

# Disseminated Paracoccidioidomycosis with Osteoarticular and Miliary Pulmonary Involvement: A Case Report

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**Abstract:** Paracoccidioidomycosis (PCM) is a systemic fungal infection endemic in Latin America, primarily affecting the lungs and mucocutaneous tissues. Osteoarticular involvement is uncommon and may mimic bacterial or mycobacterial diseases. We describe a disseminated PCM case in an immunocompetent 37-year-old woman presenting with ankle monoarthritis and diffuse miliary pulmonary infiltrates. Histopathology confirmed multiple-budding yeast forms of *Paracoccidioides* spp., while cultures and serological tests were negative. The patient was treated with liposomal amphotericin B followed by oral itraconazole, achieving complete clinical and radiological recovery. PCM should be considered in endemic regions when musculoskeletal lesions coexist with pulmonary findings, even in immunocompetent hosts.

**Keywords:** Paracoccidioidomycosis; Osteoarticular Involvement; Miliary Pattern; Case Report; Fungal Infection.

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## 1. Introduction

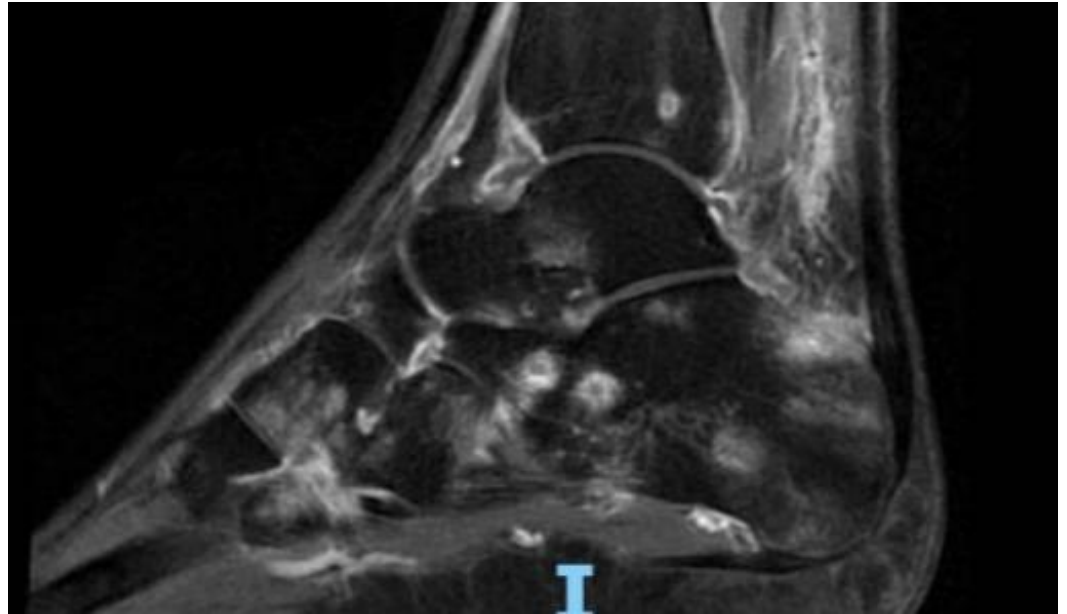
Paracoccidioidomycosis (PCM) is a systemic mycosis caused by thermally dimorphic fungi of the genus *Paracoccidioides*, remaining a major endemic infection in South America, especially in Brazil [1]. The disease predominantly affects adult males in agricultural environments, with pulmonary and mucocutaneous forms being the most frequent presentations [1]. Osteoarticular involvement is uncommon and typically results from hematogenous dissemination, often mimicking chronic bacterial osteomyelitis or tuberculosis and contributing to diagnostic delays [2–3]. We report a rare case of disseminated PCM presenting as ankle monoarthritis associated with miliary pulmonary disease in an immunocompetent woman.

## 2. Case Report

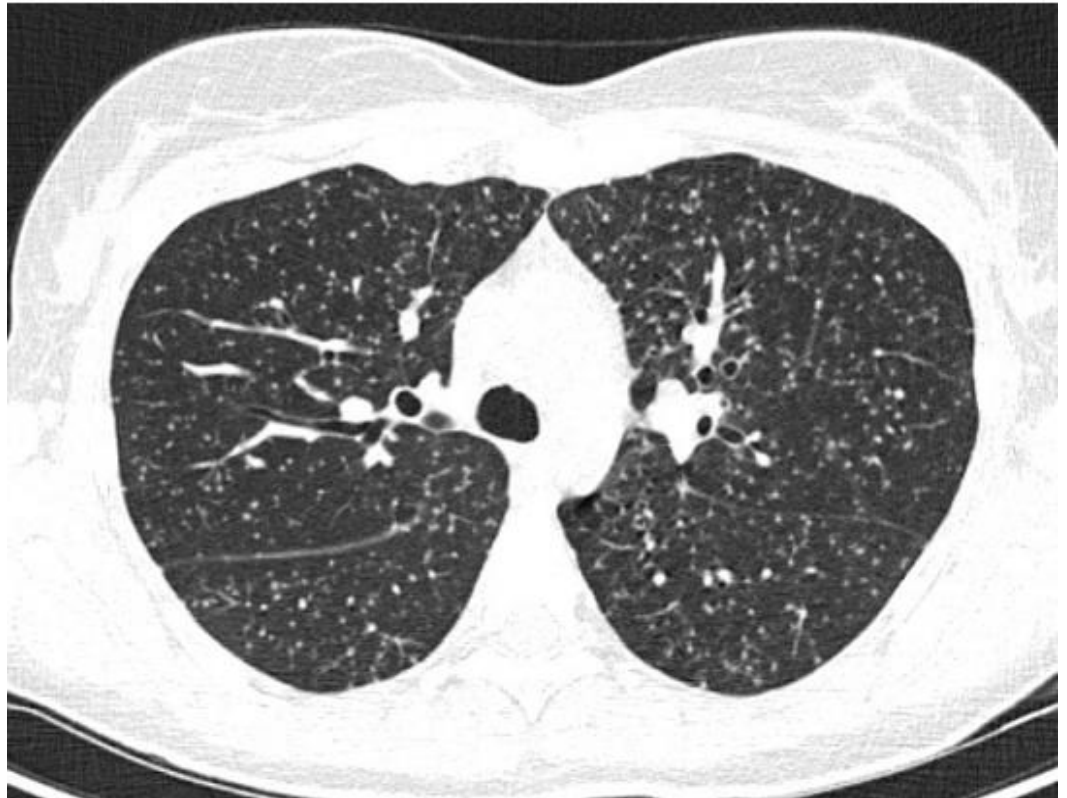
A 37-year-old woman with no prior comorbidities presented with a two-month history of progressive pain, swelling, and limited motion of the right ankle, accompanied by intermittent fever. She denied recent travel or tuberculosis exposure. Initial management with intra-articular corticosteroid injection and empirical antibiotics (ceftriaxone and clindamycin) produced transient improvement. Magnetic resonance imaging (MRI) of the ankle revealed multiple osseous signal alterations with ring enhancement and complex abscess, suggesting a granulomatous or fungal etiology (Figure 1). The patient's condition deteriorated despite broad-spectrum antibiotics. High-resolution computed tomography (HRCT) of the chest demonstrated diffuse micronodular infiltrates with a miliary pattern (Figure 2). Extensive testing, including HIV serology, interferon-gamma release assay,

bronchoalveolar lavage, and PCR for *Mycobacterium tuberculosis*, were all negative. Serology for *Paracoccidioides* antigen was non-reactive.

**Figure 1.** Ankle MRI showing multiple osseous signal alterations with ring enhancement and a complex abscess compatible with granulomatous infection.



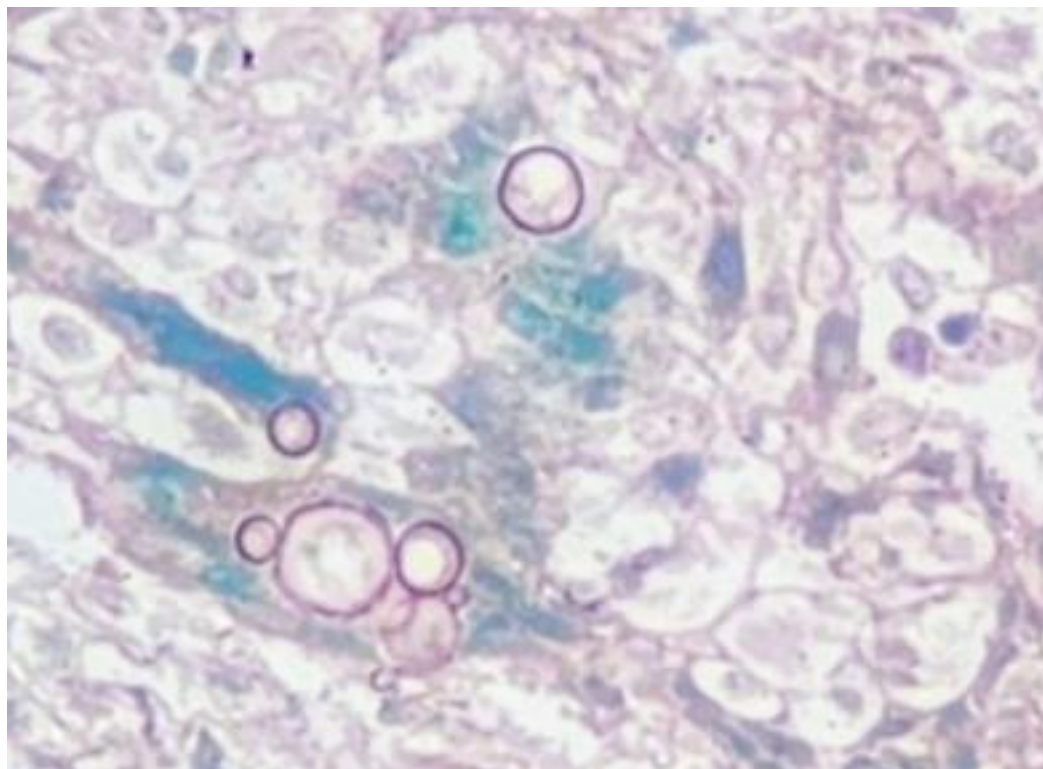
**Figure 2.** High-resolution chest CT demonstrates diffuse micronodular (miliary-like) pattern in both lungs.



A bone biopsy of the distal tibia revealed granulomatous inflammation with multiple-budding yeast forms typical of *Paracoccidioides* spp. (Figure 3). Grocott methenamine

silver stain confirmed the fungal morphology. Cultures were negative. The patient received liposomal amphotericin B at 3–5 mg/kg/day for three weeks, followed by itraconazole 200 mg/day for 12 months. Clinical symptoms were resolved, and follow-up imaging showed complete regression of pulmonary lesions.

**Figure 3.** Bone biopsy with Grocott stain showing multiple-budding yeast forms characteristic of *Paracoccidioides* spp.



### 3. Discussion

This case illustrates several atypical aspects of paracoccidioidomycosis (PCM) that merit deeper consideration. First, the patient was a 37-year-old immunocompetent woman. PCM classically affects adult males with rural or agricultural exposure, a pattern largely attributed to the protective effect of estrogen, which inhibits the mycelium-to-yeast transformation of *Paracoccidioides* spp. [1]. Although uncommon, disseminated PCM in women has been increasingly reported in Brazilian series and case reports, suggesting that hormonal protection is incomplete and may be overcome by factors such as high inoculum exposure, individual immune response variability, or infection with more virulent species within the *Paracoccidioides* complex [1,5].

From a diagnostic standpoint, the initial differential diagnoses included bacterial osteomyelitis, septic arthritis, and osteoarticular tuberculosis, which are well-known mimickers of osteoarticular PCM [2–4]. The chronic course, partial response to antibiotics, and subsequent imaging findings raised suspicion for a granulomatous process. The decision to proceed with bone biopsy, despite non-reactive serology, was driven by progressive clinical deterioration and the presence of destructive osseous lesions with abscess formation, reinforcing that histopathology remains essential when non-invasive tests are inconclusive [1,2].

The negative *Paracoccidioides* serology in this disseminated presentation deserves particular emphasis. Although disseminated disease is often associated with higher antibody titers, serological assays may yield false-negative results due to technical limitations, antigenic variability among *Paracoccidioides* species, and differences in host immune re-

sponse, particularly a predominance of cell-mediated immunity [1,5,6]. False-negative serology has also been described in extrapulmonary and osteoarticular forms of PCM [2,7]. In addition to HIV testing, no evidence of secondary immunodeficiency was identified in this patient. Prior corticosteroid exposure, even when locally administered, may further contribute to reduced antibody detection. These factors help explain the apparent discordance between disease extent and serological findings and highlight that negative serology does not exclude PCM.

Imaging played a pivotal role in raising suspicion for a fungal etiology. On MRI, the presence of multifocal bone involvement, ring-enhancing lesions, and associated soft-tissue abscess favored a granulomatous or fungal infection rather than typical bacterial osteomyelitis, which more commonly presents with diffuse marrow edema and poorly defined abscess walls [2,3]. Tuberculous osteomyelitis may show overlapping features; however, the multiplicity of lesions and lack of predominant synovial involvement supported an alternative diagnosis [2–4]. In the lungs, HRCT demonstrated a diffuse micronodular (miliary-like) pattern closely resembling miliary tuberculosis. Although this pattern is less common in PCM than classic pulmonary forms, it has been described in disseminated disease [4,6]. Subtle features such as random nodule distribution, absence of a tree-in-bud pattern, cavitation, or necrotic lymphadenopathy may aid differentiation, although significant overlap remains, making histopathological confirmation indispensable.

Regarding treatment, the patient met criteria for severe disseminated PCM according to Brazilian guidelines, based on multi-organ involvement (osteoarticular and pulmonary) and systemic symptoms [1]. The choice of liposomal amphotericin B was justified by the combination of miliary pulmonary disease and bone involvement, both associated with higher fungal burden and increased risk of complications [1,6]. Liposomal formulations are preferred in severe cases due to their improved safety profile, particularly reduced nephrotoxicity. Step-down therapy with itraconazole for 12 months aligns with current recommendations and resulted in complete clinical and radiological resolution [1].

Finally, although the patient achieved full recovery, osteoarticular PCM carries a risk of long-term sequelae, including chronic pain, joint stiffness, and structural deformities secondary to bone destruction, even after adequate antifungal therapy [2,7]. Early recognition and prompt treatment are therefore essential to prevent irreversible musculoskeletal damage. Overall, this case highlights the need for heightened clinical suspicion of PCM in endemic areas, even in immunocompetent women, and underscores the central role of histopathology when serology and cultures are negative [1,5].

#### 4. Conclusion

Disseminated PCM can present osteoarticular and pulmonary involvement in immunocompetent individuals. Clinicians in endemic areas should maintain a high index of clinical suspicion, particularly when conventional diagnostic tests are inconclusive. Early diagnosis and adherence to guideline-based antifungal treatment are essential for favorable outcomes.

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**Conflicts of Interest:** All other authors declare no conflicts of interest.

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