

## 05 CLINICS AND THERAPEUTICS

### 05.006 - PULMONARY CONSOLIDATIONS ON HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT): FREQUENCY AND REVERSIBILITY IN CHRONIC PARACOCCIDIOIDOMYCOSIS

Cerqueira, E. M. F. P.<sup>1</sup>; De Capitani, E. M.<sup>2</sup>; Nakamura, R. T.<sup>3</sup>; Kavakama, J. I.<sup>4</sup>; Balthazar, A. B.<sup>5</sup>; Quagliato Jr., R.<sup>6</sup>

<sup>1</sup>UNICAMP - RADIOLOGIA; <sup>2,5</sup>Faculdade de Ciências Médicas - Clínica Médica; <sup>3</sup>Alfa Diagnósticos - Radiologia; <sup>4</sup>Universidade de São Paulo - Instituto de Radiologia; <sup>6</sup>FCM-UNICAMP - CLÍNICA MÉDICA-PNEUMOLOGIA

**Introduction and Objectives:** Pulmonary parenchymal consolidation or air-space opacity represents the replacement of alveolar air by exudates, transudate, cells, or other substances, and is characterized on chest radiograph and high resolution computed tomography (HRCT) scan by a homogenous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls, with or without air bronchogram, with little or no volume loss. The radiological manifestations in chronic paracoccidioidomycosis (PCM) are quite variable consisting mainly of interstitial opacities, air-space opacities, or a combination of both. Pulmonary consolidations have been reported to occur in 30,1% to 71,43 % of patients who had received no treatment or treatment for three months or less. Frequency drops when studies include patients with longer times of treatment, or patients already treated. The aim of this study is to evaluate the frequency of consolidations in patients with chronic PCM evaluated by HRCT in the first 30 days of treatment (active phase), and the reversibility of these findings by comparison to HRCT obtained on post therapy follow-up (inactive phase). **Methods and Results:** Thirty-three patients (31 males, 2 females) had HRCT done in active phase of disease, and pulmonary consolidations were observed in 19 (57,5%). Ten patients had already finished treatment and had done a second HRCT, in inactive phase of disease. Six of these 10 patients (60%) had 23 pulmonary consolidations, which were mainly peripheral (47,8%), greater than 3 cm in maximum diameter (78,2%), presenting air bronchograms (91,3%) and with no cavities (65,2%). Regression of lesions was observed in all patients, and in all consolidations analyzed independently. Regression was complete in three patients (50%) and in 20 consolidations (86,9%). Partial regression was observed in three patients (50%) and in three consolidations (13%). Residual abnormalities most frequently seen were interstitial thickening (86,9%), and fibrosis, presented as architectural distortion and paracardiac emphysema (69,5%). **Conclusions:** Although our study includes only a few number of patients, the results indicate that pulmonary consolidations are probably a sign of activity in chronic PCM, and may cause focal pulmonary fibrosis after resolution.

### 05.007 - THE ASSOCIATION OF PARACOCCIDIOIDOMYCOSIS (PCM) WITH TUBERCULOSIS (TB)

Quagliato Jr., R.<sup>1</sup>; De Capitani, E. M.<sup>2</sup>; Massucio, R. A. C.<sup>3</sup>; Grangeia, T. A. G.<sup>4</sup>; Rezende, S. M.<sup>5</sup>; Balthazar, A. B.<sup>6</sup>

<sup>1,2,3,4,5,6</sup>Faculdade de Ciências Médicas - Clínica Médica

**Introduction and Objectives:** PCM and TB association has been shown to occur from 15,09% (Rev Inst Med Trop [São Paulo], 34:107-15, 1992) to 19% (Allergol Immunopathol, 8:185-8, 1980). We have noticed several PCM patients with previous TB treatment, but without positive sputum acid fast bacillus (AFB) or positive culture. At the same time, these patients did not show clinical improvement with TB treatment, but improved after PCM treatment. The aim of this study is to describe clinical, radiographic and microbiologic characteristics of patients showing this association. **Methods and Results:** 167 patients from our hospital from 1980 to 2000, diagnosed with adult chronic form of PCM were studied. From that number, 27 (16,1%) had history of previous TB treatment, but only 14 (8,3%) showed positive sputum AFB or positive culture. 13 (7,7%) were negative and did not showed improvement after specific TB treatment. **Conclusion:** Despite the relative high frequency of that association, due to the clinical and radiological similarities between both diseases, we showed almost half of the cases being misdiagnosed.

### 05.008 - ASPERGILLOMA IN A PATIENT WITH PARACOCCIDIOIDOMYCOSIS (PCM)

Quagliato Jr., R.<sup>1</sup>; De Capitani, E. M.<sup>2</sup>; Rezende, S. M.<sup>3</sup>; Schweller, M.<sup>4</sup>; Mussi, R. F. M.<sup>5</sup>; Balthazar, A. B.<sup>6</sup>

<sup>1,2,3,4,5,6</sup>Faculdade de Ciências Médicas - Clínica Médica

**Introduction and Objectives:** It is well known that residual cavities after inflammatory/infectious lung diseases can harbor fungus infections by *Aspergillus* genus as a local and limited infection called fungus ball, or mycetoma, or aspergilloma. The most common previous disease causing aspergilloma is tuberculosis. As PCM can show lung residual lesions as cavities, more cases of aspergilloma would be expected to occur, but references in the literature are rare (Clin Infect Dis, 25:1474-5, 1997). The aim of this paper is to report a case of aspergilloma in a residual cavity due to PCM. **Case Report:** A 41 years old smoking female came complaining of 6 months history of shortness of breath, fatigue, productive cough, daily fever, and weight loss of 20 kg. She had been submitted empirically to antituberculous treatment without any improvement for 4 weeks. Thorax radiogram showed bilateral

heterogeneous infiltrate predominantly in the perihilar regions. Immunodiffusion test for paracoccidioides showed positive. Sputum smears and culture were negative for AFB and fungi. After that she was put on trimethoprim plus sulfamethoxazole in November 2000 with dramatic clinical improvement. In February 2004 she presented with blood tinged sputum. Thorax HRCT at that time showed image of fungus ball in the left upper lobe. Bronchoscopy with bronchial lavage was positive for *Aspergillus fumigatus*. After that she was sent to surgeons to be submitted to lobectomy. **Conclusion:** Diagnosis of fungus ball is relatively common after TB treated patients. To our knowledge this is the second case of aspergillus ball in cavities due to paracoccidioidomycosis published in the literature.

### 05.009 - RACIAL INCIDENCE IN TUBERCULOSIS AND PARACOCCIDIOIDOMYCOSIS

Quagliato Jr., R.<sup>1</sup>; Rezende, S. M.<sup>2</sup>; De Capitani, E. M.<sup>3</sup>; Balthazar, A. B.<sup>4</sup>; Bertuzzo, C.<sup>5</sup>; Cuziol, K.<sup>6</sup>

<sup>1,2,3,4</sup>Faculdade de Ciências Médicas - Clínica Médica; <sup>5</sup>Faculdade de Ciências Médicas - Genética Médica; <sup>6</sup>FCM - Clínica Médica

**Purpose:** To study patients with Tuberculosis (TB) and Paracoccidioidomycosis (PCM) in order to compare racial incidence. **Methods:** 44 patients with TB and 44 with PCM were classified by colour skin as white or non – white people. Afterwards, using family antecedents they were reclassified and compared with state census of 2000 and our hospital out patients average racial distribution. **Results:** The TB white people percentage (45,4%) only by colour skin was lower than census (70,4%), hospital (80,7%) and PCM ( 72,5%). With family antecedents the TB white people percentage was 27,2% and PCM 50%, but marked difference continuous between both. **Conclusions:** Despite the difficult of racial classification in our country by colour skin due to miscegenation, the difference between TB and PCM was emphatic. As those patients are of similar socio – economic pattern it may suggest a genetic explanation.

### 05.010 - MALE UROGENITAL PARACOCCIDIOIDOMYCOSIS (PCM): REVIEW OF 10 CASES

Quagliato Jr., R.<sup>1</sup>; Moraes, L. B.<sup>2</sup>; Ikari, O.<sup>3</sup>; Schweller, M.<sup>4</sup>; Grangeia, T. A. G.<sup>5</sup>; Massucio, R. A. C.<sup>6</sup>; Mussi, R. F. M.<sup>7</sup>

<sup>1</sup>FCM-UNICAMP - CLÍNICA MÉDICA-PNEUMOLOGIA; <sup>2,4,5,6,7</sup>Faculdade de Ciências Médicas - Clínica Médica; <sup>3</sup>Faculdade de Ciências Médicas - Urologia

**Introduction and Objectives:** PCM is a systemic mycosis that eventually have urogenital involvement, including kidneys, ureter, bladder, prostate, spermatic duct, deferent duct, testicles and penis (Rev.Ass.med.bras,19:463-6,1973; Rev.Inst.Med.trop. S.Paulo,24:240-5,1982). The objective is to study urogenital PCM in patients followed in our Lung Division. **Methods and Results:** Ten cases of PCM with compromised urogenital system were diagnosed from 1972 to 2005, all of them with the presence of Paracoccidioides brasiliensis in urine or histopathologic examination. Different clinical and pathologic presentations, as well as diagnostic and therapeutic procedures were studied in each case. **Conclusion:** Urogenital involvement is rare in PCM but one should be aware of it, aiming the correct treatment and preventing sequelae.

### 05.011 - PARACOCCIDIOIDOMYCOSIS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS: REVIEW OF 12 CASES OBSERVED IN AN ENDEMIC REGION IN BRAZIL

Paniago, A. M. M.<sup>1</sup>; Carli Freitas, A. C.<sup>2</sup>; Aguiar, E. S. A.<sup>3</sup>; Aguiar, J. I. A.<sup>4</sup>; Cunha, R. V.<sup>5</sup>; Motta-Castro, A. R. C.<sup>6</sup>; Wanke, B.<sup>7</sup>

<sup>1,2,3,4,5</sup>Universidade Federal de Mato Grosso do Sul - Clínica Médica; <sup>6</sup>Universidade Federal de Mato Grosso do Sul - Farmácia e Bioquímica; <sup>7</sup>IPEC- Fundação Oswaldo Cruz - Micologia

**Introduction and Objective:** The association between PCM and HIV infection in Latin America, although consistently reported in the endemic areas of this mycoses is relatively low in contrast to the higher incidence of other systemic endemic mycosis, e.g. histoplasmosis and coccidioidomycosis. Moreover, little is known of the incidence and clinical manifestations of PCM among the HIV infected population. The objective is to study the clinical characteristics of 12 patients with paracoccidioidomycosis (PCM) and human immunodeficiency virus (HIV) infection. **Methods.** The clinical manifestations, diagnosis, treatment, and outcome of PCM in 12 patients infected with (HIV) attended at a University Hospital of Mato Grosso do Sul, Brazil, were evaluated. **Results.** All patients were men, mean age 36.1 years old, and eleven with had a diagnosis other than PCM as the aids-defining illness. Lymph nodes were the organs most often involved (10 patients), oral mucous membranes were involved in 8 patients and lung involvement, with a predominantly interstitial infiltrate pattern, was observed in 7 patients. Six patients presented papule-nodular skin lesions with central ulceration. Pleural involvement occurred in one patient who presented a large pleural effusion caused by *P. brasiliensis*. Seven patients presented more than one extrapulmonary organ with PCM. In most of the cases (8 patients) the diagnosis was established

by direct microscopy of clinical specimens. All patients used trimethoprim-sulfamethoxazole and seven patients were treated with amphotericin B. Eight patients died with progressive PCM manifestations, with a mean survival of 11.4 months. The cases diagnosed after 1996 (n=5), the year of the introduction of High Active Antiretroviral Treatment for aids in Brazil, showed some different characteristics, such as less dissemination, less skin involvement and lower lethality, reflecting a better immunological status of the host. **Conclusion.** Our review demonstrates that PCM, an endemic systemic mycosis in Brazil, when associated with aids, behaves clinically as an opportunistic disease. **Financial support:** This work received financial support from Department of Science and Technology of Health Ministry of Brazil (DECIT-MS)

#### 05.012 - A COMPARATIVE STUDY OF PARACOCCIDIOIDOMYCOSIS IN HIV-1-SEROPOSITIVE AND SERONEGATIVE PATIENTS

Morejon, K. M. L.<sup>1</sup>; Cardoso, V. C.<sup>2</sup>; Machado, A.<sup>3</sup>; Martínez, R.<sup>4</sup>

<sup>1</sup>Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto - USP - Clínica Médica-Divisão de Moléstias Infecciosas; <sup>2</sup>Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto - Departamento de Puericultura e Pediatria; <sup>3</sup>Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto - USP - Departamento de Clínica Médica - Divisão de Moléstias Infecciosas; <sup>4</sup>FMRP-USP - Internal Medicine

**Introduction:** Paracoccidiodomycosis (Pb) is the deep mycosis most frequently occurring in Latin America, with its incidence being highest in Brazil, especially the State of São Paulo, with an estimate of 1-3/1000 inhabitants/year in endemic areas. The University Hospital of Ribeirão Preto is the center with the largest number of cases of this co-infection. A tendency to dissemination and simultaneous involvement of various organs has been observed in immunodepressed patients. **Objectives:** To analyze in comparison to non-HIV-infected Pb patients the epidemiological, clinical, laboratory, therapeutic and evolutive aspects of patients co-infected with HIV-1 and *P. brasiliensis* in order to determine the peculiar characteristics of seropositive patients. **Methods:** A retrospective 1:2 case-control study was conducted on all HIV-1-positive patients co-infected with *P. brasiliensis*, older than 16 years, followed up at the University Hospital of Ribeirão Preto. The controls were HIV-1-seronegative Pb patients selected by drawing lots. Data were analyzed statistically using the Stata statistical software, version 8. **Results:** A total of 159 patients with Pb were evaluated, 53 of them infected with HIV-1 and 106 non-infected. HIV-infection was diagnosed on the basis of the Pb diagnosis in 43.4% of the patients. HIV-positive patients showed major visceral involvement ( $p < 0.001$ ). Skin involvement occurred in 60.4% of the HIV-positive patients and in 38.7% of the HIV-negative. The initial determination of antibodies by counterimmunoelectrophoresis (CIE) was performed for 152 patients (102 of them not HIV-1 infected and 50 HIV-1 infected). In 16 cases the exam was non-reactive (in 12 HIV-1-infected and 4 HIV-1 non infected patients). The mean CIE titer was 498.5(2-4096) for HIV-1-infected patients and 1.393.5(1-65.536) for non-HIV-1-infected patients. Seventy HIV-negative and 41 HIV-positive patients were submitted to anatomopathological study, which was positive in 97.1% and 85% of them, respectively. The initial chest radiography was altered in most cases in both groups ( $p = 0.021$ ). Mean (+SD) CD4 cell count for HIV-infected patients was 93.9 + 129.0 cells/mm<sup>3</sup> (0.76-480). The initial treatment consisted of sulfamethoxazole/trimethoprim for 64.2% of the HIV-negative patients and for 45.3% of the HIV-positive patients, while 22.6% of the HIV-positive patients were treated with amphotericin. Cure occurred in 86.25% of the HIV-negative patients and in 72.7% of the HIV-positive patients at the end of 12 months. **Conclusions:** This is the largest series reported thus far of patients with HIV/paracoccidiodomycosis co-infection. Analysis of the data led us to conclude that Pb tends to occur in a disseminated form in HIV-positive patients, who usually have severe immunodeficiency. These data support the idea that all patients with disseminated paracoccidiodomycosis should be tested serologically for HIV-1. The data suggest that *P. brasiliensis* is opportunistic for patients with acquired immunodeficiency.

#### 05.013 - PARINAUD'S OCULOGLANDULAR SYNDROME ASSOCIATED WITH PARACOCCIDIOIDOMYCOSIS

Duarte Pivetta, A. B. A.<sup>1</sup>; Neder, L.<sup>2</sup>; Fernandes, B. C. L.<sup>3</sup>; Stefanni, M.<sup>4</sup>; Kuroyanagi, F. M.<sup>5</sup>  
<sup>1,2,3,4,5</sup>UFMT - Clínica Médica

**Introduction and objectives:** Paracoccidiodomycosis is systemic mycosis caused by the dimorphic fungi *Paracoccidiodomycosis brasiliensis* originally described by Adolph Lutz, Brazil, in 1908. It is the most important endemic mycosis in South America and Brazil is responsible for eighty percent of the cases. This disease commonly affects multiples organs, although ocular involvement is rare. Parinaud's Oculoglandular Syndrome is characterized by granulomatous conjunctivitis associated with homolateral cervical and either pre or retro auricular lymph adenopathy. It has been associated with several different infectious diseases, especially the cat scratch disease (*Bartonella henselae*), but sometimes it has been reported in granulomatous chronic infections. The objective of the report is to describe the rare ocular involvement that occurs in the Paracoccidiodomycosis and especially the Parinaud's Syndrome. **Methods and results:** Descriptive Methodology of Report Case: Patient male, 44 years old, married, farm constructor, living in Pontes e Lacerda, Mato-Grosso. He complained cervical lymphadenopathy which had started 2 months before and had swollen and drained after 2 days. About a 1 week later appeared a papular lesion and nodule on the face, thorax associated with dry cough, fever in the afternoon, progressive weight loss and ulcer lesion on the right inferior eyelid with stippled hemorrhage on the surface. The submentonian lymph nodes were aspirated and the viscous yellow pus was obtained which

was contained fungi *Paracoccidiodomycosis brasiliensis* on direct examination and culture. CT thorax showed infiltration like ground glass, nodules, small cavities, scars, bronchiectasis in the bases and hilar region. A broncoscopy was carried out and revealed ulcer lesion on the right and left bronchial lobes. The direct exam of the BAL revealed fungi *Paracoccidiodomycosis brasiliensis*. The patient was given sulphamethoxazol plus trimetoprim with excellent clinical results and disappearance of radiological lesions. **Conclusion:** It was concluded that *Paracoccidiodomycosis brasiliensis* can cause typical Parinaud's Oculoglandular Syndrome. The importance is also emphasized for a systemic evaluation, as the disease is usually multifocal. **Bibliography:** [1] An bras. Dermatol. vol.78: 1,22, no.2, 2003. [2] Arq bras. Oftalmol. 67: 541-3, 2004. [3] An bras. Dermatol. 79(1):69-78. jan-fev, 2004. [4] Rev. Inst. Med. trop. 44(1):49-52, jan-fev, 2002. [5] An bras Dermatol, 78(2):135-150, mar-abr, 2003.

#### 05.014 - AUREOBASIDIN A AGAINST PARACOCCIDIOIDES BRASILIENSIS ISOLATES (PB01 AND PB18)

Amaral, A. C.<sup>1</sup>; Felipe, M. S. S.<sup>2</sup>

<sup>1</sup>UnB - Department of Cell Biology; <sup>2</sup>UnB - Department of Cell Biology

**Introduction:** The current therapy against Paracoccidiodomycosis (PCM), as for other mycosis, includes two classes of drugs, the polyenes (Amphotericin B) and the azoles (Itraconazole). The occurrence of resistant strains of fungi to these antifungal agents makes the development of alternative therapies an urgent need. Recently, some reports have shown that the new antifungal agent, Aureobasidin A, a cyclic nonapeptide obtained from the fungus *Aureobasidium pullulans*, is active against *Saccharomyces cerevisiae*, *Candida sp* and *Aspergillus sp*. The antifungal activity of Aureobasidin A is related to the Aur1 gene whose product, the inositol phosphoryl ceramide synthase, is responsible for the sphingolipid synthesis, an essential component of the fungus membrane (Curr. Drug. Targets 4:311-322, 2004). The identification of a partial sequence of the gene Aur1 in the transcriptome of *Paracoccidiodomycosis brasiliensis*, the etiologic agent of PCM, has stimulated the present experiment [J. Biol. Chem. 280(26):24706-24714, 2005]. **Objective:** The aim of this project was to evaluate the *in vitro* activity of Aureobasidin A against two isolates of *P. brasiliensis*, Pb01 and Pb18. Antifungal activity of Aureobasidin A was compared to those obtained with Amphotericin B and Itraconazole. **Method:** Aureobasidin A, Amphotericin B and Itraconazole were tested in different concentrations (ranging from 0,0156 to 64µg.mL<sup>-1</sup>) against two strains of *P. brasiliensis*, Pb01 and Pb18. These microdilution tests were performed in RPMI 1640 medium enriched with glucose 2% as suggested in the NCCLS M27A protocol. **Results:** The Minimum Inhibitory Concentration (MIC) obtained for Aureobasidin A was 1µg/mL for Pb01 and 2µg/mL for Pb18 when observed with 8 days after the beginning of the experiment. Observations made after 18 days showed MIC of 0,5µg/mL and >64µg/mL for Pb01 and Pb18 respectively. **Conclusion:** The results indicate that Aureobasidin A presents antifungal activity against two isolates of Pb (01 and 18) when observed 8 days after the beginning of the experiment. At longer periods of observation, the antifungal activity was still observed for Pb01 but lower for Pb18. One possible explanation to this difference on Aureobasidin A activity could be accounted to previous observation of the genetic variability among *P. brasiliensis* isolates. As the Aur1 gene is absent in humans, it can be considered an interesting target to the development of new therapeutic strategies against *P. brasiliensis*. Complementary studies are necessary to evaluate the *in vivo* activity of Aureobasidin A. **Financial support:** MCT, CNPq, FAP-DF.

#### 05.015 - PERIPHERAL BLOOD FINDINGS IN INFILTRATIVE MYELOPATHY BY PARACOCCIDIOIDOMYCOSIS. EVALUATION OF 19 PATIENTS, A SYSTEMATIC REVIEW AND META-ANALYSIS

Resende, L. S. R.<sup>1</sup>; Mendes, R. P.<sup>2</sup>; Bacchi, M. M.<sup>3</sup>; Marques, S. A.<sup>4</sup>; Barraviera, B.<sup>5</sup>; Souza, L. R.<sup>6</sup>; Meira, D. A.<sup>7</sup>; Niero-Melo, L.<sup>8</sup>

<sup>1,8</sup>Faculdade de Medicina de Botucatu/UNESP - Serviço de Hematologia da Clínica Médica;

<sup>2,5,6,7</sup>Faculdade de Medicina de Botucatu/UNESP - Doenças Tropicais e Diagnóstico por Imagem;

<sup>3</sup>Faculdade de Medicina de Botucatu/UNESP - Patologia; <sup>4</sup>Faculdade de Medicina de Botucatu - Dermatologia e Radioterapia

**Introduction and Objectives:** In primary or secondary bone marrow involvement from any disease, peripheral blood (PB) can reveal "clues" that indicate a cyto-histological study of this tissue. The aim of this study is to analyse PB parameters of paracoccidiodomycosis (PCM) patients that can suggest infiltrative myelopathy. **Methods and Results:** It was achieved a retrospective evaluation of PB data from 19 PCM patients, whose bone marrow involvement was diagnosed in life or necropsy, at the Botucatu University Hospital. Literature review was performed identifying 20 additional cases. Isolated or combined cytopenias (except isolated monocytopenias or anemias) and leucoerythroblastic reaction (LER) were considered indicative findings for bone marrow study. The main findings were: anemia (35/37; 94.6%), normal hemoglobin value (2/37; 5.4%); leucopenia (2/38; 5.3%), leucocytosis (16/38; 42.1%), normal leucocyte count (20/38; 52.6%); neutropenia (2/30; 6.7%), neutrophilia (13/30; 43.3%), normal neutrophil count (15/30; 50.0%); eosinophilia (21/34; 61.8%), normal eosinophil count (13/34; 38.2%); basophilia (5/30; 16.7%), normal basophil count (25/30; 83.3%); lymphopenia (9/31; 29.0%), lymphocytosis (2/31; 6.5%), normal lymphocyte count (20/31; 64.5%); monocytopenia (7/30; 23.3%), monocytosis (12/30; 40.0%), normal monocyte count (11/30; 36.7%); thrombocytopenia (22.2%), thrombocytosis (27.8%), normal thrombocyte count (50.0%). Granulocytic left shift was verified in (28/32; 87.5%). Six patients showed simultaneous erythroid left shift, characterizing LER, with or without cytopenias.

Eight presented with cytopenias, characterized as lymphocytopenia in 6, lymphocytopenia plus thrombocytopenia in 1, and pancytopenia in 1. **Conclusions:** The PB parameters varied from normal to markedly altered values in one or more hematological lineages. Only 14/39 patients (35.9%) were indicated for bone marrow examination in this study exclusively by abnormal peripheral blood parameters. Other indications should be assessed by suitable clinical and laboratory evaluation in each case, as in those with suspected simultaneous hematological neoplasia or with unsatisfactory response to treatment. **References:** Resende LSR, Mendes RP, Bacchi MM *et al.* Infiltrative myelopathy by paracoccidiodomycosis. *Histopathol*; 2005 (in press).

#### 05.016 - DYSPHONIA AND LARYNGEAL SEQUELAE IN PARACOCCIDIOIDOMYCOSIS PATIENTS. A MORPHOLOGICAL AND PHONIATRIC STUDY

Weber, S. A. T.<sup>1</sup>; Brasolotto, A.<sup>2</sup>; Rodrigues, L.<sup>3</sup>; Marcondes-Machado, J.<sup>4</sup>; Padovani, C. R.<sup>5</sup>; Carvalho, L. R.<sup>6</sup>; Mendes, R. P.<sup>7</sup>

<sup>1,3</sup>Faculdade de Medicina de Botucatu/UNESP - Oftalmologia, Otorrinolaringologia e Cirurgia de Cabeça e Pescoço; <sup>2</sup>Faculdade de Odontologia de Bauru/USP - Educação; <sup>4,7</sup>Faculdade de Medicina de Botucatu/UNESP - Doenças Tropicais e Diagnóstico por Imagem; <sup>5,6</sup>Instituto de Biociências de Botucatu/UNESP - Bioestatística

**Introduction and objectives:** Paracoccidiodomycosis (PCM) is a systemic disease caused by *Paracoccidioides brasiliensis* and the larynx is the third most frequently involved organ. The objectives of this study is to evaluate the morphological laryngeal findings and to perform the first voice analysis in paracoccidiodomycosis patients with the clinical form named sequelae. **Methods and Results:** In order to evaluate the persistent dysphonia and the laryngeal lesions we studied 15 normal male subjects and 30 post-treatment PCM patients, 15 of whom with pulmonary disease and 15 with laryngeal and pulmonary involvement. All the patients were submitted to perceptual and acoustic analysis of the voice; the 15 patients with laryngeal involvement were also submitted to an endoscopic examination. The voice analysis showed more severe dysphonia in the group of patients with laryngeal lesions ( $p < 0.01$ ), characterized by roughness and breathiness. The voices of both groups of patients showed instability at perceptual analysis ( $p < 0.01$ ). Severe dysphonia, with a dysphonia index higher than 7.0, was observed in 56% of the patients with laryngeal lesions. The program Dr. Speech, Tiger Electronics, did not accept the voices of five patients with laryngeal lesions for acoustic analysis, due to severe dysphonia. Jitter was elevated in five PCM patients with laryngeal lesions. The endoscopic examination showed that 80% of the patients with paracoccidiodomycosis laryngeal lesions had two or more laryngeal structures involved. Vocal folds alterations were observed in all the PCM patients with laryngeal involvement. Fibrous thickening was the most frequent alteration of the vocal folds. Arytenoids, epiglottis and vestibular folds were the other involved structures. **Conclusion:** This is the first functional study of the laryngeal sequelae in PCM. It revealed frequent and severe dysphonia, suggesting important social consequences.

#### 05.017 - INFILTRATIVE MYELOPATHY BY PARACOCCIDIOIDOMYCOSIS. A REVIEW AND REPORT OF 9 CASES EMPHASIZING BONE MARROW MORPHOLOGY

Resende, L. S. R.<sup>1</sup>; Mendes, R. P.<sup>2</sup>; Bacchi, M. M.<sup>3</sup>; Marques, S. A.<sup>4</sup>; Barraviera, B.<sup>5</sup>; Souza, L. R.<sup>6</sup>; Meira, D. A.<sup>7</sup>; Niero-Melo, L.<sup>8</sup>

<sup>1,8</sup>Faculdade de Medicina de Botucatu/UNESP - Serviço de Hematologia - Depto de Clínica Médica; <sup>2,5,6,7</sup>Faculdade de Medicina de Botucatu/UNESP - Doenças Tropicais e Diagnóstico por Imagem; <sup>3</sup>Faculdade de Medicina de Botucatu/UNESP - Patologia; <sup>4</sup>Faculdade de Medicina de Botucatu - Dermatologia e Radioterapia

**Introduction and Objectives:** Reports on bone marrow impairment by paracoccidiodomycosis (PCM) are rare and usually incomplete. The aims of this study are to report 9 well-defined cases with infiltrative myelopathy by PCM, and describe the specific bone marrow lesions. **Methods and Results:** A retrospective evaluation of patients with PCM whose bone marrow involvement was diagnosed in life at Botucatu University Hospital was performed. All nine patients had acute or subacute PCM. *Paracoccidioides brasiliensis* was identified by bone marrow biopsy in all cases where Hematoxylin-Eosin (HE) and/or Gomori-Grocott (GG) were used. Typical yeast forms were seen on the HE stained aspirated clot in one un-biopsied case. Bone marrow lesions due to PCM varied from compact and focal granulomas with few fungal cells, to numerous disseminated fungal cells within loose granulomatous inflammatory reaction. In all cases lesions showed reticular fibrosis. Coagulation necrosis was focal in one case, and extensive in two others. Bone marrow remnants were preserved in 7 patients and clearly impaired in two. **Conclusions:** This study reinforces that PCM causes bone marrow granulomas, and that histological specimens, mainly bone marrow biopsies, were best for demonstrating this. The different lesion patterns (size, degree of organization, fibrosis, necrosis, impact on remnants of normal tissue) suggest a wide spectrum of immune responses to the fungi. **References:** 1-BHARGAVA V and FARHI DC. Bone Marrow Granulomas: Clinicopathologic Findings in 72 Cases and Review of the Literature. *Hematol. Pathol.*, v.2, p.43-50, 1988. 2- DIEBOLD J, MOLINA T, CAMILLERI-BROËT S *et al.* Bone marrow manifestations of infections and systemic diseases observed in bone marrow trephine biopsy. *Histopathol.*, v.37, p.199-211, 2000.

#### 05.018 - BONE MARROW NECROSIS DUE TO PARACOCCIDIOIDOMYCOSIS

Resende, L. S. R.<sup>1</sup>; Mendes, R. P.<sup>2</sup>; Bacchi, M. M.<sup>3</sup>; Marques, S. A.<sup>4</sup>; Barraviera, B.<sup>5</sup>; Souza, L. R.<sup>6</sup>; Meira, D. A.<sup>7</sup>; Niero-Melo, L.<sup>8</sup>

<sup>1,8</sup>Faculdade de Medicina de Botucatu/UNESP - Serviço de Hematologia - Depto de Clínica Médica; <sup>2,5,6,7</sup>Faculdade de Medicina de Botucatu/UNESP - Doenças Tropicais e Diagnóstico por Imagem; <sup>3</sup>Faculdade de Medicina de Botucatu/UNESP - Patologia; <sup>4</sup>Faculdade de Medicina de Botucatu - Dermatologia e Radioterapia

**Introduction and Objectives:** Bone marrow necrosis (BMN) is coagulation-type and occurs due to ischemia (vascular compression by intramedullary neoplasia, diseases that cause intravascular fibrin deposition, septic or aseptic microembolization, sickle-cell diseases, severe anemia, cardiocirculatory failure, etc). Bone trabeculae can be affected promoting simultaneous osteonecrosis. Most cases of BMN are due to malignancies, 60% from primary hematological tumours, and 30% from metastatic neoplasms. Although sepsis or disseminated intravascular coagulation due to severe bacterial or fungal infections can cause BMN, paracoccidiodomycosis (PCM) was not reported as an etiology in large series. The objective of this study is to search for necrosis in bone marrow from dead patients with known PCM involvement in this tissue. **Methods and Results:** A retrospective clinical and laboratory evaluation of dead patients with PCM who had undergone necropsy at Botucatu University Hospital was performed. Twelve patients had PCM with bone marrow involvement. Seven had extensive BMN, including 4 with osteonecrosis. The necrotic areas were within loose granulomatous inflammatory reaction presenting numerous *Paracoccidioides brasiliensis* yeast forms. Bone marrow architecture was distorted, and tissue remnants were clearly impaired in all 7 cases. **Conclusions:** Rarely, severe infections cause BMN. PCM, mainly the acute or subacute form, can involve bone marrow in an extension sufficient to cause this. **References:** 1- RANAGHAN L, MORRIS TCM, DESAI ZR *et al.* Bone Marrow Necrosis. *Am. J. Hematol.*, v.47, p.225-228, 1994. 2- FOUCHAR, K. Miscellaneous Disorders of Bone Marrow Including Stromal and Bone Abnormalities. In: \_\_\_\_\_. *Bone Marrow Pathology*. 1<sup>st</sup> ed. Chicago: ASCP Press, 1995. cap.25, p.431-474. 3-JANSENS AM, OFFNER FC and VAN HOVE WZ. Bone Marrow Necrosis. *Cancer*, v.88, p.1769-1780, 2000.

#### 05.019 - COEXISTENCE OF MUCOSAL AND/OR SKIN LESIONS WITH LUNG ABNORMALITIES IN PATIENTS WITH PARACOCCIDIOIDOMYCOSIS (PCM)

Tobón, A.M.<sup>1</sup>; Agudelo, C. A.<sup>2</sup>; Ochoa, J. E.<sup>3</sup>; Cano, L. E.<sup>4</sup>; Tabares, A. M.<sup>5</sup>; De Bedout, C.<sup>6</sup>; Arango, M.<sup>7</sup>; Restrepo, A.<sup>8</sup>

<sup>1</sup>Corporación para Investigaciones Biológicas (CIB) - Hospital La María; <sup>2,8</sup>Corporación para Investigaciones Biológicas (CIB) - Facultad de Medicina, Universidad Pontificia Bolivariana; <sup>3</sup>Universidad Pontificia Bolivariana - Facultad de Medicina; <sup>4</sup>Corporación para Investigaciones Biológicas (CIB) - Escuela de Bacteriología y Laboratorio Clínico, Universidad de Antioquia, Medellín, Colombia; <sup>5,6</sup>Corporación para Investigaciones Biológicas (CIB); <sup>7</sup>Corporación para Investigaciones Biológicas (CIB) - Facultad de Medicina y Escuela de Bacteriología y Laboratorio Clínico, Universidad de Antioquia, Medellín, Colombia.

**Introduction and Objectives:** The role of the lungs as the primary infection site in PCM has not yet been proven beyond doubt as, in most cases, pulmonary manifestations are not apparent during the early stages of the infection and also, because the source and moment of infection with *Paracoccidioides brasiliensis* remain unknown. This study aimed at determining the presence of mucosal and skin lesions prompting PCM patients to seek medical attention and the coexistence, at time of diagnosis, of pulmonary abnormalities indicative of a previous respiratory process in 115 patients with this disease. **Patients and methods:** This is a retrospective study based on the scrutiny of 209 records of PCM patients who were diagnosed and clinically supervised at the CIB's Medical and Experimental Mycology Unit, Medellín, Colombia. The initial lung X-rays films were examined and the means by which diagnosis had been established (direct KOH, isolation in culture and/or biopsy specimens), as well as the type of sample examined, were also determined. Demographic and clinical data, symptoms and signs, type of radiographic abnormality at time of first consultation, were analyzed. In all patients *P. brasiliensis* was seen (direct KOH, biopsies) and/or isolated in culture. **Results:** A total of 140 (67%) patients were found to have mucosal or skin lesions with 115 being examined fully on the basis of availability of all tests and absence of concomitant tuberculosis. All patients were males, 14-75 year-old (mean 46.6) with most (83.4%) having agriculture-related occupations. Smoking was common (74%). Most (86.9%) patients had oral mucosal lesions and fewer nasal abnormalities (3.4%), either multiple or single. Skin involvement was recorded in 33.9% with single lesions predominating. According to the patients, external lesions had first been noticed in the last 3 months preceding consultation in 25 (21.7%), had been present for 4-6 months in 40 (34.7%) and for 7 months or more in 50 (43.7%) cases. Constitutional symptoms were recorded in 75.6% - with hypertrophy of reticuloendothelial organs being noticed in 30 (26%) - patients. Pulmonary symptoms were recorded in 110 (95.6%) patients with cough (68%), expectoration (63.6%) and dyspnea (49%) predominating; signs were less apparent (22%). Radiographic abnormalities were recorded in 86% of the patients with predominance of interstitial infiltrates (92.9%), followed by fibrosis (35.3%); alveolar infiltrates were less common (27%). No lung abnormalities were noticed in 16 patients but in 8 of them respiratory secretions revealed the fungus or grew *P. brasiliensis*. Intensity of the pulmonary lesions increased in parallel with the prolonged course of the external lesions and, additionally, fibrosis became significantly important ( $p < 0.01$ ) in those patients with mucosal/skin lesions that had begun 7 mos or more before the initial consultation suggesting that there was a correlation between time of appearance of external lesions and progression of residual lung lesions. **Conclusions:**

These data reveals that a large number of patients attending medical consultation due to skin or mucosal lesions had concomitant pulmonary abnormalities demonstrated by compatible lung X-rays findings (86%), respiratory symptoms (95,6%) or presence of *P. brasiliensis* in pulmonary secretions (82,5%). It became apparent that these external lesions were secondary to lung infection with pulmonary residual abnormalities increasing in frequency and severity with a more prolonged duration of such external lesions.

#### 05.020 - AN OPEN-LABEL COMPARISON OF ORAL VORICONAZOLE AND ITRACONAZOLE FOR LONG-TERM TREATMENT OF PARACOCIDIOIDOMYCOSIS

Queiroz-Telles, F.<sup>1</sup>; Goldani, L. Z.<sup>2</sup>; Goodrich, J. M.<sup>3</sup>; Schlamm, H. T.<sup>4</sup>; Shikanai-Yasuda, M. A.<sup>5</sup>

<sup>1</sup>UFPR - Hospital das Clínicas; <sup>2</sup>UFRGS - Hospital das Clínicas; <sup>3</sup>University of Wyoming, Laramie, USA - Zoology and Physiology; <sup>4</sup>Pfizer Global Research and Development - New York, NY, USA; <sup>5</sup>Fundação Pró-Sangue - Hemocentro de São Paulo

**Introduction and objectives:** Paracoccidiodomycosis (PCM), a subacute to chronic systemic mycosis caused by *Paracoccidioides brasiliensis*. The aim of this study was to investigate the efficacy, safety, and tolerability of voriconazole in the long-term treatment of acute or chronic PCM, with itraconazole as control treatment. **Methods:** This was a randomized, multicenter, open-label, comparative study conducted in Brazil in 2000-2002. Subjects were randomized (2:1) to receive oral therapy with voriconazole or itraconazole from 6 to 12 months. Satisfactory global response (incorporating clinical, mycologic, radiologic, and serologic assessments) at end of treatment (EOT) was compared for the 2 treatment groups. **Results:** Fifty-three subjects received at least 1 dose of study drug: 35 received voriconazole and 18 received itraconazole. All but 4 subjects with confirmed PCM (3 on voriconazole, 1 on itraconazole) received at least 6 months of continuous study treatment. The response rates in these treatment-evaluable patients were 100% for both treatment groups, and there were no relapses after 8 weeks of follow-up in either group. All subjects presented lung involvement at baseline; 76% mucosal lesions, 53% lymph node enlargement, 22% laryngeal involvement and 22%, cutaneous lesions due to *P. brasiliensis*. One case with both lung and CNS involvement. All subjects responded well to voriconazole. The most common treatment-related events included abnormal vision, chromatopsia, rash, and headache in the voriconazole group, and bradycardia, diarrhea, and headache in the itraconazole group. Two voriconazole subjects were withdrawn prematurely, as required by the protocol, due to study drug-related elevated alk phos and hepatic enzymes (ALT, AST, and GGT). The frequency of liver function test abnormalities was slightly higher in subjects receiving voriconazole compared to itraconazole, but the median changes in these parameters from baseline values were similar between treatment groups. One voriconazole subject expired after 52 days because of a rupture of an aortic aneurysm: an autopsy was performed and was negative for PCM. **Conclusions:** This is the first study to demonstrate that voriconazole is well tolerated and effective for the long-term treatment of PCM. **References:** [1] Brummer E, et al. *Clin Microbiol Rev.* 1993;6:89-117. [2] Blotta MH, et al. *Am J Trop Med Hyg.* 1999;61:390-4. [3] Perfect JR, et al. *Clin Infect Dis.* 2003;36:1122-31. [4] Almeida SM, et al. *J Infect.* 2004;48:193-8.

#### 05.021 - DISCUSSION ON THE NATURAL HISTORY OF THE ACUTE FORM (AF) PARACOCIDIOIDOMYCOSIS (PCM): TWO CASES WITHOUT OBVIOUS EXPOSITION

Benard, G.<sup>1</sup>; De Aquino, M. Z.<sup>2</sup>; Oliveira, P.<sup>3</sup>; Duarte Neto, A.<sup>4</sup>

<sup>1</sup>USP - Laboratório de Dermatologia e Imunodeficiências Departamento de Dermatologia; <sup>2</sup>FMUSP - ICR; <sup>3</sup>FMUSP - DMIP

**Introduction and objective:** The natural history of PCM as it is currently accepted anticipates that the AF results from recent exposition to the yeast and the chronic form from past exposition. As suggested by the antecedents of most patients, and common sense among investigators, this exposition refers to persistent (not sporadic) contact with soil such as farm working or construction activities. Surveys confirming the frequent infection of domestic (dogs, horses) or savage (armadillos) animals that have habits of soil excavation support this view. Our aim is to present 2 recent severe AF PCM cases with improbable exposition to the yeast. **Methods:** data collection from health service records. **Case reports:** 1) A middle class 16 y-old boy presented with a 1 month history of cervical adenomegaly and fever. On admission, his was well despite the painful, huge and motion-limiting cervical nodes. A

node biopsy revealed the yeasts. No pulmonary involvement was noted. He was born and had ever lived in Vila Mariana (downtown São Paulo city). His family had no rural houses, and he disliked anything related to rural activities. He has never traveled to rural areas except for 1 month before the start of the symptoms when he stayed for 2-3 hours in an area near Sorocaba (São Paulo State) for fishing. He was successfully treated with sulfadiazine and is now being followed in our out-patient service. 2) A 18 months boy, from a high middle class family, presented with a history of 30 days of fever, emaciation, visceromegaly, discrete cervical adenomegaly and cutaneous lesions. Diagnosis was made by cutaneous and bone marrow biopsies. Lungs were normal; there was only mediastinal enlargement He was successfully treated with Amphotericin B (15 days) followed by itraconazole. He has always lived in a closed condominium of houses near Ribeirão Preto (São Paulo State) that has been built 10 years before. The family denied travels to rural areas. Immunological testing of his exclusive maid and parents revealed absence of sensitization to the fungus. Both patients were immunologically evaluated and apparently do not have primary immunodeficiencies. **Conclusions:** These patients pose a puzzle on how they have got the infection. Either persistent/repetitive exposure is not necessary for development of a life threatening AF, or the AF may eventually represent the continuum of a past infection, more distant than it is currently believed. In the first case, we would expect clusters of cases (as in histoplasmosis), which have never been reported; the second possibility presumes that the immune response of AF patients can constrain the yeast for a certain period; however, this possibility does not apply to our second patient, which is the youngest ever reported in the literature **Financial support:** LIM-56, Fapesp

#### 05.022 - PARACOCIDIOIDOMYCOSIS IN NORTHERN BAHIA. A CASE REPORT

Coelho, G. V.<sup>1</sup>; Araujo, E.<sup>1</sup>; Catharin, V.<sup>2</sup>; Gonzaga, H.<sup>3</sup>; Bastos, C.<sup>4</sup>; Mascarenhas, A. V.<sup>5</sup>

<sup>1,4,5</sup>Hospital Couto Maia - Infectologia; <sup>1</sup>Hospital Couto Maia - Interno de Infectologia; <sup>2</sup>Hospital Universitário de Marília - Pneumologia; <sup>3</sup>Hospital Universitário de Marília-Unimar - Dermatologia

**Introduction:** Paracoccidiodomycosis (PCM) is a systemic fungal infection of great prevalence in Latin America. It occurs as an endemic disease in South America areas, being more frequent in Brazil, Venezuela and Colombia. In Brazil, where the number of cases is higher, they are more frequent in the states of São Paulo, Rio de Janeiro, Minas Gerais, Paraná, Rio Grande do Sul, Goiás and Mato Grosso do Sul. This disease has less prevalence in the north and the northeastern part of the country, especially in the northeast because of the extremely dry and hot weather. This report exposes the importance of an epidemiological survey of PCM in the state of Bahia, considering that the case report we are presenting occurred in an uncommon region and the clinical presentation showed the commitment of several organs and systems in the same individual. **Case report:** This report is about a male patient of 41 years old, country worker, born and resident in Alagoinhas, state of Bahia, who complained about chronic cough with yellow expectoration for 4 months. He was submitted to a chest X-ray, when the hypothesis of lung tuberculosis was made and he began the specific treatment for 1 month without success. The symptoms became worse and the patient appeared with lesions that became ulcerations in the nose, in the oral mucous, in the posterior area of the thorax and the right inguinal region. In addition, he showed enlargement of the lymph nodes in the posterior cervical area and under the mandible area. The patient was an alcoholic in the past, but stopped drinking about 4 years ago. He used to smoke, but quit 20 years ago. He reported on a weight loss of 10 kg in a 4-month period. In the physical examination, he showed vegetation lesions with ulcerations in the described places, in addition to enlarged lymph nodes with fistula points. Chest X-ray showed diffuse interstitial infiltrate in the lung. C.T. confirmed the lung images in detail, and the histopathological examination of the lymph node material, the oral and face lesions revealed the presence of *Paracoccidioides brasiliensis*. The sputum analysis also resulted positive for the fungus, configuring the diagnosis of PCM with systemic involvement. The patient began the specific treatment with clinical and laboratorial follow-up that pointed to good prognosis. **Discussion:** The PCM epidemiology is better known and researched in southern and southeastern Brazil, while the epidemiological features of the illness in northeastern Brazil are still uncertain. The present communication draws our attention to the occurrence of PCM in northern Bahia. This disease in the state of Bahia is more frequent in the south and in the Recôncavo Baiano, where the environmental conditions are more propitious to fungal development. These are, however, incomplete data, which deserve more investigation, because of the new cases in other uncommon regions such as northern Bahia, as stated in this report. On the other hand, the immunological system failures can probably explain the multiple lung, skin, mucous and lymph node manifestations of the patient. **Financial support:** FUNDAÇÃO JOSÉ SILVEIRA - ANATOMIA PATOLÓGICA.