Case Report
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A Brazilian male with typical oral and pulmonary paracoccidioidomycosis

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Abstract

An autochthonous case of paracoccidioidomycosis was reported in a city of north Iran. This condition is a well-known endemic fungal infection highly prevalent in Latin American countries, with an incidence of 1 to 3.7 cases per 100.000 annually in Brazil. The classical features are cutaneous lesions, lymph node, and pulmonary involvements, while typical oral changes are superficial ulcers with hemorrhage and moriform aspect. Herein is reported an adult male patient with characteristic oral and pulmonary lesions. Rural environment, male gender, cigarette smoking, and alcohol abuse were risk factors; and clinical history, imaging studies, and histopathologic data established the diagnosis. The patient improved well by administration of sulfamethoxazole plus trimethoprim. The aim of this case study is to enhance the awareness of generalists about this mycosis.

Keywords: Diagnosis, Oral lesions, Paracoccidioidomycosis, Pulmonary images

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Introduction

Paracoccidioidomycosis (PMC) is a major fungal endemic disease in Latin America due to *Paracoccidioides brasiliensis*, without compulsory notification (1-7). PMC was previously called South American blastomycosis as well as Lutz's disease. The first description was in Brazil by Adolpho Lutz in 1908; it is more prevalent among males from rural areas, and the annual incidence is up to 3.7 cases per 100.000 (1-7). More often, the infective

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↑What is "already known" in this topic:
Paracoccidioidomycosis (PMC) is a severe fungal endemic disease in Latin America due to *Paracoccidioides brasiliensis*, without compulsory notification. The prevalence is higher in rural areas. The annual incidence is up to 3.7 cases per 100.000. Usually, the infective forms of the fungi reach the small airways, causing primary pulmonary foci, which can disseminate by lymphatic and hematogenous routes. Males are more often affected (up to 30:1), mainly the smokers and alcohol abusers. Diabetes mellitus, malignancies, and immunosuppression are also considered predisposing factors. Diagnostic challenges have been frequently reported in primary care attention (1-7).

→What this article adds:
PCM is not a disease of compulsory notification in endemic countries yet. The possibility of imported or autochthonous cases should be included as diagnostic hypothesis in patients migrating from, or with previous work or tourist travels to the endemic areas. The aim of this article is to enhance the suspicion index of primary health care physicians about the typical features of this tropical mycosis.

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forms of the fungi reach the small airways, causing primary pulmonary foci and can disseminate by lymphatic and hematogenous routes (1-7). Males are more often affected (up to 30:1), mainly the smokers and alcohol abusers; other risk factor s may be diabetes mellitus, malignancies, and immunosuppression (1-7). The classical features are cutaneous lesions, lymph node, and pulmonary involvements; and the oral lesions are superficial ulcers with hemorrhage and moriform aspect (1, 4-7). Eyes, genital mucosa, bones and joints, and central nervous system are affected (1, 4-7). In addition to other mycosis, the diagnostic challenges about PMC include tuberculosis, mycobacteriosis, leishmaniosis, sarcoidosis, lymphoma, and carcinoma (1, 4-7).

Population migrations and work and tourist travels to endemic areas of PMC are increasing with globalization. The imported cases of Austria, Germany, Japan, Spain, Bulgaria, France, the United States, Russia, Switzerland, Belgium, and The Netherlands, are related to these factors (6). Moreover, an autochthonous case of PCM has been reported in a city of north Iran (4). The long latency of PCM makes mandatory a meticulous history, including recent and past travel or residence in endemic areas (6, 7).

Case report

A 48-year-old male smoker and alcohol abuser for 35 years worked for most of his life in rural activities and had a habit of chewing vegetables while working. He sought hospital medical care with a complaint of dry cough and dyspnea. Three months before admission, he started with insidious and progressive nonproductive cough, concomitant with oropharyngeal pain, and intermittent hoarseness. Previously, he was attended in an ambulatory and medicated with amoxicillin and ibuprofen, without improvement of the symptoms. He evolved with weight loss (6 kg in three months), odynophagia, and cough episodes, with progressive dyspnea even during small efforts.

On physical examination, he was eupneic, non-febrile, non-cyanotic, anicteric, and hydrated, without any alterations in cervical, submandibular, supraclavicular and infraclavicular lymph nodes. Two lesions were observed without bleeding on the hard palate with moriform appearance and poorly defined borders, which were submitted to biopsy (Fig. 1 A). Cardiovascular examination revealed no abnormalities; in respiratory evaluation, the vesicular murmur was bilaterally decreased, with inspiratory crackles, the respiratory rate was 16 rpm and SatO2 60% in ambient air; the abdomen was unremarkable; the extremities showed digital clubbing and cyanosis, without edema.

The investigation for acid-fast bacilli was negative in three sputum samples. Chest x-rays (Fig. 2) showed bilateral, symmetrical perihilar pulmonary infiltrates. Chest tomography with contrast (Fig. 3 A) revealed marked thickening of interlobular septa and numerous bronchiectasis in the lung parenchyma bilaterally; besides interstitial infiltrates with bilateral reticular predominance. Analysis of hemogram showed erythrocytes: 4.790.000 million/mm^3, hemoglobin: 12.7 g/dl, hematocrit: 40.6%, leukocytes: 23.630/mm3 with band forms: 15% and gran-

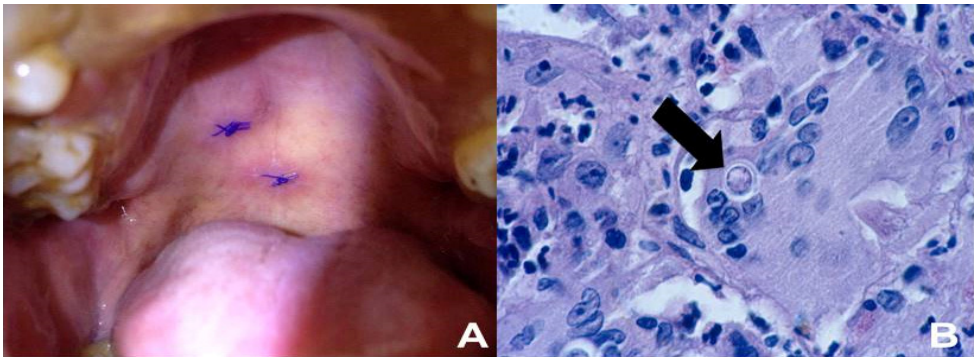

Fig. 1. A: The hard palate with moriform changes where the biopsies were done; and B: Histological findings of oral biopsy sample stained by PAS revealing pseudoepitheliomatous hyperplasia; mononuclear and polymorphonuclear infiltrates in the lamina propria; granulomatous inflammatory reaction; and ovoid yeast (arrow).

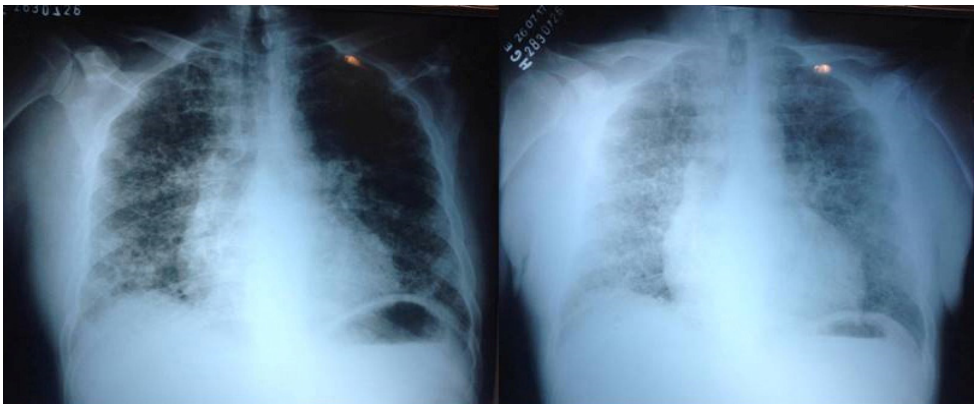

Fig. 2. Chest radiographs showing bilateral and symmetrical pulmonary infiltrates with perihilar predominance that is consistent with the “butterfly-wings” pattern.

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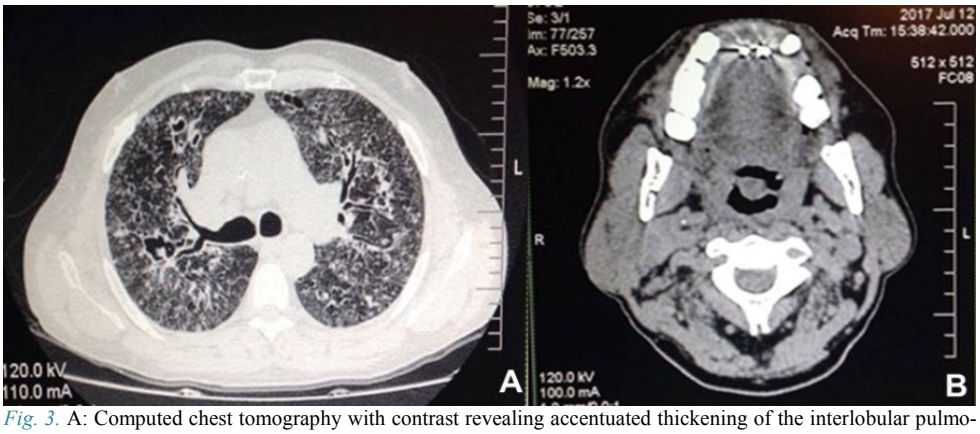

Fig. 3. A: Computed chest tomography with contrast revealing accentuated thickening of the interlobular pulmonary septa, associated with scattered bilateral bronchiectasis, in addition to bilateral interstitial infiltrates with reticular pattern predominance; and B: Computed cervical tomography showing the image of the lesion with irregular borders located in the right nasopharyngeal and oropharyngeal regions.

ulations in neutrophils.

Considering the presence of moriform lesions in the oral cavity, the cervical tomography was performed for investigation and a vegetative lesion, with irregular borders was detected in the right nasopharynx and oropharynx regions (Fig. 3 B). With the evidence shown in imaging studies, plus the data of clinical history, the main hypothesis was paracoccidioidomycosis. This diagnosis was confirmed based on the histopathological data of samples from the oral lesions at the hard palate (Fig. 1 B).

Treatment with hydrocortisone (200 mg IV thrice daily) and sulfamethoxazole plus trimethoprim (400/80 mg twice daily) for a period of 18 months was initiated. After the first month of treatment there was a significant clinical improvement, without dyspnea, with reduction of cough, and SatO2 of 92% in ambient air. He was discharged for the outpatient clinic, with corticosteroid withdrawal, using sulfamethoxazole and trimethoprim (400/80 mg twice daily) until the expected treatment period had expired.

Discussion

The 72-year-old Iranian mechanic man was not a smoker or alcohol addict (4), and lived in a region with environmental and climate characteristics diverse from the Latin American countries. The middle-aged male patient of this case study was a smoker and an alcoholic, and worked for a long time in agricultural activities in a hot and humid Brazilian region. These are risk factors described in patients with PCM; and he had moriform oral lesions and pulmonary images like butterfly-wings (1-3, 5-7). However, considering other clinical hypotheses, the initial concerns included benign and malignant conditions. Therefore, biopsy study of oral lesions was performed, the diagnosis of PMC was established in a short time, and he underwent prompt treatment.

Many factors play a role in the manifestations of PCM, like virulence of the agent, female hormones, nutrition, genetic, age, and immune status of the host (1-4,6,7). Only 2% of about 10 million people infected worldwide will have active PCM (1, 2). The mycelial forms of the fungus as found in nature can easily invade the human cells (1,4); however, the yeast forms of the agent do not pass through the cell walls and this phenomenon may explain the very rare transmission of PCM between humans (1).

The clinical forms of PCM are: 1) acute/ subacute (juvenile) affecting lymph nodes, spleen and liver; and 2) chronic (90% of the cases) predominant in adults with resistance to fungal dissemination for long time, more often with oral lesions (2, 3, 5-7).

Infection of the lower airways and primary complex are the hallmarks of PCM, followed by lymphatic and hematogenous dissemination of the fungi to other sites (1-7). Typical oral ulcers are superficial, usually affecting the gums and palate, with moriform aspect and hemorrhagic dots; bone lesions and tooth loss may also occur (1-7). Cutaneous lesions do not have a typical aspect and may be due to hematogenous dissemination, contamination by fistulas, or rare direct accidental inoculation (1, 2, 5, 6). Lymph node involvement with or without inflammatory signs and spontaneous drainage of suppurative material more often occurs in people under 30 years of age (1, 2, 5-7). Bone and joints involvement by PCM are unusual (6-20%), and meningoencephalitis also; while local granulomas can mimic tumors of central nervous system (1, 3, 5, 7).

PCM is a granulomatous disease, and the usual histopathological features are pseudoepitheliomatous hyperplasia, giant multinucleated cells and macrophages, with the presence of the fungi-free or inside the giant cells. These agents are visualized with details by hematoxylin-eosin, PAS, or Gomori-Grocott stains (1, 5-7); and yeasts with buds may have classical aspects of Mickey Mouse ears or boat steering wheels (1). Immunofluorescence, immunoelectrophoresis, immunodiffusion, immunoblotting, and PCR analysis are useful complementary resources to identify *P. brasiliensis* (1, 2, 5). Images of chest X-rays and of computed tomography may be indicative of thoracic patterns often described in PCM, including nodules with or without cavitations in the middle as well as in the peripheral and posterior lung fields, focal ground-glass opacity surrounded by a ring of consolidation (reversed halo sign), disseminated micronodules (miliary), airspace consolidation or pneumonic form, and the cavitary form (4, 5, 7).

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The treatment options depend upon the individual characteristics of patients and the severity of PCM. Itraconazole (200 mg daily for 6-18 months) or sulfamethoxazole (2400 mg daily) plus trimethoprim (480 mg daily) for 12-24 months in moderate cases; and amphotericin B (0.75 mg/kg daily IV) for the more severe cases (1, 4-7). Recurrences frequently occur, and the immunosuppressed patients have mortality rates up to 30% (1, 2). Some authors believe that PCM should be included among the opportunistic infections in HIV+ patients of the endemic regions (1-3, 5).

Imported cases are reported in people who had been in endemic regions of PCM; manifestations may appear up to 60 years later, and in a mean time of 14 years (1-3). Differing from scenarios of the endemic areas of PCM, the occurrence of autochthonous or imported infections may propitiate diagnostic challenges and misdiagnoses (5). In this setting, imported PCM in a 69-year-old Belgian man was mistaken for c-ANCA positive granulomatous vasculitis, and the consequence of corticosteroids was harmful. PCM was successfully controlled by itraconazole, and c-ANCA became negative.

Conclusion

PCM should become a disease of compulsory notification in endemic countries. The hypotheses of imported or autochthonous cases of PCM must be considered in the differential diagnosis of patients migrating from, or with antecedent of work or tourist travels to some endemic region. Therefore, primary health care physicians all over the world should get basic knowledge about the classical features of this tropical mycosis. The authors believe that case reports enhance the suspicion index about rare conditions.

Conflict of Interests

The authors declare that they have no competing interests.

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