved fever and reduced inflammatory markers but progressive inflammation occluded the fundus details and the LE vision eventually became no projection of light despite treatment. Subsequently, he developed rubeotic glaucoma and was treated conservatively because the LE was painless with poor vision. The repeated blood culture and urine was normal. In conclusion, endogenous endophthalmitis with eventual panophthalmitis is difficult to treat and has very poor visual prognosis. Our case highlights the challenges faced in the management of vision-threatening endophthalmitis and panophthalmitis in this patient.

Keywords: abscess, choroid, endophthalmitis, panophthalmitis

INTRODUCTION

Endogenous endophthalmitis is an intraocular infection which gain entry to the eye via hematogenous route in contrast to exogenous endophthalmitis in which entry into the eye is from an opening induced typically by ocular surgery and more commonly by trauma (Wong et al. 2000). The source of infection may be varied involving the urinary tract, respiratory tract or skin infections. On the other hand, panophthalmitis is a more extensive ocular inflammation involving all

layers of the globe and extending to the surrounding orbit. It usually presents with marked lid edema, proptosis, hypopyon, limited ocular movements and increased intra-ocular pressure, eventually leading to visual loss (Eagle 2012).

Both diseases pose a treatment challenge to Ophthalmologists, and visual outcome is usually guarded. We report a case of choroidal abscess with endogenous endophthalmitis in a young diabetic patient. This case highlights the importance of rapid diagnosis to prevent orbital spread and

directed systemic treatment.

CASE REPORT

A 47-year-old male with poorly controlled diabetes mellitus presented with two weeks history of progressive reduced vision and redness of the left eye (LE). He was unwell and had episodes of low-grade fever since a month previously. He complained of suprapubic pain, but denied respiratory or other symptoms of urinary tract infection. He also had reduced appetite but no loss of weight. Despite treatment with insulin, his diabetic control was not optimised due to poor compliance. He admitted to alcohol abuse and heavy smoking but denied of any intravenous drug usage (IVDU) or multiple sexual partners. There was no previous history of trauma or intraocular surgery. He had no prolonged cough or contact with tuberculosis patient. Formerly, he sought help from a private Ophthalmologist and was referred to our centre for further management.

His vision was 6/24 in the right eye (RE) while the LE was hand movement with frank afferent pupillary defect in the latter eye. The left eyelid was swollen and erythematous and the conjunctiva was injected with chemosis. There was severe anterior chamber reaction over his LE with cells of 4+ and hypopyon. Fundus examination revealed a huge dome-shaped choroidal mass covering the left macula and peripheral choroidal detachment (Figure 1). The intraocular pressures were within normal limit. Meanwhile, the RE showed proliferative diabetic retinopathy changes, necessitating laser photocoagulation which was delivered in sessions. There was limited ocular movement in all directions in the LE while RE motility was full. LE lid was oedematous and swollen. Apart from low grade fever (documented 37.5°C upon presentation, highest temperature was 37.9°C throughout the admission), systemic examination including abdominal examination was unremarkable. A B-scan showed a choroidal dome-shaped lesion over the

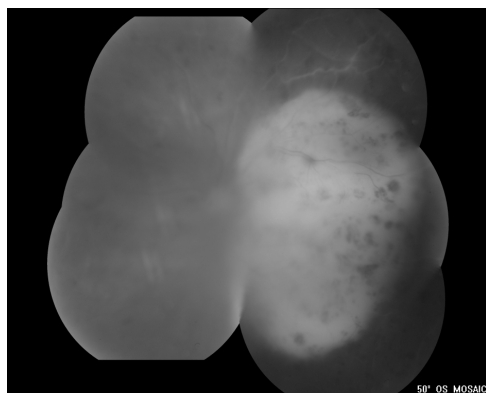


Figure 1: OS fundus showed vitritis with a huge dome-shaped choroidal mass covering the whole macula

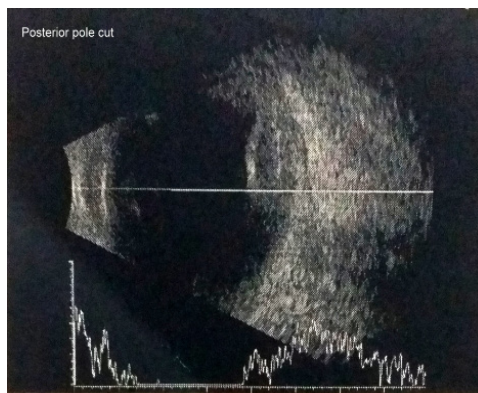


Figure 2: A choroidal dome-shaped lesion over the posterior pole of OS with increased internal hyper-reflectivity

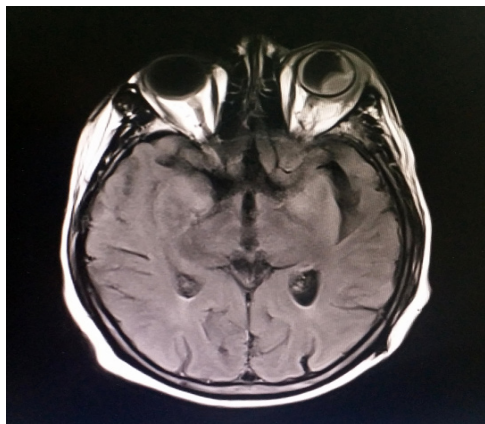


Figure 3: CT orbit (axial view) showed the left eye choroidal lesion was abscess in nature and retro-orbital tissue was inflamed

area of posterior pole with increased internal hyper-reflectivity and retinal detachment (Figure 2).

Laboratory investigation showed leucocytosis with neutrophilia, highly elevated erythrocyte sedimentation rate of 109 mm/h and C-reactive protein of (12.43 mg/L). His diabetic control was also sub-optimised evidenced by elevated HbA1c of 11.7%. As the most common sign of ocular tuberculosis is a choroidal mass followed by choroiditis due to the rich vascular plexus in choroids, we also investigated the patient for the presence of tuberculosis but his Mantoux test was normal and TB Quantiferon was negative. The chest X-ray and abdominal ultrasound were normal. CT brain & orbit showed the choroidal lesion was abscess with inflamed retro-orbital tissue (Figure 3) but there was no intracranial extension. The blood culture grew *Enterobacter sp.* which was sensitive to intravenous Ciprofloxacin and Cefepime. Intravitreal tapping attempted but it was a dry tap with less than 0.1mL

of vitreous obtained. Subsequently, intravitreal vancomycin 2mg/0.1mL and ceftazidime 2mg/0.1mL injection were given to the LE. But the vitreous sample did not grow any organism. Gram stain of the vitreous sample had scanty pus cells, no epithelial cells and no organism was seen. Topical Dexamethasone (Gutt. Maxidex) 0.1% was commenced at four-hourly intervals and tapered down slowly later. Topical cycloplegic (Gutt. Atropine 1%) was initiated once daily for pain relief. He was also referred to the endocrine team to optimise his sugar control. His symptoms of discomfort improved and inflammatory markers reduced with the treatment, but progressive inflammation and subsequent cataract occlude fundus detail. Vision of his LE deteriorated to no perception of light. He developed rubeosis iridis and secondary glaucoma with the LE intra-ocular pressure (IOP) ranged between 25-28 mmHg, which had gone beyond the normal 21 mmHg cut-off point, measured using gold standard Goldmann Applanation Tonometer (Marina et al. 2018). He was treated conservatively in view the LE was painless and had poor visual potential. Vitrectomy was not an option at this stage as the visual prognosis was guarded. Extraocular movement improved with the treatment. The choroidal abscess was monitored with serial B-scan and eventually showed some regression on B-scan.

The RE received laser photocoagulation as a treatment of proliferative diabetic retinopathy (PDR). At the last follow-up, the best corrected vision in the RE was 6/18

due to cataract development and he was no perception to light in the LE, but otherwise comfortable with well-controlled intraocular pressure on two topical anti-glaucoma eyedrops. He was followed-up regularly for monitoring his RE diabetic retinopathy status.

DISCUSSION

Endogenous bacterial endophthalmitis accounts for 2-8% of all endophthalmitis cases with generally poor visual prognosis. The eyes become blind in half of cases and some even require enucleation (Jackson et al. 2003). Visual recovery is poor as this condition is related to underlying systemic infection, which may be difficult to control. In many cases, patients are either unwell or immunocompromised. Diabetes mellitus is most commonly associated with endogenous endophthalmitis. Other systemic medical condition implicated with development of endophthalmitis include concurrent renal disease, endocarditis and immunosuppressive therapy (Wong et al. 2000; Okada et al. 1994). In East Asian nations, *Enterobacteriaceae* including *Enterobacter* sp. are frequently isolated, with *Klebsiella pneumoniae* being the major source (around 60%) of cases of endogenous endophthalmitis, usually in association with liver abscess. Interestingly, gram positive organisms from skin or joint infections, as well as endocarditis are more commonly found to be responsible for endogenous endophthalmitis for Western countries

(Durand 2013). This is believed to be due to higher incidence of cholangiohepatitis and liver abscess in East Asian populations than the Western populations. However, the incidence of gram-negative pathogen-associated endophthalmitis is also on the rise in Western nations over the last two decades (Jackson et al. 2003). Cases that are either culture-negative or are caused by coagulase-negative Staphylococci have better outcome, while the worst outcomes typically found in endophthalmitis caused by Streptococci, *Bacillus* species moulds or other more virulent pathogens (Durand 2013).

Clinical diagnosis of endogenous endophthalmitis with panophthalmitis in this patient was very challenging. Initially, he presented to us with a huge choroidal lesion involving the macula with intense anterior chamber reaction. Given that patient had fever and ocular tissue also showed signs of intense inflammation and involvement of optic nerve, the non-infectious causes of uveitis were less likely. Furthermore, his uncontrolled diabetes mellitus rendered him immunocompromised, possibly explaining the mild-to-moderate vitritis. Other than that, the laboratory tests including elevated full blood count, ESR and CRP all pointed towards ongoing systemic infection. Endogenous source of infection needs to be thoroughly investigated in this case, as the treatment often needs to be given locally and systemically. In this case, we believed the patient developed endogenous endophthalmitis at first which later rapidly progressed to panophthalmitis, as evidenced by

the clinical findings of lid edema and progressive limited extraocular eye movement, supported by radiological evidence of inflammation within the retro-orbital tissue. The choroid layer has rich vascular plexus which makes it prone to be one of the most common site of involvement in haematogenous spread of systemic infection (Ang et al. 2011) while the patient's immunocompromised state induced by his uncontrolled diabetes mellitus was an important risk factor for rapid progression to panophthalmitis.

Multimodal imaging including B-scan and MRI scan aid in delineating and evaluating the extent of infection and content of the choroidal lesion. Brain and paranasal sinus imaging is important to ensure that the infection is contained or limited to ocular structures and does not extend beyond the choroid, to rule out concurrent infection to these structures. In this case, despite empirical broad spectrum antibiotics and intravitreal injection, the severe choroidal abscess, and endogenous endophthalmitis at presentation resulted in poor visual recovery. We also postulate the severe inflammation, coupled with possible progression of diabetic retinopathy in the affected eye leads to rapid deterioration of the condition.

Negative vitreous samples in such cases have to be considered carefully, as it may be a false negative result. Endogenous endophthalmitis initially occurs as a chorioretinitis from hematogenous spread which later inoculates and breaks through into posterior vitreous resulting in a dense microbial load. In early infection

when the anterior part of vitreous has relatively less inflammation, a false-negative vitreous culture may be obtained. Furthermore, the smaller volume of vitreous tapping (0.1-0.2 mL) might decrease the sensitivity. Hence, vitrectomy sample culture i.e. vitreous tap always showed higher positive yield compared to vitreous aspirate (Durand 2013; Modjtahedi et al. 2016).

Vitrectomy is a consideration in selected patients with poor presenting visual acuity to remove infected elements and endotoxin in the vitreous that can lead to further tissue destruction (Chee & Elliot 2016). However, this surgical intervention remains controversial for endogenous endophthalmitis, as the visual prognosis is guarded. A report by Romero et al. recommended vitrectomy especially in those who developed posterior diffuse endophthalmitis and panophthalmitis (Romero et al. 1999). A differing opinion, Wong et al. proposed that the final visual outcome of the patients was unrelated to the vitrectomy but virulence of the organism itself (Wong et al. 2000). Our patient who had endogenous endophthalmitis was in poor general condition and at high risk for general anaesthesia and this had caused delay in surgical intervention timing. Moreover, the technical difficulties as well as the extent of huge lesion also made the vitrectomy and drainage difficult.

Prompt treatment should be initiated immediately when endophthalmitis is suspected even before the definitive diagnosis is made, to minimize complication and increase chance of visual recovery by performing a

vitreous and anterior chamber tap under adequate local anesthesia. The treatment includes intravitreal antibiotics, finding the infection source and giving systemic antibiotics in the case of endogenous sources (Birnbaum & Gupta 2016). Systemic antibiotics are important in controlling bacteremia and indirectly treat the intraocular infection as well. The antibiotic of choice should have good ocular penetration for eliminating the infection. Because of the blood ocular barrier, most systemic antibiotics have poor ocular penetration, making direct intravitreal injection a necessity in endophthalmitis, allowing direct access into the vitreous cavity and achievement of a higher drug concentration for a longer time (Radhika et al. 2014). Jackson et al. found that both intravitreal and systemic antibiotics are crucial as there was a trend of reducing need for enucleation compared to those who received only systemic antibiotics alone (Jackson et al. 2014).

The visual outcome of endogenous endophthalmitis is guarded with almost half of cases ending with vision worse than 20/200. Approximately 24% of eyes require evisceration or enucleation (Wong et al. 2000), despite aggressive broad-spectrum intravitreal and intravenous antibiotics. Poor presenting visual acuity, centrally located lesions and choroidal mass over the macular region are associated with very guarded visual recovery. Virulence of the organism, unilateral involvement, and presence of hypopyon also affect the visual outcome in which patients may have

higher likelihood of evisceration or enucleation (Sallam et al. 2012; Ang et al. 2011).

CONCLUSION

In summary, endogenous endophthalmitis can rapidly progress into panophthalmitis, which is a vision and life threatening serious complication of infections especially in the presence of diabetes mellitus. Despite early and aggressive treatment, visual prognosis is poor in panophthalmitis. Treatment aimed at life-saving rather than vision saving in the case above. Treatment should include controlling the ocular and orbital infection, finding all sources of infection as well as efforts to recover the immunity and counselling.

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