Keratomycosis after cataract surgery

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ABSTRACT

Purpose: To evaluate cases and results of keratomycosis that developed after cataract surgery.

Setting: Hospital de Guipúzcoa, San Sebastián, Spain.

Methods: This retrospective study comprised 8 patients who developed keratomycosis soon after cataract surgery.

Results: Culture analysis revealed 7 cases of Aspergillus fumigatus and 1 of Aspergillus flavus. After medical treatment with antifungal agents, 6 cases resolved and 2 required evisceration.

Conclusions: The presence of fungi in corneal ulcers that develop after cataract surgery should be considered. Initiation of early treatment determines the prognosis. Among the therapeutic options, collagen shields soaked in amphotericin B may be effective.

Mycotic infections after cataract surgery, while uncommon, have been occurring with increasing frequency. The infections have been diagnosed in immunosuppressed patients or those treated with corticosteroids because suppressing the ocular immunologic response favors development of mycotic infection.1

Proper collection, process staining, and culture of samples are necessary to identify the offending pathogens.1,2 Different antifungal agents and routes of administration have been suggested, with the most common being topical application, subconjunctival injection, systemic administration, and, more recently, the application of collagen shields.3–5

The clinical suspicion of infection, correct use of diagnostic tests, early treatment, and proper management of the surgical reconstructive process, when necessary, promote functional recovery.

Patients and Methods

All patients were referred to our hospital by local ophthalmologists. All cases received topical dexamethasone 0.1% 4 times a day as a routine postoperative treatment. The predisposing factors, treatments, and reconstructive techniques are shown in Tables 1, 2, and 3, respectively. Mean patient age at diagnosis was 73.60 years ± 18.23 (SD). Culture samples were obtained by scraping or biopsy. In 1 case, lactophenol blue staining was used.

Patients 1 and 2 were treated with parenteral amphotericin, according to dosing guidelines, with regular monitoring of renal function. Patients 3 to 8 were treated with oral itraconazole (200 mg/day).

Patient 1 was treated subconjunctivally with amphotericin. Topical amphotericin was administered every 2 hours in 7 cases; patient 7 received amphotericin 0.15% and the rest, a 0.25% concentration.

Patients 2, 3, and 4 received collagen shields soaked in amphotericin B and replaced daily. The Bio-Cor 24-hour collagen shields (Bausch & Lomb Pharmaceuticals) are made of porcine collagen and have a curvature...
radius of 14.5 mm and a diameter of 9.0 mm. When hydrated, they have water content of approximately 63%. These shields were soaked in 15 drops of amphotericin B 0.50% (5 mg/mL) solution for 2 hours at 25°C before application. Clinical monitoring included serial sampling. When clinical stabilization was apparent and 2 successive samples were negative, the antifungal treatment was discontinued and keratoplasty planned when necessary.

Table 1. Patient data and predisposing factors.

<table>
<thead>
<tr>
<th>Case</th>
<th>Year</th>
<th>Age/Sex</th>
<th>Eye</th>
<th>Predisposing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1990</td>
<td>64/F</td>
<td>R</td>
<td>Topical dexamethasone 0.1%/6 hours</td>
</tr>
<tr>
<td>2</td>
<td>1991</td>
<td>71/M</td>
<td>R</td>
<td>Topical dexamethasone 0.1%/6 hours; traumatic iris hernia</td>
</tr>
<tr>
<td>3</td>
<td>1992</td>
<td>81/F</td>
<td>L</td>
<td>Topical dexamethasone 0.1%/6 hours</td>
</tr>
<tr>
<td>4</td>
<td>1992</td>
<td>82/F</td>
<td>R</td>
<td>Topical dexamethasone 0.1%/6 hours; capsule rupture, anterior vitrectomy</td>
</tr>
<tr>
<td>5</td>
<td>1992</td>
<td>79/F</td>
<td>L</td>
<td>Diabetes mellitus type II</td>
</tr>
<tr>
<td>6</td>
<td>1994</td>
<td>65/M</td>
<td>R</td>
<td>Kidney transplant; systemic immunosuppression (prednisone, cyclosporine A)</td>
</tr>
<tr>
<td>7</td>
<td>1994</td>
<td>83/M</td>
<td>R</td>
<td>Topical dexamethasone 0.1%/6 hours</td>
</tr>
<tr>
<td>8</td>
<td>1994</td>
<td>64/M</td>
<td>R</td>
<td>Topical dexamethasone 0.1%/6 hours</td>
</tr>
</tbody>
</table>

R = right eye; L = left eye

Table 2. Surgical techniques, causal agents, and treatments.

<table>
<thead>
<tr>
<th>Case</th>
<th>Cataract Technique</th>
<th>Causal Agent</th>
<th>Interval* (Days)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ECCE; PC IOL</td>
<td>A fumigatus</td>
<td>20</td>
<td>Amphotericin B IV (total dose, 974 mg); amphotericin B subconjunctival</td>
</tr>
<tr>
<td>2</td>
<td>ECCE; PC IOL; iris hernia repositioning</td>
<td>A fumigatus</td>
<td>21</td>
<td>Amphotericin B IV (total dose, 726 mg); amphotericin B + collagen shields; topical amphotericin B (0.25%)</td>
</tr>
<tr>
<td>3</td>
<td>ECCE; PC IOL</td>
<td>A fumigatus</td>
<td>12</td>
<td>Oral itraconazole (200 mg/day); amphotericin B + collagen shields; topical amphotericin B (0.25%)</td>
</tr>
<tr>
<td>4</td>
<td>ECCE; capsule rupture; anterior vitrectomy; PC IOL</td>
<td>A fumigatus</td>
<td>15</td>
<td>Oral itraconazole (200 mg/day); amphotericin B + collagen shields; topical amphotericin B (0.25%)</td>
</tr>
<tr>
<td>5</td>
<td>ECCE; PC IOL</td>
<td>A fumigatus</td>
<td>15</td>
<td>Oral itraconazole (200 mg/day); topical amphotericin B</td>
</tr>
<tr>
<td>6</td>
<td>ECCE; PC IOL</td>
<td>A flavus</td>
<td>30</td>
<td>Oral itraconazole (200 mg/day); topical natamycine (5%)</td>
</tr>
<tr>
<td>7</td>
<td>Phacoemulsification; PC IOL</td>
<td>A fumigatus</td>
<td>10</td>
<td>Oral itraconazole (200 mg/day); topical amphotericin B (0.15%)</td>
</tr>
<tr>
<td>8</td>
<td>Phacoemulsification; PC IOL</td>
<td>A fumigatus</td>
<td>15</td>
<td>Oral itraconazole (200 mg/day); topical amphotericin B (0.15%)</td>
</tr>
</tbody>
</table>

ECCE = extracapsular cataract extraction; PC IOL = posterior chamber IOL; A = Aspergillus; IV = intravenous
*Between cataract extraction and keratomyocosis diagnosis
Patients 2, 4, and 7 required lamellar keratectomy with debridement of necrotic tissue. A scleral flap was created in patients 2 and 7 to cover the necrosed area. Patients 2 and 4 required keratoplasty to reconstruct the anterior segment. Patient 2 had 2 penetrating keratoplasties (PKPs), the second associated with transscleral cyclocoagulation with a thermal YAG laser, annular resection of the iris because of goniosynechias, and intraocular lens (IOL) extraction.

**Selected Cases**

**Case 2.** A 71-year-old man had uneventful extracapsular cataract extraction (ECCE) and IOL implantation to treat a cataract in the right eye. After 2 weeks, while still receiving dexamethasone 0.1%, he suffered a blunt ocular trauma with dehiscence of the wound and iris prolapse after falling to the ground; he had surgical repositioning of the iris. Ten days later, a corneal ulcer with gray stromal infiltration was diagnosed. *Aspergillus fumigatus* was isolated in this material. He was treated intravenously with amphotericin B in increasing doses until a total dose of 726 mg was reached. Renal function was monitored periodically. He also received concurrent treatment with collagen shields soaked in amphotericin B 0.50% that were replaced daily and amphotericin B 0.25% eyedrops every 2 hours between 8 AM and 12 PM. Cultures were negative by day 12, but after 30 days scleral necrosis at the level of the incision developed. Treatment consisted of necrotic tissue resection and creation of a scleral flap with a limbal autograft from the contralateral eye; the response was favorable. Final BCVA was 20/40.

**Case 6.** A 65-year-old man who was receiving oral prednisone (10 mg/day) and cyclosporine A after a kidney transplant had uneventful ECCE and IOL implantation in his right eye. One month later while receiving topical dexamethasone 0.1%, he developed an infiltration in the incisional area (Figure 1, A). Tinction of scraped material with lactophenol blue revealed *Aspergillus flavus* (Figure 1, B). He was treated with oral itraconazole (200 mg/day) and local natamycin 5% every 4 hours between 8 AM and 12 PM. Improvement was evident from day 7, with total remission on day 30 (Figure 1, C). Final best corrected visual acuity (BCVA) was 20/25.

**Case 7.** An 83-year-old man had uneventful scleral incision phacoemulsification and IOL implantation to treat a cataract in the right eye. After 10 days, he developed scleritis of the incisional area with a gray corneal infiltration and hypopyon; *A fumigatus* was isolated in the culture. He received oral itraconazole 200 mg/day and amphotericin B 0.15% eyedrops every 2 hours between 8 AM and 12 PM. Cultures were negative by day 12, but after 30 days scleral necrosis at the level of the incision developed. Treatment consisted of necrotic tissue resection and creation of a scleral flap with a limbal autograft from the contralateral eye; the response was favorable. Final BCVA was 20/40.

**Results**

Two patients had predisposing factors for the development of keratomycosis (Table 1): Patient 5 had diabetes mellitus type II and patient 6 was receiving immunosuppressing treatment after a kidney transplant. All 8 patients developed keratomycosis in the immediate postoperative period and were receiving topical treatment with dexamethasone 0.1% 4 times a day as a routine postoperative treatment.

All patients had corneal ulceration with a gray–white stromal infiltration around the incisional area as a clinical sign of keratomycosis.

Patients 1 and 8 had hypopyon. Patients 1 to 6 had ECCE, and patients 7 and 8 had phacoemulsification (Table 2). The surgical incision in extracapsular cases was anterior limbal and in the phacoemulsification
cases, scleral tunnel. In all cases, the keratomycosis was initially located at the surgical incision. The early first signs of infection were observed between 12 and 30 days after cataract surgery.

After the corneal ulcer was scraped, the procedure was as follows in all cases: The samples were processed for culture in 1 plate of blood agar, chocolate agar, and thioglucoolate medium at 37°C, and another plate of blood agar and Sabouraud’s medium were inoculated and incubated at room temperature. The following fungi were identified: *A fumigatus* in all patients except patient 6, in whom *A flavus* was isolated. The causal agent was identified by biopsy in patient 8 and by lactophenol blue staining in patient 6. All other cases were diagnosed by culturing scraped material.

Patients 1 and 5 had evisceration, although all cultures were negative after treatment (Table 2). In patients 2, 4, and 7, corneal necrosis required a lamellar keratectomy, with a PKP in patients 2 and 4 and a scleral patch and limbal autograft in patient 7. Postoperatively, 3 patients had a BCVA of 20/40 or better (Table 3).

**Discussion**

The incidence of postoperative infection has decreased because of improved aseptic methods, better use of surgical material and ocular tissues, and perhaps the use of prophylactic antibiotics. However, postoperative mycotic infections are rising because of the increasing number of ocular surgeries performed on patients who are immunosuppressed, hemodialysed, or receiving parenteral nutrition. The most frequent are caused by *Candida* and *Aspergillus* in the form of endophthalmitis acquired endogenously. Improved diagnostic techniques may also explain the higher incidence of ocular mycotic infections.
Corneal fungus infections have been described in relation to cataract surgery, keratoplasty, glaucoma, and radial keratotomy. In relation to cataract surgery, cases also have been described in which the technique used was intracapsular cataract extraction, ECCE, or phacoemulsification, although the incidence is lower in the latter than in the former 2 techniques. Thus, corneal infection can be a primary form or secondary to endophthalmitis.

The incidence of corneal mycotic infections has been reported to be between 15% and 20% in cases of stromal keratitis. Geographic differences have been recognized, with the infections occurring more frequently in rural areas and temperate climates. Factors associated with corneal infections are the fungus itself, previous trauma, the immunologic state of the host, and administration of steroidal agents. These factors (ie, surgery in immunosuppressed patients and those receiving steroidal agents; improved diagnostic techniques) may account for the increased incidence of mycotic infections over the past few years.

In our series, patient 6 was immunosuppressed as a result of treatments. Patients 1 to 8, who developed mycosis during the immediate postoperative period, were all receiving external treatment with dexamethasone 0.1%. These circumstances might lead to the conclusion that topical corticoid therapy is an avoidable predisposing factor for the development of keratomycosis because alternatives are available to manage inflammation. In all patients, the infection was localized at the incisional area.

Even though more than 35 genera of fungi related to corneal infections have been described, the most frequent infections are caused by Aspergillus and Fusarium. Before 1974, about 50% of keratomycosis cases were caused by Aspergillus, about 25% by Candida, and the rest by other genera. More recently, those caused by Aspergillus vary between 5% and 35% and those caused by Fusarium, between 23% and 50%. We believe that these variations are probably the result of geographic differences in the prevalence of the keratomycosis rather than differences in identification methods.

Keratomycosis continues to pose diagnostic and therapeutic problems in ophthalmic practice. Its clinical manifestations may be indistinguishable from other forms of inflammation. Therapeutic problems include inadequate treatment with steroidal agents, which may worsen the condition; the only solution is to use adequate antifungal agents. In 1986, up to 20% of affected eyes were enucleated despite treatment. In our series in which all patients had cataract surgery, 2 (25.0%) required evisceration.

The diagnosis of keratomycosis is based on clinical suspicion and biomicroscopic findings. In most cases, biomicroscopy makes it possible to observe epithelial ulceration with elevated edges and gray or white stromal infiltration. Fibrinous material, which could develop into endophthalmitis, may also be observed in the anterior chamber. The diagnosis is confirmed by properly obtaining samples from the edges of the stromal corneal ulcerations. Performing corneal biopsies can be useful in these situations, especially when the scrapings from the edges of the ulcers have not allowed identification of the causal agent.

In the present series, routine cultures identified fungi in 7 cases (87.5%); patient 8 required a biopsy because the cultured material was negative. The samples should be handled correctly using adequate staining and culture techniques. Direct visualization of the samples after staining techniques is the more commonly used identification technique. Staining with Calcofluor allows identification of 95% of fungi compared with 71% when potassium hydroxide tinction is used.

Three families of antimycotics generally are used clinically: polyenes (pymaricine and amphotericin B), imidazoles (miconazole and ketoconazole), and 5-fluorocytosine. The choice depends on the antifungal spectrum and its capacity to spread to the infected tissue. Amphotericin B and natamycin are the most effective agents to treat keratomycosis. The efficacy of amphotericin B against a wide variety of fungi is well documented, as is its possible toxicity, which can be avoided by administering the low-concentration preparations. Natamycin, a broad-spectrum low-toxicity agent, is available as an ophthalmic preparation, although it is not effective for treating deep stromal infections.

Miconazole and ketoconazole also have a wide spectrum of activity and low toxicity. Miconazole has been used externally and subconjunctivally and ketoconazole, orally. Their efficacy has been demonstrated experimentally and clinically.
Different routes of administration have been suggested, the most common being external application, subconjunctival injection, systemic administration, and more recently collagen shield application. Whatever route is used, intracorneal penetration increases with loss of corneal epithelial integrity. External application should be repeated frequently to reach therapeutic levels; however, this generally causes ocular irritation. Minimal penetration and severe toxicity both limit the efficacy of the subconjunctival and systemic forms. The use of moistened collagen shields to administer antifungal agents disperses the medication. Shields, especially those soaked in amphotericin B, should be considered when treating keratomycosis. However, shields soaked in natamycin are probably ineffective.

Lamellar keratectomy also has been recommended as a therapeutic alternative because it eliminates infected tissue and potentiates intracorneal penetration of antifungal drugs. This procedure has proved experimentally useful in the management of keratomycosis resulting from Candida and Fusarium, but it is not effective against Aspergillus, with which the risk of perforation is high. Occasionally, in cases in which there is minimal response to antifungal agents, debridement, lamellar keratectomy, and early keratoplasty are the most effective alternatives.

In summary, effective treatment of keratomycosis should be based on clinical findings, the correct use of available staining and culture techniques, and proper and early treatment. Collagen shields soaked in antifungal agents and lamellar keratectomy can be useful in selected cases. However, keratomycosis continues to be a serious clinical entity that occasionally requires surgery for anterior chamber reconstruction because of the characteristics of its own evolution or the toxicity of the antifungal agents used. After cataract surgery, external corticoid therapy may facilitate the development of keratomycosis because of its immunosuppression potential.

References

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