Candida albicans Endophthalmitis in Brown Heroin Addicts: Response to Early Vitrectomy Preceded and Followed by Antifungal Therapy

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The management of Candida albicans endophthalmitis in intravenous drug abusers (IVDAs) has yet to be established. Early vitrectomy was previously reported as a promising treatment for C. albicans endophthalmitis. In our series, C. albicans endophthalmitis was diagnosed for 15 IVDAs. Funduscopic examinations confirmed severe vitritis in 12 patients and chorioretinitis in three. Blood and vitreal cultures were positive for C. albicans for seven and eight patients, respectively. Patients with vitritis received antifungal therapy before and after vitrectomy. Amphotericin B or fluconazole therapy was given according to the physician’s preference. Vitrectomy was defined as early if it was performed within 1 week after the diagnosis of vitritis. All seven patients who underwent early vitrectomy had a favorable response without complications. Two of three patients who underwent late vitrectomy developed blindness or scotoma. Blindness was also described in two patients with vitritis who did not undergo vitrectomy. Early vitrectomy preceded and followed by antifungal therapy seems to be appropriate management of vitritis in IVDAs.

Candidal endophthalmitis (CE) is a common and severe complication in intravenous drug abusers (IVDAs) [1–7]. Despite improved management of CE, unfavorable outcomes have been described over the past 2 decades [4]. Consensus on medical and surgical management of CE still needs to be established [4–9].

Chorioretinitis (CR), vitritis, and panophthalmitis encompass the spectrum of endophthalmitis in IVDAs. CE is a common finding in cases of brown heroin syndrome characterized by fever and acute nodules mainly on the skin, scalp, and costochondral area [2, 4, 10, 11]. CE can also be present in non-IVDAs, and it is a specific complication of infection due to Candida serotype A biotype 153/7 [12, 13]. Patients with brown heroin syndrome are colonized by Candida in the oropharynx; however, the manipulation of contaminated material used to dissolve heroin seems to be the source of infection [14–16].

We assessed CE in IVDAs and the timing of surgical treatment of patients with vitritis who were seen at the Hospital Xeral of Vigo, University of Santiago de Compostela, Vigo, Spain.

Patients and Methods

IVDAs with CE who were seen at our center from 1990 to 1996 were assessed prospectively. CE was diagnosed if there were ocular symptoms and a culture of blood or vitreal fluid that was positive for Candida albicans, or ocular symptoms, fever, and acute lesions on the skin, scalp, and costochondral area followed by a favorable response to antifungal treatment. CE was differentiated from CR and vitritis. The initial eye examination and follow-up were performed by the same ophthalmologist. Indirect ophthalmoscopic examination with dilated pupils was done. Vitreal haze (based on the criteria of Nussenblatt et al. [17]) was assessed by clinical and photographic findings. Mild vitritis was diagnosed if the haze was <2+, and severe vitritis was diagnosed if the haze was >3+.

Following confirmation of endophthalmitis, initial antifungal treatment was given to all patients. The antifungal treatment (intravenous amphotericin B or fluconazole) was chosen on the basis of the physician’s clinical judgment (table 1). Amphotericin B was encouraged as initial treatment followed by fluconazole therapy. Vitrectomy via the pars plana was considered for treatment of all patients with severe vitritis and patients with mild vitritis whose conditions did not clinically improve after 48 to 72 hours of antifungal therapy (figure 1). Pars plana vitrectomy was performed as described previously [18]. Vitrectomy was defined as early if it was performed within 1 week after the diagnosis of vitritis. Outcomes of CR and vitritis were based on visual acuity and resolution of vitritis.

Results

Fifteen patients with CE (10 males and five females; mean age, 27 years) were enrolled in the study. CE was diagnosed
Table 1. Treatment and outcome of Candida albicans endophthalmitis in brown heroin addicts.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Form of endophthalmitis</th>
<th>Interval (d) from onset of symptoms to diagnosis</th>
<th>Initial antifungal diagnosis</th>
<th>Interval (d) from diagnosis to vitrectomy</th>
<th>Outcome at 6 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chorioretinitis</td>
<td>7</td>
<td>Amphotericin B</td>
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<td>Chorioretinitis</td>
<td>1</td>
<td>Blood</td>
<td></td>
<td>Cured</td>
</tr>
<tr>
<td>3</td>
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<td>Amphotericin B</td>
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<td>Vitreous</td>
<td>Amphotericin B*</td>
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</tr>
<tr>
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<td>1</td>
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<td>3</td>
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<tr>
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<td>30</td>
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<td>30</td>
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<tr>
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<td>Vitritis</td>
<td>7</td>
<td>Blood</td>
<td>Amphotericin B*</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Amphotericin B (0.7 mg/[kg·d]) was given for 10 to 14 days or until vitrectomy. Fluconazole (400 mg/d) was given from 2 to 8 weeks to all patients after vitrectomy.

* Patients received amphotericin B before vitrectomy.

¹ Patient received amphotericin B for 2 weeks followed by fluconazole for 2 weeks.

² Patients received amphotericin B for 2 weeks followed by fluconazole until vitrectomy.

³ Patient received 400 mg of fluconazole/d for 2 weeks and then 200 mg/d for 22 weeks.

§ Patient received 2 g of amphotericin B followed by 200 mg of fluconazole/d for 8 weeks.

for 10 patients in the last 3 years. Fourteen patients reported that they were IVDAs for >1 year, and one was an IVDA for only 4 months. Fourteen patients used brown heroin intravenously; these patients used lemon juice to dissolve heroin. Five patients (cases 5, 8, 9, 14, and 15) had HIV infection (mean CD4 lymphocyte count, 480/mm³) (table 1). Opportunistic diseases were absent in HIV-infected patients.

Funduscopic examination confirmed CR in three patients and severe vitritis in 12. Management and outcome of endophthalmitis are described in table 1. Bilateral eye involvement was present in two patients with CR and in three patients with vitritis. Fever was present in nine patients. Eight of nine febrile patients reported acute lesions on the skin and scalp that were described as painful nodules, pustules, and folliculitis.

Blurred vision was reported by all the patients. The vision of all patients except one with CR progressively worsened. Six patients reported a painful eye, and seven had a red eye with photophobia. The average time from the onset of symptoms to

Figure 1. A. Left eye of an intravenous brown heroin addict with Candida albicans endophthalmitis (case 7) before early vitrectomy; vitreal opacity adjacent to the optic nerve with vitreous haze is present. B. The same eye 4 weeks after early vitrectomy; the vitreous haze and opacity have cleared.
Figure 2. Management of candidal endophthalmitis in intravenous drug abusers. Antifungal treatment should be given at the time that the diagnosis of endophthalmitis is confirmed and after vitrectomy. * = blood culture and lesions on the skin, scalp, or costochondral area are not required to confirm the diagnosis of candidal endophthalmitis; ** = amphotericin B (0.7 mg/[kg⋅d] for 14 days) or fluconazole (400 mg/d for 2 weeks and then 200 mg/d for 4 weeks); --- = early vitrectomy should be performed for patients with mild vitritis whose conditions have not clinically and funduscopically improved after 48 to 72 hours of antifungal treatment.

the diagnosis was 5 days for patients with CR and 13 days for patients with vitritis. No patients had heart murmurs or cardiovascular symptoms. A chest roentgenogram of one patient revealed multiple nodular lesions; an echocardiogram ruled out endocarditis.

Antifungal treatment was given to all patients (table 1). All patients except two (cases 11 and 14) received amphotericin B as initial treatment. On the other hand, fluconazole was given to all patients after vitrectomy. Questionable nonfungal uveitis was described in one patient (case 11). For this patient, antifungal treatment was started 1 month later (table 1). This patient developed blindness secondary to proliferative retinopathy.

Blindness was also described in two other patients (cases 14 and 15) who did not undergo vitrectomy. One of these patients (case 14) was missing after the initial assessment, and retinal detachment was confirmed during his next visit 3 months later. The other patient (case 15) had retinal detachment at the time of presentation. At 6-month follow-ups, funduscopic examination revealed small scars in two of seven patients who underwent early vitrectomy.

Discussion

The results of this study support that early vitrectomy preceded and followed by antifungal therapy is appropriate management of vitritis in IVDA. All patients who underwent early vitrectomy completely recovered their vision; the vitreous haze in all these patients also resolved (figure 1). Favorable responses in patients treated with fluconazole or amphotericin B before vitrectomy have been reported; however, to our knowledge, no study has assessed the efficacy of both treatments for patients with CE [4–6, 8]. The small size of our series and the use of antifungals according to the physician’s preference did not allow a comparison of the efficacies of amphotericin B and fluconazole. The concentration of fluconazole in the vitreous humor is >50% of the concentration in plasma [19–22], in contrast, the intravitreal concentration of amphotericin B is low, and it is associated with high levels of toxicity [23, 24]. Fluconazole was reported as a promising alternative treatment for the management of vitritis [8, 25, 26]. In our study, fluconazole was effective in the postoperative management of all our patients treated with early vitrectomy; in addition, fluconazole allowed early discharge of our patients who continued their treatment as outpatients.

All our patients with CR had favorable responses to antifungal treatment. Poor response to treatment of vitritis was related to poor compliance, insidious onset of CE, and atypical presentation. The insidious onset of vitritis and sometimes its incorrect ophthalmologic diagnosis led to the late diagnosis of vitritis in a few of our patients, as has been reported previously [4, 10]. About one-half of our patients with ocular symptoms presented with nodules on the scalp, thus making CE the most probable diagnosis [9, 27]. The vitreous humor is an isolated medium; the diffusion of antibiotics in this medium is poor, as is the inflammatory response (both of which explain the frequent failure of antifungal treatment). In young patients, fixation of the hyaloid membrane to the retina causes retinal detachment during vitritis [7, 28], as described in one patient (case 14) in our series. The purpose of early vitrectomy is to avoid these complications [10, 23, 29], increase antibiotic diffusion [7], and provide a sample for microbiological culture.

In our center, we developed an algorithm for the management of CE in IVDA (figure 2). A drawback of this approach is the management of mild vitritis. We believe that mild vitritis should be treated with antifungals and close follow-up. In these cases, vitrectomy should be performed if there is no improvement within 48 to 72 hours.

Heroin seems to play a role in the development of CE. Opiates have a suppressor effect on peripheral T and null lymphocytes [30]. This immunosuppressive effect should facilitate
the transformation of *C. albicans* to the aggressive mycelial stage. Patients with AIDS who have bone marrow involvement or who are receiving antibiotic therapy have some risk for candidal infection. CE is not considered an AIDS-defining opportunistic disease. Few cases of CE in HIV-infected patients who responded favorably to standard treatment have been reported [8]. In our series, severe complications in two HIV-infected patients were related to poor compliance.

The goal of our case series was to show the efficacy of early vitrectomy preceded and followed by antifungal treatment. This study had a nonrandomized, uncontrolled design that limits the generalization of its conclusions. Randomized studies with larger samples of patients are needed to confirm our results.

In summary, patients with CE who were treated with early vitrectomy preceded and followed by antifungal therapy had favorable responses. Unfavorable outcomes were reported for most patients with vitritis who did not undergo early vitrectomy regardless of the antifungal treatment received.

Acknowledgment

The authors thank Benjamin Magno, M.D., for his critical review of the manuscript.

References