

Endogenous Klebsiella Pneumoniae Endophthalmitis (EKPE) case series and literature review: A one-year experience at a tertiary referral centre in Malaysia

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Abstract

To report 4 cases of Endogenous Klebsiella Pneumoniae Endophthalmitis(EKPE) by highlighting the clinical features, systemic comorbidity, source of infection, treatment modalities and visual outcome.

Method

A retrospective review of electronic medical records of patients with diagnosed with EKPE from January 2017 till December 2017 in Hospital Selayang, which is a main tertiary referral hospital in Malaysia.

Result

A total of 4 patients (5 eyes) were diagnosed with Endogenous Klebsiella Pneumoniae Endophthalmitis(EKPE). The mean age group at presentation was 55.5 years (range 49-61 years) with 3 of whom are male and one female patient. All patients had diabetes mellitus as a systemic risk factor. 3 patients presented with unilateral and one patient presented with bilateral eye involvement. Visual acuity on presentation ranged from 6/60 to perception to light. The primary source of infection were variable, with one each from urinary tract, lung, neck and gluteal infection. The most common positive culture were from blood sample with only one from vitreal fluid. All patients were treated with systemic, topical and intravitreal antibiotics. 3 patients underwent vitrectomy following which 1 patients required evisceration. Final visual acuity shows deterioration in all patients of hand movement or worse.

Conclusion

Endogenous Klebsiella Pneumoniae Endophthalmitis (EKPE) is a common human pathogen that can cause rapid and devastating ocular infection with poor visual prognosis. A high index of suspicion among patient with risk factors is needed so that early diagnosis and

adequate treatment is given thus improving final outcome.

Keywords: Endogenous endophthalmitis, Hypertension.

Introduction

Endogenous endophthalmitis (EE) is a severe intraocular infection following a hematogenous bacterial spread from a distant site usually resulting in devastating visual loss. It rarely occurs and only accounts for 2-8% of all cases of endophthalmitis.[1]EE can be due to a variety of causative organisms, which varies depending geographical location[2].

Klebsiella species are gram-negative, encapsulated, facultative anaerobic bacteria which forms the normal flora in the gastrointestinal tract and the nasopharynx[3]. Klebsiella species specifically Klebsiella Pneumoniae is the second leading cause of gram negative bacteremia following Eschericia Coli[4] In Asia, Klebsiella species have been recognized as a leading cause of EE in 54-61 % of cases[5]. Local studies shows similar results with Klebsiella Pneumoniae as the leading cause for EE ranging from 32.5%-44.4% of cases[6,7].Dismal visual outcome are commonly seen among patients following EE. We would like to report the clinical features, systemic comorbidity, source of infection, treatment modalities and visual outcome of patients with Endogenous Klebsiella Pneumonia endophthalmitis (EKPE) in a tertiary hospital in Malaysia.

Materials and Methods

This is a retrospective observational study conducted in Selayang Hospital which is a main tertiary referral centre in Malaysia from January 2017 till December 2017. The search terms endogenous endophthalmitis and Klebsiella were entered in the electronic medical record to identify all patients with the diagnosis over the defined period. All identified records were reviewed to ensure diagnosis of EKPE.

Data regarding demographic details such as age, gender and race, presenting complaints, time of onset, systemic comorbidity, source of infection, laterality, presenting and final

visual acuity, ocular examination, microbiologic and sensitivity profile, treatment modalities were collected.

It is compliant according to Malaysian Good Clinical Practise and registered to National Medical Research Register (NMRR).

Results

Demographic data

A total of 4 patients (5 eyes) were collected in this case series. The mean age group is 55.5 years which ranged from 49-61 years. Three patients were male (3,75%) . Racial distribution is equal between Malays (2, 50%) and Chinese (2, 50%) patients.

Systemic features

Systemic comorbidity

Diabetes mellitus was present in all cases with EKPE. Meanwhile 2 patients have multiple comorbidities including hypertension (Case 1 and 4) and goitre (Case 1). None of the patient had underlying liver disease, immunosuppressive state either due to malignancy or on systemic immunosuppressant .

Source of infection

Source of infection were able to be identified in all cases. There is a variety site consisting of urinary tract, lung, gluteal and neck infection.

Ocular features

Ocular symptoms

Majority of our patients presented with unilateral eye presentation (3, 75%).Only one patient had bilateral eye involvement (1, 25%). All patients had similar ocular symptoms which was blurring of vision with redness. Pain was noted in all patients except in case number 4. None of patients complaint of floaters during initial presentation.

The first presentation to an ophthalmologist following the onset of ocular symptom was a fast as one day duration. All the patients presented within a week of symptoms to the ophthalmologist.

Ocular signs

On presentation, the anterior segment inflammation is assessed base on Standardization of Uveitis Nomenclature (SUN). All cases (5 eyes, 100%) had anterior chamber grade 3 or worse. Fibrin was seen in all eyes (5 eyes, 100%), with hypopyon in 4 eyes (80%).

No fundal view was seen in all eyes (5 eyes, 100%). Ultrasound was performed on all the eyes with no fundal view .Vitreous loculation was documented in all eyes (5 eyes, 100%), meanwhile subretinal abscesses was seen in case 3 and 4 (3 eyes ,60%). No retinal detachment was documented.

Microbiology

All of the cases had cultures taken from blood, vitreous and relevant site during presentation. 100% positive culture were obtained in all patients. Blood culture had the highest yield with positive result (3, 75%). 2 cases (50%) had combination of positive culture of blood with either vitreous or other body fluid. Positive culture for other body fluid includes from one from urine and swab culture respectively.

Vitreous sample was taken in all cases (5 eyes, 100%), however only one vitreous culture came back positive case 3(1, 25%). Antibiotic sensitivities following positive culture ranged widely among antibiotic groups. Klebsiella Pneumoniae is sensitive mostly towards Penicillin, Cephalosporin, Beta lactamase inhibitor and Fluoroquinolone group of antibiotics. However 2 cases reported resistant towards ampicillin.

Treatment

All of our patients were co-managed with our infectious disease colleague. Patients were started on medical therapy consisting of systemic, topical and also intravitreal antibiotics. A combination of systemic antibiotics were started for all the patients. Its consist of combination of ciprofloxacin and other groups of antibiotic which are tailored to the culture sensitivity. Intravitreal antibiotic consisting of vancomycin and ceftazidime were given in all the eyes. Repeated intravitreal injection was given in all the eyes and ranged from 2 till 12 times. Surgical intervention such as vitrectomy was performed in 3 eyes (60%).Case 2 and 4 had early vitrectomy done within the first 2 week of presentation. Meanwhile case 4 had the vitrectomy within 4 weeks of presentation. One eye (20%) further progressed and required evisceration.

Outcome

On presentation, visual acuity ranged from 6/60 to perception to light. Most of the patients presented with a visual acuity of perception to light (3 eyes, 60%). None of the eyes had initial vision better than 6/60.Following completion of treatment, all the cases documented deterioration of visual acuity comparing initial presentation. One patient each achieved final visual acuity of HM and perception to light. Meanwhile other patients had perception to light, 3 eyes(60%). 1 eyes (20%) in case 3, further complicated with panophthalmitis which required evisceration. None of our patient succumb to death due to sepsis or multiorgan failure in this series.

Discussion

As we know, Klebsiella Pneumonia is common gram negative bacteria which forms the normal flora of the body. However this organism may also turn into a highly virulent bacteria leading to a devastating endophthalmitis. Increasing incidence of EKPE in Asia has been postulated due to the organism virulence factors and to a certain extent due to genetic susceptibility of certain races[8,9]. Klebsiella species are resistance toward phagocytosis by neutrophil which is due to its polysaccharide capsule with specific capsular serotype[10]. Klebsiella Pneumoniae specifically with serotype K1 and K2 have shown enhanced virulence with lesser susceptibility toward destruction by neutrophil as compared to other Klebsiella serotype. This ability

is further enhanced among patients with poorly controlled diabetes mellitus[11]. The extreme virulent nature of *Klebsiella Pneumoniae* was demonstrated in experimental animal models as rapid and severe destruction of retinal photoreceptor occurs within 48 hours of infection.

In our series, endogenous *Klebsiella Pneumoniae* endophthalmitis (EKPE) predominantly occurs among male patient with a mean age of 55.5 years. Most patient presented with unilateral involvement, with only one case presented to bilateral eye involvement. Our findings were similar as to previous studies in regards to age, gender and laterality involvement[12,13]. All of our patients presented within a week of symptoms upon onset of ocular symptoms. 3 patients even presented within a day of onset. Vision on presentation ranged from 6/60 to perception to light. The main presenting symptoms was blurring of vision, pain and redness. In our series, all eyes had severe diffuse endophthalmitis. Hypopyon was seen in 4 eyes during presentation. None of the eyes had fundal view on presentation. B scan in all eyes revealed loculation with 3 eyes having subretinal abscess documented. Otherwise no retinal detachment was seen on presentation. Our findings were similar to other previous series. Initial presentation exhibit the extreme virulence nature and rapid destruction caused by this organism.

In terms of risk factor, diabetes mellitus has been reported as a significant risk factor for developing *Klebsiella* sepsis.[14] Other risk factor includes concurrent pyogenic liver abscess, systemic immunocompromise status, disseminated intravascular coagulation, and delayed treatment of systemic bacteremia. [15] However in our series, patients with poor glycaemic diabetes control was identified as the risk factors for developing EKPE.

Several literature reviews identified hepatobiliary tract infection as the commonest site of infection in EKPE as high as 90%, followed by urinary tract and lung infection[16]. In contrast to other studies, Muda et al. reported urinary tract infection(33.3%) as the commonest source of infection for EKPE followed by lung infection (15.8%) and hepatobiliary infection (10%). In our small series, a variety source of infection was documented one each from urinary, lung, gluteal and neck infection. In case one, patient further had disseminated infection involving the liver, lung and thyroid gland.

Early diagnosis and prompt treatment is crucial in managing this condition. EKPE is diagnosed based on clinical and confirmed isolation of *Klebsiella Pneumoniae* from blood, ocular or non-ocular sample from all patients. In our series, positive culture was most seen using blood culture with only one from vitreous sample. Blood culture tends to have higher rate of positivity as compared to vitreous aspirate possibly due to larger volume sampled, meanwhile early or localized infection on the retina surface may result in lower yield from vitreous aspirate[17,18]

In treating metastatic bacterial endophthalmitis, Greenwald et al.[19] suggested intensive and prompt intravenous antibiotic was crucial. All of our patients received immediate systemic, intravitreal and topical antibiotic within 1 hour of diagnosis. Our patients were co-managed with the infectious disease unit in

determining the antibiotic regimen which was tailored on the basis of the culture and sensitivity result. *Klebsiella Pneumoniae* cultured in our series were sensitive towards aminoglycoside, beta lactamase inhibitor, carbapenem, 3rd generation cephalosporin, 2nd generation fluoroquinolones and sulfa trimetoprim. However resistance toward ampicillin were seen in two cultures. The sensitivity profiles in our series were similar with other series. Intravenous antibiotic target both source and ocular infection thus reduces the risk of further embolization of organisms[20]. All of our patients completed at least 2 weeks of antibiotic until the systemic infection was resolved. Meanwhile intravitreal antibiotics improves the antibiotic penetration into the vitreous cavity. In our series all patients received a combination of intravitreal ceftazidime and vancomycin.

Surgical intervention can function as both diagnostic and therapeutic purposes. The purpose for early vitrectomy is to rapidly reduce the organism and inflammatory load in the vitreous, and also to allow diffusion of systemic blood stream into the vitreous cavity. However it should only be reserved for patients with progression of infection despite adequate treatment. The value of early vitrectomy for patient with endogenous endophthalmitis is still controversial as some studies favour early meanwhile other studies were unable to replicate similar result.[21,22,23] Systemic instability and bleeding tendency may limit surgical intervention. In our series, three eyes had vitrectomy done within a period of 2-4 weeks duration since the commencement of treatment. One patient was not fit for vitrectomy had later complicated with panophthalmitis which required evisceration.

In our series, all eyes demonstrated extremely poor visual outcome despite adequate treatment. Only one achieve vision of hand movement, with the rest of the eyes showed further deterioration either perception or no perception towards light. Our outcome was similar with several case series[24]. However, few studies reported favourable visual outcome as result from early and rapid treatment.

Conclusion

In conclusion, our paper highlights the grim outcome among patient with EKPE despite aggressive and adequate treatment. Thus, it is crucial for ophthalmologist and physician to have high index of suspicion regarding the possibility of EKPE among patients with *Klebsiella* sepsis as early diagnosis and treatment may improve the final outcome.

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