IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 9 Ser. 9 (September. 2024), PP 29-37
www.iosrjournals.org

Serious Pulmonary Paracoccidoidomycosis: Case Report

Priscilla Dos Santos Decembre Montalvão[1], Marcela Marques Abbes[1], Aline Cristina Couto Da Silva[2], Giovana Casarini Yamasehiro[3], Gabriel Queiroz Sabbag[4], Bruna Estefani Rocha De Brito[5], José Carlos Ferreira Da Silva[2], Maria Clara Guimaraes Costa[2], Júlia Da Silva Toledo [6], Délio Tiago Martins Malaquias [2], Ana Laura Nogueira Ervilha[6], Aline Andressa Ferreira Schröder[7], Cristiana Do Nascimento O.Beloto[2], Roselene De O. Carvalho[2], Daniella Campos Furtado[2]; Lucimara Pigaiani[2], Diógenes Trabuco Da Silva Oliveira[2], Rubens Rodrigues Tudela[8], Hamilton Roberto M. De Oliveira Carriço[9], Leonardo T. Da Silva[2], Rafael Pinheiro Do Nascimento[10], Danilo A. De Oliveira Panebianco[2], Rayssa Pince Cardoso[2], Thalita Pinheiro M.Alineri[12], Thiago Gaban Trigueiro[13], Isabela Marini Ferreira[11], Juliana Fontes Beltran Paschoal[2-14], Kauan Santos Amorim De Oliveira[16]; Daniela Costa De Souza [17], Laura Yurico Mizuno[18], Thiago Augusto Rochetti Bezerra[2-15].

Medical Doctor. Unievangelica, Santa Casa De Misericórdia De Goiânia. Goiás, Brazil
Medical Student. Unaerp. Guarujá, São Paulo, Brazil.
Medical Student. Nove De Julho University. São Paulo, Brazil.
Medical Doctor. São Leopoldo Mandic, São Paulo, Brazil.
Medical Student. Centro Universitário Vértice Univértix, Matipó, Minas Gerais, Brazil.
Medical Student. Faculty Of Medical Sciences, São José Dos Campos, São Paulo, Brazil.
Medical Doctor. Puc. Goiás, Brazil.
Medical Student. São Judas, Cubatão, São Paulo, Brazil.
Medical Student. Unisul. Tubarão, Santa Catarina, Brazil.
Medical Student. Uninove Vergueiro. São Paulo, Brazil.
Medical Student. Nove De Julho University, São Bernardo Do Campo, São Paulo, Brazil.
Medical Student. Unoeste, Guarujá, São Paulo, Brazil.
Medical Student. Potiguar University. Natal, Rio Grande Do Norte, Brazil.
Phd In Biotechnology, Usp, São Paulo, Brazil.
Phd In Medical Sciences. University Of São Paulo. Ribeirão Preto, São Paulo, Brazil.
Medical Student. Faculdade Santo Agostinho De Vitória Da Conquista, Bahia, Brazil.
Nursing Student, Unicsul.Sp, Brasil
Physiotherapist Graduated. Unicid Sp, Brasil.

Abstract:
Introduction: *Paracoccidioidomycosis (PCM) is a systemic granulomatous mycosis caused by fungi of the genus Paracoccidioides. Its gateway is generally the respiratory system, with the lungs being the most affected organ.*
Objective: *To demonstrate how the diagnosis, treatment and management of possible complications associated with the disease are carried out, as well as the development of material to raise awareness among the scientific population about Paracoccidioidomycosis.*
Methodology: *This is an observational, descriptive case report study, discussing the clinical case of a male patient with Severe Pulmonary Paracoccidioidomycosis admitted to the Santa Casa de Misericórdia de Goiânia between April and May 2024.*
Discussion: *The gold standard for diagnosing PCM is the finding of fungal elements suggestive of Paracoccidioides spp in a fresh examination of sputum or other clinical specimen (lesion scrapings, lymph node aspirates) and/or biopsy fragments of supposedly affected organs.*

Conclusion: *Although common in endemic regions, it is often not considered as an initial diagnostic hypothesis by health professionals. The scientific dissemination of this disease is important for improving care in the clinical practice of health professionals in Brazil and around the world.*

Keywords: *Paracoccidioidomycosis. Fungal lung diseases.*

Date of Submission: 17-09-2024 Date of Acceptance: 27-09-2024

I. Introduction

Paracoccidioidomycosis (PCM) is a systemic granulomatous mycosis caused by fungi of the Paracoccidioides genus. [1]

All organs can be affected, with cutaneomucosal (especially mouth and upper airways), lymphatic, pulmonary, adrenal, central nervous, spleen, liver, bone and joint involvement being frequent. [2]

Endemic areas are located in tropical and subtropical forest regions. [3]

Brazil has the highest number of described cases of PCM, followed by Colombia, Venezuela and Argentina. [1]

The natural habitat of the Paracoccidioides complex is unknown. It appears that the mycelium is its saprophytic life form and that the production of infective spores occurs in soil and plant debris.[4-8]

Paracoccidioidomycotic infection is acquired through inhalation or by inoculation of the spores in a continuity solution on the skin or mucous membranes, especially in the oral or anal region. [2] Person-to-person transmission has not yet been documented. [9]

An important risk factor for PCM is exposure to soil in rural areas, and it is considered an occupational disease for farmers in endemic regions.[10,11]

The real prevalence of the disease PCM is not established, because in most Brazilian states it is not compulsorily notifiable.[12,13,14]

The causative agent is a dimorphic fungus that can remain viable in the host for long periods, with reactivation of the disease up to several years after the initial infection.[15]

Generally, epidemiological findings indicate that the infection is acquired mainly in the first 2 decades of life, with a peak incidence in the second decade. [10]

The appearance of clinical manifestations or the development of the disease is uncommon in this group, occurring more frequently in adults between 30 and 50 years of age, when there is reactivation of a latent endogenous focus. [10]

The gateway is usually the respiratory tract, with the lung being the most affected organ.16 Chronic infection with severe lung disease and progression to terminal fibrosis can occur even in the absence of pronounced symptoms. [15]

Dissemination from a primary lung lesion can affect other organs, most frequently the skin and mucous membranes.[16]

The most common sequelae of this mycosis include fibrosis with respiratory failure, cor pulmonale, Addison's disease and intestinal malabsorption. [17]

PCM is part of the group of neglected infectious diseases, as it does not receive attention from institutions involved in public health policies and from the pharmaceutical industry, which does not invest in the development of new antifungals. [2]

The usual progression of PCM-disease, without specific therapeutic intervention, is death. [18,19]

II. Objectives

To demonstrate how the diagnosis, treatment, and management of possible complications associated with the disease are performed, as well as the development of material to raise awareness among the scientific population about Paracoccidioidomycosis.

III. Methodology

This is an observational descriptive case report study, discussing the clinical case of a male patient with Severe Pulmonary Paracoccidioidomycosis admitted to Santa Casa de Misericórdia de Goiânia between April and May 2024.

The patient's authorization for the disclosure of clinical data will be obtained through the signing of the Free and Informed Consent Form by the patient or his/her legal representative. The data collected will be used only for scientific research purposes and may be published in scientific events and/or journals. They will be archived for 5 years by the researcher in charge and then incinerated.

The study subject's identity will be protected and may stop participating in the research at any time prior to the publication of the work in a scientific journal or event, without incurring any costs or receiving any

remuneration in relation to this study. The data collection procedure will be through an interview with the patient, review of electronic medical records and collection of results of laboratory and imaging tests performed during the hospital stay. They will be used after the signing of the Medical Record Access Authorization and Authorization of the Head of Medical Clinic documents by the current authorities of Santa Casa de Misericórdia de Goiânia. The integrity of the medical record and any other document evaluated will be protected, in accordance with the Data Use Commitment Term.

The risks associated with this research would be the breach of confidentiality and secrecy; breach of anonymity; exposure to embarrassing situations; exposure of third parties; discomfort at the site where the interview technique is applied; severe exposure to uncomfortable situations; inaccuracy in the dissemination of results.

This research will have the benefits of recognizing the local reality of Paracoccidioidomycosis for the development of research and treatment actions; the possibility of discovering new procedures that are beneficial to health (clinical treatment, pain relief, rehabilitation, etc.); a better understanding of the disease as a whole from a clinical and epidemiological point of view; evidence to support the incorporation of actions and the development of strategies for preventing or treating the disease; the discovery of new potentials to avoid serious complications; and the development of material to raise awareness among the scientific population about Paracoccidioidomycosis.

The bibliographic review will be carried out by collecting scientific articles through the electronic addresses Pubmed, Scielo and Google Scholar, with the research based on the term "Paracoccidioidomycosis". The analysis of patient data will be compared in light of the medical literature and national and international scientific production. The study proposal must be submitted via Plataforma Brasil (PB) and approved by the Research Ethics Committee - CEP in compliance with Resolution 466/12 prior to its publication or dissemination. The research, therefore, may bring benefits in improving the management of severe cases of Pulmonary Paracoccidioidomycosis.

IV. Clinical Case

Patient A.R.B., 56 years old, male, Brazilian, born in Xinguara, Pará. He has worked with fencing of agricultural fields for 3 decades and is a long-time ex-smoker, having previously smoked for 40 years and abstained for 6 years.

He reports the onset of a recurrent dry cough for 22 years, with worsening in frequency in the last 6 months, associated with the onset of dyspnea on moderate exertion and a feeling of chest tightness, in addition to weight loss of 16 kilograms in the last 6 weeks prior to his hospitalization.

He seeks medical care due to progressive worsening of symptoms, with dyspnea at rest and inability to perform his work activities in the last 3 months.

During the physical examination upon admission, diffuse lymphadenopathy was noted in the anterior and posterior cervical chains, bilateral, of soft consistency, not adhered to adipose tissue, without local inflammatory signs, with a diameter of less than 2 centimeters and painless.

The patient underwent a chest X-ray [FIGURE 1], with the appearance of reticulonodular opacities distributed bilaterally in the middle lung fields, sparing the bases and apices. Antibiotic therapy was initiated due to an initial suspicion of Community-Acquired Pneumonia with Ceftriaxone for 24 hours, and was subsequently escalated to Piperacillin with Tazobactam.

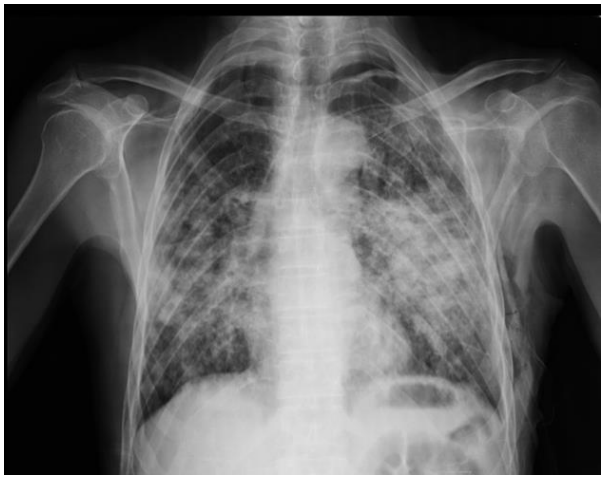

Figure 1: Chest X-ray in anteroposterior view showing diffuse reticulonodular opacities bilaterally, predominantly in the middle lung fields. Source: Authors.

Soon after, a chest tomography scan [FIGURES 2, 3 and 4] without contrast was performed for better diagnostic elucidation, demonstrating extensive consolidations with intervening air bronchograms and areas of ground-glass infiltrate in the surrounding parenchyma, with intervening cavitated lesions associated with consolidations in both lungs and mediastinal lymph node enlargement, the largest infracarinal measuring 3.0 x 2.7 centimeters.

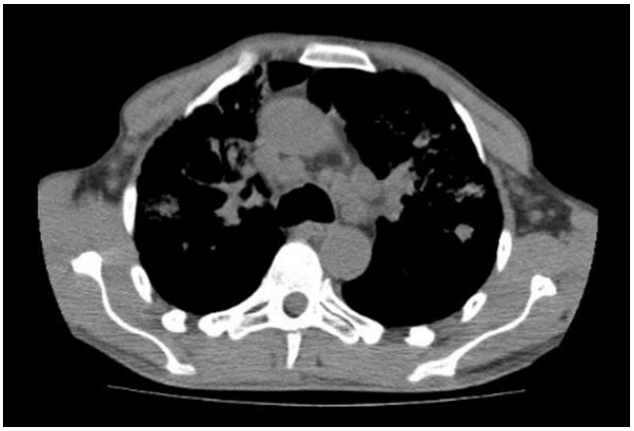

Figure 2: Chest CT scan in axial view, through the mediastinal window, showing multiple mediastinal lymph node enlargement, demonstrated by white arrows. Source: Authors.

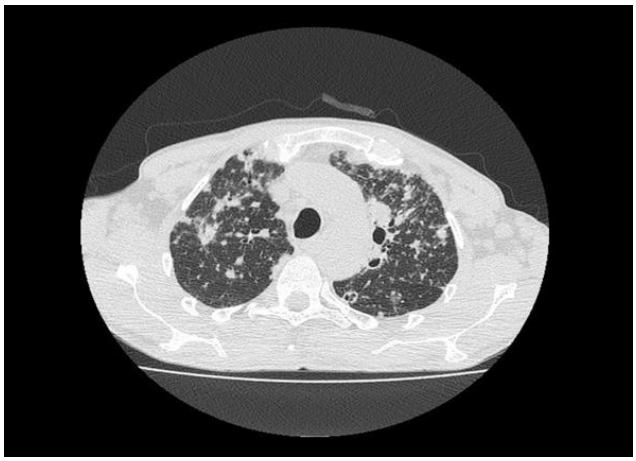

Figure 3: Chest CT scan in axial view, through the lung window, showing multiple bilateral consolidations, with ground-glass opacities in the adjacent lung parenchyma. Source: Authors.

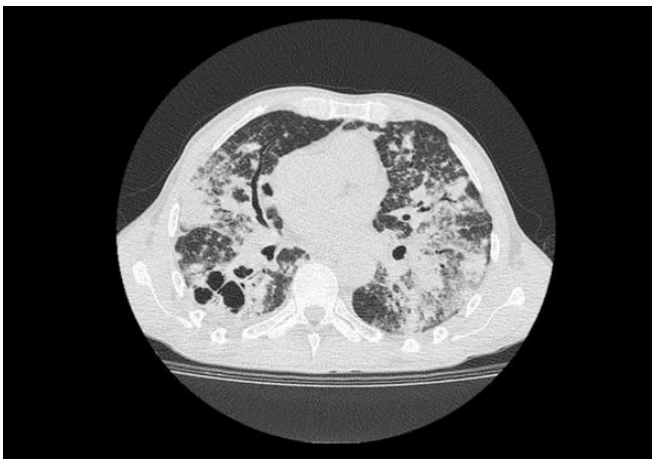

Figure 4: Chest CT scan in axial view, through the lung window, showing multiple bilateral consolidations, with adjacent ground glass. And cavitations in the left lung base. Nonspecific bronchial dilatation in the left middle lung field. Source: Authors.

Initially, 3 sputum samples were collected for tuberculosis testing and culture for fungi, bacteria and mycobacteria. While waiting for the test results, the patient developed clinical worsening of cough and dyspnea, requiring supplemental oxygen therapy via nasal catheter, with the suspension of the use of Piperacillin with Tazobactam and the start of the use of Meropenem. Direct fungal testing and culture for fungi, bacteria and mycobacteria in sputum were negative in 2 samples. As well as negative bacterioscopy of sputum for acid-fast bacilli in 2 samples. In the meantime, an anatomopathological collection and culture of samples from the right cervical lymph node were performed. The result was a negative culture for fungi and mycobacteria, as well as direct testing for acid-fast bacilli not detected in 2 samples of lymph node tissue. The anatomopathological report describes a granuloma with extensive necrosis, surrounded by epithelioid cells and multinucleated giant cells and the presence of numerous structures identifiable as Paracoccidioides, with no signs of malignancy. Meropenem was then suspended and Amphotericin B was started via a left subclavian central venous catheter after the diagnosis of Paracoccidioidomycosis.

Evolving with Acute Renal Failure due to Acute Tubular Necrosis 72 hours after starting Amphotericin B, with recurrent hypokalemia and hypomagnesemia, requiring repeated intravenous potassium and magnesium replacements. There was a progressive improvement in dyspnea with the start of therapy, with subsequent weaning from supplemental oxygen therapy after 12 days of treatment with intravenous antifungal. As well as a progressive drop in nitrogenous excreta levels after its suspension, with subsequent normalization of electrolyte levels.

The therapy was subsequently transitioned to Itraconazole 200 milligrams orally, 1 tablet once a day.

The patient also reported the appearance of an ulcerative lesion measuring approximately 2 centimeters in diameter and 0.5 centimeters in depth in the anterior portion of the scalp for 5 months, without local pain or bleeding. An excisional biopsy of the lesion was performed during hospitalization [FIGURE 5]. The anatomopathological report also shows a chronic granulomatous inflammatory reaction containing epithelioid cell granulomas and multinucleated giant cells that encompass fungal structures with a birefringent capsule containing "steering wheel" buds in the dermis - compatible with Paracoccidioides sp.

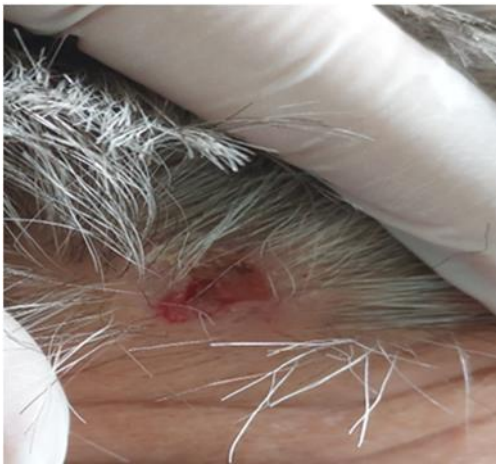

Figure 5: Ulcerous lesion approximately 2 centimeters in diameter and 0.5 centimeters deep on the anterior portion of the patient's scalp. Source: Authors.

Due to improvement in renal function and resolution of dyspnea, the patient is discharged from hospital with a prescription for Itraconazole 200 mg/day and referral for outpatient follow-up with an infectious disease specialist and pulmonologist.

V. Discussion

Paracoccidioidomycosis is the most important deep mycosis in Latin America, first described in 1908 in Brazil by physician Adolfo Lutz. [20]

It can affect people of all ages, and its clinical manifestations range from benign to severe and life-threatening. [2]

The causal agent is a dimorphic fungus that can remain viable in the host for long periods, with reactivation of the disease up to several years after the initial infection. [15]

The real prevalence of PCM-disease has not been established, because in most Brazilian states it is not subject to mandatory reporting. [12,13,14]

All organs can be affected, with frequent involvement of the cutaneous and mucous membranes (especially the mouth and upper airways), lymphatic, pulmonary, adrenal, central nervous system, spleen, liver, bones, and joints. [2]

PCM is considered a neglected infectious disease due to the following characteristics: it occurs mainly in poor and rural environments.

Disproportionately in low-income populations; perpetuates a vicious cycle of disease (between poverty and inadequate health care); receives no attention from the developed world and the pharmaceutical industry (which does not invest in the development of new antifungals); receives no attention from institutions involved in public health policies; generally incapacitates rather than kills; promotes poverty, causing lasting consequences and devastating impacts on the ability to work and quality of life; involves patients who cannot easily obtain drug therapy; and, finally, affects patients who often seek medical care late, when the disease is already in an advanced stage. [21,22]

It is estimated that in endemic regions there are approximately 10 million people infected with P. brasiliensis. [23]

However, most do not present clinical symptoms. [23]The disease is associated with professions and activities that involve soil management, such as agriculture, transportation of plant products, earthmoving and gardening. It mainly affects rural workers (44.3-76.2%) and construction workers (5-20%), who generally come from rural areas. [24-27]

It is a systemic granulomatous disease, with pulmonary and cutaneous-mucosal forms predominating.16 The lungs are affected in 50-100% of cases. [16]

The main route of infection is respiratory, by inhalation of spores present in the soil.16,28,29 It can also be acquired by inoculation of spores in a discontinuous solution in the skin or mucous membranes, especially the oral or anal region.2 This disease is not transmitted between humans. [29,30]

The initial contact between the host and the fungus usually evolves into a subclinical infection, with initial formation of a pulmonary granuloma, which may have characteristics similar to the primary tuberculosis complex. [16,28]

Eventually, the fungi contained in the primary complex may spread rapidly to other organs, via hematogenous and/or lymphatic routes, causing the juvenile or acute form of the disease.[24]

However, most cases usually evolve to prolonged latency, with a primary scar complex containing viable fungi (quiescent focus) that can evolve into chronic PCM many years after infection.[25]

The factors involved in the reactivation of the residual or quiescent focus have not yet been established.[2,33-35]

Humans are resistant hosts to the fungus, since the number of people exposed (PCM-infection) to the fungus is much higher than the number of patients with PCM (PCM-disease).[2]

PCM-disease can manifest in two forms: acute (juvenile type) and chronic (adult type).[10]

The acute form accounts for 5-25% of cases, demonstrates rapid evolution and is considered the most severe form, which presents marked depression of the immune cellular response and high antibody titers.[10,25]

It predominates in children, adolescents and young adults, and may occasionally affect adults over 30 (up to 40) years of age. The gender distribution is practically equal, particularly among children. [36-39]

It usually originates from a primary infection, spreading rapidly through the lymphatic pathways to the monocytic-macrophagic system, highlighting the presence of localized or generalized lymphadenomegaly, which may, as it progresses, present with suppuration and fistulization and hepatosplenomegaly, in addition to possible bone marrow dysfunction10. Mucosal lesions are uncommon, occurring in 15% to 20% of cases; Pulmonary involvement is rare, being present in only 5% to 11% of patients.[5,36,39]

Intra-abdominal lymph node enlargement may coalesce, producing tumor masses that exert compression on several organs, such as the common bile duct and intestinal loops. [38)Fever, weight loss, anorexia, and emaciation frequently accompany the clinical picture.[10] One notable laboratory alteration in this form is peripheral eosinophilia, which may occur in 30 to 50% of cases. [38,39,40]

The chronic form (in adults) is responsible for the majority of cases of PCM, with a prevalence of 74 to 96%.(10) It frequently affects adult males between 30 and 60 years of age, with a male-to-female ratio of 22:1.10 The disease arises from a quiescent focus and may affect a single organ (unifocal) or spread to other organs (multifocal).[25]

The disease sets in more slowly, with symptoms lasting for more than four to six months and sometimes more than a year. (10) In some cases, the onset is silent and the disease is detected by an exam requested for work purposes or check-up.(10) Pulmonary involvement is present in 90% of patients.(36,41) In addition to the lungs, the mucosa of the upper aerodigestive tract and skin are the sites most affected by Chronic PCM.[10]

The evolution of PCM can be cured, with sequelae or death.(2) The appearance of sequelae is very common in PCM.[3]

Scars can promote changes in lung function, upper airways or digestive tracts, in addition to promoting severe aesthetic skin-mucosal retractions. [29,31,33-35]

Pulmonary sequelae are characterized mainly by fibrosis and emphysema, standing out for their frequency, severity and limitations that they impose on patients' lives. patients.[3]

Even with appropriate treatment, patients can develop Addison's syndrome and often require lifelong hormone replacement therapy. [3]

Neurological sequelae vary greatly depending on the location of the lesions, but generally impose considerable limitations on the patients' activity Tracheal lesions are difficult to treat and occasionally require surgical intervention.[3]

Lesions in the gastrointestinal tract can cause obstruction or subobstruction of the digestive tract, requiring surgical correction. Skin and mucosal lesions are often disfiguring.(3) Laryngeal involvement can cause considerable and often irreversible impairment of the patient's voice.[3]

Chest radiography in PCM infection can show several alterations: linear and reticular opacities, nodules of variable dimensions, poorly defined infiltrates, areas of airspace consolidation and cavitation.[40]

However, this examination has limited capacity in the evaluation of diffuse lung diseases.[15] Thus, HRCT has become the method of choice in the evaluation of patients with clinical suspicion and/or laboratory findings of pulmonary PCM.[15]

Alterations in the lung parenchyma usually have a bilateral, practically symmetrical distribution and, although affecting the entire lung, are predominant in the middle thirds. [43]

They may simultaneously include lesions in the active phase and chronic and fibrosing changes.[15]

Pulmonary disease manifests on high-resolution computed tomography (hrct) as areas of consolidation, ground-glass opacities, scattered parenchymal nodules (granulomas or paracoccidiomas), interlobular septal thickening, spiculated pleural thickening, bronchial wall thickening, traction bronchiectasis, tracheal dilatation, architectural distortion, parenchymal bands, and paracicatricial emphysema.[41-43]

Hilar and mediastinal adenopathies are frequently present. [40,42]

Parenchymal consolidation translates into focal pneumonia, which usually begins with a desquamative alveolitis (associated with ground-glass opacities) and consists microscopically of a fungal-rich inflammatory infiltrate.[43]

The reversed halo sign (defined as a central ground-glass attenuation surrounded by dense peripheral consolidation in the shape of a crescent or ring) appears in about 10% of patients with active infection. [41,42]

Pulmonary fibrosis is a frequent finding with thickening of the inter and intralobular septa, thickening of the bronchial walls, architectural distortion, parenchymal bands, intralobular reticulation and irregular thickening of the perihilar axial interstitium, involving hilar lymph nodes, main bronchi and branches of the pulmonary artery.[15,16,41-43]

The gold standard for the diagnosis of pcm is the finding of fungal elements suggestive of paracoccidioides spp in a fresh examination of sputum or other clinical specimen (scrape of lesion, aspirate of lymph nodes) and/or biopsy fragment of supposedly affected organs.[10]

Serological techniques (specific antibody titers) allow the diagnosis to be inferred with a certain degree of certainty, in addition to assisting in the evaluation of the response to treatment and detection of recurrence.[17,19,31-32]

Although a vast therapeutic arsenal is available for disease management, in practice, treatment is mainly done with sulfomethoxazole-trimethoprim or itraconazole.[10,19,40]

The most severe cases of chronic or acute disease can be treated with amphotericin b.[19,40]

The expression "definitive cure" may never be applied to patients with pcm, due to the impossibility of eradicating p. brasiliensis from the organism.[10]

The objective of treatment is to reduce the fungal load in the patient's organism, allowing the recovery of cellular immunity and the reestablishment of the balance between parasite and host.[10]

It is important to emphasize that pcm, especially in its pulmonary form, must be differentiated from other mycoses and tuberculosis.[41]

Clinical and radiological findings are nonspecific; however, extensive calcification, pleural effusion and apical location are indicative of histoplasmosis and tuberculosis.[41]

The differential diagnosis with leishmaniasis is also very important, since the endemic regions for this pathology often coincide with those of pcm, and the oral, cutaneous and nasal cavity lesions are quite similar.[43] Involvement of the lymphatic system simulates hodgkin's disease and other malignant diseases.[41]

VI. Conclusion

Although common in endemic regions, it is often not considered as an initial diagnostic hypothesis by health professionals.

The scientific dissemination of this disease is important for improving care in the clinical practice of health professionals in brazil and worldwide.

REFERENCES

[1]. Fortes, Maria Rita Parise Et Al. Imunologia Da Paracoccidioidomicose. Anais Brasileiros De Dermatologia, V. 86, P. 516-524, 2011.
[2]. Rodrigues, Gustavo Da Silva Et Al. Associação Entre Paracoccidioidomicose E Câncer. Jornal Brasileiro De Pneumologia, V. 36, P. 356-362, 2010.
[3]. Romitti, Julia Picua; Barbosa, Adriano Batista; Furlanetto, Rosecler Canossa. Paracoccidioidomicose. Revista Mato-Grossense De Odontologia E Saúde, V. 3, N. 1, P. 43-61, 2024.
[4]. Nogueira, Maria Gorete Dos Santos; Andrade, Gláucia Manzan Queiroz. Paracoccidioidomicose Em Crianças E Adolescentes. 2015.
[5]. Millington, Maria Adelaide Et Al. Paracoccidioidomicose: Abordagem Histórica E Perspectivas De Implantação Da Vigilância E Controle. Epidemiologia E Serviços De Saúde, V. 27, P. E0500002, 2018.
[6]. Cavalcante, Leandro. Aplicação Das Técnicas De Diagnóstico Da Paracoccidioidomicose No Brasil: Revisão Sistemática. South American Journal Of Basic Education, Technical And Technological, V. 6, N. 2, P. 762-775, 2019.
[7]. De Souza Tolentino, Elen Et Al. Manifestações Bucais Da Paracoccidioidomicose–Considerações Gerais E Relato De Caso. Revista Da Faculdade De Odontologia-Upf, V. 15, N. 1, 2010.
[8]. GÓES, Alfredo Miranda De Et Al. Paracoccidioidomicose (Doença De Lutz-Splendore-Almeida): Etiologia, Epidemiologia E Patogênese. Rev. Méd. Minas Gerais, 2014.
[9]. Rosario, Jéssica Stuchi Et Al. Diagnóstico E Tratamento De Paracoccidioidomicose: Relato De Caso Clínico. Revunivap, V. 22, N. 40, P. 641, 2017.
[10]. Moraes, Cristian Saievicz De Et Al. Análise Das Alterações Radiográficas Pulmonares Durante A Terapêutica Da Paracoccidioidomicose. Radiologia Brasileira, V. 44, P. 20-28, 2011.
[11]. Armas, Mónica Et Al. Paracoccidioidomicose Pulmonar: Relato De Caso Clínico Com Aspetos Em Tomografia Computorizada De Alta Resolução. Revista Portuguesa De Pneumología, V. 18, N. 4, P. 190-193, 2012.
[12]. Santos, Aline Ferreira Dos. Qualidade De Vida E Função Pulmonar De Pacientes Com Sequela Pulmonar De Paracoccidioidomicose. 2015.
[13]. Boscardin, Roberto Nogueira. O Lavado Broncoalveolar Na Paracoccidioidomicose Pulmonar. 2013.
[14]. Finato, Angela Carolina. Avaliação De Terapias Antifibróticas Associadas Aos Antifúngicos Itraconazol E Cotrimoxazol Em Modelo Murino De Paracoccidioidomicose Pulmonar. 2017.
[15]. Freitas, Ricardo Miguel Costa De Et Al. Paracoccidioidomicose Pulmonar: Radiologia E Avaliação Clínico-Epidemiológica. Revista Da Sociedade Brasileira De Medicina Tropical, V. 43, P. 651-656, 2010.
[16]. Guedes, Carlos Ivan Andrade. Quantificação De Fibrose E Enfisema Pulmonares Em Pacientes Tratados De Paracoccidioidomicose Pulmonar. 2015.
[17]. Queiroz, Rodolfo Mendes; Gomes, Michela Prestes; Valentin, Marcus Vinicius Nascimento. Paracoccidioidomicose Pulmonar Exibindo Sinal Do Halo Invertido Com Margens Nodulares/Rugosas. Radiologia Brasileira, V. 49, P. 59-60, 2016.
[18]. Rosario, Jéssica Stuchi Et Al. Diagnóstico E Tratamento De Paracoccidioidomicose: Relato De Caso Clínico. Revunivap, V. 22, N. 40, P. 641, 2017.
[19]. Queiroz-Telles, Flavio; Escuissato, Dante L. Pulmonary Paracoccidioidomycosis. In: Seminars In Respiratory And Critical Care Medicine. © Thieme Medical Publishers, 2011. P. 764-774.
[20]. Vio De Queiroz-Telles, Flá Et Al. New Insights On Pulmonary Paracoccidioidomycosis. In: Seminars In Respiratory And Critical Care Medicine. Thieme Medical Publishers, 2020. P. 053-068.
[21]. Feriotti, Claudia Et Al. Nod-Like Receptor P3 Inflammasome Controls Protective Th1/Th17 Immunity Against Pulmonary Paracoccidioidomycosis. Frontiers In Immunology, V. 8, P. 786, 2017.
[22]. Venturini, James Et Al. Altered Distribution Of Peripheral Blood Dendritic Cell Subsets In Patients With Pulmonary Paracoccidioidomycosis. Acta Tropica, V. 173, P. 185-190, 2017.
[23]. Naranjo, Tonny W. Et Al. Combined Itraconazole-Pentoxifylline Treatment Promptly Reduces Lung Fibrosis Induced By Chronic Pulmonary Paracoccidioidomycosis In Mice. Pulmonary Pharmacology & Therapeutics, V. 24, N. 1, P. 81-91, 2011.
[24]. Costa, Tania A. Et Al. In Pulmonary Paracoccidioidomycosis Il-10 Deficiency Leads To Increased Immunity And Regressive Infection Without Enhancing Tissue Pathology. Plos Neglected Tropical Diseases, V. 7, N. 10, P. E2512, 2013.
[25]. Cano, Luz E. Et Al. Pulmonary Paracoccidioidomycosis: Clinical, Immunological And Histopathological Aspects. Lung Diseases-Selected State Of Art Reviews. Rijeka: Intech-Europe, P. 359-91, 2012.
[26]. Santos, Patricia Campi Et Al. The Pivotal Role Of 5-Lipoxygenase-Derived Ltb4 In Controlling Pulmonary Paracoccidioidomycosis. Plos Neglected Tropical Diseases, V. 7, N. 8, P. E2390, 2013.
[27]. Restrepo, Angela; Gonzalez, Angel; Agudelo, Carlos A. Paracoccidioidomycosis. In: Essentials Of Clinical Mycology. New York, Ny: Springer New York, 2010. P. 367-385.
[28]. Marchiori, Edson Et Al. Paracoccidioidomycosis: High-Resolution Computed Tomography–Pathologic Correlation. European Journal Of Radiology, V. 77, N. 1, P. 80-84, 2011.
[29]. Costa, André Falcão Pedrosa Et Al. A Brazilian Male With Typical Oral And Pulmonary Paracoccidioidomycosis. Medical Journal Of The Islamic Republic Of Iran, V. 33, P. 145, 2019.
[30]. Shikanai-Yasuda, Maria Aparecida. Paracoccidioidomycosis Treatment. Revista Do Instituto De Medicina Tropical De São Paulo, V. 57, P. 31-37, 2015.
[31]. Bernardino, Simone Et Al. Tnf-A And Cd8+ T Cells Mediate The Beneficial Effects Of Nitric Oxide Synthase-2 Deficiency In Pulmonary Paracoccidioidomycosis. Plos Neglected Tropical Diseases, V. 7, N. 8, P. E2325, 2013.
[32]. Menna Barreto, Miriam Et Al. Ct Morphological Features Of The Reversed Halo Sign In Pulmonary Paracoccidioidomycosis. The British Journal Of Radiology, V. 88, N. 1055, P. 20150246, 2015.
[33]. Menna Barreto, Miriam Et Al. Ct Morphological Features Of The Reversed Halo Sign In Pulmonary Paracoccidioidomycosis. The British Journal Of Radiology, V. 88, N. 1055, P. 20150246, 2015.
[34]. Bazan, Silvia B. Et Al. Loss-And Gain-Of-Function Approaches Indicate A Dual Role Exerted By Regulatory T Cells In Pulmonary Paracoccidioidomycosis. Plos Neglected Tropical Diseases, V. 9, N. 10, P. E0004189, 2015.
[35]. Pereira, Mariana Leite Et Al. Spontaneous Pneumothorax As An Atypical Presentation Of Pulmonary Paracoccidioidomycosis: A Case Report With Emphasis On The Imaging Findings. Case Reports In Medicine, V. 2010, N. 1, P. 961984, 2010.

[36]. Amorim, Barbara Casella Et Al. Enhanced Expression Of Nlrp3 Inflammasome Components By Monocytes Of Patients With Pulmonary Paracoccidioidomycosis Is Associated With Smoking And Intracellular Hypoxemia. Microbes And Infection, V. 22, N. 3, P. 137-143, 2020.
[37]. Angela C. Et Al. Evaluation Of Antifibrotic And Antifungal Combined Therapies In Experimental Pulmonary Paracoccidioidomycosis. Medical Mycology, V. 58, N. 5, P. 667-678, 2020.
[38]. Rad, Mojgan Naeimi Et Al. Pulmonary Paracoccidioidomycosis: A Case Report. Iran Red Crescent Med J, V. 19, N. 2, P. E28319, 2017.
[39]. Peçanha-Pietrobom, Paula Massaroni Et Al. Diagnosis And Treatment Of Pulmonary Coccidioidomycosis And Paracoccidioidomycosis. Journal Of Fungi, V. 9, N. 2, P. 218, 2023.
[40]. Loures, Flávio V. Et Al. Dectin-1 Induces M1 Macrophages And Prominent Expansion Of Cd8+ Il-17+ Cells In Pulmonary Paracoccidioidomycosis. The Journal Of Infectious Diseases, V. 210, N. 5, P. 762-773, 2014.
[41]. Abud, Lucas Giansante; Queiroz, Rodolfo Mendes; Abud, Thiago Giansante. Concomitant Pulmonary And Central Nervous System Paracoccidioidomycosis With Cerebellar Abscess. Revista Da Sociedade Brasileira De Medicina Tropical, V. 48, N. 6, P. 789-789, 2015.
[42]. Batah, Sabrina Setembre Et Al. Pulmonary Paracoccidioidomycosis-Induced Pulmonary Hypertension. Clinical And Translational Medicine, V. 10, N. 7, 2020.