

Clinical outcome of bacterial endogenous endophthalmitis in 15 patients

Dear Editor,

Endophthalmitis refers to the inflammation of the ocular cavities and their immediate adjacent structures without extension beyond the sclera, usually secondary to infection. Endogenous endophthalmitis (EE) results from haematogenous spread of microorganisms in patients with bacteraemia or fungaemia into the eye and represents 2–15% of endophthalmitis cases.¹⁻³ The last study conducted on the incidence of bacterial endogenous endophthalmitis (BEE) in Singapore was published in 2000 by Wong et al.⁴

The study reported *Klebsiella* spp. as the most common organism causing BEE especially among patients with hepatobiliary infections. Since then, it has become a routine practice to refer patients with *Klebsiella* bacteraemia to the ophthalmology service for endophthalmitis screening, independent of visual symptoms. However, there has been little new Singapore data evaluating the incidence and profiles of BEE, especially that of *Klebsiella* endogenous endophthalmitis in recent years.

We retrospectively reviewed the charts of all patients diagnosed with BEE in a tertiary centre in Singapore from 1 January 2014 to 31 December 2021. In this study, endophthalmitis was defined clinically by the presence of inflammation of the posterior segment with or without anterior chamber inflammation. We also collected the blood culture results positive for *Klebsiella pneumoniae* over the study period to review the incidence of EE among patients with *Klebsiella* bacteraemia.

We found 15 patients diagnosed with BEE at our tertiary centre during the study period. All patients had unilateral BEE. The patients' ages ranged from 36 to 74 years, with the median being 57 years. There was a slight male preponderance seen in our cohort (60.0%, n=9). Eleven (73.3%) patients were Chinese, 3 (20.0%) were Malay and 1 (6.7%) was Indian.

Seven patients (46.7%) initially presented to the emergency department for evaluation of their visual symptom(s), while the remaining 8 patients were diagnosed and treated for BEE as inpatients. All patients received intravenous antimicrobial therapy (Table 1). Twelve out of 15 patients (80.0%) had underlying diabetes mellitus.

Most of the patients (86.7%, n=13) presented with blurring of vision, with 3 of them reporting concomitant floaters (Table 1). One patient reported having floaters without blurring of vision. Presenting visual acuity (VA) ranged from 6/7.5 to perception of light with 7 patients (46.7%) having vision of hand movement only or worse. Eight patients (53.3%) had hypopyon. All patients had vitritis, with 5 of them (33.3%) having retina and/or choroidal abscess on presentation.

The number of intravitreal injections received by the group during their treatment period ranged from 1 to 6 injections, with both the mean and median being 3 injections. Each injection might constitute either a monotherapy or combination of either vancomycin, amikacin, and/or ceftazidime. Seven patients (46.7%) underwent vitrectomy (Table 1). Final VA ranged from 6/6 to no perception of light. One patient had an eye eviscerated, and 2 patients passed away from their systemic infection.

Liver abscess (n=4, 26.7%) and urinary tract infection (n=3, 20%) were the most frequent sources of systemic infection. The infective sources of bacteraemia in the rest of our patients are summarised in Table 1. One (6.7%) patient (Patient 10) had septicaemia without any localising foci of infection despite extensive investigations.

Nine (60.0%) patients had positive blood cultures with gram-positive bacteria being the predominant organism—4 patients with *Streptococcus agalactiae* (Group B) bacteraemia and 2 patients with methicillin-sensitive *Staphylococcus aureus* bacteraemia. Three patients (20.0%) had gram-negative bacteraemia and all 3 had *K. pneumoniae* detected in their blood cultures. Six patients (40.0%) had negative blood cultures. Of these, 4 patients (26.7%) had culture-proven sources of extra-ocular infection (Patients 3, 6, 9 and 13). The remaining 2 patients (13.3%; Patients 1 and 5) had their sources of infection established clinically and radiologically.

During the same study period, there were 2,014 patients with blood cultures positive for *K. pneumoniae* being treated in our centre. Three of these patients were diagnosed with endogenous endophthalmitis (Patients 12, 14 and 15). Patient 12 had his blood culture done in another centre and was subsequently transferred to our hospital for further treatment of his liver abscess.

Table 1. Clinical details of patients diagnosed with bacterial endogenous endophthalmitis in our cohort

Patient no.	Year	Age/ Sex	Ethnicity	Systemic conditions	Laterality	Source(s) of infection	Blood culture	Cultures from vitreous fluid	Other cultures	Visual symptoms	Signs	No. and types of intravitreal injections	Vitreotomy	Initial VA	Latest VA	Systemic antibiotics	On antibiotics prior to diagnosis of EE*	Mortality
1	2014	57M	Malay	DM, IHD, previous hepatic and retropharyngeal abscess, ESRF	R	Pyelonephritis	No growth	No growth	NA	Blurring of vision	Hypopyon, vitritis	1-4 : V/A	Yes (x2)	PL	6/30	Ciprofloxacin	No	No
2	2014	53M	Chinese	DM	R	UTI	MSSA	MSSA	Urine: MSSA	Blurring of vision, eye pain	Hypopyon, vitritis	1 : V/A 2 : V/C	Yes (x1)	PL	PL	Cloxacillin	No	No
3	2015	60M	Chinese	DM	R	UTI	No growth	<i>Klebsiella pneumoniae</i>	Urine: <i>Klebsiella pneumoniae</i>	Blurring of vision, eye pain	Hypopyon, vitritis	1-5 : V/C 6 : G	Yes (x1)	HM	NPL	Ciprofloxacin	No	No
4	2015	64M	Chinese	DM, HTN, IHD	R	Infective endocarditis	GBS	No growth	NA	Blurring of vision, eye pain, floaters	Vitritis, choroidal abscess	1 : V/A 2 : V	nil	CF	6/7.5	Ceftriaxone	No	No
5	2016	49M	Chinese	DM, HLD	L	Liver abscess	No growth	No growth	NA	Blurring of vision, eye pain	Hypopyon, vitritis	1 : V/C 2 : C 3 : A	nil	PL	NPL	Ciprofloxacin, ceftriaxone, meropenem	Yes	No
6	2016	74M	Chinese	HTN, IHD, AF, COPD	R	Septic arthritis	No growth	Mixed bacterial growth ^a	Joint fluid: <i>Pseudomonas aeruginosa</i>	Blurring of vision, eye pain	Hypopyon, hyphema, vitritis	1 : V/C 2 : V/A	nil	PL	-	Piperacillin/tazobactam, voriconazole, fluconazole, vancomycin, levofloxacin	Yes	Yes
7	2017	58F	Chinese	HTN, ESRF, NPC, hypothyroidism	R	Infective endocarditis	GBS	No growth	NA	Blurring of vision, eye pain	Hypopyon, vitritis	1 : A/C 2-4 : V	nil	CF	-	Ampicillin, vancomycin, ceftriaxone, meropenem, gentamicin, penicillin G	No	Yes
8	2017	57F	Chinese	DM	R	Septic arthritis	MSSA	No growth	Joint fluid: MSSA	Blurring of vision, floaters	Vitritis	1 : V	Yes (x1)	N18	6/7.5	Cefazolin	Yes	No
9	2017	36F	Malay	DM	R	Large axillary abscess	No growth	No growth	Abscess: MSSA	Floaters, eye redness	Vitritis, choroidoretinal abscess	1 : V/C	nil	6/7.5	6/6	Cloxacillin	Yes	No

Table 1. Clinical details of patients diagnosed with bacterial endogenous endophthalmitis in our cohort (Cont'd)

Patient no.	Year	Age/ Sex	Ethnicity	Systemic conditions	Laterality	Source(s) of infection	Blood culture	Cultures from vitreous fluid	Other cultures	Visual symptoms	Signs	No. and types of intravitreal injections	Vitreotomy	Initial VA	Latest VA	Systemic antibiotics	On antibiotics prior to diagnosis of EE ^a	Mortality
10	2018	68M	Chinese	Nil	R	Unknown ^b	GBS	GBS	Urine: no growth	Blurring of vision, eye pain	Hypopyon, vitritis	1-5 : V/C	Yes (x2)	HM	- (Eviscerated)	Ceftriaxone	No	No
11	2019	56F	Chinese	DM, CKD, HTN	L	Gastrointestinal tract infection	GBS	No growth	Peripheral line: <i>Candida albicans</i>	Blurring of vision	Vitritis, choroidoretinal abscess	1 : V	Yes (x2)	CF	CF	Meropenem, clindamycin, vancomycin, piperacillin/tazobactam, levofloxacin, amiodulafungin, fluconazole	Yes	No
12	2020	42M	Indian	DM	L	Liver abscess	<i>Klebsiella pneumoniae</i>	No growth	Abscess: <i>Klebsiella pneumoniae</i>	Blurring of vision	Vitritis, retinal abscess	1 : V/A 2 : A 3-4 : V/C	Yes (x1)	CF	PL	Ceftriaxone, ciprofloxacin	Yes	No
13	2021	57F	Chinese	DM	R	Disseminated abscesses (lung and kidney)	No growth	No growth	Perinephric abscess: <i>Escherichia coli</i>	Blurring of vision	Hypopyon, vitritis, choroidal abscess	1-3 : V/C 4-5 : C	nil	HM	CF	Ceftriaxone	No	No
14	2021	50M	Chinese	DM, HLD	R	Liver abscess	<i>Klebsiella pneumoniae</i>	No growth	Abscess: <i>Klebsiella pneumoniae</i>	Blurring of vision, floaters	Vitritis	1-4 : C	nil	N6 ^b	6/6	Ceftriaxone, ciprofloxacin	Yes	No
15	2021	66F	Malay	DM	L	Liver abscess	<i>Klebsiella pneumoniae</i>	No growth	Abscess: <i>Klebsiella pneumoniae</i>	Nil	Retinal infiltrates, mild vitreous haze	1 : V/C	nil	N12 ^c	6/9	Meropenem, ceftriaxone, piperacillin/tazobactam, ciprofloxacin	Yes	No

AF: atrial fibrillation; A: amikacin; C: ceftazidime; CF: counting finger; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; EE: endogenous endophthalmitis; ESRF: end-stage renal failure; F: female; GBS: *Streptococcus agalactiae* (Group B); HLD: hyperlipidaemia; HM: hand movement; HTN: hypertension; IHD: ischaemic heart disease; L: left; M: male; MSSA: methicillin-sensitive *Staphylococcus aureus*; NA: not available; NPC: nasopharyngeal carcinoma; NPL: no perception of light; PL: perception of light; R: right; UTI: urinary tract infection; V: vancomycin ; VA: visual acuity

^a Endogenous endophthalmitis was the first presentation in patients who were not on systemic antibiotics prior to diagnosis

^b *Pseudomonas stutzeri*, Coagulase-negative *Staphylococcus*, *Moraxella* spp., *Micrococcus* spp.

^c Bedside assessment with handheld near chart

This brought the incidence of *Klebsiella* BEE in our centre to 0.1% (2 out of 2,014) over 8 years.

Diabetes mellitus is the most common underlying systemic risk factors among our patients having BEE, with liver abscess and urinary tract infection being the most frequent sources of systemic infection in our cohort, similar to the trend observed in earlier studies on BEE.^{2,4,5} The last Singapore study on BEE by Wong et al. found gram-negative bacteria, particularly *Klebsiella spp.*, to be the predominant causative organism in their cohort.⁴ In comparison, despite having an all-Asian cohort, our study found that gram-positive bacteria accounted for 60.0% of positive blood cultures. Interestingly, all 3 patients with gram-negative bacteraemia in our study had *K. pneumoniae* in their blood cultures.

An overwhelming proportion of our patients were symptomatic at the point of presentation, with 14 out of 15 patients reported to have blurring of vision and/or floaters. It was not possible to obtain history in one patient as she had altered mental status from underlying septic shock upon initial review. Of note, it is a routine practice in our centre to refer all patients with *Klebsiella* bacteraemia to the ophthalmology service for endophthalmitis screening. Considering the low incidence of *Klebsiella* EE among patients with *Klebsiella* bacteraemia, it may be worthwhile to reconsider the current workflow of routine *Klebsiella* EE screening to one that is based on visual symptoms. Patients who are unable to give reliable history should still be screened for endophthalmitis by an ophthalmologist.

In summary, BEE was exceedingly rare, averaging around 2 cases per year in our centre. Hepatobiliary and urinary tract infections are the most frequent infective

sources of our patients with BEE, with diabetes being the most common underlying comorbidity. As most patients with BEE are symptomatic upon presentation, routine endophthalmitis screening is of low value and should be reserved for patients with symptoms and those who cannot provide reliable history.

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