Fungal Endophthalmitis Developing in Asthmatic Individuals Treated With Inhaled Corticosteroids

Candida albicans is a normal component of human microbial flora of the skin and gastrointestinal tract. When it gains access to the bloodstream, resulting in fungemia, susceptible patients may develop endogenous fungal endophthalmitis (EFE). A number of risk factors have been associated with Candida endophthalmitis and are shown in the Table. These include long-term intravenous therapy, intravenous drug abuse, and even lithotripsy. In this article, we propose another risk factor for EFE—the use of inhaled corticosteroids in the treatment of asthma.

Oral candidiasis secondary to the treatment of asthma with inhaled corticosteroids has been well-documented in the medical literature. We hypothesize that oral candidiasis may cause transient fungemia, which can seed the choroid and lead to EFE.

### Table. Risk Factors for Endogenous Fungal Endophthalmitis

<table>
<thead>
<tr>
<th>Iatrogenic</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indwelling bladder catheter</td>
<td>Trauma</td>
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<td>Long-term intravenous line</td>
<td>Malignancy</td>
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<tr>
<td>Hemodialysis</td>
<td>Diabetes</td>
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<td>Prolonged antibiotic use</td>
<td>HIV</td>
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<td>Abdominal procedures or surgery</td>
<td>Alcoholism</td>
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<td>Immunosuppression</td>
<td>Fungemia</td>
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<td>Lithotripsy</td>
<td>Low-birth-weight infants</td>
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<td></td>
<td>Hyperalimentation</td>
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<td></td>
<td>Debilitated state</td>
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</tbody>
</table>

Abbreviation: HIV, human immunodeficiency virus.

Report of a Case. Case 1. The patient was a 68-year-old woman with a history of asthma and decreased, “cloudy” vision in both eyes for a period of 2 days. She had recently experienced an asthma exacerbation treated with inhaled corticosteroids and subsequently developed oral candidiasis treated with local application of nystatin.

Examination revealed a visual acuity of counting fingers at 1 foot in both eyes, 1+ conjunctival injection, and 4+ cell in the anterior chamber with 1-mm hypopyon and posterior synechiae bilaterally (Figure). The anterior vitreous of the right eye was poorly visualized owing to a small pupil, while the left eye revealed vitreous cells. The media was hazy, and vitreous debris was seen on B-scan bilaterally.

A clinical diagnosis of bilateral EFE was made, and she was treated with 200 mg of oral fluconazole twice daily for 1 month. In addition, she was given topical corticosteroids and cycloplegic eye drops.

At the 1-month follow-up, her visual acuity was 20/25 in both eyes. As a result of fluconazole treatment, the patient resolved her infection and experienced a significant improvement in visual acuity, confirming our clinical diagnosis.

Case 2. The patient was a 67-year-old woman with a history of steroid-dependent asthma and chronic obstructive pulmonary disease who presented with 2 days of decreased visual acuity in the left eye and retroorbital and facial pain. In the 2 months prior, she had 3 hospital admissions for asthma exacerbations that were treated with inhaled corticosteroids. During these episodes, she developed oral candidiasis treated locally with nystatin.

The patient’s left eye had a visual acuity of counting fingers at 6 inches, 2+ conjunctival injection, 4+ cell and flare in the anterior chamber with 0.5 mm hypopyon, 3+ anterior vitreous cells, hazy fundus view with dull red reflex, and a “chalky white” lesion in the posterior pole. She was diagnosed clinically with EFE and treated with an intravitreal injection of 5 µg/0.1 mL of amphotericin B as well as corticosteroid and cycloplegic eye drops.

At the 2-week follow-up, the patient had decreased vision and increased pain in the left eye. Exami-
nation revealed a large, tender posterior cervical lymph node on the right side, and she appeared systemically ill. The patient was admitted for evaluation for systemic fungal infection and taken to the operating room for pars plana vitrectomy and another intravitreal amphotericin B injection. During surgery, she was found to have a white fluffy vitreous abscess attached to the retina just above the supratemporal arcade; however, results of vitreous culture testing were negative for C albicans. She was treated with 400 mg of amphotericin B lipid complex every other day, 200 mg of oral fluconazole every other day, topical corticosteroids, and cycloplegic eye drops for 5 weeks.

Two months later, the patient’s visual acuity was 20/50 in the affected eye, with mild vitreous debris in the left eye. The initial intravitreal antifungal injection was unsuccessful; however, systemic antifungal treatment was able to resolve the ocular and presumed systemic infection.

Comment. Endogenous fungal endophthalmitis can be difficult to diagnose. It should be suspected in any patient who presents with decreased vision or mild anterior uveitis, with or without hypopyon and one of the risk factors listed in the Table. A positive result on vitreous culture testing serves as the criterion standard for diagnosis, while testing of cultures from blood or urine can support the diagnosis without an invasive eye procedure. Even when vitrectomy is performed, growth on culture media has been reported at only 47%, so diagnosis is often made clinically and supported by response to empirical antifungal treatment. In our experience, cultures must include the abscess to test positive for C albicans. Polymerase chain reaction also has the capability to detect C albicans; however, it is not widely available at this time.

Here we describe 2 asthmatic patients who use inhaled corticosteroids who developed oral candidiasis that was treated locally with nystatin only and were diagnosed clinically with EFE. We propose that a careful medical history should include not only the typical risk factors listed in the Table but also the additional risk factors of asthma, inhaled corticosteroids, and oral candidiasis highlighted in these cases. We hypothesize that the pathogenesis of the EFE in these cases originated from oral candidiasis due to inhaled corticosteroids used in the treatment of asthma, a well-established phenomenon.

Another clinical point derived from these cases is that local treatment with intravitreal amphotericin B may not be sufficient, as patients are at risk for the development of a systemic infection that requires treatment as well, as in case 2. Systemic treatment with oral fluconazole has been shown to be effective, as in case 1, with or without vitrectomy and intravitreal amphotericin B, depending on vitreal involvement. In the cases presented here, resolution of infection occurred with treatment with systemic antifungals. These cases demonstrate another underlying etiology of fungal endophthalmitis that should be added to the list of risk factors.

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Cataract operating does not require as much dexterity as is shown by many artisans who are specially skilled in their own line. But the difficulty about cataract is that there is so little material available to train the apprentice upon.