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CASE REPORT

Paracoccidioidomycosis in a 16-year-old adolescent patient: a case report from Bolivia

Paracoccidioidomicosis en paciente adolescente de 16 años: un reporte de caso en Bolivia

Carlos Alberto Paz-Román[1], Jhossmar Cristians Auza-Santivañez[2], Daniel Ramiro Elías Vallejos-Rejas[3], Diego Javier La Fuente Padilla[4], Marlon Carbonell González[5], Jose Luis Diaz-Guerrero[6], Leonel Rivero Castedo[7], Jaykel Evelio Gómez Triana[8]

[1]Hospital de Niños Mario Ortiz. Clínica de las Américas. Santa Cruz, Bolivia.
[2]Ministerio de Salud y Deportes. Instituto Académico Científico Quispe-Cornejo. La Paz, Bolivia.
[3]Facultad de Medicina. Universidad Privada del Valle Bolivia. Santa Cruz, Bolivia.
[4]Clínica de las Américas. Santa Cruz, Bolivia.
[5]Hospital Clínico Quirúrgico Miguel Enríquez. Unidad de Cuidados Intensivos. La Habana, Cuba
[6]Seguro Social Universitario Tarija (SSUT). Servicio de Ecografía. Tarija, Bolivia.
[7]Hospital Municipal Dr. Julio Manuel Aramayo. Santa Cruz, Bolivia.
[8]Centro de Salud Nuestra Señora del Castillo. Sevilla, España.

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Corresponding Author: Jhossmar Cristians Auza-Santivañez

ABSTRACT

Introduction: paracoccidioidomycosis (PCM) is the most common systemic mycosis in Latin America.
Case Report: a 16-year-old female patient from Bolivia presented with a 6-month history of ulcerative nasal lesions and cervical lymphadenopathy. Initial histopathology suggested tuberculosis with a positive Ziehl-Neelsen stain. Direct KOH examination revealed characteristic "steering wheel" yeasts of Paracoccidioides brasiliensis. Antituberculosis treatment was discontinued and itraconazole was started with a favorable response.
Conclusions: juvenile paracoccidioidomycosis represents a significant diagnostic challenge due to its variable clinical presentation and its ability to mimic other more prevalent pathologies such as tuberculosis and lymphoproliferative syndromes. This case illustrates the importance of maintaining a high index of clinical suspicion in adolescent patients from endemic areas who present with lymphadenopathy and mucocutaneous lesions, especially when tuberculosis studies are negative. A broad differential diagnosis is important, as is the need for specific complementary testing in the event of clinical discrepancies. Direct mycological examination is crucial as a rapid and definitive diagnostic method for paracoccidioidomycosis.

Keywords: Paracoccidioidomycosis; Paracoccidioides Brasiliensis; Juvenile Tuberculosis.

RESUMEN

Introducción: la paracoccidioidomicosis (PCM) es la micosis sistémica más frecuente en América Latina.
Reporte de caso: paciente femenina de 16 años de Bolivia, consultó por cuadro de 6 meses con lesión ulcerosa nasal y adenopatías cervicales. La histopatología inicial sugirió tuberculosis con Ziehl-Neelsen positivo. El examen directo con KOH reveló levaduras características en "Rueda de timón" de Paracoccidioides brasiliensis. Se suspendió tratamiento antituberculoso e inició itraconazol con respuesta favorable.

Conclusiones: la paracoccidioidomicosis juvenil representa un desafío diagnóstico significativo debido a su presentación clínica variable y su capacidad de simular otras patologías más prevalentes como la tuberculosis y los síndromes linfoproliferativos. Este caso ilustra la importancia de mantener un alto índice de sospecha clínica en pacientes adolescentes procedentes de áreas endémicas que presentan adenopatías y lesiones mucocutáneas, especialmente cuando los estudios para tuberculosis resultan negativos. Es de importancia un diagnóstico diferencial amplio, la necesidad de pruebas complementarias específicas ante discordancias clínicas y destaca el rol fundamental del estudio micológico directo como método diagnóstico rápido y definitivo en la paracoccidioidomicosis.

Palabras clave: Paracoccidioidomicosis; Paracoccidioides Brasiliensis; Forma Juvenil Tuberculosis.

INTRODUCTION

Paracoccidioidomycosis (PCM) is a deep, granulomatous, suppurative systemic mycosis caused by dimorphic-thermic fungi of the genus Paracoccidioides spp., mainly Paracoccidioides brasilensis and Paracoccidioides lutzii.[1,2] This disease, which is endemic, is the most common systemic mycosis in Latin America, occurring in subtropical and tropical regions, especially in rural areas associated with agricultural activities, mainly related to coffee, sugar cane, and tobacco.[3,4] It is mainly acquired through inhalation of conidia or fragments of hyphae of the fungus present in the environment, which transform into the yeast-like phase, their pathogenic form, upon reaching the lungs; This can spread to the oropharyngeal mucosa, the reticuloendothelial system, the skin, bones, and viscera.[5,6] Although the primary disease is usually primary and often asymptomatic, the disease can manifest acutely/subacutely (juvenile), chronically (adult), or residually.[4,7]

As for skin manifestations and lymph node involvement, these are among the most important extrapulmonary manifestations and may be the main reason for consultation. Skin lesions are observed in 8 to 10 % of cases,[8] although other reports indicate a frequency ranging from 19 %[5] to 25 %[6] or up to 61,2 % in the chronic form of the disease.[3] The skin is commonly affected by hematogenous spread of the fungus from the lungs, or by contiguous spread from mucosal lesions, or they are also secondary to lymph node fistulization, or in less common cases by direct inoculation or trauma.[1,4,9] The similarity of the lymph node presentation of PCM to other diseases is a key point in the differential diagnosis. Adenopathies in PCM can be confused with those observed in lymph node tuberculosis or lymphoma, with tuberculosis being the disease most closely related to the differential diagnosis of PCM. Their coexistence is not uncommon in approximately 10 to 30 % of cases.[1]

We present the case of an adolescent female patient with cutaneous-lymphatic PCM, whose initial misdiagnosis of tuberculosis illustrates the diagnostic complexity and importance of clinical suspicion in endemic areas, as well as the correct use of diagnostic techniques.

CASE REPORT

A 16-year-old female patient, resident of Santa Cruz of the Sierra, presented with a clinical picture that had been evolving for approximately six months. The history began with the appearance of a small lesion on the right nasal wing, which grew progressively until it became an ulcerative-crusty lesion. Simultaneously, she developed cervical lymphadenopathy, the largest being in the right laterocervical region. The condition was accompanied by asthenia, hyporexia, unquantified weight loss, and episodes of intermittent dry cough. On physical examination, the patient was afebrile and had stable vital signs. An ulcerative-crusty lesion with an infiltrated base measuring approximately 2 cm in diameter was observed on the skin of the right nasal wing (figure 1A). Cervical palpation revealed multiple adenopathies, the largest of which was in the right cervical chain, measuring approximately 3x5 cm, firm in consistency, mobile, not adherent to deep planes, painless, and without signs of inflammation (figure 1B).

Initially, she was evaluated by a pediatric surgeon who performed an excision of a right cervical lymph node and a histopathological study was performed, which described the lymph node parenchyma replaced by an inflammatory process with chronic granulomatous reaction, Langhans-type giant cells, and positive Ziehl-Neelsen staining (+++), concluding a result “compatible with chronic granulomatous tuberculous lymphadenitis.” A subsequent immunohistochemical study on the same paraffin blocks reported positivity for CD68 and CD163 and “weakly positive mycobacterium,” which was interpreted as “compatible with a chronic granulomatous inflammatory process of the tuberculous type.” Due to the discrepancy between the skin lesion and the TB diagnosis, the patient was reevaluated. Additional tests were requested to definitively rule out *M. tuberculosis* infection. The purified protein derivative (PPD) test resulted in 0.0 mm induration, and the interferon-gamma release assay (QuantiFERON-TB Gold Plus) was “NEGATIVE.” In addition, the posteroanterior chest X-ray showed no infiltrates or lesions consistent with active pulmonary TB.

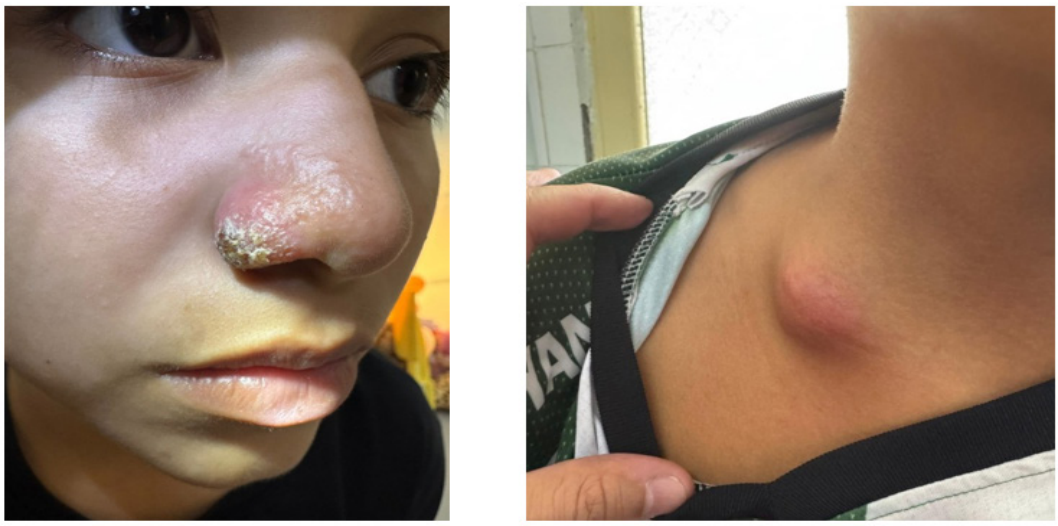

Figure 1. (A) Lesion on the right nasal wing. (B). Adenopathy with lymph nodes larger than 3 cm in diameter

Given the high suspicion of systemic mycosis, a sample of the nasal mucosal lesion was taken for mycological study. Direct microscopic examination with potassium hydroxide (KOH), performed by the National Center for Tropical Diseases (CENETROP), which provided the definitive diagnosis, which revealed thick-walled, birefringent yeasts with multiple peripheral buds, forming the pathognomonic image of a "steering wheel" or "ship's rudder" (Figure 2), identifying the agent as *Paracoccidioides brasiliensis*. The mycological culture was negative after two weeks of incubation. With these findings, the final diagnosis of Paracoccidioidomycosis, subacute (juvenile) form, with skin and lymphatic involvement, was established. Specific therapy with oral Itraconazole 200 mg/day was initiated. The patient showed favorable clinical progress within a few days after starting antifungal treatment.

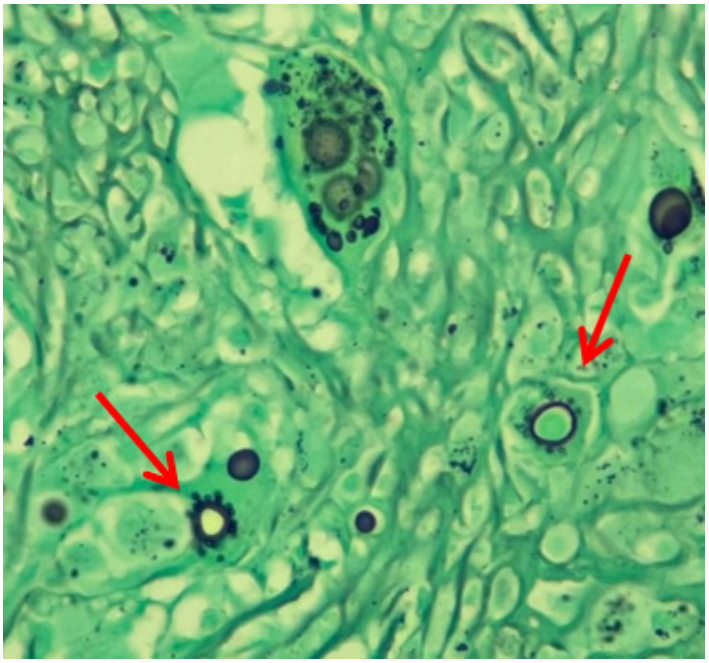

Figure 2. Lymph node biopsy and anatomopathological evaluation show a chronic granulomatous inflammatory process and fungi in the form of a "ship's rudder," *a* characteristic *red spot* of PCC

DISCUSSION

Although PCM is prevalent in the adult population, especially between the ages of 30 and 60 [7], the juvenile form (acute or subacute) accounts for between 5 % and 25 % of cases[11] and occurs in children, adolescents, and young adults, generally under the age of 30.[4,7] In contrast to the chronic form in adults, where pulmonary and mucocutaneous manifestations are prominent, the juvenile form is characterized by a more rapid and aggressive course, with a predominance of reticuloendothelial system involvement, manifested by generalized

lymphadenopathy, hepatosplenomegaly, and bone marrow dysfunction.[10] ·Our clinical case is relevant due to the rarity of the juvenile form of the disease and its presentation in females, which challenges the epidemiological and clinical characteristics classically described for PCM in adults.[10]

The simultaneous presence of visible skin lesions in the nasal region is an unusual manifestation in this clinical form and suggests an atypical presentation within the juvenile spectrum of paracoccidioidomycosis. Added to this is the presence of respiratory symptoms suggestive of clinical pulmonary involvement, a finding that, although it may be present, is less frequently reported in the acute/subacute form, in which extrapulmonary findings predominate. A distinctive feature of this case is its presentation in a female patient. It has been postulated that female hormones, such as 17-beta estradiol, exert an inhibitory effect on the transformation of the fungus from conidia to yeast, which is essential for the onset of infection, explaining the lower incidence in adult women.[12] Although PCM is markedly more common in men, with ratios ranging from 9:1 to 45:1 in the chronic adult form[1], the subacute or acute form tends to be distributed more evenly between the sexes.[9]In children, there is no significant difference, with a male-to-female ratio of approximately 1:1;[1] however, the hormonal influence of estrogen during puberty begins to generate the male predominance typical of the adult form, enhancing the atypical nature of the case.[4] Mucocutaneous lesions in PCM are common, becoming a frequent reason for consultation, affecting between 40 and 60 % of patients; painful ulcers with a grainy appearance and hemorrhagic spots (morphiform stomatitis) are observed on the oral mucosa,[1,2,6] as well as skin lesions such as papules, nodules, ulcers, and warts in the nasal area, which are slow to develop and asymptomatic.[12] In this patient, the mucocutaneous and lymphatic involvement is similar to the descriptions in the literature, highlighting the variability in the presentation of the disease.[2,7] Although pulmonary involvement is rare in the juvenile form, PCM is primarily a pulmonary infection.[5,8,10] The possibility of silent pulmonary involvement in the patient, despite the absence of prominent respiratory symptoms, where the juvenile form of the infection is usually asymptomatic, is consistent with findings in studies where up to 89 % of patients with extrapulmonary lesions had radiologically demonstrable pulmonary pathology. The polymorphism of PCM makes its differential diagnosis challenging, as it can mimic various pathological conditions, including neoplasms, such as carcinomas, squamous cell, pharyngeal, or oral; and acute systemic processes such as leukemia or lymphomas.[9,13] As well as granulomatous diseases and various infections, such as leishmaniasis, actinomycosis, blastomycosis, coccidioidomycosis, syphilis, leprosy, mucormycosis, sarcoidosis, and leprosy.[2,12,13,14] Tuberculosis is the most frequent differential diagnosis, due to the similarity of its clinical and radiological presentations, as well as reports showing the coexistence of PCM and tuberculosis in 10 to 30 % of cases[1]; other sources report ranges of 5,5 to 19 %.[15] In juvenile forms, it is often confused with lymphoproliferative syndromes, such as leukemia or lymphomas, due to marked lymphadenopathy and hepatosplenomegaly.[8,9]

The definitive diagnosis of PCM is established through laboratory tests, with direct microscopy of clinical samples being the fastest and most specific method.[3,8] Where the observation of spherical or oval double-walled yeasts with multiple budding, in the shape of a “steering wheel” or “Mickey Mouse” head, is pathognomonic. Histopathological study of biopsies reveals granulomas with the characteristic presence of the fungus. Cultures confirm the isolation of the fungus, although its growth is slow. Serological tests, such as agar gel immunodiffusion and complement fixation, are useful for diagnosis and follow-up.[6,11] Treatment is essential to control the disease and prevent sequelae.[4] Sulfa drugs were the first effective drugs; currently, itraconazole is the first-line treatment for mild to moderate forms.[1,8] For severe or disseminated forms, amphotericin B is the drug of choice, followed by maintenance therapy with azoles or clotrimazole. Treatment is prolonged, lasting from months to years, to prevent relapse.[6,8] In children, trimethoprim-sulfamethoxazole is commonly used because of its efficacy and availability.[9,13]

The rarity of juvenile PCM, especially in females, and its ability to mimic other more common diseases, such as tuberculosis or lymphomas, highlight the importance of high clinical suspicion in patients from endemic areas, even with atypical presentations. The detailed documentation of this case, with its clinical evolution and diagnostic confirmation, is a strength that contributes to the knowledge of this mycosis. The main lesson learned is the need to consider PCM in the differential diagnosis of lymphoproliferative syndromes and tuberculosis in the pediatric and adolescent population in endemic areas to ensure early diagnosis and timely treatment, which can prevent multisystem involvement and fatal outcomes.

CONCLUSIONS

Juvenile paracoccidioidomycosis represents a significant diagnostic challenge due to its variable clinical presentation and its ability to mimic other more prevalent pathologies such as tuberculosis and lymphoproliferative syndromes. This case illustrates the importance of maintaining a high index of clinical suspicion in adolescent patients from endemic areas who present with lymphadenopathy and mucocutaneous lesions, especially when tests for tuberculosis are negative. The presentation of a 16-year-old female patient with simultaneous skin and lymphatic involvement is an atypical manifestation within the spectrum of the juvenile form, emphasizing the clinical polymorphism of this systemic mycosis. Diagnostic confirmation by direct microscopic observation

of the yeast characteristics with multiple budding in a "steering wheel" pattern allowed timely initiation of specific antifungal treatment, resulting in a favorable clinical outcome. This case reinforces the importance of a broad differential diagnosis, the need for specific complementary tests in the event of clinical discrepancies, and highlights the fundamental role of direct mycological study as a rapid and definitive diagnostic method in paracoccidioidomycosis.

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CONSENT

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTION

Conceptualization: Carlos Alberto Paz-Román, Jhossmar Cristians Auza-Santivañez.
Data curation: Carlos Alberto Paz-Román.
Formal analysis: Carlos Alberto Paz-Román, Jaykel Evelio Gómez Triana.
Research: Jhossmar Cristians Auza-Santivañez, Carlos Alberto Paz-Román.
Methodology: Jhossmar Cristians Auza-Santivañez.
Project management: Carlos Alberto Paz-Román.
Resources: Diego Javier La Fuente Padilla.
Supervision: Jaykel Evelio Gómez Triana.
Validation: Marlon Carbonell González.
Visualization: Marlon Carbonell González.
Drafting – original draft: Carlos Alberto Paz-Román, Jhossmar Cristians Auza-Santivañez, Daniel Ramiro Elías Vallejos-Rejas, Diego Javier La Fuente Padilla, Marlon Carbonell González, Jose Luis Diaz-Guerrero, Leonel Rivero Castedo, Jaykel Evelio Gómez Triana.
Writing – review and editing: Carlos Alberto Paz-Román, Jhossmar Cristians Auza-Santivañez, Daniel Ramiro Elías Vallejos-Rejas, Diego Javier La Fuente Padilla, Marlon Carbonell González, Jose Luis Diaz-Guerrero, Leonel Rivero Castedo, Jaykel Evelio Gómez Triana.