

Endogenous endophthalmitis: A 5-year Retrospective Study at Thammasat Hospital

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Purpose: To study clinical features, risk factors, microbiological characteristics, and visual outcomes in patient with endogenous endophthalmitis

Design: Retrospective, observational case series study

Methods: Review of medical records of 16 patients 18 eyes with endogenous endophthalmitis between 2017 -2022 at Thammasat Hospital which had completed in medical record more than 12 months. The initial visual acuity, underlying disease, method of treatment, method of culture etc. had been recorded. From the results of this study, we compared the treatment outcomes between intravenous antibiotics, pars plana vitrectomy, and a combined method. Endophthalmitis from other causes had been ruled out from the study.

Results: 18 eyes of 16 patients who were diagnosed with endogenous endophthalmitis. Mean($\pm$ SD) age was 52.75 ($\pm$ 18.58) years. Mean($\pm$ SD) onset was 5.43($\pm$ 7.44) days. Seventy-five percent of patients had underlying disease. The most common risk factor was diabetes mellitus and the most common primary site of infection is the urinary tract. Causative organisms were identified in 87.5% of patients. The most common organism was *Streptococcus agalactiae* (43.75%). The final visual outcomes were no light perception in 29.41%.

Conclusion: Endogenous endophthalmitis is the cause of severe visual loss. Risk factor of endogenous endophthalmitis comes from various causes but diabetes mellitus is still the most common risk factor. Primary vitrectomy with intravitreal antibiotics may be the better option for treatment than intravitreal antibiotics alone.

Key word: Endogenous endophthalmitis, Intravitreal antibiotics, Pars plana vitrectomy
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Introduction

Endogenous endophthalmitis is an infection in the eye that occurs when an infectious agent is carried from an internal source in the body through the bloodstream, subsequently entering the eye by crossing

the blood-retina barrier, leading to an eye infection. This condition is relatively uncommon, accounting for approximately 2-17% of all eye infections.¹⁻⁵ Additionally, it represents a severe form of eye infection that can result in blurred or distorted vision.

The main causative agents of endogenous endophthalmitis are predominantly bacteria and fungi, while the occurrence of protozoal infections is very rare. Moreover, the types of bacterial pathogens responsible for endogenous endophthalmitis differ in various geographical regions around the world.^{3,5} According to

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studies conducted in Western countries such as the United States and Europe, the predominant bacterial pathogens^{3,5-7} causing endogenous endophthalmitis are gram-positive bacteria, including species like *Staphylococcus* spp. Bacterial^{7,21} induced endophthalmitis which consequence of primary infections in other parts of the body, such as urinary tract infections (UTIs) and infective endocarditis, before spreading to the eye and causing endophthalmitis.

In studies conducted in the East Asian side, there are still variations in research findings regarding the causative agents of diseases. It has been observed that the majority of bacterial pathogens found in this region are gram-negative bacteria^{3-5,8-10}, such as *Klebsiella* spp. and *Pseudomonas aeruginosa*, which differs from the results seen in Western countries. These infections often occur as a consequence of primary infections in the liver and the biliary tract, for example, in cases of liver abscesses. However, some studies in the East Asian region have shown results consistent with findings in Western countries. In these studies, gram-positive bacteria have been found to be the predominant causative agents, similar to what is observed in Western regions.¹² For example, gram-positive bacteria such as *Streptococcus* species and *Staphylococcus aureus* have been commonly identified as the main bacterial pathogens. Regarding fungal infections, the most frequently encountered pathogen is *Candida* spp. *Aspergillus* spp. is the second most frequently found fungal pathogen.^{4,6,9,10,13-15} This diversity in research findings highlights the complexity of the epidemiology of endogenous endophthalmitis in different regions of the world. The variations in causative agents may be influenced by factors such as local microbial flora, prevalence of underlying medical conditions, and other region-specific factors.

The predisposing factors associated with endogenous endophthalmitis include patients with impaired immune systems^{4,13, 16-19}, such as those with poorly controlled diabetes, kidney failure^{5,8,17,19}, liver abscesses^{4,8,10,12,17,19}, cancer^{5-9,16,19}, or receiving immunosuppressive drugs⁶ like organ transplant^{3,4,6,8,12,13,18} recipients or individuals taking immunomodulating and antineoplastic agents⁴ for cancer treatment. The use of broad-spectrum antimicrobial agents and intravenous drug abuse can also

increase the risk. Additionally, patients with conditions like HIV/AIDS, long-term indwelling catheters^{3,4}, intravenous hyperalimentation⁴, kidney dialysis^{4,6}, and premature infants²⁰ are also considered at higher risk for developing endogenous endophthalmitis. It's essential to recognize and manage these risk factors to help prevent or diagnose the condition promptly and effectively.

To identify the causative pathogens of the disease, several diagnostic methods can be employed, including vitreous aspiration, vitrectomy, aqueous tapping, and blood culture. Recent studies²⁹ have shown that the rate of positive vitreous cultures has increased to 41.7% for cases in which antibiotic treatment was not received before sample collection. From studies conducted by Okada et al., it was found that diagnostic vitrectomy had a higher chance of detecting infectious agents compared to vitreous aspiration (92% vs. 44%, respectively).²² Bacterial infections had a higher likelihood of being detected through culturing (96% overall), whereas the chance of detecting fungal infections decreased to 55.8%.²³ The use of real-time polymerase chain reaction (RT-PCR)²⁴ to detect microbial genetic material showed a higher probability of detecting infectious agents (74.4%)²³ compared to conventional culture methods.

The primary treatment approach for Endogenous endophthalmitis typically involves administering intravenous antimicrobial therapy to combat the bloodstream infection and intravitreal injections of antimicrobial agents directly into the vitreous cavity of the eye. This combination therapy aims to target and eliminate the causative pathogens effectively. Moreover, there have been studies suggesting that early pars plana vitrectomy in patients with relatively good initial visual acuity may lead to better treatment outcomes. This early vitrectomy can potentially preserve better visual acuity compared to cases where severe vision loss occurs. Additionally, it may reduce the need for more invasive procedures such as evisceration or enucleation. The choice of treatment strategy depends on various factors, including the severity of the infection, the causative pathogen, and the patient's overall health condition. Prompt and appropriate management is essential to improve the chances of preserving vision and preventing complications in Endogenous endophthalmitis.

Patients and methods

This study was a retrospective, observational case series which was approved by the institutional review board (IRB) of the faculty of medicine at Thammasat University. The patient's medical were reviewed and data was collected pertaining age, gender, underlying disease, microbial culture results, causes and treatments received. The requirement for informed consent was therefore waived. This study was a historical review of 72 patients, however only 16 patients had complete data. 18 endogenous endophthalmitis patients (18 eyes) at Thammasat Hospital from January 2017 to December 2022 were included in this study. Statistical analysis used SPSS version 23.

The data was obtained from medical records. The patients who had a history of intraocular surgery, ocular trauma, and previous ocular infection were excluded from this study. The patient's demographic, clinical, and laboratory data were recorded. Visual acuity was obtained in a Snellen test with a measurement distance of 20 feet (20/20). VA below 20/200 was grouped into 4 categories: Counting fingers (FC), Hand movement (HM), Perception of light (PL), and No perception of light (no PL)

Visual acuity improvement or worsening was defined as a gain or loss of more than one line of Snellen VA consecutively. If VA was below 20/200 (FC to no PL), it was defined as one step improvement or worsening for evaluation.

Results

Table 1: Demographic data and risk factor of endogenous endophthalmitis

Total patient (No)	Total patient (N=16 (18 eyes))		Associated diseases		
	Patient (N)	%		Patient (N)	%
Male	11	68.75%	DM	4	25%
Female	5	31.25%	No risk factor	4	25%
Age (years)			Valvular heart disease	3	18.75%
Mean (SD)	52.75 (18.58)	16-78	HT	1	6.25%
Laterality			Cirrhosis	1	6.25%
Unilateral	14	87.5%	HIV	1	6.25%
Bilateral	2	12.5%	Malnutrition	1	6.25%
Side			Heavy Alcoholic	1	6.25%
Right	9	56.25%	Malignancy	1	6.25%
Left	5	31.25%	Hemodialysis	1	6.25%
Bilateral	2	12.5%	Indwelling catheter	1	6.25%

Sixteen patients (18 eyes) with endogenous endophthalmitis were analyzed. There were 11 males' eyes (68.75%) and 5 females' eyes (31.25%). The mean ($\pm$ SD) age was 52.75 ($\pm$ 18.58) years old, and the range was 16-78 years old. (Table 1) The laterality of involvement was unilateral 14 cases (87.5%, right 9 cases, left 5 cases) and bilateral 2 cases (12.5%). The total eyes in this study were 18 eyes. The mean ($\pm$ SD) onset was (5.43 ± 7.44) days (ranging 1-30 days). The median onset was 3 days (Table 1).

The patient's risk factor was found in 12 cases (75%). The risk factors in this study were diabetes mellitus in 4 cases (25%) and valvular heart disease in 3 cases (18.75%). On the other hand, the various following risk factors were each present in a single case (6.25%); essential hypertension, liver cirrhosis, human immunodeficiency virus, malnutrition, heavy alcoholism, malignancy, hemodialysis, and indwelling catheter (Table 1).

Table 2: Source of Primary infection endogenous endophthalmitis

Source of infection	Patient (N)	%	Source of infection	Patient (N)	%
UTI	3	18.75%	Bacterial meningitis	1	6.25%
Unknown	3	18.75%	Bursitis	1	6.25%
Septicemia	2	12.5%	Soft tissue infection	1	6.25%
Liver abscess	2	12.5%	IE	1	6.25%
Septic arthritis	1	6.25%	Tonsillitis	1	6.25%
Infectious hepatitis	1	6.25%	Epidural abscess	1	6.25%

The primary sites of infection were urinary tract infection in 3 cases (18.75%), unknown 3 (18.75%), septicemia 2 (12.5%), liver abscess 2 (12.5%). While one case each of the following were found; septic arthritis, infectious hepatitis, bacterial meningitis, bursitis, soft tissue infection, infectious endocarditis, tonsillitis and epidural abscess (Table 2).

Overall culture identification was positive in 12 eyes (66.6%) from 18 eyes. The highest-yield methods were vitreous from pars planar vitrectomy, positive in 8 eyes (44.4%), while vitreous aspiration yielded positive results in 3 eyes (16.6%), and aqueous tapping in 1 eye (5.5%) (Table 3).

Table 3: Method of culture and result in endogenous endophthalmitis

Method of culture	N=16 (18 eyes %)	Result(eyes%)	
		Positive	Negative
Vitreous from PPV	9 (50%)	8 (44.4%)	1 (5.5%)
Vitreous aspiration	6 (33.33%)	3 (16.6%)	3 (16.6%)
Aqueous tapping	3 (16.67%)	1 (5.5%)	2 (11.1%)

Table 4: Culture identification and Microbiologic results of endogenous endophthalmitis

Culture results	Patient(N)	Patient(%)
Bacteria	13	81.25%
- Gram positive	9	56.25%
Streptococcus agalactiae	7	43.75%
Staphylococcus aureus (MSSA)	2	12.5%
- Gram negative	4	25%
Klebsiella pneumoniae	2	12.5%
Stenotrophomonas maltophilia	1	6.25%
Pseudomonas aeruginosa	1	6.25%
Fungus	1	6.25%
Candida albican	1	6.25%
No growth	2	12.5%

In this study, the culture results showed bacteria in 13 cases (81.25%), fungus in 1 case (6.25%), and no growth in 2 cases (12.5%) whereas Streptococcus agalactiae was the most common pathogen in this study (7 cases,

43.75%), with *Klebsiella pneumoniae* being the most prevalent among Gram-negative bacteria, found in 2 cases (12.5%). Only 1 case showed positive culture for the fungus *Candida albicans* (6.25%) (Table 4).

Table 5: Treatment modalities and outcome in overall

Overall outcome	Eyes (N)	(%)
Better	6	33.33 %
Worse	12	66.66 %
Intravenous antibiotics		
Yes	18	100 %
NO	0	0
IVT antibiotics		
Yes	17	94.44%
NO	1	5.56%
Pars plana vitrectomy		
Yes	11	61.11%
NO	7	38.89%

Overall, patients who had endogenous endophthalmitis seem to have worsened even after receiving treatment in 12 eyes (66.66%). of which all of them were treated with intravenous

antibiotics. Intravenous antibiotics were received in 17 eyes (94.44%) and 11 eyes (61.11%) underwent pars plana vitrectomy (Table 5).

Table 6: Compare Initial and Final visual acuity after treatment

Initial visual acuity			Final visual acuity		
	Eyes (N)	(%)		Eyes (N)	(%)
no PL	2	11.11%	no PL	5	27.77%
PL	3	16.67%	PL	1	5.55%
PJ	2	11.11%	PJ	1	5.55%
HM	6	33.33%	HM	0	0.00%
FC	1	5.56%	FC	1	5.55%
≤ 20/200	3	16.67%	≤ 20/200	3	16.66%
> 20/200	1	5.56%	> 20/200	2	11.11%

The initial visual acuity (VA) results were as follows: no perception of light (NPL) in 2 eyes (11.11%), perception of light (PL) in 3 eyes (16.67%), projection of light (PJ) in 2 eyes (11.11%), hand motion (HM) in 6 eyes (33.33%), finger counting (FC) in 1 eye (5.56%), worse than 20/200 in 3 cases (16.67%), and better than

20/200 in 1 case (5.56%). The final visual acuity (VA) outcomes were: NPL in 5 cases (27.77%), PL in 1 eye (5.55%), PJ in 1 eye (5.55%), FC in 1 eye (5.55%), worse than 20/200 in 3 cases (16.66%), better than 20/200 in 2 cases (11.11%), evisceration in 3 eyes (16.66%), and enucleation in 2 eyes (11.11%) (Table 6).

Table 7: Subgroup analysis of Outcomes of treatment between combine PPV with IVT and IVT alone.

Combine PPV with IVT		
Outcome	Eyes(N)	(%)
Better	5	45.45%
Worse	5	45.45%
Not change	1	9.09%

Outcome IVT alone		
Outcome	Eyes(N)	(%)
Better	2	11.11%
Worse	5	88.88%
Not change	0	0

Discussion

Endogenous endophthalmitis can originate from various pathways, but hematogenous spreading is the most common cause, leading to a high mortality rate and poor visual acuity outcomes. A major review of systemic conditions related to endogenous endophthalmitis revealed that diabetes mellitus was reported in approximately 9.3% to 85.7% of patients.⁶ Our recent study similarly showed that an identifiable preexisting predisposing condition was present in a significant number of cases, with diabetes mellitus being the most common systemic condition (25%).²⁵ Other underlying conditions included valvular heart disease (18.75%), hypertension (6.25%), and others.

The culture-positive rate from our series was 87.5%, with the majority of positive cultures obtained through the pars plana vitrectomy (PPV) method, accounting for 66.67% of cases. Similarly, Nicoleta A. et al.²⁹ reported that not only did the yield from vitreous culture was high usually more than 93% of endogenous endophthalmitis compared with other methods but also hemoculture had a high positive culture rate with a variable range of between 20% to 100% which can help the clinician when vitreous culture returns negative. To maximize the rate of positive results, the blood sampling should be performed during peak of fever and before systemic antibiotics are given.

Systemic infections such as liver abscesses, meningitis, and infective endocarditis can lead to the subsequent development of endogenous endophthalmitis. According to Zenith et al.²⁷, gram-negative bacteria endogenous endophthalmitis was more common than gram positive bacterial causes. However, our case series found that the majority of pathogens were bacteria (81.25%), while only a small percentage was fungus (6.25%). Among the bacterial cultures, *Streptococcus agalactiae* (*S. agalactiae*) accounted for 43.75% of cases, making it the most prevalent in contrast of previous study that found *Klebsiella* sp. the most.

S. agalactiae is recognized as a major human pathogen, and it is part of the normal flora found on the skin, throat, and lower gastrointestinal tract. Primary sources of *S. agalactiae* have been reported by different studies. According to Yu Ra Sim et al.²⁸ the most common primary source of *S. agalactiae* was skin

and soft tissue infections (22.7%), followed by septic arthritis and urinary tract infections (13.6% both). In contrast, a recent study found different patterns. In this study, the most common primary source of *S. agalactiae* was arthritis (28.57%), followed by bacterial meningitis (14.28%), and cases with an unknown cause (42.85%). Similar to the results of the recent study, patients who tested positive for *S. agalactiae* in case series had chronic immunosuppressive diseases, such as diabetes, malignancy, valvular heart disease, and malnutrition, prior to developing endogenous endophthalmitis. Despite this, it can still lead to endogenous endophthalmitis, which is very rare but visually a devastating disease.^{20,23,26} Similar to the findings of our recent study, patients who tested positive for *S. agalactiae* in their cultures had final visual outcomes ranging from Perception of Light (PL) to No Perception of Light (NPL). In the worst-case scenarios, enucleation had to be considered due to the severity of the condition. The prevalence of bacterial pathogens, particularly *S. agalactiae*, our case series showed the importance of understanding the diverse nature of endogenous endophthalmitis and its potential to cause severe visual impairment or even lead to the loss of the affected eye (Figure 1).

In a study conducted by Zhang et al.¹⁵, the treatment results from PPV showed that almost all cases had a high anatomical success rate of 85% and retained a vision of finger counting (FC) or better after surgery in 80% of cases. However, in contrast to the findings in Zhang et al.'s study, our cases underwent PPV as well, but the final visual acuity results were still Perception of Light (PL) or No Perception of Light (NPL). Combined Pars plana vitrectomy with intravitreal antibiotics seem to be more than effective than intra vitreous antibiotics alone which 5 eyes from 18 showed improvement (Table 7). Despite this, none of the PPV cases had to undergo evisceration or enucleation when compared with other methods like intravitreal antibiotic injection (4 out of 16 cases required evisceration or enucleation). This indicates that PPV is the preferred method for treating endogenous endophthalmitis because it allows us to save the globe even if the visual outcomes may be poor. Overall, despite the poorer visual acuity results in our cases compared to Zhang et al.'s study¹⁵, the avoidance of more drastic measures like evisceration or enucleation

highlights the favorable impact of PPV in the treatment of endogenous endophthalmitis.

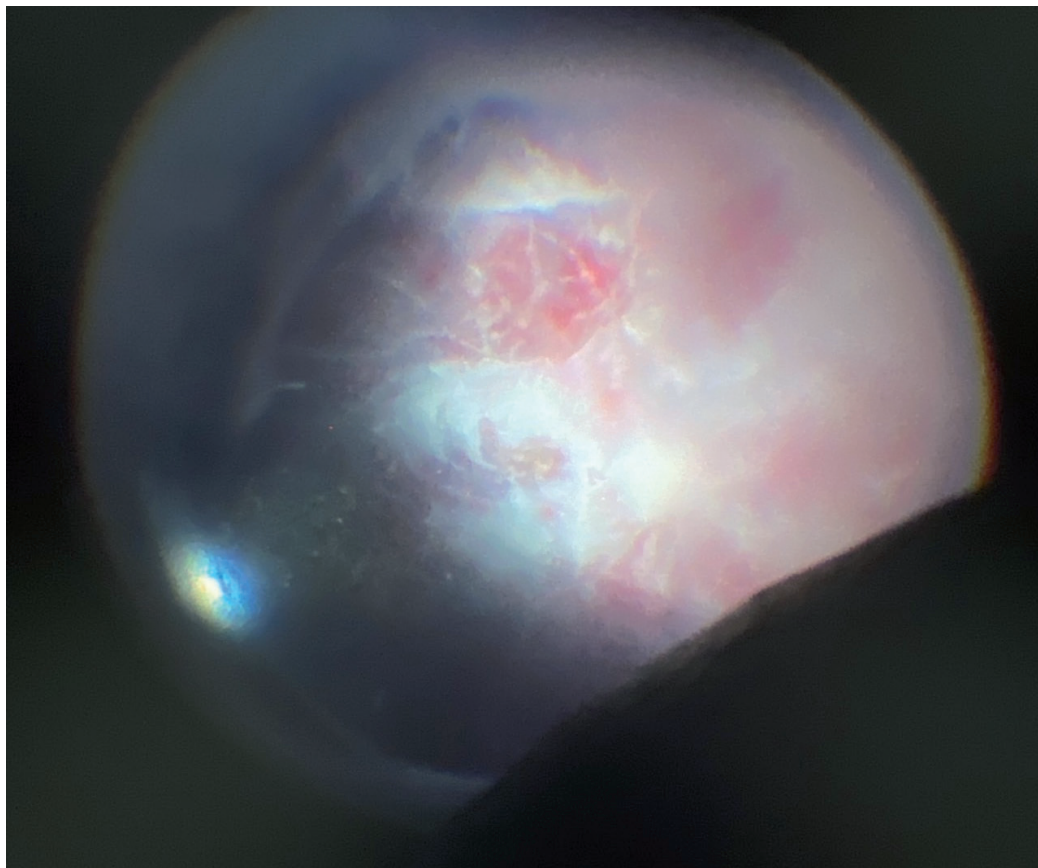


Figure 1: A 67-year-old Thai male with unknown underlying conditions was referred from a private hospital due to acute painful visual loss experienced three days ago. Upon initial examination, his visual acuity was found to be Perception of Light (PL). Further examination revealed a hypopyon of 4 mm, corneal edema, and vitreous haze of grade IV. As a result, the patient underwent an emergency pars plana vitrectomy. During the vitrectomy procedure, after clearing the core vitreous, numerous instances of retinitis and vasculitis were discovered. Culture in this case from vitrectomy was *S. agalactiae*.

The most important in the treatment of endogenous endophthalmitis was prompt appropriate systemic antibiotic therapy. The treatment modality for endogenous employed in our case series included combined intravitreal and systemic antibiotics, PPV, and Intravitreal antibiotics are generally essential in treating bacterial endogenous endophthalmitis as most topical or systemic antibiotics do not reach a sufficient therapeutic level in the vitreous.⁶ The use of intravitreal antibiotics has been reported to reduce the chance of evisceration or enucleation,

but it did not significantly improve the visual prognosis.¹⁴ PPV is another important treatment option, as a previous study has demonstrated that PPV can result in an 85% anatomical success rate, with 80% retaining a vision of FC or better after surgery.¹⁴ In addition, the chance of requiring enucleation or evisceration was also reduced after PPV.

The limitation of this study is the small sample size due to the rare disease, the loss of medical documents in some patients, and incomplete medical records.

Conclusion

Endogenous endophthalmitis is a cause of severe visual loss. Diabetes mellitus is the most common risk factor. Primary vitrectomy with intravitreal antibiotics may be a better option for treatment than intravitreal antibiotics alone.

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