Treatment of Fungal Corneal Ulcers With Amphotericin B Ointment

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PURPOSE: To report two patients with severe fungal corneal ulcers who were treated successfully with topical amphotericin B ointment.

METHODS: Two eyes of two patients developed corneal ulcers and hypopyon after corneal foreign body removal. Aspergillus fumigatus and Fusarium solani were isolated in Patients 1 and 2, respectively. By antifungal susceptibility testing, amphotericin B was shown to have the lowest minimal inhibitory concentration.

RESULT: Topical administration of amphotericin B ointment resulted in dramatic improvement in fungal corneal ulcers.

CONCLUSIONS: Antifungal susceptibility tests may aid with selection of antifungal agents. Amphotericin B ointment is one of the promising therapies for keratomycosis caused by antifungal-resistant fungi.

With the development of new broad-spectrum antifungals, treatment of ophthalmic infections with fungal causes has improved. However, cases of severe infection caused by antifungal-resistant fungi are increasing, making treatment more difficult. We present two patients with severe fungal corneal ulcers successfully treated with topical amphotericin B ointment.

• CASE 1: A 59-year-old man developed a corneal ulcer and hypopyon 5 days after a corneal foreign body was removed from his left eye. Systemic and topical antibiotics (flomoxef and sisomicin sulfate) were ineffective. On fungus culture, Aspergillus fumigatus was isolated from the lesion. Systemic and topical antifungals (fluconazole, miconazole, flucytocine, and natamycin) were introduced and continued for 1 month, but there was no improvement. The patient was referred to us 26 days after onset of the corneal ulcer (Figure 1, left). Antifungal susceptibility testing for A fumigatus disclosed highest susceptibility to amphotericin B (minimal inhibitory concentration, 0.78 μg/ml) compared with other antifungals (fluconazole, 200 μg/ml; miconazole, 12.5 μg/ml; flucytocine, >200 μg/ml). Forty-two days after onset, amphotericin B was introduced gradually, beginning with 1 mg in 500 ml of saline solution for the first day and increased 2 mg daily up to 15 mg.

Simultaneously, amphotericin B ointment was administered four times daily. Hypopyon disappeared 10 days after amphotericin B administration, and the corneal ulcer resolved in 2 weeks. Systemic amphotericin B administration was stopped after 1 month and amphotericin B ointment after 3 months.

• CASE 2: A 68-year-old woman was initially examined with corneal ulcer and hypopyon 1 month after a corneal foreign body was removed from her right eye (Figure 2, left). Systemic antibiotic therapy (flomoxef and gentamicin sulfate) and antifungal therapy (fluconazole, miconazole, flucytocine, and natamycin) did not cause improvement. A culture of corneal epithelium showed Fusarium solani that was susceptible to amphotericin B (minimal inhibitory concentration, 1.56 μg/ml). Amphotericin B ointment only was introduced four times daily instead of systemic administration because of mild dysfunction of the patient’s liver and pancreas. Sixteen days after amphotericin B ointment administration, the hypopyon disappeared.
FIGURE 1. Patient 1. (Left) Photograph of the corneal ulcer in Patient 1 shows extreme corneal thinning with suppuration into the deep stroma and massive hypopyon. (Right) Photograph of the cornea with moderate stromal opacity 6 months after termination of treatment by amphotericin B ointment.

FIGURE 2. Patient 2. (Left) Photograph of the eye in Patient 2 shows a corneal ulcer with stromal suppuration and hypopyon. (Right) Photograph of the cornea with moderate opacity 5 months after termination of treatment by amphotericin B ointment.

and the corneal ulcer had improved remarkably. Amphotericin B ointment treatment was ceased 1 month later.

In our practice, we often administer broad-spectrum antimycotics as soon as possible to treat severe fungal corneal ulcers. However, fungal susceptibility tests may be useful in determining the most effective antifungal agent. We administered systemic and topical amphotericin B in Patient 1 and amphotericin B ointment only in Patient 2, followed by antifungal susceptibility tests, and had good results. In both the above cases, no side effects were seen throughout the course of treatment, and there was no recurrence (Figures 1 and 2, right).

Clinicians are often reluctant to administer amphotericin B because of severe side effects, including nausea, vomiting, and renal dysfunction. However, if introduced by way of gradual dose increases, most patients do not demonstrate such side effects. Furthermore, if amphotericin B is introduced topically, there is even less risk of side effects. Amphotericin B
ointment (a concentration of 5 mg/g) was prepared by adding 9 g of white Vaseline to 50 mg of the intravenous preparation (Fungizone Intravenous, Bristol Meyers, Squibb Co, Ltd, Tokyo, Japan) mixed with 1 g of liquid paraffin in a sterile process. Amphotericin B ointment may provide a greater concentration of amphotericin B than other topical usages and can be stored for up to 1 month if not exposed to light and kept in a refrigerator. Our patients indicate that amphotericin B ointment is a promising topical therapy for keratomycosis caused by an antymycotic-resistant fungus.

REFERENCES


Serum Beta Carotene, Alpha Tocopherol, and Age-Related Maculopathy: the Blue Mountains Eye Study

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PURPOSE: To assess associations between serum beta carotene, alpha tocopherol, and age-related maculopathy.

METHODS: We studied 156 subjects with age-related maculopathy matched for age, sex, and month of blood collection to 156 control subjects without age-related maculopathy. Subjects were identified from the Blue Mountains Eye Study: those with late age-related macular degeneration and early age-related maculopathy using examination and grading of retinal photographs, and control subjects without age-related maculopathy randomly sampled from the study population.

RESULT: Neither serum alpha tocopherol nor beta carotene was significantly associated with age-related maculopathy.

CONCLUSION: These findings provide no evidence of a protective association between serum alpha tocopherol or beta carotene and age-related maculopathy.

IN RECENT YEARS, MUCH EDITORIAL SPACE HAS BEEN occupied by discussions of the possible association between antioxidant vitamins and age-related maculopathy. Findings from cross-sectional and case-control studies have not resulted in clear evidence in support of or in clear evidence against associations between age-related maculopathy and either dietary intake or serum levels of antioxidant vitamins. Identifying preventive factors, as hypothesized for antioxidant vitamin intake, is very important because age-related maculopathy is a leading cause of blindness, and treatment is rarely effective.

The Blue Mountains Eye Study has surveyed a geographically defined population aged 49 years and older living west of Sydney, Australia. The details of the survey, examination, and photographic methods used have been previously described. During a 2-year period, 3,654 subjects were examined, representing a response rate of 87.9%.

The Wisconsin Age-Related Maculopathy Grading System was used to grade individual age-related maculopathy lesions. Late age-related macular degeneration included neovascular age-related macular degeneration and geographic atrophy, defined previously. Early age-related maculopathy was defined as either the presence of soft indistinct or reticular drusen, or the presence of both soft distinct drusen and retinal...