Paracoccidioidomycosis in Turkey: A Case Report

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Abstract

Paracoccidioidomycosis is known to be an important mycosis in Latin America. We recently treated a sailor with paracoccidioidomycosis in Turkey. The patient had a travel history to Brazil and had been treated with amphotericin B and itracanazol. He died of pulmonary embolism.

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Case Report

The patient was a 45-year-old male, who was a sailor with addiction to drinking and smoking. He had presented to another hospital with complaints of sore throat and feeling weak and had received antibiotherapy with a diagnosis of upper respiratory tract infection. His complaints did not recede and he underwent a punch biopsy from the ulcerative lesions on the soft palate. While waiting for the results of the biopsy, he started having complaints of fever, weight loss and a productive cough. A computed tomography of the thorax showed an interstitial pattern in the upper lobes; bronchiolar disease with centrilobular nodule formation and a cavitary lesion in the right lower lobe. The pathology of the soft palate showed granulomatous inflammation. Respiratory function tests were consistent with an obstructive condition. Fiberoptic bronchoscopic examinations were normal. Examination and cultures of clinical materials were negative for *Mycobacterium tuberculosis*. Bronchoalveolar lavage showed lymphocytic alveolitis. The CD_4/CD_8 ratio was 0.58. Transbronchial biopsies were inadequate for diagnosis. Serum angiotensin converting enzyme level was 73 U/L (N: 8.00 U/L-52 U/L). Open lung biopsy was offered to the patient for definitive diagnosis, but he did not accept.

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Treatment for sarcoidosis with prednisolone in a dose of 40 mg/day was initiated. As the disease progressed, the patient consented to thoracoscopic lung biopsy and was referred to us. At the time of referral, he still was under treatment and also had gastrointestinal bleeding.

On examination, the patient was cachectic, had a fever of 39°C. The lymph nodes were enlarged in the neck and in the axillary and inguinal regions. Inspiratory and expiratory ronchi were heard bilaterally throughout all lung areas and an ulcerative lesion was detected in the right pharyngeal area. All biochemical parameters, immunoglobulin levels and serological markers including HIV were normal except for presence of a normochromic anemia, leucocytosis, and hypoproteinemia. A chest x-ray showed bilateral hilar enlargements with nodular infiltrations all over the lung parenchyma. Pathological investigation of the lung biopsy revealed non-necrotizing granulomatous lesions with Langhans type giant cells. Many fungal spores were detected in the cytoplasm of the Langhans cells and in the extracellulary matrix, a finding compatible with paracoccidioidomycosis (Figure 1). Amphotericin B (1 mg/kg/day) (Fungisone; Geneva Pharmaceuticals, Inc., Princeton, NJ) and supportive treatment were initiated. To rule out coexisting malignancy, biopsy materials were also taken from the soft palate, cervical lymph nodes, and from the ulcerative lesion seen in the second portion of the duodenum. Pathologic examination of these showed necrotizing granulomatous inflammation due to fungal infection. The culture of cervical lymph node biopsy showed coagulase negative staphylococci and the patient was started on treatment with cefepime hydrochloride (2 mg/kg/day) (Maxipime; Elan Biopharmaceuticals; San Diego, CA). None of the fungal cultures nor cultures for M. *tuberculosis* were positive. Bone marrow biopsies showed a normocellular pattern with an increase in the granulocytic series. Cranial, cervical, abdomino-pelvic tomographies showed only lymphadenomegaly. Screening for collagen vascular diseases was negative. Lesions of the patient regressed with treatment and he gained two kilograms in one month. He was discharged from the hospital with amphotericin B, itracanazol (100 mg/day) (Itraspor; Eczacıbaşı, Istanbul, TR), amoxicillin/clavulanic acid (3 g/day) (Augmentin; GlaxoSmithKline; Five Moore Drive Research Triangle Park, NC) treatment. Two days later he was re-admitted with severe dyspnea. His blood pressure was 60/40 mmHg, liver function tests were highly elevated, and an electrocardiogram showed right ventricular loading, D-dimer level was 2.6 mg/l (<0.3 mg/l), cortisole level was normal. Treatment for pulmonary embolism and toxic hepatitis was given. The patient died without any change in his condition. Consent for autopsy was not given.

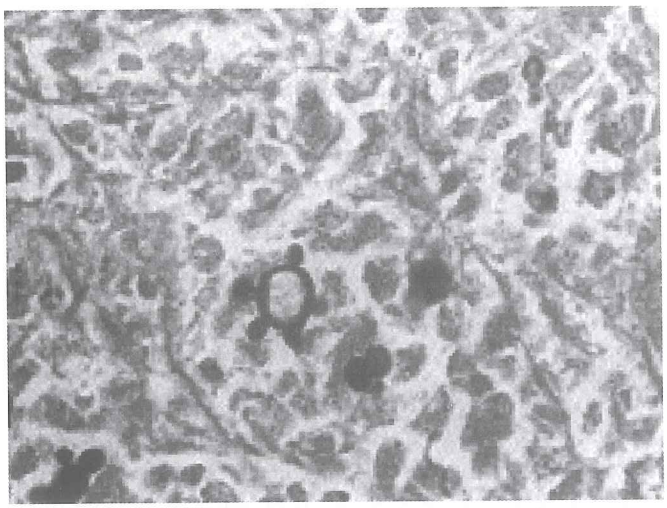

Figure 1. *Pilot wheel cell; blastoconidia surround the mother cell, to which they are connected by means of short cytoplasmic bridges and fungal spores. (Grockott Gomori methenamine silver nitrate staining - X 1250).*

Discussion

Paracoccidioidomycosis is an important mycosis in Latin America (1). Its chronic progressive adult form accounts for the majority of cases and affects predominantly males (2,3). Adult disease can be disseminated at onset (as it is in 75% of all patients) or can be restricted to the lungs (4). Lung involvement usually presents with cough, progressive dyspnea, and diffuse inspiratory crackles on examination. The chest x-ray often reveals nodules and/or cavities superimposed on a diffuse interstitial or fibrotic pattern typically involving the mid and lower lung zones (5). Mucosal lesions are usually painful and appear infiltrated or ulcerative. They can be located on the lips, the tongue and in the nasopharynx or larynx (6,7). Adenopathy may involve cervical, axillary, or mediastinal lymph nodes (2). In centers that rarely encounter paracoccidioidomycosis, definitive diagnosis involves culture and histology of tissue specimens. Typical histologic findings include granulomas and intracellular fungal elements (2). The differential diagnosis includes tuberculosis, which coexists in 10-25% of cases, histoplasmosis, and disseminated malignancy (1).

This patient's clinical presentation had many features of paracoccidioidomycosis including oral mucosal and pulmonary lesions, lymphadenopathies, and systemic symptoms including weight loss, anorexia. The diagnosis was delayed because of lack of attention to the patient's travel history. He was first considered to have tuberculosis because of the high incidence of tuberculosis in Turkey (8). If the disease had been suspected clinically, fungal cultures and histological examinations might have led to an earlier diagnosis. Also if the lung biopsy could have been performed at an earlier stage, there would perhaps be no need to give the high dose corticosteroid treatment.

Cell mediated immunity is usually depressed in paracoccidioidomycosis (1,2). The disseminated nature of this patient's disease might imply an immunocompromised state, but none

of the biopsy materials nor serologic tests were positive. However, the PPD and Candidin skin tests were nonreactive. Alcoholism and smoking are reported as predisposing factors to paracoccidioidomycosis in this patient, and this was probably true also for this patient (1).

Although we believed that our patient received optimal treatment with amphotericine B and itraconazole (9), he died of complications related to the emboli. There are two reports in the literature regarding arterial emboli associated with paracoccidioidomycosis (4,10).

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