Prolonged Curvularia Endophthalmitis Due to Organism Sequestration

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Curvularia is a dematiaceous or darkly pigmented fungus. Endophthalmitis due to Curvularia species is exceedingly rare, with only isolated case reports in the literature. Large series of endogenous and exogenous fungal endophthalmitis in the United States do not mention Curvularia as a separate causative organism. The present series of 6 cases of Curvularia endophthalmitis demonstrates the difficulty of timely and proper diagnosis and challenges in the eradication of the microorganism.

Methods
An institutional review board-approved retrospective review of the archives of the microbiology laboratory at Bascom Palmer Eye Institute from January 1, 1980, through September 30, 2013, identified all cultures positive for Curvularia. The substrate (blood agar, chocolate agar, Sabouraud agar, Lowenstein-Jensen agar, or thioglycolate broth) on which Curvularia grew...
was documented with the time from initial specimen plating to organism growth. We identified a total of 7 patients with vitreous cultures positive for *Curvularia*. One additional patient had culture-confirmed *Curvularia* endophthalmitis with a vitreous culture performed at another hospital. Because the patient was treated for her condition at Bascom Palmer Eye Institute and we had access to the patient’s complete medical records, she was included in the study. Thus, we reviewed the records of 8 patients. Two patients were excluded after review of the clinical history because they did not develop clinical endophthalmitis. Therefore, we included a total of 6 cases of *Curvularia* endophthalmitis, with 2 of these patients previously described in separate reports4-5 (cases 1 and 2 in the Supplement [eAppendix]).

### Results

A total of 6 patients with endophthalmitis caused by *Curvularia* species were identified and reviewed in chronological order (Table). In 5 patients (mean age, 75.2 years), endophthalmitis occurred after cataract surgery with intraocular lens implantation; in 1 patient (age, 21 years), endophthalmitis occurred after trauma. The diagnosis was established rapidly at 6 weeks in the trauma case. In the postoperative cases, the time from surgery to the first signs of inflammation ranged from 2 to 5 months. The time from the surgery to correct diagnosis of *Curvularia* endophthalmitis ranged from 7 to 24 months. The patients with postoperative endophthalmitis were treated with topical corticosteroids (n = 5), sub-Tenon or subconjunctival injection of triamcinolone acetonide (n = 3), or systemic methotrexate sodium and azathioprine sodium (n = 1). These patients underwent a mean of 2 (range, 0-5) intraocular procedures and operations, including anterior chamber culture, vitreous culture, intraocular injection, or pars plana vitrectomy. In 5 postoperative cases, the definitive surgery that established the diagnosis of *Curvularia* endophthalmitis was pars plana vitrectomy with vitreous cultures, partial or complete capsullectomy or lensectomy, and intravitreal injection of antimicrobials. The time from the inciting event (surgery or trauma) to eradication in all 6 patients ranged from 8 to 27 months. During this time the patients were treated with topical, oral, and, in 1 case, intravenous antifungals. They underwent a mean of 1.8 intraocular procedures, usually with concurrent intravitreal antifungal treatment, with a mean of 6.8 separate intravitreal antifungal injections. Despite aggressive antifungal therapy, eradication of the infection could be achieved only by identification and removal of the nidus of sequestration. This process required the use of imaging studies, such as ultrasonography, and use of endoscopy during the pars plana vitrectomy. The nidi of sequestration included an iris lesion, a corneal endothelial plaque, ciliary body mem-

<table>
<thead>
<tr>
<th>Case No./ Age, y</th>
<th>Eye</th>
<th>Comorbidities</th>
<th>Cause</th>
<th>Date of Surgery/ Trauma</th>
<th>Time From Inciting Event To Symptoms (mo)</th>
<th>Time From Inciting Event To Diagnosis (mo)</th>
<th>Specimen</th>
<th>Curvularia Substrate (Time From Plating to Growth)</th>
<th>VA (Time)</th>
<th>Time From Inciting Event to Eradication, mo</th>
<th>Presumed Area of Sequestration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/79 R</td>
<td>R</td>
<td>DM, hypertension, anemia, possible RA</td>
<td>CE/IOLI</td>
<td>November 2006</td>
<td>5</td>
<td>12</td>
<td>Vitreous wash of iris lesion</td>
<td>Blood agar, Sabouraud agar (3 d)</td>
<td>HM (POM 12)</td>
<td>20/100 (POM 34)</td>
<td>23</td>
</tr>
<tr>
<td>2/21 L</td>
<td>L</td>
<td>None</td>
<td>Trauma</td>
<td>July 2007</td>
<td>0</td>
<td>6 wk</td>
<td>Vitreous</td>
<td>Chocolate agar, blood agar, Sabouraud agar, thiglycolate broth (48 h)</td>
<td>2/200 (POW 2)</td>
<td>20/200 (POM 35)</td>
<td>16</td>
</tr>
<tr>
<td>3/76 R</td>
<td>R</td>
<td>DM, hypertension, hypercholesterolemia</td>
<td>CE/IOLI</td>
<td>November 2009</td>
<td>3</td>
<td>7</td>
<td>Vitreous</td>
<td>Chocolate agar, blood agar, Sabouraud agar, thiglycolate broth (3 d)</td>
<td>20/70 (POM 6)</td>
<td>20/60 (POM 11)</td>
<td>14</td>
</tr>
<tr>
<td>4/67 L</td>
<td>L</td>
<td>DM, hypertension, fibromyalgia, cerebral aneurysm, stroke</td>
<td>CE/IOLI</td>
<td>September 2010</td>
<td>2</td>
<td>19</td>
<td>Vitreous</td>
<td>Unknown</td>
<td>20/400 (POM 23)</td>
<td>20/300 (POM 28)</td>
<td>25</td>
</tr>
<tr>
<td>5/84 L</td>
<td>L</td>
<td>COPD, asthma, hypertension, hyperlipidemia</td>
<td>CE/IOLI</td>
<td>March 2011</td>
<td>3</td>
<td>7</td>
<td>Vitreous</td>
<td>Chocolate agar (blood agar)</td>
<td>CF (POM 3)</td>
<td>20/400 (POM 11)</td>
<td>8</td>
</tr>
<tr>
<td>6/70 R</td>
<td>R</td>
<td>Hypothyroidism, hypertension</td>
<td>CE/IOLI</td>
<td>August 2011</td>
<td>2</td>
<td>24</td>
<td>Vitreous</td>
<td>Chocolate agar, blood agar, Sabouraud agar, Lowenstein-Jensen medium (3 d)</td>
<td>1/200 (POM 24)</td>
<td>LP (POM 27)</td>
<td>27</td>
</tr>
</tbody>
</table>

Abbreviations: CE/IOLI, cataract extraction with intraocular lens implantation; CF, counting fingers; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; FU, follow-up; HM, hand motions; L, left; LP, light perception; NA, not available; POM, postoperative month; POW, postoperative week; R, right; RA, rheumatoid arthritis; VA, visual acuity.
branes, capsular bag, and subretinal abscess (several of these nidi are shown in the Figure). The visual acuity at presentation ranged from 20/70 to hand motions. The median follow-up was 29.5 (range, 11-35) months. The final visual acuity ranged from 20/60 to light perception.

Discussion

We report the first, to our knowledge, clinical series (6 patients) with intraocular cultures positive for Curvularia species. Curvularia, a widespread septate mold that is black owing to melanin in its hyphae and conidia, is found in tropical climates, lives in the soil and on plants, and is spread by airborne spores.11 In the literature, the number of reports of Curvularia keratitis has increased through the last half of the 20th century, with most of the reports coming from India, the United States, and Asia.11 Nevertheless, fungal keratitis due to Curvularia is less frequent than that due to Candida, Fusarium, or Aspergillus species.11 Cases of Curvularia endophthalmitis are rare, but reports are increasing. The first reports of Curvularia endophthalmitis are from India in early 2000.3-6,12 Review of the records of the microbiology laboratory at our institution disclosed that the first case of clinically significant Curvularia endophthalmitis was documented in 2006 (case 1; Table). Four large studies focusing on endogenous and exogenous fungal endophthalmitis at our institution spanning 1984 through 199310 and 1990 through 20098 for endogenous and 1969 through 19867 and 1990 through 20069 for exogenous infections did not identify any cases of Curvularia endophthalmitis.

Curvularia was not documented as a human pathogen until 1959.13 Curvularia species most commonly cause skin infections, invasive sinusitis, and allergic fungal sinusitis.14,15 Cases of pulmonary and cerebral infection and arthritis, osteomyelitis, fungemia, endocarditis, peritonitis, and gastrointestinal tract disease have been reported.14,16-18 Infections with Curvularia do not appear to require an immunosuppressed host, and inhalation and skin inoculation are the main routes of infection.15,18

In the present study, 1 patient was otherwise healthy (case 2). The other patients had several comorbidities such as hypertension, diabetes mellitus, cerebral aneurysm, stroke, anemia, hypothyroidism, and possible rheumatoid arthritis (Table). However, none of them were significantly immunocompromised.

In Curvularia keratitis, trauma with plant matter or dirt is the leading cause of infection.11 In the present trauma-related case of Curvularia endophthalmitis, the trauma was due to nail injury. No unusual exposure was seen in surgery-related cases. However, Curvularia species have been isolated in the conjunctival sac of healthy individuals.19 In the trauma-related case of endophthalmitis, the diagnosis was established rapidly because the signs suggestive of infectious endophthalmitis increased the level of suspicion. The patients with Curvularia endophthalmitis after cataract surgery had delayed diagnosis and appropriate therapy. The time from surgery to first symptoms ranged from 2 to 5 months. The time from surgery to correct diagnosis ranged from 7 to 24 months. In fact, 3 of 5 patients were treated with sub-Tenon or subconjunctival injection of corticosteroids in addition to topical corticosteroid application before the appropriate diagnosis, and
1 patient received oral immunosuppressive therapy. *Propionibacterium acnes* is the most common causative organism of delayed-onset endophthalmitis and presents with similar low-grade inflammation and a slowly progressive course; a posterior capsular plaque is present in about 65% of patients. In *Curvularia* endophthalmitis, the plaque was seen in 3 of 5 patients who had undergone surgery for cataract. Compared with *P acnes*, *Curvularia* infection presented with a variety of locations of sequestration, including an endothelial corneal plaque, the posterior lens capsule, a vitreous fungus ball, membranes on the ciliary body, and the subretinal space.

In the present case series, the patients received an aggressive treatment consisting of combined intravitreal, oral, topical, and occasionally intravenous antifungals and surgical intervention. Diagnostic and therapeutic vitrectomy was necessary in all cases. All the reported cases clearly demonstrate the importance of identification and elimination of the possible source of sequestered infection. This process may require use of preoperative high-resolution ultrasonography and thorough intraoperative depression or endoscopy to visualize the retinal periphery and the retroiridal space.

**Conclusions**

*Curvularia* infection represents a rare cause of endophthalmitis. The diagnosis and treatment are often delayed, especially in the postoperative cases. The eradication of the organism requires identification and removal of the nidus of sequestration.

**REFERENCES**