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Vitrectomy for Endogenous Fungal Endophthalmitis

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ABSTRACT

Purpose: The purpose of this study was to evaluate the predisposing risk factors and treatment outcomes of endogenous fungal endophthalmitis (EFE). *Methods*: Records of 25 patients (29 eyes), diagnosed with EFE and treated at Shanghai Eye, Ear, Nose & Throat Hospital from January 2002 to December 2006, were retrospectively reviewed. Four patients had bilateral disease. Final visual acuity and recurrence of EFE were evaluated. *Results*: Of these 25 patients diagnosed with EFE, 20 patients (22 eyes) were treated by pars plana vitrectomy. Of the remaining 5 patients (7 eyes), 3 cases (4 eyes) were cured by antifungal drugs through systemic treatment and intravitreal injection, but another 2 cases (3 eyes) were only given intravitreal injection because of severe general conditions. Of the 22 eyes that underwent pars plana vitrectomy, 16 (73%) eyes gained visual acuity of counting fingers or better. Recurrent EFE was happened in 2 eyes. Vitrectomy was repeated in 1 eye, another was subsequently enucleated due to phthisis. Vitreous culture-proven or smear-proven EFE occurred in 27 or 2 eyes, respectively. *Candida albicans* occurred in 17 of 29 eyes (59%), and other causative organisms were yeast fungus (3 eyes), *Aspergillus niger* (3 eyes), *Actinomyces* (2 eyes),*Aspergillus flavus* (1 eye), and *Fusarium* (1 eye). *Conclusion*: *Candida albicans* were the most common causative organisms in EFE. The most common predisposing risk factors include recent major operation and intravenous administration in rural settings. Most patients with EFE will gain useful vision (counting fingers) after pars plana vitrectomy.

Keywords: Causative organism; endogenous; fungal endophthalmitis; predisposing risk factors; vitrectomy

Endogenous fungal endophthalmitis (EFE) is a complication of disseminated fungal infections, which is a potentially blinding intraocular infection.[1,2] It is estimated that about 2–10% of endophthalmitis cases are endogenous,[3,4] which is associated with immunocompromised state, debilitating diseases, and invasive procedures, and a major part of them is EFE. Recent reports suggested that the incidence of EFE is increasing.[5] Most patients with EFE are immune-compromised hosts, and the number of this kind of host is increasing with the advance of medical therapy and diagnosis. In clinical practice, due to the unfolding diagnosis and treatment, many patients with EFE are misdiagnosed, and the prognosis of these patients is still poor.[2] It is important to be aware of EFE because early diagnosis and prompt aggressive treatment are imperative to avoid vision loss. We retrospectively reviewed the cases of all patients with EFE who were treated in our hospital from January 2002 to December 2006.

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MATERIALS AND METHODS

This was a retrospective observational case study, which was approved by Department of

Ophthalmology, Shanghai Eye, Ear, Nose & Throat Hospital, Fudan University. This retrospective medical record review included all patients treated for vitreous culture-proven or smear-proven EFE (without mixed infection of bacteria) in our hospital from January 2002 to December 2006. The patients who were highly suspected for EFE without evidence of culture or smear of specimens were excluded. The review included sex, age, recent predisposing risk factors that might prone to infection, microbiologic findings, clinical findings, treatment modalities, initial as well as final visual acuity, and recurrence of EFE. Patients with a history of penetrating ocular trauma, intraocular surgery within 1 year of presentation, or any evidence of a primary external ocular infection were excluded.

RESULTS

In our study series, 25 patients (29 eyes) were diagnosed with EFE. Four patients had bilateral disease and 21 patients had unilateral EFE. The average patient age was 43.2 years (range, 22–62 years). Twelve patients were men and 13 patients were women. The average length of follow-up was 12.5 months (range, 3–28 months). The clinical characteristics for our patient population are listed in Table 1.

Of all 25 patients diagnosed with EFE, 24 patients had associated predisposing risk factors for EFE, and no underlying cause was found in 1 patient (Table 2). The most common predisposing risk factors were recent major operation (6 cases, 24%) and intravenous administration in rural settings (4 cases, 16%). All patients undergoing major surgery encountered systemic malignancy. Among them, 2 had cancer of pancreas, 1 had liver cancer, 1 had stomach cancer, 1 had abdomen liomyosarcoma, and 1 had breast cancer. In our study, another common predisposing risk factor is related to postpartum or abortion (3 cases, 12%). Deep abscess (liver or buttocks abscess) and diabetes mellitus were founded in 2 patients (8%), respectively. Other predisposing risk factors were hemodialysis (1 case), disseminated intravascular coagulation (1 case), kidney transplant (1 case), lymphoma (1 case), pancreatitis (1 case), current history of dental extraction (1 case), and ulcerative colitis (1 case). Most patients had recently received or were receiving immunosuppressive therapeutic agents (such as chemotherapy, systemic corticosteroids, or immunomodulating medications) or antibiotic agents.

Five patients (cases 6, 10, 13, 15, 16) in whom EFE was highly suspected were directly treated with vitrectomy and intravitreal amphotericin B injection because of severe vitreous inflammation and retinitis, without surgical intervention for biopsy or intravitreal antifungal medication before vitrectomy. Cultures of vitreous of the 5 patients, gained by vitrectomy, were all positive for fungi. Blood culture was done in all cases, but only 2 patients' blood cultures were positive (8%). The initial vitreous needle biopsies were performed in the remaining 20 patients for diagnosis, due to their ocular signs with mild to moderate vitreous inflammation, but firstly a lot of vitreous cultures and smears were negative (11 cases, 55%). In our series, the initial biopsies proved both vitreous culture- and smear-positive in 3 cases, vitreous culture-positive in 4 cases, and only vitreous smear-positive in 2 cases. Although the initial biopsies showed no evidence of fungi infection in 11 cases, cultures or smears of specimens obtained from the opacity near the retina by vitrectomy were all positive for fungi. Of all 25 cases, it was found finally that 13 cases (17 eyes, 59%) were due to *Candida albicans*; 3 cases were due to yeast fungus, and another 3 cases were due to *Aspergillus niger*; 2 cases were due to *Actinomyces*; 1 case each was due to *Aspergillus flavus* and *Fusarium*; and 2 cases had only a positive fungal smear.

Five patients directly treated with vitrectomy also received systemic antifungal treatment (fluconazole) after surgery. Of the remaining 20 patients, 9 cases were diagnosed with EFE definitely by initial biopsy. Although the remaining 11 cases had no evidence of fungi infection through culture or smear of specimens by initial biopsy, their clinical characteristics implied they had EFE highly. Consequently, for the 20 patients, in addition to systemic antifungal treatment (fluconazole), intravitreal amphotericin B injection was also used. Of the 20 cases, 3 cases (4 eyes) were cured by antifungal drugs through systemic treatment and intravitreal injection. Two cases (3 eyes) were given only intravitreal antifungal medication because of severe general conditions. The remaining 15 cases (17 eyes) received vitrectomy with or without intravitreal amphotericin B injection due to uncontrolled EFE and systemic antifungal treatment were also used after surgery. Of all 22 eyes treated with vitrectomy, 11 eyes had combined lensectomy, 10 had long-lasting gas tamponade, 6 had silicone oil, and 8 had sclera encircling.

Sixteen of the 22 eyes that underwent pars plana vitrectomy gained visual acuity of counting fingers or better. Visual acuity was improved in 14 eyes (64%) after surgery. Visual acuity findings before and after vitrectomy are summarized in Table 3. Recurrent EFE happened in 2 eyes. Vitrectomy was repeated in 1 eye (case 8) and another eye was subsequently enucleated due to phthisis and loss of light perception (case 7). Among the 22 eyes treated with vitrectomy, 2 eyes experienced retinal detachments in follow-up duration and they were cured with vitrectomy again finally. Of the remaining 7 eyes, 4 eyes (3 patients), with mild to moderate vitreous involvement, were cured by treatment with antifungal

Table 1. Clinical characteristics of patients

Case	Sex,	age(yr),	eye	Fungus	Predisposing risk factors	Vitrectomy	Recurrence	Initial vision	Fina vision	Length of follow-up (mo)
1	F,	32,	OD	*Candida albicans*	Abortion	Yes	No	FC	20/30	10
2	M,	43,	OU	*Candida albicans*	Cancer of pancreas	Yes	No	FC, LP	FC, LP	7
3	M,	53,	OU	*Candida albicans*	Cancer of stomach	No	No	HM, HM	Died	/
4	M,	32,	OU	*Candida albicans*	Pancreatitis	Yes	No	20/400, FC	20/400, 20/50	22
5	F,	22,	OD	*Candida albicans*	Abortion	No	No	FC	20/30	6
6	F,	31,	OS	*Candida albicans*	Postpartum	Yes	No	HM	20/400	15
7	M,	52,	OD	*Aspergillus niger*	Liver abscess	Yes	Yes	LP	NLP	3
8	M,	48,	OD	*Aspergillus flavus*	Buttocks abscess	Yes	Yes	HM	20/400	5
9	M,	39,	OD	*Candida albicans*	Cancer of pancreas	No	No	LP	NLP	8
10	M,	51,	OS	*Candida albicans*	Cancer of liver	Yes	No	HM	20/80	11
11	F,	43,	OD	*Fusarium*	Breast cancer	Yes	No	20/400	HM	15
12	F,	62,	OS	*Candida albicans*	Abdomen liomyosarcoma	Yes	No	20/200	20/60	6
13	F,	40,	OD	*Actinomyces*	Intravenous administration in rural settings	Yes	No	HM	HM	4
14	F,	57,	OD	*Candida albicans*	Diabetes mellitus	Yes	No	HM	20/200	6
15	M,	58,	OD	*Aspergillus niger*	Diabetes mellitus	Yes	No	LP	FC	8
16	F,	38,	OS	*Candida albicans*	Toxuria	Yes	No	LP	FC	9
17	F,	29,	OU	*Candida albicans*	Disseminated intravascular coagulation	No	No	20/200, 20/200	20/100, 20/50	13
18	M,	47,	OD	*Aspergillus niger*	Kidney transplant	Yes	No	HM	FC	17
19	M,	50,	OS	*Actinomyces*	Lymphoma	Yes	No	LP	FC	25
20	F,	38,	OD	Yeast fungus	History of dental extraction	Yes	No	HM	HM	28
21	M,	44,	OS	*Candida albicans*	Ulcerative colitis	Yes	No	20/100	20/50	21
22	F,	38,	OD	Yeast fungus	Intravenous administration in rural settings	Yes	No	HM	HM	12
23	F,	41,	OS	Yeast fungus	Unknown	Yes	No	HM	20/200	14
24	M,	53,	OD	Smear +	Intravenous administration in rural settings	No	No	FC	20/400	15
25	F,	38,	OD	Smear +	Intravenous administration in rural settings	Yes	No	FC	20/200	20

Note. NLP, no light perception; HM, hand motion; CF, counting fingers.

drugs through systemic medication and intravitreal injection (cases 5, 17, and 24). The final vision acuities in these eyes were 20/400 to 20/30. The further 3 eyes (2 patients, cases 3 and 9) received intravitreal amphotericin B injection only because of severe general health. One of the 2 patients died 2 months later due to complicated failure of heart and lung (case 3). Phthisis and loss of light perception were found in another patient (case 9).

DISCUSSION

Endogenous fungal endophthalmitis (EFE) is a rare entity, which usually occurs from teens to

Table 2. Associated predisposing risk factors

Associated predisposing factors	No. of patients
After surgery	6
Cancer of pancreas	2
Cancer of liver	1
Cancer of stomach	1
Abdomen liomyosarcoma	1
Cancer of breast	1
Intravenous administration in rural settings	4
Postpartum or abortion	3
Abortion	2
Postpartum	1
Deep abscess	2
Liver abscess	1
Buttocks abscess	1
Diabetes mellitus	2
Hemodialysis	1
Disseminated intravascular coagulation	1
Kidney transplant	1
Lymphoma	1
Pancreatitis	1
History of dental extraction	1
Ulcerative colitis	1
Unknown	1

octogenarian.[1,2,5,6] Bilateral involvement is seen in a lot of patients with EFE. There is no sex preponderance. It is prone to underlying disorders, including chronic immune-compromising illnesses (diabetes mellitus, renal failure), venous cannulation, immunosuppressive diseases and therapy (malignancies, AIDS, chemotherapeutic agents), after surgery (especially malignant tumor procedures), abortion or delivery, invasive diagnostic or dental manipulation, and intravenous drug abuse.[1,2,5–10] On the basis of our results, the most frequent predisposing risk factors were recent major surgery, intravenous administration in rural settings for minor ailments, and abortion or delivery. These medical disorders were present in 52% of the cases. No underlying cause was founded in 1 patient.

Table 3. Visual acuity before pars plana vitrectomy and at follow-up in 22 eyes

Time	NLP	LP	HM	CF	20/400 to 20/200	Better than 20/200
Before surgery	0	5	9	4	3	1
Follow up	1	1	4	5	6	5

Note. NLP, no light perception; LP, light perception; HM, hand motion; CF, counting fingers.

Our initial biopsy showed that 55% of ocular sample cultures or smears are negative, which was identical to what Binder reported.[11] Although initial biopsy with needles showed no evidence of fungi infection in some cases, cultures or smears of samples obtained by vitrectomy from the cases were all positive for fungi in our series. It was considered that adequate samples could be gained by vitrectomy biopsy. Furthermore, the samples were near the retina and it may have more organisms, because it is known that in EFE, the organism first appears in the choroidal vessels and then spreads through the retina into the vitreous. It was found that *Candida albicans* were the most common causative organisms in EFE (59%), which was consistent with what Essman and Takebayashi showed.[2,5] The reason for *Candida albicans* predominance in EFE hasn't been known clearly until now, although some studies reported that it was usually due to candidemia after major surgery or iatrogenic causes, such as administration of contaminated infusion in rural settings.[7,13]

EFE is a diagnostic and a treatment challenge for ophthalmologists. It is known that EFE can masquerade as uveitis, especially for *Candida* endophthalmitis. Some studies have reported rates of misdiagnosis for *Candida* endophthalmitis approaching 50%.[9] When a patient has uveitis symptoms with the predisposing risk factors described previously, a diagnosis of EFE should be sought. Once the diagnosis has been made or strongly considered, prompt treatment is needed. Final visual outcome is mainly dependent on timely diagnosis and treatment.[13] In cases with massive vitreous opacities, diffused infiltration in the retina, and visual acuity equal to or worse than hand motion, we think that vitrectomy is necessary. In our series, 5 patients had the severe conditions when they first came to our clinic. Based on our experience, they were directly treated with vitrectomy. In the EFE cases with mild to moderate vitreous involvement, they were treated with intravitreal administration of amphotericin B and systemic antifungal administration. It is effective for some cases. In our study, 3 cases were cured by the treatment. If the condition could not be controlled, vitrectomy would be applied. A lot of studies revealed the importance and effectiveness of vitrectomy for EFE.[1,2,5,14–17] In this series, following vitrectomy, 73% of patient achieved a visual acuity of count fingers or better, and visual acuity was improved in 14 eyes (64%) after surgery.

Patients with EFE caused by *Aspergillus* usually had worse visual outcomes compared with those caused

by *Candida*; our finding agrees with the Essman or Weishaar series.[2,17] In our series, none of the *Aspergillus* cases achieved a final visual acuity of 20/200 or better, but 53% of *Candida* eyes gained final visual acuity equal to or than 20/200. The phenomemon has not been elucidated clearly. Maybe EFE caused by *Candida* could be diagnosed easier than that caused by *Aspergillus* due to the characteristic clinic manifestation, and the patients with endogenous *Candida* endophthalmitis could be treated in a timely manner. It was also reported that endogenous *Aspergillus* endophthalmitis damaged macula in a short duration,[2,9,10,17] which may decrease vision seriously.

In conclusion, according to our experience with EFE, it is suggested that any patient with intraocular inflammation and systemic risk factors should raise suspicion of endogenous endophthalmitis, especially EFE. In our series, it is found that the most common predisposing risk factors include recent major surgery and intravenous administration in rural settings. *Candida albicans* were the most common causative organisms in EFE.When the diagnosis is made based on clinical and history findings, vitrectomy and treatment with intravitreal and systemic antifungal agents may achieve stabilization and improvement in visual function.

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