

# Endojen Endoftalminin Klinik Özellikleri

## Clinical Features of Endogenous Endophthalmitis

Ziya AYHAN<sup>1</sup>, Ezgi KARATAŞ<sup>2</sup>, Aylin YAMAN<sup>3</sup>, Ali Osman SAATCİ<sup>3</sup>

### ÖZ

**Amaç:** Endojen endoftalmi (EE) tanılı hastaların klinik özelliklerinin gözden geçirilmesi.

**Gereç-Yöntem:** Ocak 2012 – Ağustos 2017 yılları arasında EE tanısı konulan ve 3 ay ve üzeri takibi olan 8 hastanın verileri geriye dönük incelendi. Hastaların klinik özellikleri, predispozan faktörler, uygulanan tedavi ve sonuçları değerlendirildi.

**Bulgular:** Çalışmaya 8 hastanın (6 kadın, 2 erkek) 12 gözü dahil edildi. Ortalama yaş 56,1±17,0 (Aralık: 26-76 yıl) yıl, ortalama takip süresi 5,7±4,3 ay (Aralık: 3-15 ay) olarak bulundu. 6 hastada diyabet, 1 hastada hem diyabet hem de immüsupresan ilaç kullanımını mevcuttu. Hastalarda üriner sisteme invaziv girişim, kalp kapak değişimi, böbrek transplantasyonu, intravenöz santral kateter uygulaması, by-pass cerrahisi öyküsü, septisemi olması predispozan faktörler olarak değerlendirildi. Predispozan işlem ile endoftalmi tanısı arasında geçen süre ortalama 5,6±4,4 hafta (Aralık: 1-12 hafta) olarak bulundu. Septisemi tablosu olan hasta hariç diğer tüm hastalardan vitreus örneği alınarak, işlem esnasında ampirik olarak intravitreal geniş spektrumlu antibiyotik uygulanmıştı. Takiplerde 5 göze pars plana vitrektomi uygulandı. Görme keskinliği 8 gözde artarken, 2 gözde aynı düzeydeydi. Ancak 2 gözde görme keskinliğinde düşüş olduğu görüldü.

**Sonuç:** Endojen endoftalmi genellikle kötü görsel prognoza sahip olup immün sistem bozukluğuna yol açan klinik antitelere görülür. Erken tanı, erken müdahale ve daha iyi görsel prognoz için gereklidir.

**Anahtar Kelimeler:** Endojen endoftalmi, immüsupresyon, intravitreal enjeksiyon, pars plana vitrektomi.

### ABSTRACT

**Purpose:** To review the clinical features of patients diagnosed as endogenous endophthalmitis (EE).

**Subjects and methods:** We retrospectively reviewed records of 8 patients with a diagnosis of EE who were followed-up for at least three months in between January, 2012 and August, 2017. The clinical features of patients, predisposing factors, treatment modalities and outcomes were evaluated.

**Results:** Twelve eyes of 8 patients (6 female, 2 male) were included to the study. The mean age was 56.1±17.0 years (range: 26-76 years) and the mean follow-up time was 5.7±4.3 months (Range: 3-15 months). Six patients had diabetes mellitus (DM), an additional patient using immunosuppressive agent also had DM. The history of urinary system procedure, central venous catheter application, kidney transplantation, cardiac valve surgery, by-pass surgery and septicemia were the predisposing factors. The time from predisposing procedure to EE diagnosis was 5.6±4.4 weeks (range: 1-12 weeks). Five eyes underwent vitrectomy surgery in addition to intravitreal antibiotic administration. Best-corrected visual acuity was improved in 8, remained unchanged in 2 and worsened in 2 eyes.

**Conclusion:** Endogenous endophthalmitis is characterized by poor visual outcome and it should be kept in mind that patients with immune system pathology are prone to EE. Early diagnosis is warranted for early intervention and better visual outcome.

**Key Words:** Endogenous endophthalmitis, immunosuppression, intravitreal injection, pars plana vitrectomy.

1- Uz. Dr., Dokuz Eylül Üniversitesi Tıp Fakültesi, Göz Hastalıkları AD, İzmir, Türkiye

2- Asist. Dr., Dokuz Eylül Üniversitesi Tıp Fakültesi, Göz Hastalıkları AD, İzmir, Türkiye

3- Prof. Dr., Dokuz Eylül Üniversitesi Tıp Fakültesi, Göz Hastalıkları AD, İzmir, Türkiye

Geliş Tarihi - Received: 05.03.2018

Kabul Tarihi - Accepted: 25.04.2018

Ret-Vit 2019; 28: 45-50

Yazışma Adresi / Correspondence Address:

Ali Osman SAATCİ  
Dokuz Eylül Üniversitesi Tıp Fakültesi, Göz Hastalıkları AD,  
İzmir, Türkiye

Tel: +90 505 433 0331

E-mail: osman.saatci@deu.edu.tr

## INTRODUCTION

Endogenous endophthalmitis (EE) is an intraocular infectious entity caused by hematogenous spread from a remote source, which is characterized by pathogens passing across blood-retina barrier and spread within eye and can lead devastating visual outcomes if left untreated.<sup>1-3</sup> Although it accounts for 2-8% of all cases with endophthalmitis, mortality rate is 4% in cases diagnosed as EE.<sup>4-6</sup> The causative agents generally gain access to eye from vascular structures of posterior segment, spreading to choroid and retina where they pass to vitreous and anterior chamber. In addition, direct spread through optic nerve from central nervous system is also possible.<sup>1-6</sup> In this study, we reviewed patient characteristics, etiological factors, treatments employed and outcomes in patients diagnosed as EE.

## MATERIAL AND METHOD

We retrospectively reviewed records of 8 patients who were diagnosed as EE at Ophthalmology Department of 9 Eylül University, Medicine School between January, 2012 and August, 2017 and had at least 3 months of follow-up. Classical endophthalmitis findings were present in all cases but there was no history of intraocular surgery or ocular trauma which may cause exogenous endophthalmitis. Clinical characteristics of patients, predisposing factors, treatments employed and outcomes were assessed.

## FINDINGS

The study included 12 eyes of 8 patients (6 women and 2 men). The mean age was  $56.1 \pm 17.0$  years (range: 26-76 years) and the mean follow-up time was  $5.7 \pm 4.3$  months (Range: 3-15 months). Six patients had diabetes mellitus (DM) while an additional patient on immunosuppressive agent also had DM. The history of urinary system procedure, central venous catheter application, kidney transplantation, cardiac valve surgery, by-pass surgery and septicemia were the predisposing factors. The time from predisposing procedure to EE diagnosis was found as  $5.6 \pm 4.4$  weeks (range: 1-12 weeks). The vitreous samples were obtained from all patients other than a patient with septicemia. Empirical broad-spectrum antibiotic injection was performed via intravitreal route after vitreous sampling. In vitreous culture tests, *Candida* spp. were detected in 3 patients while causative agent could not be isolated in 4 patients. *Klebsiella pneumoniae* and *Neisseria gonorrhoeae* were isolated from blood cultures in 2 patients. In cases with *Candida* growth, additional injection with antifungal agent was performed via intravitreal route. Pars plana vitrectomy was performed in 5 eyes with inadequate response to treatment and opacity. The infection was controlled in all eyes after treatment. During follow-up, cataract surgery was undertaken in 2 cases. Best-corrected visual acuity was improved in 8, remained unchanged in 2 and worsened in 2 eyes.

None of the patients required enucleation or evisceration

surgery. Table shows demographic data and clinical characteristics of the patients. The pictures 1, 2, 3, 4 and 5 shows clinical appearance of patients 2, 6 and 8.

## DISCUSSION

Endogenous endophthalmitis is a serious clinical entity associated with severe loss of vision, which is generally encountered in patients with diabetes mellitus, urinary system infection, intravenous drug use and those with disorders resulting in immunocompromise such as tumor, neutropenia or HIV infection.<sup>1-3,6-10</sup> The infective endocarditis is an important cause of endogenous endophthalmitis in Western countries.<sup>11,12</sup> In addition, EE was also described following colonoscopy procedure.<sup>13</sup> In a study by Jackson et al.<sup>14</sup> a systemic disease was detected in 56% of cases with endogenous endophthalmitis, as diabetes mellitus being most common systemic disease. In another study, it was found that there was hypertension in 69%, heart disease in 62%, diabetes mellitus in 39% and renal pathology in 31% of patients with EE.<sup>12</sup> There was diabetes mellitus in 7 cases and systemic immunosuppressive agent use in one case in our study. To best of our knowledge, this is largest case series of EE published in Turkey.<sup>8-10</sup>

The diagnosis of endogenous endophthalmitis can be made by meticulous ophthalmological examination in the presence of high level of clinical suspicion. The EE should be kept in mind in all patients having ocular inflammation findings with underlying diabetes mellitus, cardiovascular and renal disorders, and immune disorders.<sup>15</sup> The patient with EE generally presents with decreased vision, photophobia and pain. In ocular examination, various findings such as eyelid edema, cilia infection, corneal edema, hypopyon, posterior synechiae, vitreous opacity, rubeosis or iritis can be observed. The findings such as uveal tissue abscess, hypopyon > 1.5 mm, presence of exudate in vitreous, visible septic arteriolar embolus, necrotizing retinitis, perivascular bleeding with infiltration and panophthalmitis can also be seen.<sup>6,16</sup> In addition, it is also possible to recognize causative agent-specific findings. In the EE secondary to *Candida* septicemia, cotton-like lesions extending from retinal surface to vitreous are seen while yellow-white focal or diffuse foci can be seen in *Aspergillum* infections. Sub-retinal or choroidal abscesses may be present in bacterial endogenous endophthalmitis. The methicillin-resistant *Staphylococcus aureus* (MRSA) infections can lead retinal detachment within 2 weeks.<sup>17-19</sup>

The causative agents generally include gram-positive and gram-negative bacteria and fungi with variations in incidence according to geographic location. Fungal infections are more common than bacterial endogenous endophthalmitis.<sup>6,20-24</sup> In Northern America and Europe, fungi and gram-positive agents are leading cause of EE while gram-negative agents are more common in Southeast Asia. Although underlying cause of this finding is unknown, it is attributed to higher incidence of hepatic and biliary disorders in Asian countries.

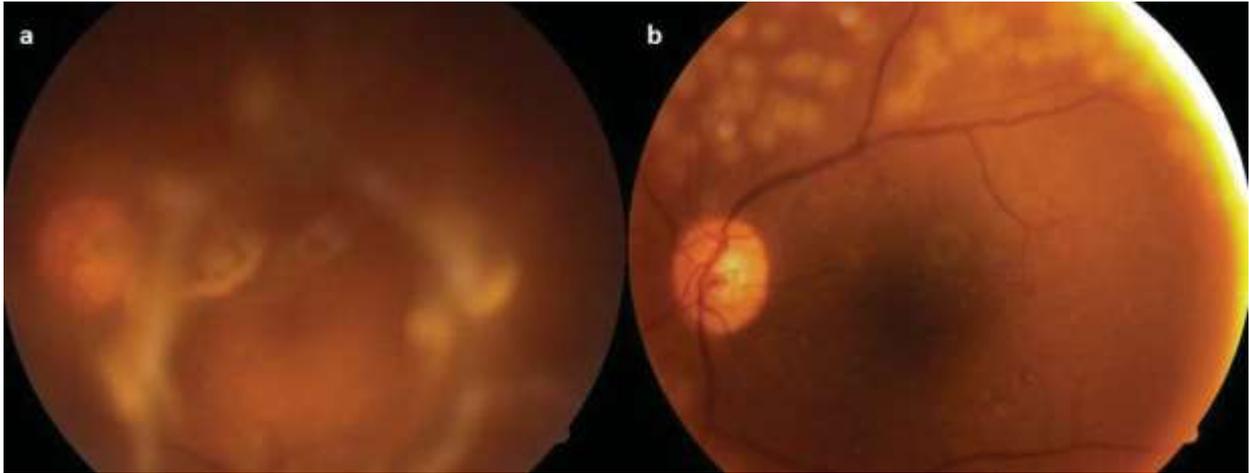
**Table 1:** Demographic and clinical characteristics of patients

No/A/G	Eye	Risk factor	Systemic disease	Time from intervention and clinical (week)	Culture	Treatment	Surger y	Visual acuity®		Follow-up (mo)
								Baseline	Final	
1/63/F	Right	Cardiac valve replacement	DM	8	No growth in vitreous sample	Intravitreal vancomycin +ceftazidime	-	P+P-	2mps	3
2/26/F	Right + Left	Renal transplantation	DM, Systemic immunosuppression (mycophenolic acid)	12	No growth in vitreous sample	Right: Intravitreal vancomycin+ ceftazidime +amphotericine B Left: Intravitreal vancomycin+ ceftazidime+ amphotericine B	Right: PPV Left: PPV	Right: EH Left: 1 CF	Right: 5mps Left: 5 CF	3
3/76/M	Right	Vascular catheter	DM	2	No growth in vitreous sample	Intravitreal vancomycin +ceftazidime +amphotericin B	-	1 CF	1 CF	3
©4/52/F	Right	Nephrosotomy + urinary stent	DM	2	No growth in vitreous sample Klebsiella Pneumonia in blood culture	Intravitreal vancomycin +ceftazidime + clindamycin	-	0.1	0.1	4
5/56/M	Left	Coroner bypass surgery	DM	4	Candida tropicalis (vitreous)	Intravitreal vancomycin +amikacin + amphotericine B	PPV, (follow-up) Phaco+IO L	2 CF	0.2	15
6/61/F	Right + Left	Urinary stent	DM	4	Candida Albicans (vitreous)	Right+left: 1. injection: Intravitreal vancomycin +ceftazidime +amphotericine B Right+left: 2. injection: intravitreal amphotericine B + voriconazole	Left: PPV, (Follow-up) Phaco+IO L	Right:1 mps Left: 1 CF	Right: 0.3 Left: 3 CF	9
7/75/F	Right + Left	Renal lithotripsy	DM	12	Candida Albicans (vitreous)	Right+Left: 1. injection: Intravitreal vancomycin +ceftazidime + +amphotericine B Right+left: 2. injection: intravitreal amphotericine B Right+left: 3. injection: Intravitreal Caspofungin	Left PPV	Right:0.7 Left:0.1	Right :0.2 Left: P-	6
8/39/F	Right + Left	Gonococcal septicemia	-	2	No vitreous sampling; Neisseria Gonorre (Blood)	Sulbactam-ampicillin (SAM) (IV)	-	Right:0.16 Left: 0.5	Right: 0.9 Left: Tam	3

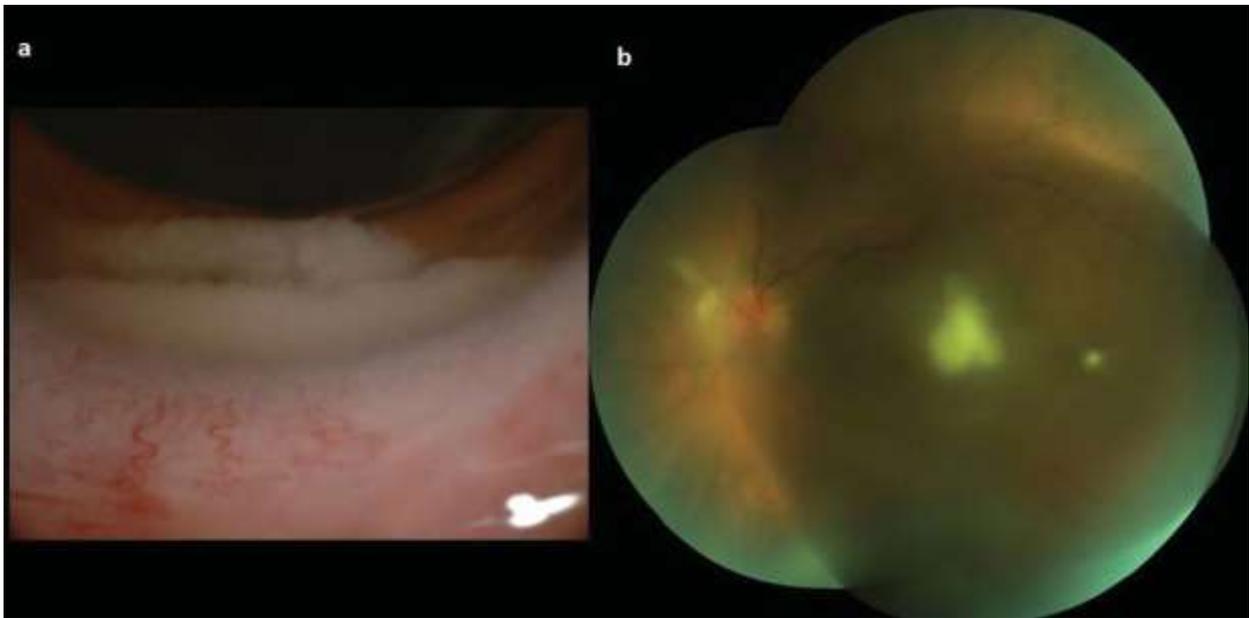
®: Snellen chart; A: age; G: gender; DM: diabetes mellitus; P+P-: perception +projection -; CF: counting finger from distance (m); PPV: pars plana vitrectomy, IV: intravenous ©: Published as case report. (Takes O, Kocaoglu G, Ayhan Z, Saatci AO. Successful treatment of a case of unilateral endogenous Klebsiella pneumoniae endophthalmitis European Ophthalmic Review 2015;9(1):23-4)

*Staphylococcus Aureus* is most common gram-positive whereas *Klebsiella Pneumonia* is most common gram-negative and *Candida* spp. are most common fungal agents.<sup>22,24-29</sup> Blood culture in addition to vitreous and humor aqueous cultures will be helpful in revealing etiology as microorganisms gain access to vitreous through choroid by hematogenous spread.<sup>1, 13, 15, 20, 27</sup> It is important to obtain vitreous sampling before initiation of infusion during

vitrectomy in order to enhance likelihood positive growth in culture. The samples are inoculated into blood agar, chocolate agar, Sabouraud agar and Thioglycollate agar. The sensitivity of culture tests varies from 50% to 70%; however, PCR with sensitivity up to 92% has been introduced as valuable method.



**Picture 1.** Patient 2, Left eye, Color fundus images, posterior pole image and inflammatory deposits in vitreous at presentation (a) fundus image on day 3 after pars plana vitrectomy and endolaser (b).

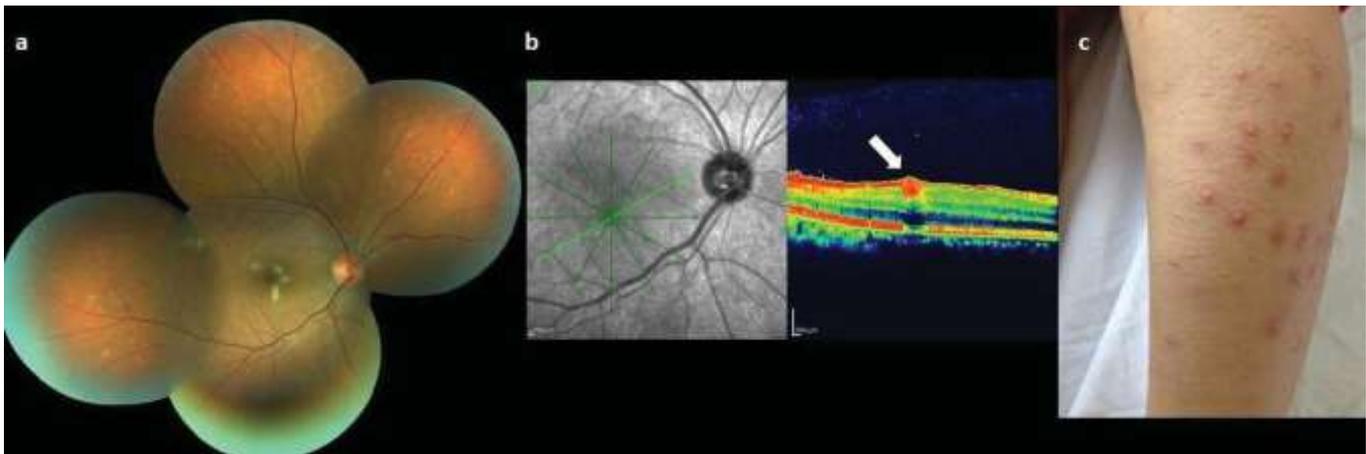


**Picture 2:** Patient 6; Left eye, hypopyon and anterior chamber at time of diagnosis on color image (a) and fungal balls obscuring posterior pole in anterior segment (b).

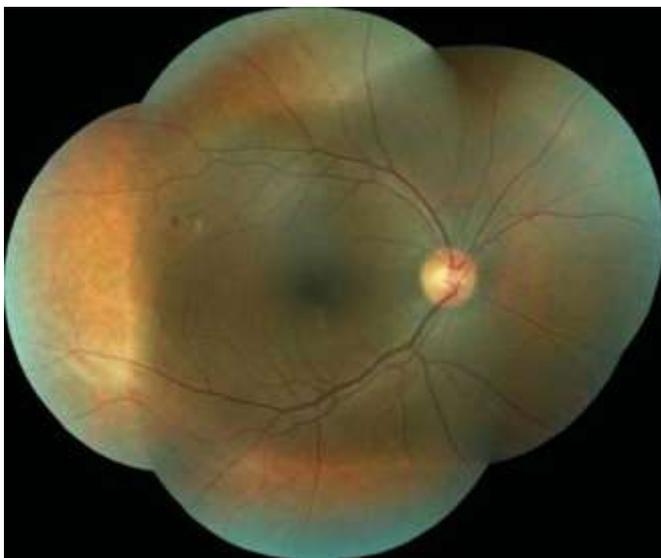


**Picture 3:** Patient 6; color fundus image on month 3 after pars plana vitrectomy

It is particularly helpful in the detection of microorganisms with slow proliferation rate such as *P. acnes*, *A. israeli* and fungi, in cases with failure to detect causative agent in microscopy, and in cases without growth in culture tests. Although PCR allows identification of causative agent in rapid and sensitive manner, culture tests are still reasonable as they do not only identify causative agent but also antibiotic sensitivity.<sup>30-31</sup> In an one-year screening study from UK, 62 patients with EE were reported. The survey outcomes were available at baseline in 48 patients whereas at month 6 in 26 patients. It was reported that the EE was accompanied by diabetes mellitus, genitourinary infection, endocarditis or septic arthritis. There was vitritis in 37 eyes at time of diagnosis while retinal structures were obstructed in 19 eyes during fundus examination. In addition, it was seen that there was retinitis in 19 eyes and choroiditis in 8 eyes.



**Picture 4:** Patient 8; diffuse, infiltrative retinitis foci in color fundus image (a), on OCT, hyper-reflective area in inner retina (arrow) and masking just beneath the area (b), diffuse pustular lesion at skin (c).



**Picture 5.** Patient 8; marked regression in retinitis foci on color fundus image obtained on day 25 after intravenous ampicillin-sulbactam therapy

The causative agent was detected in 58% of 36 patients with blood culture test and 23% of 35 patients with vitreous culture test. In the treatment, intravitreal antibiotic injection was performed in addition to oral or intravenous systemic treatment following vitreous sampling. It was found that vancomycin plus ceftazidime or vancomycin plus amikacin were most commonly used antibiotic combinations. Authors suggested that improved vision could be achieved in at least one-half of patients with early diagnosis and appropriate treatment.<sup>29</sup>

Based on etiological agent, intravitreal antibiotic/antifungal treatment, vitrectomy and systemic therapies should be considered in combination.<sup>1-10,26-29,32-34</sup> In particular, vitrectomy can reduce bacterial/fungal load and remove inflammatory agents, decreasing need for enucleation or evisceration.<sup>33</sup> In their study, Zhang et al.<sup>26</sup> performed pars plana vitrectomy in 20 eyes diagnosed as EE. Anatomic success was achieved in 17 eyes (85%) while visual acuity gain was at least counting level in 16 eyes (80%).

Minimum  $\geq 20/200$  visual acuity was achieved in 8 eyes.

Visual outcome is generally poor in endogenous endophthalmitis although it depends on causative agent and time to onset of treatment. In a study by Binder et al.<sup>2</sup> it was suggested that visual outcomes were better in cases with visual acuity  $> 20/200$  at time of diagnosis and no hypopyon. In a study, Esman et al.<sup>7</sup> achieved  $\geq 20/400$  visual acuity in 13 of 17 (76%) eyes with EE caused by *Candida* spp. However, authors reported that visual acuity gain was not at this level in 3 eyes with EE caused by *Aspergillum*. In another study, vitrectomy outcomes were reported in 10 eyes with fungal EE developed following invasive urinary system intervention. In all eyes, infection could be controlled and visual acuity was improved in eyes while it remained stable in 2 eyes and worsened in 1 eye. Authors suggested that baseline visual acuity, macular involvement and retinal detachment are important to predict final visual acuity.<sup>34</sup>

In conclusion, this is largest case series of EE in Turkey. Endogenous endophthalmitis is a rare infectious entity with poor visual prognosis. It should be kept in mind that EE may be encountered particularly in patients with immune disorder and that early diagnosis should prompt timely management.

## REFERENCES

1. Schiedler V, Scott IU, Flynn HW, Jr., et al. Culture-proven endogenous endophthalmitis: clinical features and visual acuity outcomes. *Am J Ophthalmol* 2004;137:725-31.
2. Binder MI, Chua J, Kaiser PK, et al. Endogenous endophthalmitis: an 18-year review of culture-positive cases at a tertiary care center. *Medicine* 2003;82:97-105.
3. Riddell J 4tt, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis* 2011;52:648-53.

4. Greenwald MJ, Wohl LG, Sell CH. Metastatic bacterial endophthalmitis: a contemporary reappraisal. *Survey of Ophthalmol*. 1986;31:81-101.
5. Samiy N, D'Amico DJ. Endogenous fungal endophthalmitis. *Int Ophthalmol Clin* 1996;36:147-62.
6. Jackson TL, Paraskevopoulos T, Georgalas I. Systematic review of 342 cases of endogenous bacterial endophthalmitis. *Surv Ophthalmol* 2014;59:627-35.
7. Essman TF, Flynn HW, Jr., Smiddy WE, et al. Treatment outcomes in a 10-year study of endogenous fungal endophthalmitis. *Ophthalmic Surg Lasers*. 1997;28:185-94.
8. Düzgün E, Çakır A, Ünal MH, et al. Endojen kandida endoftalmisi: Tedavi seçenekleri. *Retina-Vitreus* 2014;22:159-67.
9. Güçlü H, Özal SA, Gürlü VP, et al. Escherichia Coli'ye bağlı gelişen endojen endoftalmi ve yönetimi. *Retina-Vitreus* 2016;24:169-72.
10. Dinç UA, Tatlıpınar S, Yenerel M, et al. Fungal endoftalmi saptanan bir olgunun tedavisi ve klinik seyri. *Turk J Ophthalmol* 2009;39:52-55.
11. Buzzacco DM, Carroll CP. Intravitreal daptomycin in a case of bilateral endogenous endophthalmitis. *Arch Ophthalmol* 2012;130:940-1.
12. Yonekawa Y, Chan RV, Reddy AK, et al. Early intravitreal treatment of endogenous bacterial endophthalmitis. *Clin Exp Ophthalmol* 2011;39:771-8.
13. Wu AY, Oestreicher JH. Endogenous bacterial endophthalmitis after routine colonoscopy. *Can J Ophthalmol* 2011;46:556-7.
14. Jackson TL, Eykyn SJ, Graham EM, et al. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. *Surv Ophthalmol* 2003;48:403-23.
15. Wu ZH, Chan RP, Luk FO, et al. Review of clinical features, microbiological spectrum, and treatment outcomes of endogenous endophthalmitis over an 8-year period. *J Ophthalmol* 2012;2012:265078.
16. Chee SP, Jap A. Endogenous endophthalmitis. *Curr Opin Ophthalmol* 2001;12:464-70.
17. Ho V, Ho LY, Ranchod TM, et al. Endogenous methicillin-resistant *Staphylococcus aureus* endophthalmitis. *Retina* 2011;31:596-601.
18. Lingappan A, Wykoff CC, Albin TA, et al. Endogenous fungal endophthalmitis: causative organisms, management strategies, and visual acuity outcomes. *Am J Ophthalmol* 2012;153:162-6.e1.
19. Sridhar J, Flynn HW, Jr., Kuriyan AE, et al. Endogenous fungal endophthalmitis: risk factors, clinical features, and treatment outcomes in mold and yeast infections. *J Ophthalmic Inflamm Infect* 2013;3:60.
20. Ness T, Pelz K, Hansen LL. Endogenous endophthalmitis: microorganisms, disposition and prognosis. *Acta Ophthalmol* 2007;85:852-6.
21. Connell PP, O'Neill EC, Fabinyi D, et al. Endogenous endophthalmitis: 10-year experience at a tertiary referral centre. *Eye* 2011;25:66-72.
22. Zhang H, Liu Z. Endogenous endophthalmitis: a 10-year review of culture-positive cases in northern China. *Ocul Immunol Inflamm* 2010;18:133-8.
23. Leibovitch I, Lai T, Raymond G, et al. Endogenous endophthalmitis: a 13-year review at a tertiary hospital in South Australia. *Scand J Infect Dis* 2005;37:184-9.
24. Wong JS, Chan TK, Lee HM, et al. Endogenous bacterial endophthalmitis: an east Asian experience and a reappraisal of a severe ocular affliction. *Ophthalmology* 2000;107:1483-91.
25. Chung KS, Kim YK, Song YG, et al. Clinical review of endogenous endophthalmitis in Korea: a 14-year review of culture positive cases of two large hospitals. *Yonsei Med J* 2011;52:630-4.
26. Zhang YQ, Wang WJ. Treatment outcomes after pars plana vitrectomy for endogenous endophthalmitis. *Retina* 2005;25:746-50.
27. Yoon YH, Lee SU, Sohn JH, et al. Result of early vitrectomy for endogenous *Klebsiella pneumoniae* endophthalmitis. *Retina* 2003;23:366-70.
28. Keswani T, Ahuja V, Changulani M. Evaluation of outcome of various treatment methods for endogenous endophthalmitis. *Indian J Med Sci* 2006;60:454-60.
29. Maling S, King C, Davies N. A British Ophthalmological Surveillance Unit Study on metastatic endogenous endophthalmitis. *Eye* 2018; [Epub ahead of print]
30. Sandhu HS, Hajrasouliha A, Kaplan HJ, et al. Diagnostic utility of quantitative polymerase chain reaction versus culture in endophthalmitis and uveitis. *Ocul Immunol Inflamm* 2018; [Epub ahead of print]
31. Rishi E, Rishi P, Therese KL, et al. Culture and reverse transcriptase polymerase chain reaction (RT-PCR) proven mycobacterium tuberculosis endophthalmitis: A case series. *Ocul Immunol Inflamm* 2018;26:220-227.
32. Bae JH, Lee SC. Intravitreal liposomal amphotericin B for treatment of endogenous candida endophthalmitis. *Jpn J Ophthalmol* 2015;59:346-52.
33. Microbiologic factors and visual outcome in the endophthalmitis vitrectomy study. *Am J Ophthalmol* 1996;122:830-46.
34. Ghoraba HH, Ellakwa AF, Elgemai EM, et al. Results of pars plana vitrectomy for the management of endogenous fungal endophthalmitis after urinary tract procedures. *Retin Cases & Brief Rep* 2017;11:171-4.