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Acremonium nail bed mycetoma masquerading as subungual squamous cell carcinoma

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Abstract

Acremonium is a large fungal genus that is comprised of approximately 150 species, found ubiquitously in nature. Although the majority are recognized as being saprophytes in soil and pathogens of plants, several species are emerging as causative agents of a variety of human infections, including mycetomas. Herein, we present a young man that was referred to our department with a painful subungual mass that developed following traumatic inoculation of Acremonium spp. In recent years, the role of Acremonium spp. has been increasingly recognized in localized infections, such as mycetoma, in humans. Other locally invasive as well as disseminated infections are also described. Optimal treatment of Acremonium spp. mycetoma is not well-defined owing to the rarity of cases, thus posing a therapeutic challenge.

Keywords: Acremonium, mycology, nails, malformed, mycetoma

Introduction

The role of *Acremonium species*, a genus of fungi in the family *Hypocreaceae,* in human infections has been recognized for a long time. The cephalosporins, a group of broad-spectrum, semisynthetic beta-lactam antibiotics, were derived from *Acremonium,* which was formerly known as "*Cephalosporium*." The genus currently contains roughly 150 recognized named species, most of them being environmental saprophytes [1, 2]. Although once believed to have no obvious pathogenic potential for humans, during the past two decades certain species of *Acremonium spp*. have emerged as etiologic agents for a variety of clinical conditions, including mycetomas [2-3].

Mycetoma is a rare, slowly developing, chronic granulomatous disease of infectious etiology involving the skin, subcutaneous tissue, fascia, and bone [4]. On 28th May, 2016, this clinical entity was recognized as a neglected tropical disease by the World Health Organization [5]. Mycetoma prevails in many tropical and subtropical regions between latitudes 15°S and 30°N, which is also known as the mycetoma belt, but is uncommon in Europe and the USA [5, 6]. It can be caused by filamentous bacteria (actinomycetoma) or fungi (eumycetoma) and typically involves exposed areas of the body that are likely to sustain traumatic injury to the skin that involves contamination with soil [6]. Thus, the lesion is usually located on the lower extremities, especially the foot of agriculture workers and people who walk barefoot [4]. The triad of tumefaction, draining sinus

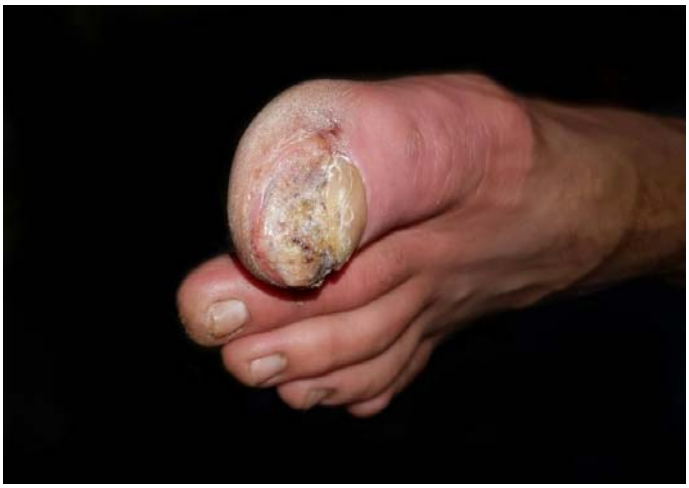

Figure 1. *Painful, purulent subungual nodular lesion associated with an ill-defined broad halo of surrounding rubor and edema.*

formation, and a purulent or seropurulent discharge containing grains is considered pathognomonic [7]. Mycetoma can become progressively worse and may cause life-long disabilities if it remains undiagnosed. Timely diagnosis, identification of the causative agent, and prompt treatment are critical in order to prevent complications, such as dissemination of the infection or muscle and bone destruction [4, 8].

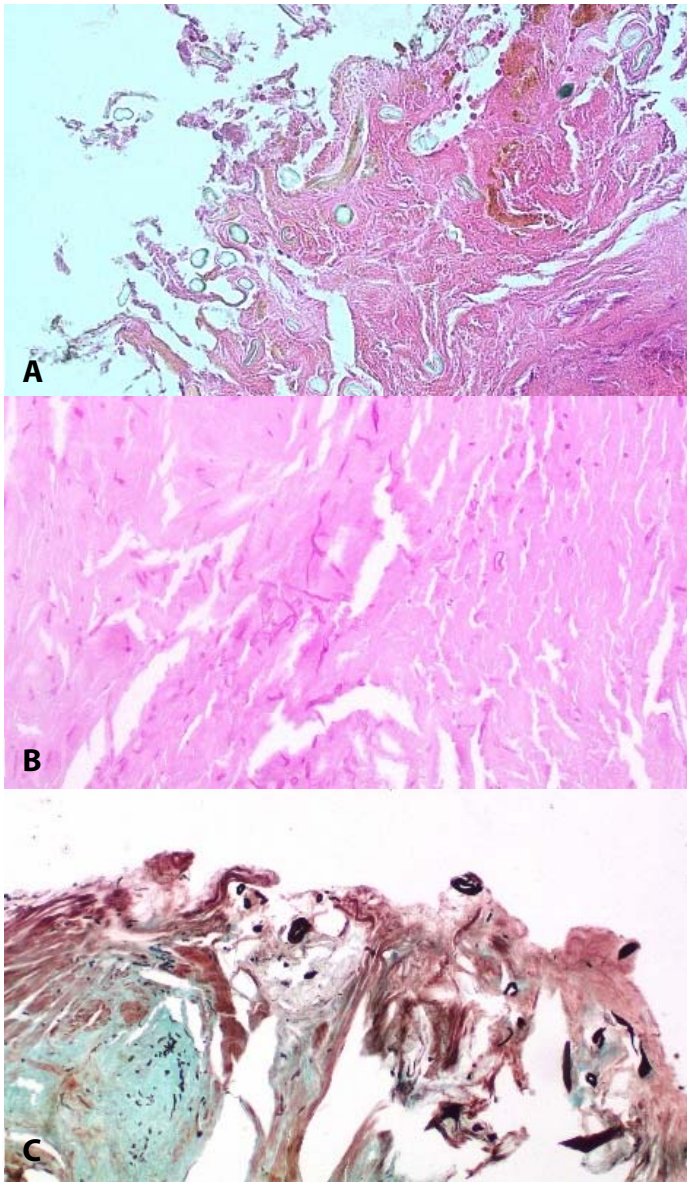

Figure 2. ***A)*** *Histopathological examination of the biopsy specimen revealing necrosis of the epidermis and upper dermis, acute inflammation, crescent and round conidia, as well as aggregates of numerous oval to round grains. H&E, 200×.* ***B)*** *Periodic acid–Schiff stain demonstrated long, narrow, poorly staining septate hyphae, 400×.* ***C)*** *Characteristic Acremonium circular and crescent nonseptate conidial structures were also demonstrated with Crocot stain, 200×.*

Case Synopsis

A 34-year-old man was referred to our department with a painful subungual mass on the left great toe of three months duration, following minor trauma to the digit. Dermatological examination demonstrated an ulcerated, oozing nodule, causing elevation and deformity of the nail plate, without restriction of movement of proximal and distal interphalangeal joints. There was surrounding diffuse erythema and edema involving the proximal part of the great toe and extending to the second digit (**Figure 1**). The nodule presented non-characteristic dermoscopic features and closely resembled squamous cell carcinoma. Histopathological examination of two biopsy specimens obtained from the nail bed nodule demonstrated necrosis of the epidermis and upper dermis, acute inflammation, crescent and round conidial structures and aggregates of numerous grains containing narrow septate hyphae (**Figure 2**). Direct microscopic examination and tissue cultures obtained from the nail bed revealed infection by *Acremonium spp*. in the absence of any dermatophyte growth. The mold was identified on the basis of its colony morphology and its morphology on microscopic observation of lactophenol cotton blue preparations. The diagnosis of eumycetoma was based on clinical features, detection of the fungal elements in histopathologic sections, and identification of fungal species in culture. The patient responded satisfactorily to treatment with intravenous liposomal amphotericin B (4mg/kg/d) for ten days followed by surgical debridement and a three-month course of oral voriconazole (200mg twice daily). There was no evidence of relapse at his follow-up visit, six months later.

Case Discussion

Acremonium spp. are filamentous fungi found ubiquitously in nature in materials such as soil, plant debris, decaying food, and hay. Human infections by fungi belonging to this genus occur uncommonly, but unlike infections related to other filamentous fungi, usually affect immunocompetent individuals. In recent years the number and the diversity of

human infections caused by *Acremonium* species have increased and numerous species have been implicated [2, 9].

The majority of infections produced by *Acremonium* species are cutaneous infections including foot mycetoma and onychomycosis, followed by other locally invasive infections such as corneal infections, osteomyelitis, arthritis, and peritonitis. However, disseminated infections including meningitis, endocarditis, colonizing disease of the gastrointestinal tract, pneumonia, and cerebritis have also rarely been reported [1-2, 10].

Acremonium mycetoma can be easily misdiagnosed in clinical practice because of its nonspecific clinical features, its notable rarity, and lack of awareness of the disease. Reported *Acremonium* mycetomas account for only about 50 cases among the several thousand cases of mycetoma of different etiology throughout the world [2, 7]. The disease is thought to arise after sustaining penetrating injury by sharp objects, such as thorns or splinters [8, 11]. However, such infections are also recognized to occur in patients who do not recall any skin injury [11, 12]. The rarity of human infections by *Acremonium* despite their high occurrence in soil or air may suggest either infrequent wound inoculation or low virulence associated with infection [7].

Several species of *Acremonium* are emerging as causative agents of mycetomas and hitherto pose a therapeutic challenge since they are generally resistant to the most commonly used antifungal agents. Optimal treatment has yet to be determined owing to the rarity of cases. Nevertheless, a combination of surgical intervention, sometimes requiring amputation of the affected part, and a regimen of antifungals, especially amphotericin B and ketokonazole for long periods seems to be the gold standard based on anecdotal reports [2, 8, 11]. Other reports have cited resistance to ketoconazole and successful treatment with other azoles, such as voriconazole, itraconazole, or posaconazole in patients with refractory forms of mycetoma [7-8, 11]. Recurrences are common and may be related to prolonged duration of infection, non-compliance to the treatment, and an absence of response to standard therapeutic measures [4, 6].

Conclusion

To our knowledge, this is the first case of *Acremonium spp.* nail bed mycetoma mimicking a malignant subungual tumor. Clinicians should have an acute awareness of this clinical entity and retain a high index of suspicion when encountering patients with atypical cutaneous infections following penetrating trauma. Although the optimal combination therapy has yet to be clearly defined, early identification of the causative agent and aggressive management, as in our patient, appears to represent the best chance for cure in *Acremonium* mycetoma.

Potential conflicts of interest

The authors declare no conflicts of interests.

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