

Paracoccidioidomycotic Prostatitis: Two Case Reports and Literature Review

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ABSTRACT

Paracoccidioidomycosis (PCM) is considered endemic in various Latin American countries, with the highest incidence reported in humid tropical and subtropical regions. A few cases of PCM are reported in the non-endemic region. The authors report two cases of PCM prostatitis, which is considered a rare form of this entity presentation, with only a few cases reported globally. In the first case, a 57-year-old patient was incidentally diagnosed with PCM prostatitis by post-radical-

prostatectomy examination of a piece of a surgically removed tissue. In another case, a 52-year-old patient was diagnosed with PCM prostatitis, who was initially thought to have benign prostatic hyperplasia. A review of the medical literature indicates that a histopathological examination can confirm the diagnosis of PCM prostatitis and may be employed in symptomatic cases to avoid surgical intervention and associated adverse effects.

Keywords: Prostatitis; Paracoccidioidomycosis; Paracoccidioidesbrasiliensis; Paracoccidioideslutzii; Benign Prostatic Hyperplasia; Prostate Adenocarcinoma

INTRODUCTION

Paracoccidioidomycosis (PCM), also known as South American blastomycosis or Lutz-Spledore-Almeida mycosis, is a granulomatous fungal infection caused by *Paracoccidioidesbrasiliensis* and *P. lutzii* [1-4]. *P. brasiliensis* is a thermally dimorphic fungus, that is, it can occur in two morphologies depending on the temperature and other environmental conditions [4]. PCM infection is usually acquired by inhalation of the conidia or mycelium fragments of the fungus commonly present in the soil. The parasite can eventually affect any organ in the body through the lymphatic or hematogenous spread. However, a long latency period is generally observed between pathogen exposure and the appearance of clinical manifestation [1-4]. PCM usually affects the skin, mucous membranes, lymph nodes, reticuloendothelial system, bones, and viscera (lungs, and less frequently gastrointestinal tract, genitourinary tracts, and central nervous system) [2,4,5]. Most incidences are reported in male-farmers age between 20 and 59 years with some cases reported in children and young adults (about 5% to 10% of all cases)

[2,3,5]. The disease is considered endemic in Latin American countries, such as Brazil, Venezuela, Colombia, Ecuador, and Argentina, with the highest incidence reported in humid tropical and subtropical regions. Only a few cases of PCM are reported in the non-endemic regions [4,5]. Almost all reported cases outside of the endemic region are believed to be traveler's disease, that is, past visit(s) to the endemic location is reported in nearly all cases [4,5]. The purpose of this case report is to present a primary atypical manifestation of prostatic paracoccidioidomycosis, thus, alerting urologists and clinicians.

CASE REPORT

Case 1: A 57-year-old male presented to the urology clinic for evaluation of a prostatic nodule. His primary care physician detected the nodule and ordered a serum prostate-specific antigen (PSA) test. Physical examination did not reveal any other significant finding other than obesity. External sex organs were normal. A digital rectal examination revealed a prostate with an estimated mass of 40 grams and a firm,

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non-tender nodule at the right lateral apex. His PSA level was elevated at 8 ng/mL. Analysis of biopsy specimens obtained through ultrasonography-guided needle biopsy technique showed adenocarcinoma in the right lobe of the prostate with a Gleason score of 6 (3+3). Radical prostatectomy was performed and the specimen obtained from the procedure showed adenocarcinoma along with paracoccidioidomycosis (Figure 1).

Case 2: A 52-year-old white male, who was admitted to the Coronel Mota Hospital, was having difficulty in urination for about 3 months, incomplete emptying of the bladder, pollakiuria, nocturia, urinary urgency, urinary jet, and intermittent jet. He did not report dysuria or hematuria. In the antecedents, he denied alcoholism, smoking, diabetes, systemic arterial hypertension, or sexually transmitted diseases. He did not report any other clinical condition except for two previous hydrocele surgeries (30 years ago) and a left knee surgery (23 years ago). On physical examination, he was in good general condition, hydrated, and afebrile. His blood pressure was 110/80 mmHg, pulse 88bpm, and cardio-respiratory examination was normal. His urological examinations revealed a fibro-elastic, regular prostate with an estimated mass of 50 grams. International Prostate Symptoms Score (IPSS) was 15 and ultrasound showed a prostate volume of 42g. The urofluxometry was 9ml/second. Adenomatous changes were observed in the prostate without nodules. His PSA level was 3 ng/mL. Other laboratory tests, such as hemogram, glycemia, electrolytes, urea, and creatinine were normal. Radiological examination of the chest and abdomen did not reveal any abnormality. The diagnostic hypothesis derived from the above findings was benign prostatic hyperplasia with severe lower urinary tract symptoms and incomplete voiding. Thus, transurethral resection of the prostate was employed. The pathological examination of the specimen revealed a chronic granulomatous PCM prostatitis (Figure 2).

DISCUSSION

Fungal infection of the prostate is rare and mostly observed in immune-compromised patients. Common fungal species affecting prostate include *Candida albicans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Aspergillus* sp., and *Cryptococcus neoformans* [1,2]. Prostate infection with *P. brasiliensis* is

uncommon and mostly results from hematogenic dissemination of the fungus [2]. PCM infection is usually a disseminated disease that may cause concomitant manifestations in multiple organs or can elicit symptoms in a specific location [4]. According to an estimate, the incidence rate of prostate involvement is 2.7% to 9% in all reported cases of disseminated PCM infection [2]. The penis, testicles, epididymis, urethra, ureters, and kidneys are the most commonly affected sites in the urogenital tract [1,2].

Two main clinical presentations have been reported for PCM-acute or subacute (juvenile) form that usually affects children and young adults and chronic unifocal or multifocal (adult) form that usually affect adults and older population (especially males) [3,4]. The juvenile form is generally present as a moderate to severe disseminated acute disease that usually involves the reticuloendothelial system. Conversely, the common adult form is generally present as a mild, moderate, or severe chronic disease that is believed to result from fungal reactivation [4].

PCM is generally diagnosed when the disease has progressed due to an early asymptomatic presentation or associated symptoms are presented by certain other disorders [1,6,7]. Common signs and symptoms of the disseminated disease include lymph node enlargement, hepatomegaly or splenomegaly, diarrhea, vomiting, abdominal pain, ascites, pulmonary manifestations (consolidations, infiltrates, or pleural effusion), and lesions in joints, bones, or skin [4,7]. Increased erythrocyte sedimentation rate, anemia, hypoalbuminemia, and high serum levels of IgA, IgG, and IgE antibodies are common laboratory findings with the magnitude of abnormality depending on the disease severity [4]. The typical clinical manifestations of PCM prostatitis include symptoms that arise due to vesical irritation and/or intravesical obstruction [1]. In line with our experience, physical examinations usually show irregular prostate enlargement or fluctuation that depends upon various factors like chronic inflammation, abscesses formation, necrosis, and fibrosis. The formation of the granuloma is a defense mechanism that prevents parasitic dissemination. This response is also observed in the case of other fungal infections [1,6]. The PCM should be differentiated from conditions that may mimic its clinical manifestations, for example, adenocarcinomas or benign hyperplasia, allergic disorders, viruses, other fungal species, and certain common bacterial infections (caused by *Mycobacterium*

Figure 1: Granulomatous inflammation, characterized by collections of epithelioid macrophages and multinucleated giant cells (colored by PAS)

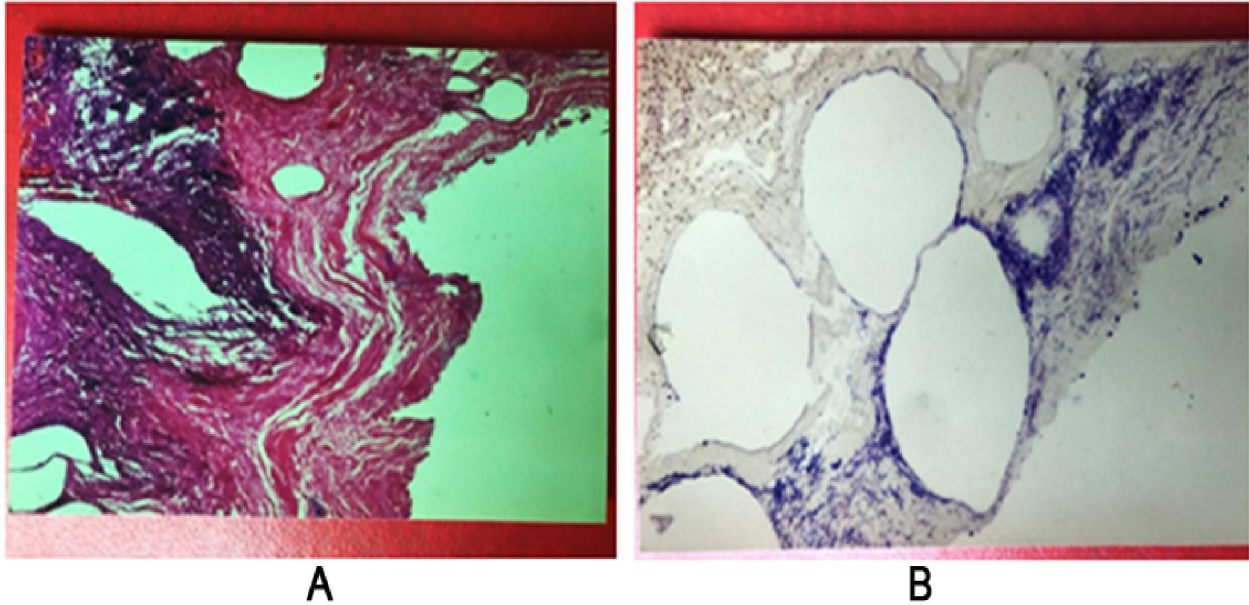
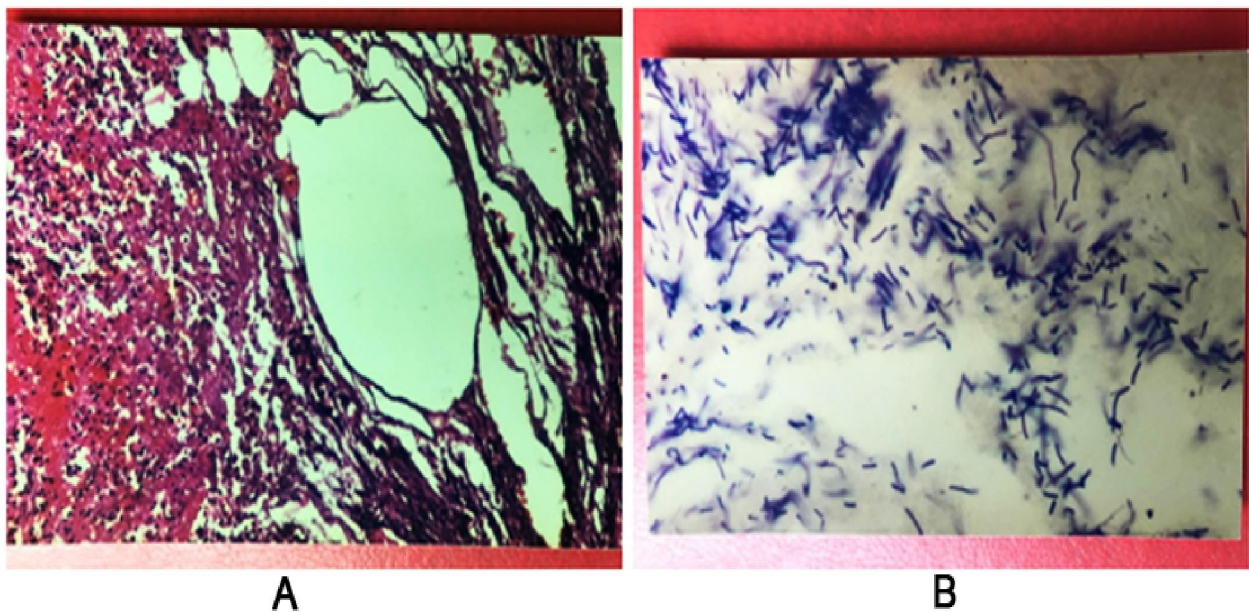


Figure 2: *Paracoccidioides brasiliensis* surrounded by multinucleated cells (colored by PAS)



tuberculosis, *Treponema pallidum*, *Brucella* sp.) [1].

The skin reactivity test for *P. brasiliensis* antigen generally indicates an asymptomatic infection and cannot establish the diagnosis of active PCM [4]. The gold standard for establishing the diagnosis of PCM is the identification of the *P. brasiliensis* through culture and/or microscopic examination of the biological sample (secretion, mucous, biopsy). *P. brasiliensis* has unique morphological characteristics like typical multiple budding yeast cells of different sizes (2-40 µm), bi-refringent cell wall, and multiple-sprouting blastospores attached to the cell wall [1,3,4]. However, this technique is time-consuming and results are available after a few weeks [4]. Certain specific staining (e.g, Grocott silver methenamine) may help in the diagnosis of PCM in case granulomas are observed in the biological sample [6,4]. Detection of extracellular antigens or PCM specific membrane protein (e. g. MEXO, Pb28, Pbgp43) via enzyme-linked immunosorbent assays (ELISA) technique provides fast and reliable results in symptomatic patients [1,4]. PCR and immunohistochemistry are other useful advanced techniques that have shown promising results in the diagnosis of *P. brasiliensis* in both symptomatic and asymptomatic patients irrespective of fungal burden [4].

Once the diagnosis is made, systemic treatment of the condition is indicated, which consists of two phases: induction and maintenance. Treatment compliance is the key to successful disease remission, as poor treatment compliance may lead to drug-resistance [3]. The induction phase usually includes anti-fungal agents with higher efficacy that help in controlling fungal growth, alleviate disease symptoms, and bring the laboratory parameters in the normal range. The maintenance phase usually includes drugs that prevent disease recurrence [3]. A combination of sulfamethoxazole and trimethoprim (cotrimoxazole) has been reported effective in the treatment of non-life-threatening PCM infections [3,4]. Itraconazole is the first choice of agent (among other azoles, ketoconazole, fluconazole, and voriconazole) due to its superior efficacy at a relatively lower dosage and favorable safety profile [3,4]. Amphotericin B, an excellent fungistatic and fungicidal agent, is recommended for the management of severe cases due to its higher toxicity [3,4].

CONCLUSION

These cases were reported because of two reasons; first, due to the rarity of this prostatic lesion and second, due to the possibility of diagnostic confusion with prostate cancer or benign prostatic hyperplasia. In the first case reported, the preoperative diagnosis was adenocarcinoma through needle biopsy, and radical prostatectomy was indicated for the same. In the second case, the clinical diagnosis was benign prostatic hyperplasia, based on the clinical presentation and urological examinations, and the recommendation was the transurethral resection of the prostate.

Clinical manifestations alone cannot indicate paracoccidioidomycosis infection. However, histopathological diagnosis can confirm the diagnosis of infectious prostatitis and should be employed in suspected cases to avoid surgical intervention and start an appropriate anti-infective treatment in-time.

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