# Septic Arthritis and Osteomyelitis due to the Chromoblastomycosis Agent *Fonsecaea pedrosoi*

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## Abstract

***Fonsecaea pedrosoi*** **is the most common agent of chromoblastomycosis, a chronic localized fungal infection of the skin and subcutaneous tissues mainly involving the lower extremities. We report a rare case of septic arthritis and osteomyelitis due to the chromoblastomycosis agent *F pedrosoi,* which was successfully treated with arthrotomy and debridement, followed by a long course of oral antifungal therapy. To our knowledge, this is the second case of *F pedrosoi* osteomyelitis treated successfully to be ever reported.**


*Fonsecaea pedrosoi* is the most common agent of chromoblastomycosis, a chronic localized fungal infection of the skin and subcutaneous tissues mainly involving the lower extremities.[1] The agents of chromoblastomycosis belong to the group of dark-walled or dematiaceous fungi found in the soil, particularly in association with cacti, thorny plants, and other live decaying vegetation. The fungus does not generally invade intact skin but instead is usually introduced through trauma. Infection typically develops at the site of introduction and involves the epidermis, dermis, and subcutaneous tissue, causing lesions that range from small papules, to nodules, to warty, cauliflower-like plaques.[2,3] Osseous involvement is rare with few cases reported and thus, data regarding optimal treatment of bone involvement are sparse.[4,5] Here we report a case of septic arthritis and osteomyelitis due to *F pedrosoi* which was successfully treated with surgical debridement, oral antifungals, and subsequent arthrodesis of the first tarsometatarsal joint. The patient provided written informed consent for written and electronic publication of the case report.

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## Case Report

A 50-year-old female presented with a painful pruritic nodule over the right first tarsometatarsal joint. Five years earlier, she had a lesion on the same site that was excised and cultured. Fungal cultures at that time grew *F pedrosoi* and she received oral itraconazole for 1 year.

The current lesion developed 1 year prior to presentation as an erythematous swelling of the skin over the joint and progressed to formation of a pruritic non–painful nodule over 10 months. The lesion continued to progress over 2 months and she also developed pain. The patient denied trauma to the area. There was no fever, night sweats, weight loss, or other joint involvement. She had a history of hypothyroidism, for which she was taking levothyroxine. She denied smoking and illicit drug use. She worked as an academic adviser and had traveled to Mexico 3 times in the previous 25 years.

Examination of the right foot revealed an erythematous tender nodule over the right first tarsometatarsal joint. X-ray of the right foot showed narrowing of the first tarsometatarsal joint with erosion of the articular surfaces with marked periarticular soft tissue edema

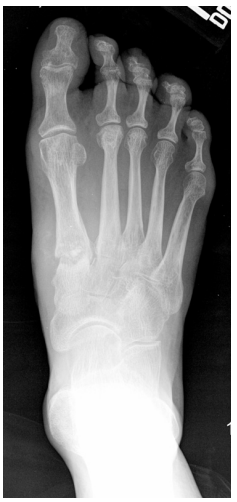

**Figure 1.** X-ray of the right foot showing narrowing of the first tarsometatarsal joint with erosion of the articular surfaces and marked periarticular soft tissue edema.

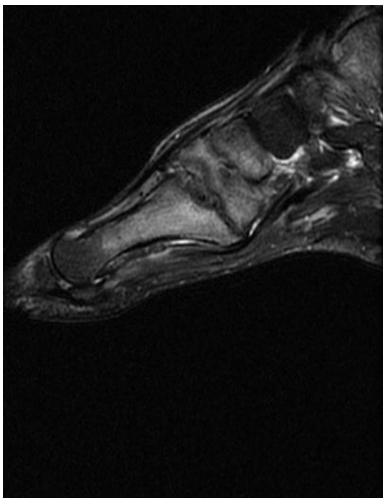

**Figure 2.** Magnetic resonance imaging of the right foot showing erosion of the articular surfaces of the right first tarsometatarsal joint with joint effusion and prominent periarticular bone marrow edema.

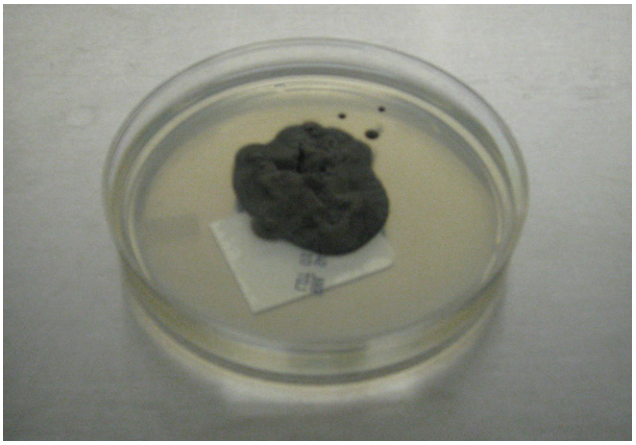

**Figure 3.** Culture on Saboraud dextrose agar showing olive-black velvety colony.

**Figure 4.** Fungal colony stained by lactophenol cotton blue showing branching septate brown hyphae (original magnification x 40).

(Figure 1). Magnetic resonance imaging of the right foot showed erosion of the articular surfaces of the right first tarsometatarsal joint with joint effusion and prominent periarticular bone marrow edema consistent with septic arthritis and periarticular osteomyelitis (Figure 2).

The patient underwent arthrotomy with debridement of the right first tarsometatarsal joint, which showed grossly thickened synovium and areas of bone necrosis. Histopathology revealed fragments of synovium, fibroconnective, and granulation tissue showing abundant embedded bone detritus, chronic inflammation, and focal foreign body type giant cell reaction with adherent fibrinous changes. She was empirically started on itraconazole 100 mg orally twice a day. Staining studies revealed rare neutrophils, no organisms, no acid fast bacilli, and no fungal elements. Bacterial culture of the soft tissues and bone grew *Proteus mirabilis,* for which she was treated with ciprofloxacin. Fungal culture of the soft tissues and bone grew a dark velvety mold (Figure 3) after 3 weeks of incubation, which was later identified as *F pedrosoi* (Figure 4).

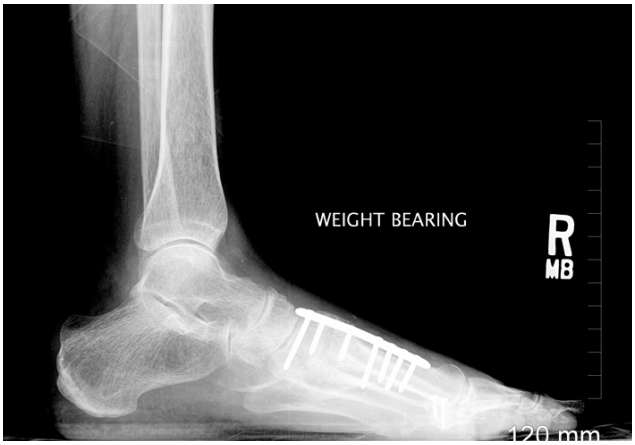


**Figure 5.** X-ray of the right foot showing fixation of the first tarsometatarsal joint with plates and screws along the first metatarsal and medial cuneiform.

The patient continued to take itraconazole for 7 months. An erythrocyte sedimentation rate after 5 months of therapy was 11 mm/hr. A few weeks after she completed 7 months of itraconazole, she underwent right first tarsometatarsal arthrodesis with interpositional tricortical iliac crest bone graft (Figure 5). Repeat cultures from the joint and bones revealed no growth. Pathology showed fragments of partially devitalized bone and cartilage with fibrosis and a Gomori's methenamine silver stain was negative for fungal organisms. The patient went on to uneventful healing of her arthrodesis and was satisfied with her outcome.

## Discussion

The agents of chromoblastomycosis have a worldwide prevalence, but the disease is most common in tropical and subtropical areas of Latin America, the Caribbean, Africa, and Asia, with particular foci in the Amazon region of Brazil, Madagascar, Mexico, the Dominican Republic, Venezuela, India, Japan, and Australia.[1]

Most cases of chromoblastomycosis are due to *Fpedrosoi* (95%).[6] Less common agents include *Phialophora verrucosa, Cladosporium carrionii, Fonsecaea compacta,* and *Rhinocladiella aquaspersa.*[3]

Chromoblastomycosis commonly affects immunocompetent individuals with 5-9:1 male predominance. Infection results from traumatic implantation and most patients have occupational exposure in agricultural or related activities as laborers, lumberjacks, or agricultural product sellers and a consistent feature is their lack of adequate protective footwear and clothing.[7,8] In our case, there was no report of trauma or injury to the foot but she had traveled to Mexico a few times.

Traumatic inoculation of the agents of chromoblastomycosis results in a mixed chronic suppurative and granulomatous host response and foci of neutrophils and microabscesses are seen in both the epidermis and dermis. Granulomas with multinucleated giant cells and epithelioid cells with varying amounts of fibrosis

may be seen. The hallmark of chromoblastomycosis, the muriform cells, or sclerotic bodies, are darkly pigmented, thick-walled, rounded cells, 4-15 µm in diameter with cross-walls in 1 or 2 planes. These may be found intracellularly in macrophages or extracellularly in abscesses.[9]

Chromoblastomycosis is slow to develop. Weeks to months following inoculation of the causative organism, subjects typically develop a small scaly papule at the site of the trauma. These then progress into nodules, plaques, verrucous, or exophytic lesions.[1]

The lesions are seldom painful but pruritus is frequent and can be severe. Pruritus is hypothesized to lead to dissemination by autoinoculation and contiguous spread.[7,9]

Ulceration and discharge have also been reported and can be suggestive of bacterial superinfection, which can occur in up to 63% of patients.[3] Infection is usually confined to the skin and subcutaneous tissues and does not invade underlying muscle or bone except in immunosuppressed patients. Our case is unusual because the patient had no known immunocompromising condition. There is only one other English language case report of *F pedrosoi* osteomyelitis in a 50-year-old male immunocompetent farmer with tibial osteomyelitis.[5] Hematogenous dissemination has rarely been described but does include reports of CNS involvement. As with chronic osteomyelitis due to other pathogens, malignant transformation of chronic chromoblastomycosis lesions into squamous cell carcinoma has also been reported.[1]

The length of time between the appearance of the lesion and diagnosis has ranged from 1 month to 25 years, with an average of 87 months.[2] Lesions have also been reported to persist for up to 24 years.[3] Differential diagnosis includes other cutaneous mycosis such as phaeohyphomycosis, mycetoma, sporotrichosis, blastomycosis, coccidioidomycosis, paracoccidioidomycosis, cutaneous tuberculosis, leishmaniasis, keratoacanthoma, and squamous cell carcinoma. Diagnosis is made by finding the pathognomonic muriform cells on direct microscopy of scrapings from lesions mounted with 10% potassium hydroxide. Cultures are required for species identification but may take 10 or more days for the mold to grow.

The pathogen grows as deep green to black velvety colonies on Sabouraud dextrose agar. Species identification relies on morphological examination of the colonies. Hematoxylin–eosin stained specimens will demonstrate inflammatory infiltrate with multinucleated giant cells, fibrosis, papillomatosis, epithelioid giant cells, and muriform cells may also be seen with this technique.[8]

Comparative clinical trials are lacking for the treatment of chromoblastomycosis.[9]

Treatment is associated with low cure rates and high relapse rates. In addition, there is no standard method to test in vitro susceptibility. Despite being the most common etiological agent, *F pedrosoi* appears to be less susceptible to antifungal therapy than either *P verrucosa* and *C carrionii*.[1] Currently, the best pharmacotherapy from case series appears to be itraconazole or terbinafine, combined with local treatment like cryotherapy, liquid nitrogen, topical heat, photocoagulation, and surgical removal of lesions. Itraconazole (200-400 mg/day) combined with local treatment results in 27% to 91% cure rate.[7,10,11] Pulse therapy with itraconazole 400 mg daily for 7 days a month for 6-12 months has also been shown to be effective in 1 small series.[12] The 1 case of *F pedrosoi* tibial osteomyelitis was successfully treated with debridement and itraconazole 200 mg/day for 12 weeks.[5] The allylamine antifungal terbinafine has been shown to have an 82.5% mycologic cure rate in 1 series. Use of terbinafine has also been reported to be associated with partial reversal of fibrosis.[13]

Posaconazole was effective in treating chromoblastomycosis in a small number of patients with disease refractory to itraconazole and terbinafine.[14] Voriconazole has also been shown to have in vitro activity comparable to that of itraconazole against a number of dematiaceous molds including, *Fonsecaea, Cladophialophora, Exophiala,* and *Bipolaris*.[15] Fluconazole and flucytosine has been used in some series but was associated with incomplete response and relapse.[7] Our case was managed with a combination of surgical debridement and itraconazole, which resulted in apparent clinical and mycologic cure.

## Conclusion

This case report demonstrates the occurrence of *F pedrosoi* osteomyelitis in an immunocompetent patient whose only risk factor was travel to an endemic area.

Chromoblastomycosis rarely involves the bone and data regarding the optimal treatment of osteomyelitis secondary to agents of this disease is lacking. The patient in our case was successfully treated with combination of surgical debridement, tarsometatarsal arthrodesis, and itraconazole, and while further follow-up is needed, to our knowledge, this is the second case of *F pedrosoi* osteomyelitis treated successfully to be ever reported.

## Authors' Disclosure Statement & Acknowledgements

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