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Case Report

Mixed fungal keratitis of *Penicillium* species and *Acremonium* species

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ABSTRACT

Mixed fungal keratitis of two different genera has rarely been reported. We described a case of mixed fungal keratitis of *Penicillium* sp and *Acremonium* sp. A 67-year-old male developed severe keratitis after undergoing superficial corneal trauma of his right eye while picking herbs (*Ficus erecta Thunb. var.*) 3 days earlier. Corneal stromal infiltration with a feathery border and a surrounding immunological reaction ring was noted without epithelial defect. Direct smear examination of corneal scraping showed the presence of filamentous fungi, and topical natamycin (5%) hourly was prescribed along with systemic voriconazole. However, hypopyon soon developed. Culture revealed growths of *Penicillium* sp and *Acremonium* sp. Combined treatment with topical amphotericin B (0.1%) and natamycin, alternated hourly, and systemic ketoconazole resulted in resolution in a fluctuating course. The culture results were important for the diagnosis of a mixed infection and together with careful follow-up were critical for a good result.

1. Introduction

Fungal corneal ulcers or coinfection of bacteria and fungi are common in developing countries, among which *Aspergillus*, *Fusarium*, and *Candida* are the most common agents [1,2]. However, mixed fungal keratitis of two different genera has rarely been reported. Here, we reported a case of mixed fungal keratitis of *Penicillium* sp and *Acremonium* sp.

2. Case report

A 67-year-old male was injured in his right eye during the picking of herbs (*Ficus erecta Thunb. var.*). He came to our clinic for painful blurred vision 5 days later. On examination, biomicroscopy revealed no epithelial defect, but there was corneal stromal infiltration (two-thirds in depth) with a feathery border and an immunological reaction ring (Fig. 1A). A smear of corneal scraping showed the presence of hyphae (Fig. 1B). Topical natamycin (5%) hourly and oral voriconazole were prescribed immediately. However, hypopyon soon developed, which was resolved after adding topical amphotericin B (0.1%), alternated hourly with natamycin, from Day 3 onward to the treatments. Oral voriconazole was changed into ketoconazole (400 mg/d) on Day 6 because of a skin rash and intolerable pruritus and increased hypopyon (Fig. 1C). Fungal culture with Sabouraud's dextrose agar showed growths of *Penicillium* species and *Acremonium* species (Fig. 1D and E). The hypopyon was completely resolved on Day 22. Amphotericin B was discontinued on Day 28 but was represcribed on Day 35 because of the reappearance of hypopyon. The lesion became almost a scar, and amphotericin B and ketoconazole was discontinued on Day 56. Unfortunately, a recurrence of an anterior chamber reaction was noted again on Day 58. Natamycin, amphotericin B, and systemic ketoconazole were used from this point for 2 more weeks until complete resolution (Fig. 1F). The final visual acuity was 20/40, and there was no recurrence in the following 6 months.

3. Discussion

Direct microscopy and culture results are both important tools in diagnosing infectious keratitis. Bharathi et al [3] even suggested a greater diagnostic value of KOH smear. However, diagnosis of a mixed infection depends on culture results. Mixed fungal keratitis has been rarely reported. Chin [4] reported a corneal perforation because of mixed infection of *Helminthosporium* sp and *Mima polymorpha*. In our patient, the corneal ulceration was caused by mixed infection of *Penicillium* sp and *Acremonium* sp. *Penicillium* and *Acremonium* sp are filamentous fungi wildly spread in the

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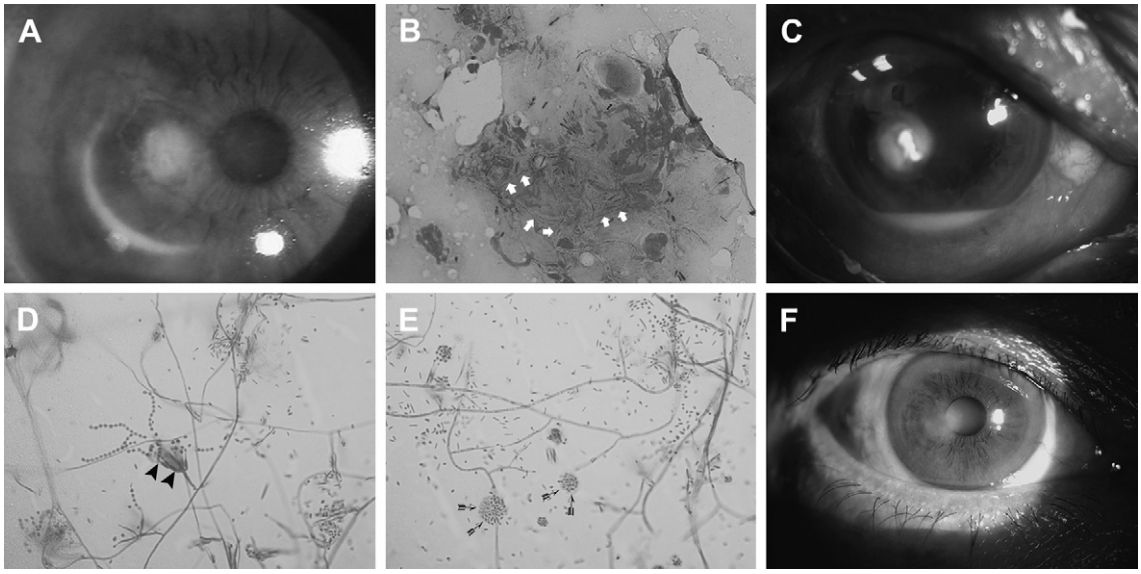

Fig. 1. (A) Slit lamp examination on referring to our clinic showed corneal stromal infiltration with a feathery border and an immunological reaction ring. (B) The smear of corneal scraping revealed septated fungal hyphae (white arrows). (C) Hypopyon increased suddenly on Day 6 of treatment with topical natamycin, amphotericin B, and oral voriconazole. (D and E) The culture of the corneal scraping demonstrated growths of Penicillium sp with brush-like phialides (D, black arrow heads) and Acremonium sp with conidia (E, dart arrows) aggregated at the apex of phialide. (F) Biomicroscopy showing complete resolution with faint scar.

environment, such as soil or tap water [5,6] and have been occasional etiologic pathogens of corneal ulceration, respectively [2]. *Acremonium* keratitis has been reported to be retractable and prone to recurrence and might require surgical interventions [7,8]. *Penicillium* keratitis has also led to penetrating keratoplasty [9]. The culture result of mixed infection of the above two fungi made us observe carefully for the corneal stromal infiltrate and ulceration, corneal edema, anterior chamber reaction, and also subjective symptoms.

Antifungal treatment is empirical conventionally [10]. It is not practical for the clinical ophthalmologist to ask a microbiology laboratory for identification and sensitivity studies to initiate and plan therapeutic management [11]. Many laboratories, including ours, are not equipped or experienced to perform sensitivity studies on fungi. Even laboratories with the necessary expertise may exhibit variability within their own results with the same fungi and may take days to weeks to perform the tests. Once obtained, the *in vitro* data and the clinical sensitivity response may not correlate [12]. It is most practical to consult published table of sensitivities for general groups of identified fungi against common available antifungal agents [12]. Careful clinical monitoring of the infiltrate and antifungal testing plays a role in the outcome of treatment [13]. Natamycin was reported the drug of choice for filamentous fungi keratitis, including *Acremonium* keratitis and *Penicillium* keratitis [2,14]. Natamycin has better penetration than amphotericin B in corneas with intact epithelium [15]. However, intensive topical natamycin application with oral voriconazole or ketoconazole was ineffective against the mixed *Acremonium* and *Penicillium* keratitis in our patient. The keratitis relapsed twice with an increased anterior chamber reaction after topical amphotericin B was discontinued. A regime involving a combination with topical amphotericin B seemed vital to cure. Therefore, we suggested that therapy for a fungal keratitis might be started with 5% natamycin hourly, but if the infection appeared to be progressing, then consideration should be given to adding or substituting another antifungal agent, such as amphotericin B or miconazole.

Fungal keratitis can easily become a surgical disease because of a delay in initiating medical treatment. Even with alertness and a prompt diagnosis of fungal infection, accurate culture results and a careful follow-up over the whole course are necessary for a good result.

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