BRIEF COMMUNICATIONS

Paracoccidioidomycosis in a Spanish Missionary

Germán Ramírez-Olivencia, PhD,∗ Oriana Ramírez-Rubio, MD,† Pablo Rivas González, PhD,∗ María Dolores Herrero, PhD,∗ and Sabino Puente Puente, MD∗

∗Tropical Medicine Unit, Hospital Carlos III, Madrid, Spain; †Service of Preventive Medicine, Hospital La Paz, Madrid, Spain

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Paracoccidioidomycosis is the most important systemic mycosis in South America. In Europe the disease is very rare and only found in returning travelers. Here we report on a 56-year-old Spanish missionary with respiratory symptoms but no other affected systems. Diagnosis was made based on serology and PCR for Paracoccidioides brasiliensis.

Case Report

A 56-year-old male, born in Spain, presented to our Tropical Medicine Unit in January 2007. He lived in Venezuela (Maracaibo and Caracas) from November 1996 to July 2006. His past medical history included an episode of pneumonia when he was 25 years old and a bilateral inguinal hernia repair in 1996. Since June 2006 he presented with progressive dyspnea, initially with physical activity and then at rest, a cough productive of brown–yellow sputum, occasionally hemoptysis, and fever. The fever was high (39°C) and intermittent with episodes lasting 3 days occurring at 15-day intervals. Other symptoms included night sweats, loss of appetite, and weight loss.

On physical examination the patient appeared pale. He was tachypnoeic, and pulmonary auscultation revealed scattered rhonchi with some expiratory wheeze. Oxygen saturation was 89% on air. Blood tests showed leukocytosis (15,800 cells/μL), trombocythaemia (442,000/μL), elevated serum IgE (498 UI/mL), and a high erythrocyte sedimentation rate (ESR; 43 mm/h). Other hematological and biochemical parameters were normal. Urinalysis was unremarkable. The initial chest X-ray and computed tomography scan findings showed diffuse infiltrates and nodular lesions, some of them cavitates (Figure 1). Both the ECG and the echocardiogram were normal. An abdominal ultrasound revealed no adenopathies. No intestinal parasites were found in the stool test.

A bronchoscopy with bronchoalveolar aspiration and lavage was carried out. Gram stain, microscopy, and culture of the aspirate were all negative. Bacterial, fungal, and mycobacterium cultures were also negative after 6 weeks. Bronchoscopy was repeated and a transbronchial lung biopsy was performed, revealing acute inflammatory interstitial pulmonary infiltrates. Serologies for Influenza A and B virus, adenovirus, respiratory syncytial virus (RSV), Mycoplasma pneumoniae, Coxiella, Chlamydia, Blastomyces dermatitidis, Coccidioides immitis.

Figure 1 CT scan showing diffuse infiltrates and nodular lesions, some of them cavitates.

Corresponding Author: Germán Ramírez-Olivencia, MD, Hospital Carlos III, Calle Sinesio Delgado 10, E-28029 Madrid, Spain. E-mail: germanro.76@gmail.com
and *Histoplasma capsulatum* were all negative. Other serologies including HIV, HCV, HBV, Dengue, Chagas, syphilis, and *Legionella* were also negative. Serology and a molecular diagnostic technique based on real-time PCR in sputum for *Paracoccidioides brasiliensis* were performed. Briefly, a molecular beacon probe was used, labeled with FAM and directed at the ITS1 region of ribosomal DNA. The detection limit of the technique developed was 1 fg of fungal DNA per microliter of sample. Serology and real-time PCR were both positive.

As a result of this positive finding on PCR, treatment with itraconazole (100 mg/d) was initiated. Weekly follow-up in the outpatient setting was performed. Unfortunately, 4 weeks later the symptoms worsened, and the patient reported continuous fever and increased dyspnea. New thoracic chest X-ray and Ga67 gammaphotography were performed, which showed progression of the infiltrates and increased uptake in the lungs. In response to these signs of clinical progression, and after excluding a bacterial or mycobacterial coinfection, treatment with liposomal amphotericin B (200 mg/d, up to 3 g) was initiated, followed up by sulfadiazine (1 g/6 h). Tolerance to both drugs was good, except for a discrete hypokalemia (secondary to the amphotericin use) which was controlled with oral supplements. Once on these medications, clinical progress was good. The fever resolved, and the cough and thoracic pain settled. At 14th week, the patient remained well with no active pulmonary lesions, oxygen saturation of 96% on air, and normal leucocytes, platelets, ESR, and IgE on blood tests. Spirometry done at this time showed a restrictive pattern [forced vital capacity (FVC) 2.83 L (74%); forced expiratory volume in first second (FEV1) 2.36 L (77.7%); FEV1/FVC 83.70%]. Treatment was stopped after 18 months. A new spirometry revealed a total improvement [FVC 4.13 l (108.7%), FEV1 3.20 l (105.9%); FEV1/FVC 77.43%]. After 9 months of discontinuing treatment, there is no relapse. Paracoccidioidomycosis is the most prevalent systemic mycosis in South America. Sporadic case reports are becoming more frequent in non-endemic regions due to increasing international travel by immigrants or tourists.1–3

Less than 20 cases have been reported in Spain in the last 40 years.4,5 Failing to recognize these cases due to inexperience in non-endemic regions may have fatal consequences.6,7 Diagnosis is usually done by direct observation or a microorganism culture. In this case, diagnosis was made by a combination of a positive serology and a positive PCR in a sputum sample. Elevation of serum IgE has been described previously—this appears to be high inactive disease but decreases its value during treatment.8 Extension diagnosis and follow-up of the disease were performed with Ga67 gammaphotography. This method has proved useful in both situations, despite its low sensitivity for intra-abdominal or central nervous system involvement, and its low specificity.9,10 Even when clinical and radiological evidence of disease seems to be resolving, an increase in the captation indicates active disease and is regarded as an indication for extending treatment.

When patients with paracoccidioidomycosis deteriorate, rescue treatment with amphotericin B is recommended. Even though the use of lipid formulations remains controversial, continuation of amphotericin B with sulfadiazine in our patient produced a satisfactory response. Monitoring of disease progression is performed using clinical, radiological, and microbiological criteria. In our patient, both clinical and radiological improvements were seen. Unfortunately antibody titer levels were not available, so we were unable to demonstrate an improvement in the microbiological criteria. Paracoccidioidomycosis should be suspected in patients with an appropriate travel history who experience weight loss and have progressive pulmonary deterioration.

**Declaration of Interests**

The authors state that they have no conflicts of interest to declare.

**References**