Introduction

CBM is a fungal infection of cutaneous and subcutaneous tissue that occurs mainly in tropical and subtropical areas around the globe. The infection begins following traumatic inoculation of one of the causative organisms into the skin. CBM is often chronic, difficult to treat, and can rarely progress to squamous cell carcinoma of the skin. The causative organisms are dematiaceous, or melanin-producing, fungi. The most common organisms include Fonsecaea pedrosoi, Phialophora verrucosa, and Cladophialophora carrionii. Less commonly it is caused by Rhinocladiella aquaspersa and Exophiala dermatitidis. There has been confusion in the literature regarding the nomenclature of these organisms, as they have been referred to by multiple different names based on history and locale. Moreover, advances in culturing these organisms have unified prior nomenclature.1,5

The epidemiology of CBM varies based on the region that is studied. The incidence rate in Madagascar is thought to be 1:6,800, compared to 1:8,625,000 in the United States and 1:100,000 in Brazil. The male-to-female ratio ranges from 5:1 to 9:1 depending on the study. Middle-aged men are thought to be at higher risk because they are more likely to work outdoors, increasing their exposure to the fungi. CBM is considered an occupational disease affecting outdoor workers. CBM classically has been described as having five clinical presentations: nodular, tumoral, verrucous, plaque, and cicatricial. First-line treatment of CBM is often surgical removal or physical destruction of smaller lesions, often with concomitant use of oral antifungal agents. Surgery on larger lesions is generally not performed as there is concern for dissemination of the underlying organism. Larger lesions are often treated with oral antifungal therapy and/or physical destruction. We present a patient from central Florida with plaque-type CBM of the left knee that autoinoculated to the left forearm, forming nodular CBM. The left forearm completely resolved following shave biopsy/removal and the use of topical ketoconazole 2% cream. The left knee partially responded to topical ketoconazole alone.

Case Report

A 77-year-old male with a past medical history of hypertension, atrial fibrillation, and hypercholesterolemia presented with a chronic, pruritic, erythematous, scaly rash present for many years on his left upper knee, as well as a newer, 8-mm, scaly red papule on his left forearm, which had been present for weeks to months (Figure 1). The rash on his left upper knee was diagnosed seven years prior as a dermatophyte infection. Of note, the patient was retired and stated he often did yardwork outside. He had no other known risk factors and was immunocompetent. The patient last travelled outside of the United States more than 50 years prior, well before his rash started. A shave biopsy, encompassing the whole papule, was performed on the left forearm. The biopsy demonstrated acanthosis, pseudoepitheliomatous hyperplasia, and a granulomatous infiltrate with multinucleate giant cells extending down to the reticular dermis (Figure 2). A culture of the specimen was obtained and grew Fonsecaea pedrosoi. The biopsy of the left upper knee seven years prior, which had been diagnosed as tinea corporis, was requested and on second look was also consistent with CBM. After an in-depth discussion with the patient, he declined oral therapy, surgery, and physical destruction of his lesions. The patient did agree to use topical ketoconazole 2% cream to his left forearm and left knee. On follow-up at six weeks, the patient’s left forearm was 100% improved. Moreover, the left knee was less scaly in nature (Figure 4), and the patient stated it was no longer pruritic. The patient again declined physical destruction and oral therapy.

Figure 1. Scaly, erythematous papule on the left forearm.

Figure 2. Shave biopsy from left forearm demonstrating acanthosis, pseudoepitheliomatous hyperplasia, and a granulomatous infiltrate extending down to the reticular dermis.

Figure 3. On higher magnification, multiple sclerotic bodies are observed within a multinucleated giant cell. Surrounding the granuloma are neutrophils and a lymphohistiocytic infiltrate.

Figure 4. Scaly, erythematous plaque on the left knee.
**Discussion**

CBM classically begins, following traumatic inoculation, as a smooth macule that grows into a papule or warty growth. The most common cause of CBM, accounting for up to 96% of lesions, is *Fonsecaea pedrosoi*. The time to lesion onset after inoculation can range from weeks to months. Patients often experience pruritus and/or pain. The infection can occur anywhere but is most common on the extremities. The disease can spread via autoinoculation.

There are five classic clinical presentations of CBM: nodular, tumoral, verrucous, plaque, and cicatricial. Nodular is often the earliest form of the disease, and it can progress to tumors. The nodules are soft, raised, and pink to purple in color and can have a smooth, verrucous, or scaly surface. The tumor lesion is much larger and has a lobulated, cauliflower-like appearance. The verrucous type is characterized by hyperkeratosis and looks like verruca vulgaris; it occurs most commonly on the feet. The plaque type is the least common and has large areas of infiltration with a red-to-violaceous color, often with scale. Cicatricial lesions are flat and can involve large areas of the body. They enlarge peripherally and centrifugally, with atrophic scarring in the center.

CBM has traditionally been classified as mild, moderate, or severe. Mild lesions are small, single nodules that are less than 5 cm in diameter. Moderate lesions consist of single or multiple tumoral-, verrucous-, or plaque-type lesions that are adjacent and less than 15 cm in diameter. Severe type involves single or multiple lesions covering large areas of skin (adjacent or nonadjacent) that can involve large areas of the body. They enlarge peripherally and centrifugally, with atrophic scarring in the center.

Complications associated with CBM include systemic spread, secondary infections, and malignancy. Chronic infection with CBM can lead to squamous cell carcinoma, presumably due to long-standing inflammation and scarring. Onset of malignancy is about 20 to 30 years after inoculation, and it is most commonly seen in males after the age of 60. Diagnosis of CBM is made by direct examination, histology, and culture. Lesions often contain pigmented fungal elements on the surface that can be seen with the naked eye, appearing as small black dots. A potassium-hydroxide (KOH) test of scrapings may reveal fungal elements. Muriform cells, also known as sclerotic bodies, Medlar bodies or copper pennies, are needed to diagnose CBM. These cells are darkly pigmented round or polyhedral cells with septa. These cells can germinate filaments. Histology of CBM may show hyperkeratosis, pseudopitheliomatous hyperplasia, and neutrophilic microabscesses. Treatment can be started upon visualization of the muriform cells, but a culture is often recommended, as the *Fonsecaea* species may be less sensitive to itraconazole compared to *C. carrionii*. Serologic studies are not routinely performed.

CBM is often recalcitrant to therapy. Pharmacologic and nonpharmacologic therapies are available to treat CBM, but the disease is often persistent. Surgery or physical destruction and/or antifungal therapy are often first-line treatment modalities for smaller lesions. Oral itraconazole or terbinafine can be given three months prior to a wide and deep excision and then continued for another six to nine months. For larger lesions, or if the patient declines surgery, destructive modalities and/or antifungal therapies are often utilized. Destructive methods include cryosurgery, electrocoagulation, heat therapy, laser therapy, photodynamic therapy, and curettage. First-line pharmacologic treatment for CBM is generally itraconazole 200 mg/day to 400 mg/day for six to 12 months or until the lesions have cleared. Itraconazole is often used by itself but may be combined with 5-fluorocytosine 30 mg/kg four times a day for six months. Terbinafine 250 mg/day to 500 mg/day for 12 months is also commonly used. For extensive and systemic disease, intravenous amphotericin B at 1 mg/kg or lipid-complex at 3 mg/kg/day to 5 mg/kg/day may be used. Treatment can stop when all lesions have cleared. Modified classification systems have been proposed that also encompass response to treatment and symptomatology.

**Conclusion**

CBM is a cutaneous and subcutaneous fungal infection most commonly caused by *Fonsecaea pedrosoi*, *Phialophora verrucosa*, and *Cladosiphialophora carrionii*. It occurs more commonly in tropical and subtropical regions. Our patient presented with a persistent rash for years that had been previously misdiagnosed as tinea corporis. The rash had spread from the left knee to the left forearm, likely by autoinoculation. The 8-mm left forearm papule resolved via shave biopsy/removal followed by topical 2% ketoconazole cream twice a day. CBM is an uncommon fungal infection in the United States that is difficult to treat and can become widespread and rarely systemic. Early diagnosis and treatment are best for optimal results, as chronic lesions are often more resistant to treatment.

**References**