

Clinical Review of Endogenous Endophthalmitis in Korea: A 14-Year Review of Culture Positive Cases of Two Large Hospitals

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Purpose: To identify the clinical features and outcomes of endogenous endophthalmitis in Korea. **Materials and Methods:** We reviewed 18 patients with endogenous endophthalmitis at 2 Korean hospitals, treated over a 14 year period between January 1993 and December 2006. **Results:** The comorbidities observed in these cases were diabetes mellitus and liver cirrhosis. The most common pathogens, which were found in 7 patients each (38.9%), were *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. All patients were treated with systemic antibiotics and fortified topical antibiotics. A surgical approach including vitrectomy was performed in 9 cases (50.0%). The prognosis was generally poor, and visual acuity improved slightly in 6 patients (33.3%). **Conclusion:** In this study, diabetes mellitus and *Klebsiella pneumonia* showed a close relationship with endogenous endophthalmitis, respectively. Endogenous endophthalmitis is a serious risk to sight and careful attention to establishing the diagnosis and management may decrease the ocular morbidity.

Key Words: Endophthalmitis, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, liver abscess, diabetes mellitus

INTRODUCTION

Endogenous endophthalmitis is an infectious disease in which systemic infection spreads through the bloodstream to the ocular space without an associated incidence of ocular surgery or trauma.¹ Endogenous endophthalmitis is a rare disease in East Asian countries, especially in Korea, but still remains as a potentially devastating disease that carries a grave visual prognosis in spite of seemingly appropriate antibiotics and aggressive treatment options.²

The causative organism, risk factors and source of the infection have been well

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described previously, however, the pattern in East Asia differs from western countries in that *Klebsiella pneumoniae* is more likely to cause endogenous endophthalmitis.^{3,4} Similarly, liver abscesses and diabetes mellitus have been linked with endogenous endophthalmitis in East Asia.⁵⁻⁸

The current review examined the related medical comorbidity, pathogens, treatment, and prognosis of endogenous endophthalmitis through a retrospective study of 18 patients during a 14-year period at two large hospitals in Korea.

MATERIALS AND METHODS

We reviewed the case notes of all patients diagnosed with endogenous endophthalmitis at Severance Hospital and Wonju Christian Hospital, Korea, during a 14-year period (from January 1993-December 2006). Severance Hospital is a 2000-bed, teaching hospital affiliated with Yonsei University in Seoul. Wonju Christian Hospital is a 750-bed teaching hospital in Wonju. Information on demographic characteristics, comorbid condition, underlying infection, and treatment was obtained through chart review.

The diagnosis of endogenous endophthalmitis was established by the presence of iritis and vitritis together with the presence of positive blood or vitreous or aqueous culture. We excluded patients who underwent ophthalmic surgery within 1 year of diagnosis, post-traumatic endophthalmitis, corneal ulcers, diabetic maculopathy or ocular disease-associated diabetes mellitus. Visual acuity is a quantitative measure of the ability to identify black symbols on a white background at a standardized distance, estimated by ophthalmologist. During the period, 332 patients were diagnosed with endophthalmitis, whereas 18 patients (18 eyes, 5.4%) were diagnosed with endogenous endophthalmitis.

Our study included information regarding presenting complaints, the time from onset of symptoms to diagnosis, microbiologic results, treatment, and visual outcome.

The study protocol was approved by the ethics committee of the Severance Hospital and Wonju Christian Hospital.

RESULTS

Eighteen patients were included in the study. The study population consisted of 13 men (72.2%) and 5 women (27.8%) with a mean age of 63.5±14.5 years. The average duration of hospitalization was 42.3±13.7 days. Medical record re-

view revealed, 9 patients (50.0%) with diabetes mellitus and 3 patients (16.7%) with liver cirrhosis. Underlying infections were community-acquired in 13 patients (72.2%) and nosocomial-acquired in 5 patients (27.8%). Pneumonia was the underlying infection in 4 patients (22.2%), and liver abscesses in 3 patients (16.7%).

Among the classic symptoms of endogenous endophthalmitis,⁹ conjunctival injection and corneal edema were observed in 16 cases (88.9%), and subconjunctival hemorrhage and hypopyon were observed in all patients (100%). Eight patients (44.4%) had ocular pain, 5 (27.8%) had blurred vision at time of diagnosis. Diabetic maculopathy or ocular disease-associated diabetes mellitus was not found in all 9 patients with diabetes mellitus.

In 8 patients (44.4%), a primary source of infection was not identified although all 8 patients had positive blood cultures (Table 1). Blood cultures were obtained from 13 patients (72.2%) and 10 patients out of 13 patients (76.9%) were culture positive. Sixteen patients (88.9%) had both vitreous and aqueous samples taken, and 11 patients of these (68.8%) showed the infective organism (Table 2). A vitreous biopsy was performed on 12 patients (66.7%), leading to identification of bacteria in 7 cases (58.3%). There were 4 patients (22.2%) who had aqueous taps and they were all culture positive.

The organism identified in blood cultures included *Klebsiella pneumoniae* (6 patients, 33.3%), and *Pseudomonas aeruginosa* (2 patients, 11.1%) and the organism identified in vitreous cultures included *Klebsiella pneumoniae* (2 patients, 11.1%), and *Pseudomonas aeruginosa* (6 patients, 33.3%) (Table 2).

All patients were treated with systemic antibiotics and fortified topical antibiotics, and intravitreal steroid injection was combined with intravitreal antibiotics in 9 patients (50.0%). Surgical approaches including vitrectomy were performed on 9 patients (50.0%) considering the severity and extent of inflammation. Six patients (6 of 9 patients with surgical treatment, 66.7%) underwent only trans pars plana vitrectomy, and 1 patient (11.1%) was treated with pars plana lensectomy and vitrectomy together because lens abscess existed with endophthalmitis. Two patients (22.2%) were treated with evisceration because severe infection was accompanied with pain and no visual potential was expected. In 3 patients (16.7%), only intravenous antibiotics were administered without intravitreal antibiotics or surgery due to their poor physical condition or refusal of treatment.

Table 1. Clinical Characteristics

Case	Age	Gender	Comorbidity	Source of infection	Causative Microorganism	Primary culture	Secondary culture	Acquired place
1	50	F	None	Not identified	<i>Pseudomonas aeruginosa</i>	Blood	None	Community
2	70	M	DM	Not identified	<i>Pseudomonas aeruginosa</i>	Blood	None	Community
3	67	F	DM, CRF	UTI	<i>Klebsiella pneumoniae</i>	Blood	None	Community
4	56	M	Liver cirrhosis	Pneumonia	<i>Escherichia coli</i>	Vitreous	None	Nosocomial
5	61	F	Liver cirrhosis	Not identified	<i>Klebsiella pneumoniae</i>	Vitreous	None	Community
6	80	M	DM	Liver abscess	<i>Klebsiella pneumoniae</i>	Blood	Abscess	Community
7	43	M	DM, liver cirrhosis	Thigh abscess, pneumonia	<i>Staphylococcus aureus</i>	Blood	Sputum	Nosocomial
8	86	M	COPD	Pneumonia	<i>Pseudomonas aeruginosa</i>	Vitreous	Sputum	Nosocomial
9	55	F	None	Liver abscess, pneumonia	<i>Klebsiella pneumoniae</i>	Blood	Sputum, Abscess	Nosocomial
10	54	M	Hypertension	Liver abscess	<i>Klebsiella pneumoniae</i>	Blood	Abscess	Community
11	66	M	DM, CAOD, hypertension	Cellulitis, infective endocarditis	<i>Staphylococcus coagulase negative</i>	Blood	None	Community
12	60	F	DM, pancreatic cancer	Prostate abscess, necrotizing pancreatitis	<i>Klebsiella pneumoniae</i>	Blood	None	Community
13	69	M	DM, COPD	Not identified	Beta-hemolytic group G Streptococcus	Aqueous	None	Community
14	82	M	None	Not identified	<i>Pseudomonas aeruginosa</i>	Vitreous	None	Community
15	61	M	Rectal cancer	Not identified	<i>Pseudomonas aeruginosa</i>	Vitreous	None	Community
16	34	M	DM, mental retardation	Cellulitis	<i>Klebsiella pneumoniae</i>	Blood	None	Community
17	85	M	Asthma	Not identified	<i>Pseudomonas aeruginosa</i>	Vitreous	None	Community
18	70	M	DM	Not identified	<i>Pseudomonas aeruginosa</i>	Vitreous	None	Community

DM, diabetes mellitus; CRF, chronic renal failure; COPD, chronic obstructive pulmonary disease; CAOD, coronary artery occlusive disease; UTI, urinary tract infection.

DISCUSSION

Endogenous endophthalmitis is an uncommon form of endophthalmitis. In our study only 18 patients were diagnosed in a 14 year period. Another study from Korea also reported 9 cases in 10 years.¹⁰ While the incidence in East Asia is undoubtedly low, the incidence may be increasing.¹¹

Reviewing our baseline characteristics, we found that duration of hospitalization was quite long (42 days). The reason for long duration of hospitalization could be explained by combined comorbidity, high proportion of severe infection, and old age in our population. Indeed, 15 of 18 patients (83.3%) had a serious underlying disease, including diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease and liver cirrhosis, while 8 patients (44.4%) had severe infection, including pneumonia, liver abscess, infective endocarditis and necrotizing pancreatitis (Table 1). Moreover, mean age of our study populations (63.5 years) seemed to be higher than that in other studies.^{11,12} These characteristics could also be one of the factors which resulted in poor prognosis in our study.

In our experience, blood culture was the most reliable method of diagnosing endogenous endophthalmitis, but both aqueous and vitreous samples proved equally to be useful in some cases.^{13,14}

Table 2. Microbiology

Causative microorganism	Blood isolates (n=18)	Vitreous or aqueous isolates (n=18)
<i>Klebsiella pneumonia</i>	6 (33.3%)	2 (11.1%)
<i>Pseudomonas aeruginosa</i>	2 (11.1%)	6 (33.3%)
<i>Escherichia coli</i>	0 (0.0%)	1 (5.6%)
<i>Staphylococcus, coagulase negative</i>	1 (5.6%)	1 (5.6%)
<i>Staphylococcus aureus</i>	1 (5.6%)	0 (0.0%)
Beta-hemolytic group G Streptococcus	0 (0.0%)	1 (5.6%)
No growth or not done	8 (44.4%)	7 (38.9%)

Table 3. Diagnostic Elapsed Time and Visual Outcome

Case	Elapsed interval*	Initial visual acuity	Final visual acuity
1	15	LP (-)	HM (+)
2	10	LP (+)	LP (-)
3	2	LP (-)	LP (-)
4	5	20/60	HM (+)
5	3	LP (+)	HM (+)
6	2	HM (+)	LP (-)
7	5	LP (+)	LP (-)
8	3	Unknown	Unknown
9	4	Unknown	LP (-)
10	5	20/125	Loss of vision
11	3	20/800	0.1
12	2	LP (+)	Loss of vision
13	14	20/800	FC(+)/30 cm
14	7	LP (-)	LP (-)
15	5	LP (+)	HM (+)
16	14	HM (-)	HM (-)
17	1	HM (+)	FC (+)/1 m
18	1	HM (+)	FC (+)/30 cm

LP, light perception; HM, hand motion; FC, finger count.

Unknown: visual acuity are not estimated because patient were on ventilator care.

*Elapsed interval: time from the onset of symptom to diagnosis.

In our present study, *Klebsiella pneumonia* and *Pseudomonas aeruginosa* were the most common infecting pathogens [in 7 patients each (38.9%)]. In East Asia countries, Gram-negative organisms have been reported to make up 70% of infecting pathogens responsible for endogenous endophthalmitis.^{3,9,11} This compares with reports from western countries where Gram negative organism comprises only 30% of the pathogens isolated in patients with endogenous endophthalmitis. Several studies suggest that the reason for the differing pathogen distribution is related to high prevalence of hepatobiliary infections in Asian populations,^{6,11} Of hepatobiliary infections, liver abscess showed a close relationship with the presence of endogenous endophthalmitis, according to several reports.^{15,16} Additionally, many studies suggested a strong association between liver abscess and

Klebsiella pneumonia.^{17,18} In our study, *Klebsiella pneumonia* was cultured in all 3 patients with liver abscess.

Diabetes mellitus was found to be a risk factor for endogenous endophthalmitis and show a close relationship with *Klebsiella pneumonia* infection.^{4,8,9} Yang, et al.⁵ showed that diabetes mellitus is a risk factor for developing endogenous endophthalmitis in patients who already have liver abscesses. Of the 9 patients with diabetes mellitus in our study, *Klebsiella pneumonia* was the infecting pathogen in 4 of those patients (44.4%). Although we reviewed only 18 patients, this rate, nevertheless, suggests a close relationship between *Klebsiella pneumonia*, endogenous endophthalmitis, diabetes mellitus, and liver abscess. In our study, diabetes mellitus patients showed poor prognosis: We observed worsening visual acuity in 5 patients (55.6%, 1 patient went completely blind), and no interval change in 2 patients (22.2%) among 9 diabetes mellitus patients. We suggest that there are two reasons for these results. First, *Klebsiella pneumonia* with endogenous endophthalmitis, which showed a close association to diabetes mellitus, was related to poor prognosis. Secondly, injury to the microvasculature of the retina and ocular space, which occurs in diabetes mellitus patients, is associated with poor prognosis when infected with endogenous endophthalmitis. In conclusion, high proportion of *Klebsiella pneumonia* as pathogen in our study population and role of diabetes could be an another explanation of poor prognosis in our study.

In treatment of endogenous endophthalmitis, physicians should consider intravitreal antibiotics and surgical approaches including vitrectomy. Even though, the role of surgical treatment, including vitrectomy, is still debatable, potential benefits of surgical treatment are expected to remove vitreous scaffold, bacterial load, and toxic bacterial and inflammatory product.¹⁹ Previous study suggested that immediate pars plana vitrectomy could be beneficial to postoperative bacterial endophthalmitis patients with poor visual acuity (only light perception or loss of light perception in visual acuity).²⁰ We suggest that surgical treatment, includ-

ing vitrectomy, needs to be decided, depending on the severity and extent of inflammation.

One study showed better results with early diagnosis and intravitreal antibiotics administered within 48 hours,⁷ whereas another study showed that a delay in treatment was a predictive factor for poor results in the resolution of endogenous endophthalmitis.⁴ In our study, the average time from the onset of symptoms to diagnosis was 5.61 days, and 4 patients were diagnosed with endogenous endophthalmitis more than 10 days after symptoms appeared. Finally, 9 patients (50.0%) had decreased visual acuity in our study. These results support the hypothesis that a delay in diagnosing endogenous endophthalmitis is related to poor visual outcome.

In our study, 6 patients (33.3%) with slightly improved visual outcome had underlying infections that were community acquired (except one case), non-combined, but not as severe as those in other patients. Moreover, they were diagnosed relatively early except one case. Treatment included vitrectomy, and intravitreal antibiotics were given to these patients. These results suggest that early diagnosis, severity of underlying infection, and active treatment are related to a good prognosis of endogenous endophthalmitis.

In conclusion, physicians must pay attention to ocular symptoms such as conjunctival hemorrhage, ocular pain, and decreased visual acuity in severely infected patients. Particularly, greater attention must be paid to ocular symptoms in patients with diabetes mellitus or liver abscesses. As for the treatment, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are considered common causative pathogens, and consultation with an ophthalmologist is necessary and should not be delayed. Proper treatment including intravitreal antibiotics should be done with supportive care.

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