

# Treatment of Chromoblastomycosis Due to *Fonsecaea Pedrosoi* with Low-Dose Terbinafine

Gina M. Sevigny, MD, Gainesville, FL

Francisco A. Ramos-Caro, MD, Gainesville, FL

*Chromoblastomycosis, or chromomycosis, is a chronic fungal infection of the skin and subcutaneous tissues caused by a species of dematiaceous fungi. We present a patient with chromoblastomycosis due to Fonsecaea pedrosoi, who was treated with 8 months of terbinafine 250 mg by mouth daily with histologic and mycologic cure.*

## Case Report

A 58-year-old white male presented with a 12-year history of a slowly enlarging plaque of the right ventral wrist and forearm. This plaque was not pruritic or painful. The patient was retired but worked for many years picking and sorting oranges. He was otherwise healthy except for hypertension, for which he was taking benazapril and metoprolol. On physical examination, there was a large erythematous psoriasiform plaque with white scale on the right ventral wrist and forearm (Figure 1). Potassium hydroxide examination of the scale revealed several pigmented spores (Figure 2). A biopsy revealed a granulomatous dermatitis with microabscess formation and scattered pigmented spores consistent with chromoblastomycosis. Tissue sent for fungal culture grew *Fonsecaea pedrosoi*. The patient was started on terbinafine 250 mg by mouth every day. Four months later, on examination, the plaque of the right forearm and wrist was much smaller in size with central clearing. Potassium hydroxide examination of the site was negative, but a punch biopsy specimen at the center of the le-



FIGURE 1. Psoriasiform plaque of 12 years' duration.

sion, which clinically appeared clear, revealed hyperkeratotic epidermis with pigmented septate spores. Tissue sent for fungal culture did not grow any organism. The patient was continued on terbinafine 250 mg by mouth every day for an additional 4 months, at which time the lesion has totally resolved; the histologic and mycologic studies were negative and the treatment was discontinued. Complete blood counts and liver function studies were unchanged from baseline during the duration of the therapy.

## Discussion

*F. pedrosoi* is the most common causative agent for chromoblastomycosis, followed by *Cladosporium carrionii* and *Phialophora verrucosa* and, less commonly *Fonsecaea compactum* and *Rhinocladiella aquaspersa*.<sup>1,2</sup> These fungi are present in soil, wood, and decomposing vegetation, with the most common route of infection being traumatic inoculation.<sup>1</sup> While the fungi are distributed worldwide, they are most fre-

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Dr. Sevigny is from the University of Florida College of Medicine, Division of Dermatology, Gainesville, Florida. Dr. Ramos-Caro is from the University of Florida College of Medicine, Division of Dermatology, and the Gainesville Veterans Medical Center, Gainesville, Florida.

REPRINT REQUESTS to Division of Dermatology and Cutaneous Surgery, PO Box 100277, Gainesville, FL 32610-0277 (Dr. Ramos-Caro).



**FIGURE 2.** "Copper-penny" spores in the potassium hydroxide examination of the scale (original magnification,  $\times 10$ ).

quently found in tropical and subtropical regions, especially Madagascar.<sup>1,3</sup> Clinically the lesions of chromoblastomycosis evolve slowly over many years, and although characteristically verrucous, they may have a nodular, papillomatous, plaque-like, cicatricial or ulcerative presentation.<sup>1,4</sup>

Histologically, hyperplasia of the epidermis is seen with multinucleated giant cells and neutrophils seen throughout the dermis.<sup>5</sup> The organisms may be found in the giant cells as well as free in the tissue, and have a dark brown, oval appearance, ranging in size from 6 to 12  $\mu\text{m}$ .<sup>5</sup> They have a thick wall and may appear singly or in chains and clusters, and because of the brown pigmentation, the spores are usually seen without special stains.<sup>5</sup>

Treatment of chromomycosis may be difficult. In the early stages, physical modalities such as surgical excision, curettage, cryotherapy hyperthermia, and laser therapy alone or in combination with systemic therapy have been used with variable results.<sup>1,2,4</sup> Chromomycosis appears to be relatively resistant to systemic amphotericin B.<sup>1</sup> Thiabendazole, flucytosine ketoconazole, and fluconazole have been used also systemically with modest cure rates of less than 50%.<sup>1</sup> Itraconazole with a response rate of about 65%, and terbinafine with a response rate of about 82%, seem to be promising agents.<sup>1,3</sup> *C. carrionii* seem to respond more rapidly than do *F. pedrosoi* to both itraconazole and terbinafine, with significant improvement occurring within few months of therapy.<sup>1,3,4</sup> Dosages for itraconazole range from 200 to 400 mg daily.<sup>1,4</sup> Terbinafine used at doses of 500 mg/day for 6 to 12 months showed a mycologic cure judged by skin scrap-

ings of 82.5% at 12 months of therapy.<sup>3</sup> About 6 to 12 months of therapy seems to be effective to accomplish cure with either agent in most cases, although some cases may require longer treatment.<sup>1,4</sup>

Terbinafine is an allylamine with broad activity against dermatophytes and dimorphic fungi and is primarily fungicidal.<sup>3,6</sup> The terbinafine inhibits ergosterol formation at an earlier stage than the azoles, blocking the step in which squalene is transformed to squalene epoxide, and not involving cytochrome P-450.<sup>6</sup> This results in an intracellular accumulation of squalene that is thought to be fungicidal by disrupting the fungal cell membrane.<sup>6</sup> Terbinafine exhibits low minimal inhibitory concentrations *in vitro* with *F. pedrosoi* and other dematiaceous fungi.<sup>3</sup> Terbinafine therapy seems to be safe, with few serious adverse reactions reported.<sup>7,8</sup> Most side effects are minor, transient, and reversible upon discontinuation of therapy.<sup>8</sup> Since it does not interact with cytochrome P-450, it does not seem to have significant drug-drug interactions.<sup>8</sup>

We treated our patient with a lower dose of terbinafine than previously reported, with an apparent comparative result.

*Acknowledgment* —We would like to thank Joan McTigue, PA and Christine Dortch for their assistance with this case.

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