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EPIDEMIOLOGICAL ASPECTS OF PARACOCCIDIOIDOMYCOSIS IN THE CITY OF SINOP – MT

Ricardo Souza Gomes

Fabiana Cristina Donofrio

Abstract: Paracoccidioides *brasiliensis* is a dimorphic fungus that causes paracoccidioidomycosis, a systemic fungal infection. The main risk factor for acquiring this infection are activities for acquiring the infection are professions or activities related to soil management related to the fungus with the fungus, such as agricultural activities, earthworks, soil preparation, gardening practices, transportation of plant products, among others. The first host-parasite interaction occurs in the pulmonary alveoli; from the lungs, the fungus can spread through the hematogenous or lymphatic route, affecting other organs and systems such as the liver, spleen, bones and central nervous system. Given the geographic and demographic characteristics of the municipality of Sinop - MT, this project aimed to evaluate the epidemiological aspects of paracoccidioidomycosis in this region and to isolate the etiological agent from sputum samples. The project was duly approved by the Research Ethics Committee and authorized by the Municipal Health Department of Sinop - MT. The screening of suspected cases of paracoccidioidomycosis was carried out with the collaboration of a pulmonologist in the city of Sinop - MT. Interviews were conducted with these suspected patients through a questionnaire to assess epidemiological factors. The sputum was processed for direct examination with KOH (potassium hydroxide) between the slide and the coverslip, and cultured on Sabouraud agar plus 0.05% chloramphenicol, Mycobiotic agar, and on BHI heart and brain infusion agar plus 5% sheep's blood, incubated at room temperature (25°C) and in an oven at 37°C, for approximately 1 month before being considered negative. After the appearance of fungal colonies, the analysis of the macroscopic/microscopic characteristics was performed by visualizing the presence or absence of fruiting and ornamentation structures. Of the total number of patients diagnosed so far, 6 (85.7%) were male and 1 (14.3%) were female, as shown in Figure 1 below. The most affected age group was over 40 years, with 2 (28.6%) cases between 40-50 years, 2 (28.6%) between 51-60 years and 3 (42.8%) between 61-70 years. years old. Our findings corroborate other studies, in which the most affected age group is between 30 and 60 years of age and more than 90% of the cases are male, a group that is more exposed to alcoholism and smoking, possible factors of risk for the development of this disease. The low prevalence of the disease in women is due to the inhibitory influence of estrogen, however, it can affect young women and post-menopausal age. Data analysis allows us to infer that we are facing a factor that is in line with the literature. Several studies demonstrate that the region of Mato Grosso can be considered endemic for the microorganism and knowing the epidemiological aspects of the infection, as well as the risk factors related to the pathogen are fundamental to devise strategies against paracoccidioidomycosis, a systemic mycosis that, when diagnosed early, gives good results. therapeutic adherence and cost reduction to the public health system.

Keywords: Paracoccidioidomycosis, systemic mycosis, sputum, Sinop-MT.

INTRODUCTION

The study of paracoccidioidomycosis (PCM), formerly called Brazilian blastomycosis, is increasingly important, given the increasing increase in this mycosis and, due to the severity of some of its anatomical-clinical forms (LACAZ et al., 2002).

PCM has the dimorphic fungus *Paracoccidioides brasiliensis as its etiological agent* and represents an important public health problem due to its high disabling potential, in addition to causing premature

deaths (WANKE, 2009). This presents itself as a filamentous fungus in the saprobiotic phase with the form of septate, hyaline mycelium, chlamydoconidia and conidia that can be present in soil, water and in plants at room temperature and which would be its infective forms, and as yeast with multi-sprouted appearance. of "rudder wheel" when cultivated at 37°C or in the host tissue (parasitic phase) (DISMUKES, 2001). It is believed that *Paracoccidioides brasiliensis* finds its natural habitat in the plant kingdom and in the soil (FRANCO et al., 2000).

The infection is endemic in Latin America, with a high incidence in Brazil, Colombia, Venezuela and Argentina. In Brazil, the highest prevalence occurs in the South and Southeast regions. Recent studies show that individuals living in rural areas, in an endemic area for PCM, are more exposed to *P. brasiliensis* than those in urban areas, acquiring the subclinical form of PCM (MARTINEZ, 2015).

PCM is a disease of pulmonary onset, and the fungus is acquired mainly through the respiratory route by inhaling sessile conidia of the filamentous form of *P. brasiliensis*. This primary focus of infection can be eliminated, forming the primary complex, or it can form foci that remain quiescent until the host's immune system declines, then clinical manifestations appear. The acute or subacute form of the disease can affect both sexes, with an abrupt onset, with deterioration of the host's conditions. The chronic form of the disease is more frequent in male adults aged between 30 and 50 years, with pulmonary predominance and/or mucocutaneous involvement and slow evolution, being distinguished into two subtypes: unifocal, which manifests itself by signs and symptoms referred to a single organ or system (lungs, adrenals, skin, nervous system, etc.), slightly depressed or conserved cellular immunity and antibodies present in moderate levels, and multifocal which is characterized by signs and symptoms referred to more than an organ (skin, mucous membranes and lungs, adrenals and lungs, etc.) with variable cellular and humoral changes (PALMEIRO; CHERUBINI; YURGEL, 2005).

The decisive diagnosis of PCM includes the direct observation of multi-bud, refractive, double-contour yeast cells in biological fluids and tissues or the isolation of the fungus from clinical material. This diagnosis most often takes time, due to the slow growth of the fungus, and depending on the clinical conditions of the patient and the laboratory technician, it may have low sensitivity (MENDES-GIANNINI; MELHEM, 2001). The rapid and accurate diagnosis of PCM enables early treatment, thus preventing the spread of the disease to other organs.

Several antifungals can be used to treat this disease, such as amphotericin B, sulfamidics (sulfadiazine, sulfamethoxazole/ trimethoprim combination), azoles (ketoconazole, fluconazole, itraconazole). Itraconazole is a therapeutic option that allows the control of mild and moderate forms of the disease in a shorter period of time. However, this drug is not available in the public network in most states, and the sulfamethoxazole-trimethoprim combination is the most used in outpatient therapy for patients with PCM. Patients with severe forms of the disease require hospitalization, and the antifungal amphotericin B or the sulfamethoxazole/trimethoprim combination is used intravenously. The patient will remain in treatment and follow-up until all cure criteria are met in clinical, radiological and serological parameters (SHIKANAI-YASSUDA et al., 2006).

According to the Consensus on Paracoccidioidomycosis (YASUDA et al., 2006), the greatest risk factor for acquiring the infection is the professions or activities related

to the management of soil contaminated with the fungus, such as agricultural activities, earthworks, soil preparation, gardening practices, transport of plant products, among others. Thus, the municipality of Sinop - MT configures an area conducive to the habitat of the fungus, both for the geographical aspect, as for the socioeconomic activities developed and characteristics in the region, such as agriculture. In order to identify and estimate the prevalence of the dimorphic fungus *Paracoccidioides brasiliensis,* the present study aims to isolate and identify *Paracoccidioides brasiliensis* from sputum samples from suspected patients in the city of Sinop - MT.

LITERATURE REVIEW

Paracoccidioides brasiliensis is a thermoregulated dimorphic fungus, human pathogen and etiologic agent of paracoccidioidomycosis (PCM), a systemic mycosis geographically restricted to Latin America. The fungus was isolated for the first time by Adolpho Lutz in 1908. (RESTREPO; TOBÓN, 2005).

Brazil is responsible for 80% of the cases described in the literature, followed by Colombia and Venezuela (COUTINHO *et al.,* 2002).

The states of the South, Southeast and Midwest are, in Brazil, the places where the disease is most frequently found (PANIAGO *et al.,* 2003).

Infection of the human host usually occurs by inhaling propagules of the fungus. The fungus grows as yeast on infected tissues or when cultured *in vitro* at 36°C. The mycelial form, considered infective, is observed under saprobiotic conditions in the environment, or when cultivated at temperatures below 28°C (SAN BLASS *et al.,* 2002).

The yeast cells of *P. brasiliensis* are characterized by having multiple buds, formed by the evagination of the mother cell, where a central cell is surrounded by several peripheral cells, giving an aspect of a ship's rudder wheel. The mycelial form can be identified by septate filaments with terminal or intercalated conidia (RESTREPO-MORENO, 2003).

The fungus *P. brasiliensis* belongs to the kingdom Fungi, phylum Ascomycota, subdivision Euascomycotina, class Plectomyceto, subclass Euascomycetidae, order Onygenales, family Onygenaceae, subfamily Onygenaceae Anamorphic, genus *Paracoccidioides,* species *Paracoccidioides brasiliensis* (SAN-BLAS *et al.,* 2002).

The first parasite-host interaction occurs in the pulmonary alveoli; from the lungs, the fungus can spread via hematogenous or lymphatic routes, affecting other organs and systems such as the liver, spleen, bones and central nervous system (VALERA *et al.,* 2008).

The disease generally has a chronic course, is relapsing and can leave anatomical and functional sequelae. There is a large number of patients who need long-term medical care in regions with greater endemicity, making the disease, due to its prevalence, an important public health problem. (FERREIRA et al., 2012)

METHODOLOGY

TARGET POPULATION AND SAMPLE COLLECTION

The project was duly approved by the Research Ethics Committee number CAAE: 66850217.4.0000.8097, from the Federal University of Mato Grosso, Campus Sinop and authorized by the Municipal Health Department of Sinop – MT. The study was carried out in adults with suspected paracoccidioidomycosis who underwent clinical evaluation by a pulmonologist in the city of Sinop - MT, after signing the free and informed consent form in accordance with MS Resolution 196/96.

The screening of suspected cases of paracoccidioidomycosis was carried out with the collaboration of a pulmonologist in the city of Sinop - MT. Interviews were conducted with suspected patients through a questionnaire to assess epidemiological factors such as occupational activity, city of origin, age and history of previous illness, as shown in Table 1 below. Afterwards, two sputum samples were collected and sent to the Laboratory of Microbiological and Parasitological Analysis (LAMP) at UFMT – Campus Sinop to be processed.

The sputum sample was the biological material collected for the research. The collection of 2 samples was established. The first was collected at the time of the medical consultation, and the patient was asked to provoke a cough and eliminate the secretion in the disposable and sterile pot, which was identified and stored for analysis. The individual received another container for the second collection, which was carried out by him at his home the following morning, after waking up and after fasting, before oral hygiene and tooth brushing, with only a simple mouthwash with water for 3 times, in order to eliminate possible food particles and in an attempt to reduce the associated microbiota present in the oral region.

The sputum samples were sent to the Laboratory of Microbiological and Parasitological Analysis – LAMP, at the Federal University of Mato Grosso, Sinop campus.

MYCOLOGICAL ANALYSIS

Sputum collection was performed in adults with suspected paracoccidioidomycosis, that is, the presence of clinical manifestations and radiological parameters suggestive of PCM. The sputum was processed for direct examination with KOH (potassium hydroxide) between the slide and the coverslip, and cultured on Sabouraud agar plus 0.05% chloramphenicol, Mycobiotic agar and on BHI heart and brain infusion agar plus 5% sheep's blood, incubated at room temperature (25°C) and in an oven at 37°C, for approximately 1 month before being considered negative. After the appearance of the fungal colonies, the analysis of their macroscopic characteristics was carried out through the appearance of the colonies and microscopic by the visualization of the presence or absence of fruiting and ornamentation structures. The potato agar microculture technique will provide a detailed study of the different fungal structures. The positive cases were referred to the Center for Medical Specialties in the city of Sinop – MT for treatment and follow-up by the pulmonologist at the outpatient clinic.

STATISTICAL ANALYSIS

The data obtained through the techniques of analysis of sputum samples, direct examination and culture, were tabulated and grouped to statistically determine the microbiological percentage evaluated in the secretion collected from individuals suspected of having systemic mycosis.

RESULTS AND DISCUSSION

During the project, 2 sputum samples were collected, only one positive for paracoccidioidomycosis and also evaluated medical records of patients diagnosed with paracoccidioidomycosis in the municipality of Sinop - MT from 2014. 85.7%) were male and 1 (14.3%) were female as shown in Figure 1 below. The most affected age group was over 40 years, with 2 (28.6%) cases between 40-50 years, 2 (28.6%) between 51-60 years and 3 (42.8%) between 61-70 years. years (Figure 2). Our findings corroborate other studies, in which the most affected age group is between 30 and 60 years of age and more than 90% of the cases are male, a group that is more

Home

- Rural area
- masonry house
- House of wood
- Water piped
- Pit artesian
- asphalt paving
- Septic tank
- Sewerage system

life habits

smoker

- Yes / number of cigarettes per day:_____/ Years:___
- Not

Alcoholic

- Yes / daily dose: 3 to 4 doses- frequency: occasionally on weekends
- Not

Practiced or practice activity in rural areas

- Yes

  Which one?

  - Agriculture
  - soil management
  - mining
  - rural property mechanic
  - Others: Rural property warehouse - PR (agricultural inputs) and MT (grains) - for more than 5 years
- Não

Do you live or have you ever lived in a rural area?
Yes/ period in years _____ location
Not

Do you have family farming?
Yes
Not

Pathological History Progress
Arterial hypertension
Tuberculosis
Cutaneous Leishmaniasis
leprosy
Chagas disease
Others

Medications in use
Glicocoricoides
Antifungicos
Others: Doxa doxazosin mesylate

Present signs and symptoms

Cough with expectoration
cough without sputum
dyspnea
hemoptysis
Hoarseness
odynophagia
Dysphagia
Sialorrhea
Dysphonia
cervical adenomegaly
generalized adenomegaly

Others:

Ulcerated lesion on nasal mucosa
Ulcerated lesion on the oral mucosa
skin lesions
Ulcers
vegetations
nodules
plates
hepatosplenomegaly
abdominal tumor

Table 1: Epidemiological data evaluated from the patients in this study.

exposed to alcoholism and smoking, possible factors of risk for the development of this disease (SHIKANAI-YASUDA et al., 2006; BLOTTA et al, 1999; IKUTAA et al., 2015). The low prevalence of the disease in women is due to the inhibitory influence of estrogen, however, it can affect young women and post-menopausal women (AZENHA et al., 2012).

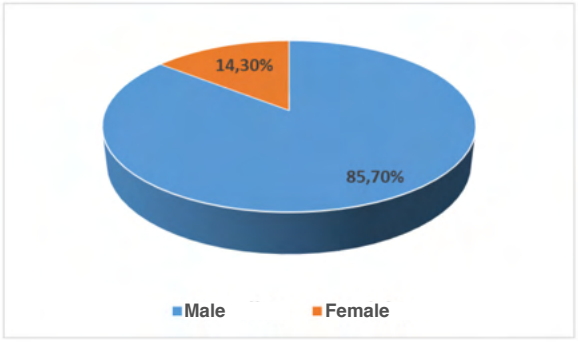

Figure 1: Percentage of cases of paracoccidioidomycosis diagnosed by gender.

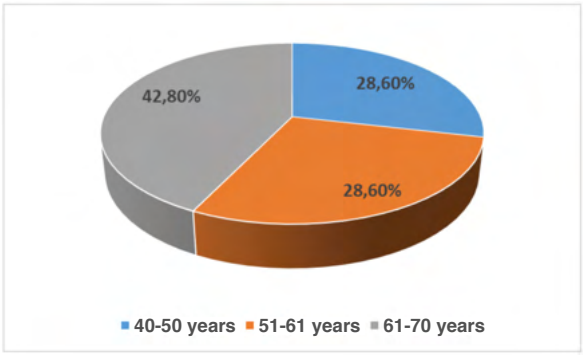

Figure 2: Percentage of cases of paracoccidioidomycosis diagnosed by age group.

Over the last few decades, there have been changes in the demographic characteristics of the affected population and in the geographic distribution of PCM. The increase in urbanization, improved diagnosis and the presence of environmental factors were crucial for these changes. With the opening of new agricultural frontiers and the clearing of forests, especially in the Midwest and North regions, they contributed to the current scenario of mycosis.

The most relevant epidemiological variants found for the study were: housing in a brick house, with running water, asphalt paving and septic tank; drinking habits with the amount of 3 to 4 doses of alcohol and occasional frequency, on weekends; practice of rural activity for more than 5 years in a warehouse of agricultural inputs in different Brazilian states (PR and MT) and signs and symptoms related to the pulmonary form, presence of cough, expectoration, dyspnea, hoarseness and drooling. Several studies have shown that most patients were agricultural workers, and that smoking and alcoholism are often associated with ringworm (SHIKANAI-YASUDA et al., 2006; ALMEIDA. 2014)

CONCLUSION

The analysis of the collected data and the positive result of the sputum sample for *Paracoccidioides brasiliensis* allows us to infer that we are facing a factor that is in line with the literature. Several studies demonstrate that the region of Mato Grosso can be considered endemic for the microorganism and knowing the epidemiological aspects of the infection, as well as the risk factors related to the pathogen are fundamental to devise strategies against paracoccidioidomycosis, a systemic mycosis that, when diagnosed early, gives good results. therapeutic adherence and cost reduction to the public health system.

Thus, the final result obtained configures an alert to health professionals, who must understand the relevance of this clinical condition and the importance of its differential diagnosis.

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