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Sistemic mycosis associated to tuberculosis in Bolivar state, Venezuela

Micosis Sistémicas Asociadas a Tuberculosis, Estado Bolívar, Venezuela

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Resumen

Se determinó la frecuencia y características clínicas de las micosis sistémicas endémicas asociadas a tuberculosis en el estado Bolívar. Se revisaron las historias clínicas de los casos con diagnóstico confirmado de micosis sistémicas y tuberculosis en un período de cinco años. Se detectaron 7 casos de las micosis sistémicas endémicas en la región, Paracoccidioidomicosis e Histoplasmosis, asociadas a tuberculosis. Todos los pacientes procedían del estado Bolívar, sólo uno era del sexo femenino y ninguno tenía serología positiva para la infección por el Virus de Inmunodeficiencia Humana. Todos presentaron manifestaciones pulmonares, la mayoría sintomáticos y con pérdida de peso (6 de 7). En todos los casos, se evidenciaron alteraciones en el estudio radiológico del tórax, con diferentes patrones, predominando el compromiso alveolar difuso bilateral. En 6 de los 7 pacientes, se observaron bacilos ácidos resistentes en muestras de esputo. La micosis más frecuentemente asociada a tuberculosis fue Paracoccidioidomicosis (6 de 7). Todos los pacientes recibieron tratamiento antimicótico y tratamiento antituberculoso con cuatro drogas y todos mostraron mejoría. La asociación de micosis sistémicas endémicas con tuberculosis no es rara en el estado Bolívar, por tanto, la asociación de estas infecciones deberían investigarse sistemáticamente.

Palabras clave: Histoplasmosis, paracoccidioidomicosis, micosis sistémicas, tuberculosis.

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Abstract

The frequency and clinical characteristics of endemic systemic mycosis associated with tuberculosis were determined in Bolívar State. Clinical case records with confirmed diagnoses of systemic mycosis and tuberculosis were reviewed for a 5-year period. Seven cases of systemic mycoses endemic to the region were detected: Paracoccidioidomycosis and Histoplasmosis, associated with tuberculosis. All patients came from Bolivar state; only one was feminine and no one was seropositive for the Human Immunodeficiency Virus. All presented pulmonary compromise, mostly symptomatic, accompanied by weight loss (6 of 7). In all cases, alterations appeared on the radiological study of the thorax, mainly diffuse bilateral alveolar compromise. In 6 of the 7 patients, acid-resistant bacilli were observed in sputum samples. The mycosis most frequently associated with tuberculosis was Paracoccidioidomycosis (6 of 7); the other associated mycosis was Histoplasmosis (1 of 7). All patients received antimycotic and 4-drug anti-tuberculosis treatments and all of them improved. The association of endemic systemic mycosis with tuberculosis is not unusual in Bolivar state and therefore, the association of these infections should be systematically investigated.

Key words: Histoplasmosis, paracoccidioidomycosis, systemic mycosis, tuberculosis.

Introduction

Tuberculosis (TB) has remained as a public health problem of enormous importance, particularly in the developing world; it is the first cause of mortality in the world due to a single infectious agent (1). According to World Health Organization evaluation, ten million people are infected every year and more than three million die every year, so tuberculosis remains one of the most feared diseases on the planet (1, 2). The frequency of invasive fungal infections has increased together with the increase in number of high risk patients (3). In Venezuela, since 1961, sistemic mycosis have been considered a public health problem (4) Diagnoses of fungal infections in Bolívar state, , particularly systemic mycosis, that are also endemic infections, have shown an increase in their prevalence (5, 6). Clinical manifestations of TB and mycosis such as Histoplasmosis or Paracoccidioidomycosis can be very variable and it may be difficult to clinically differenciate them (7, 8), even more, one patient may show both (9). Given the increasing prevalence of these infections, the aim of this study was to detect the frequency of the association of these systemic mycoses, which are endemic in this region, with TB.

Patients and Method

Clinical records of patients with both diagnoses: systemic mycosis and clinical and microbiological diagnosis of TB, from January 1999 to January 2004 in the "Complejo Hospitalario Universitario Ruiz y Páez" (CHURP), the reference hospital for Bolívar state, Venezuela, were reviewed. In systemic mycosis, the fungus was identified by direct mycologic study of samples using KOH 20% and/or anatomopathological studies using special stains (Grocott method). Neither micological culture nor serology were realised in any cases. In all cases, epidemiological and clinical data were recorded. Cases with no-microbiologically confirmed diagnosis were excluded. Descriptive analysis was made using the statistical package SPSS 11.0 was used.

Results

During this period of 5 years, 43 cases of systemic mycoses endemic in this region (Paracoccidioidomycosis: 21 and Histoplasmosis: 22) and 78 cases of confirmed TB were diagnosed. Seven cases of these systemic mycoses, were found associated to TB (18,6%). All patients came from Bolívar state, 6 were male, 1 were indigenous and 3 were farmers. All of them showed pulmonary disease manifestations with symptoms (n= 6) like cough with mucous expectoration and dyspnea. Six patients showed a remarkable weight loss. Chest x-ray showed mainly bilateral diffuse alveolar infiltrates. There was evidence of acid-alcohol resistant bacillus in sputum of 6 patients (Table 1 and Figure 1).

Paracocidiodomycosis was more frequently associated to TB (6 cases) than Histoplasmosis (1 case). *Paracoccidioides brasiliensis* was shown in different samples from sputum, skin and oral ulcers, lymphatic ganglion and joint liquid. There were 4 cases of chronic paracoccidioidomycosis and 2 cases were of the juvenile type. Five cases were initially treated with Amphotericine B followed by sulfa therapy, 2 cases received only sulfa treatment and 1 case Itraconazole. All of them showed clinical improvement.

Histoplasma capsulatum was demostrated in biopsie from bone marrow and bronchus. The case of Histoplasmosis was disseminated type and was treated with Amphotericine B and showed a satisfactory evolution.

All patients received anti-TB therapy with 4 drugs: Rifampicine, Isoniacide, Pirazinamide and Ethambutol.

Discussion

Paracoccidioidomycosis and Histoplasmosis are endemic diseases in the south of Venezuela, representing a public health problem (10). Paracoccidioidomycosis (PCM) a mycosis caused by the dimorphic fungus *Paracoccidioides brasiliensis* is a systemic disease that affects predominantly male adults living in rural areas in endemic countries of South and Central America (11,12). The primary lesion occurs in lung, but often disseminates to other organs and systems, notably oral mucose, adrenal glands, fagocytic-mononuclear system, skin and less frequently to other organs like central nervous system (13-15).

PCM clinical forms vary from a benign self-limited infection to a severe, progressive and sometimes fatal disease involving pulmonary and extrapulmonary tissues (16) as it was observed in this study.

Active TB can precede, coexist or follow to PCM in 24% of patients in endemic areas (8). In adults, PCM is a chronic, progressive pulmonary infection clinically similar to TB. Bronchogenic, hematogenic or lymphatic dissemination eventually may occur and then it may affect different organs like tracheobronchial mucose, skin, adrenal glands, gastrointestinal tract and central nervous system. It is more frequent in male adults and it has been reported a male/female ratio of 13:1 (8, 17, 18) and a higher frequency in males was also observed in this study.

Fungal infections are a major cause of morbidity and mortality in increasing numbers of immunocompromised patients (3, 19, 20).

Histoplasmosis is an endemic mycosis more frequent in patients with AIDS (21-23). However, in this study these patients were not seropositive for HIV. Demographic characteristics and clinical manifestations were similar to that described elsewhere (22-24).

In a recent study realised in Argentine, PCM was demostrated associated with TB in

Tabla 1. Cases of systemic mycosis associated to tuberculosis.

Case (year)	Age / Sex	Antecedents	Clinical manifestations	Chest x-ray	Sample
1 (1999)	53y/ M	Radio speaker, diabetes mellitus.	Cough, expectoration, dyspnea, pleuritic pain, fever, hyporexis, weight loss.	Multiple diffuse alveolar radiopacities and reticular infiltrate.	Sputum: ARB + KOH + *P. brasiliensis*.
2 (2001)	25y/ M	Farmer, convict	Arthritis of right ankle and left elbow and foot.Ulcers in ankle,ear,hemithorax and left gluteus.	Radiopacity in middle 1/3 of left hemithorax. Bilateral reinforcing of hilum.	Sputum: ARB + KOH + Bp ulcers and joint liquid: *P. brasiliensis*.
3 (2001)	37y/ M	Farmer	Cough, expectoration, thoracic pain, dyspnea. Fever, hyporexis, weight loss. Hepatomegaly.	Radiopacity in parahilum, some cavities	Bronchus Bp and BM aspirate: *H. capsulatum*. Sputum: ARB ++
4 (2001)	54y/ M	Farmer	Cough, expectoration, dyspnea. Cervical ulcer, weight loss, odynophagy, oral ulcer. Hepatoesplenomegaly.	Bilateral diffuse radiopacity of interstitial type.	Cervical ulcer: ARB +. KOH +. Cervical ganglion and oral ulcer Bp. *P. brasiliensis*.
5 (2002)	25y/ F	Indigenous	Cough, hemoptysis, dyspnea, weight loss	Diffuse radiopacity of bronchopneumonic type	Sputum: ARB + *P. brasiliensis*+
6 (2002)	38y/ M	Trader. "Crack" and cocaine consumer.	Dyspnea, fever, weight loss.	Bilateral diffuse infiltration.	Sputum: ARB + KOH + *P. brasiliensis*.
7 (2003)	43y/ M	Homosexual, hair dresser in mines	Odynophagy, ulcer in oropharinx. Cough, fever, weight loss. Plaque in finger of hand.	Bilateral diffuse reticulonodular infiltration	Ganglion Bp: ARB +.Sputum and scraping of skin and oral ulcer: KOH + *P. brasiliensis*.

y= years; M=masculine; F=feminine; ARB=acid resistant bacillus; Bp= biopsy TB= tuberculosis; BM= bone marrow.

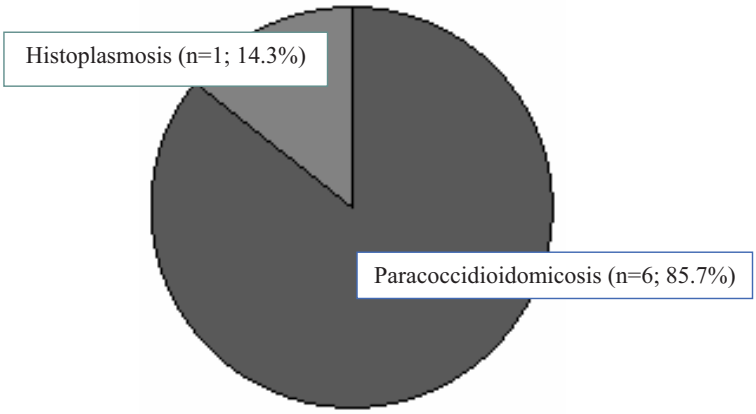

Figure 1. Cases of systemic mycosis associated to tuberculosis.

a half of respiratory symtomatic patients diagnosed (5 from 10 patients) (25). Association of pulmonary TB with endemic systemic mycosis is not unusual in our environment and therefore it should be systematically searched using different methods. It should be remarked the need to be aware about this possibility in order to set the appropriate strategies to prevention, diagnosis and therapy for these mycosis and their association to other diseases like TB in our region.

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