Paracoccidioidomycosis of external genitalia: report of six new cases and review of the literature *

Paracoccidioidomicose de localização genital externa: relato de seis novos casos e revisão da literatura

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Abstract: BACKGROUND: Paracoccidioidomycosis is a systemic mycosis of dermatological interest due to the frequency of cutaneous and mucosal lesions. The involvement of the external genitalia is extremely rare and few cases have been reported.
OBJECTIVE: To study the prevalence of external genitalia lesions in paracoccidioidomycosis patients, identify clinical characteristics and compare with what is observed in the specific literature.
METHODS: This is a cross-sectional, descriptive study, with focus on paracoccidioiodomycosis patients with external genitalia lesions. The demographic and clinical aspects of cases were compared with what has been reported so far on LILACS, SciELO e MEDLINE data bases.
RESULTS: Data of 483 cases of paracoccidioidomycosis were studied in a 42-year period. Six (1.2%) patients showed specific lesions on external genitalia. Five patients were male with mean age of 47.2 years and all of them presented with the chronic multifocal clinical form. Only one, a 15-year-old female patient was observed who showed a subacute clinical form, juvenile type.
CONCLUSIONS: Compromise of the genitourinary tract among paracoccidioidomycosis patients is rare and even rarer when only the external genitalia are considered. As observed in the classical picture of paracoccidioidomycosis patients, the male gender and the chronic multifocal clinical form prevailed in the present study.
Keywords: Dermatology; Genitalia; Mucous membrane; Paracoccidioidomycosis

Resumo: FUNDAMENTOS: Paracoccidioidomicose é micose sistêmica de interesse dermatológico pela freqüência de lesões tegumentares. Sua localização em genitália externa é extremamente rara e pouco descrita.
OBJETIVOS: estudar a prevalência de lesões de paracoccidioidomicose de localização genital, identificar suas características clínicas e compará-las com a literatura específica.
MÉTODOS: estudo descritivo, transversal, de série de casos, com inclusão de casos com lesões específicas de paracoccidioidomicose de localização genital externa, estudo das características demográficas e clínicas dos casos, confrontados com dados de revisão da literatura nas bases LILACS, SciELO e MEDLINE.
RESULTADOS: foram revisados de 483 pacientes de paracoccidioidomicose diagnosticados no período de 42 anos. Seis (1,2%) pacientes apresentavam lesão específica de genitália externa. Cinco eram do sexo masculino com idade média de 47,2 anos e todos com a forma crônica multifocal da doença, O único caso do sexo feminino, de 15 anos de idade, apresentava a forma subaguda, tipo juvenil.
CONCLUSÕES: o comprometimento do trato geniturinário na paracoccidioidomicose é raro e mais ainda quando se considera apenas as localizações de genitália externa. Como na paracoccidioidomicose clássica, o sexo masculino e a forma crônica da doença predominaram na amostragem estudada.
Palavras-chave: Dermatologia; Genitália; Membrana mucosa; Paracoccidioidomicose

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INTRODUCTION

Paracoccidioidomycosis is a systemic mycosis of acute, subacute or chronic progression, caused by a thermodimorphic fungus, the *Paracoccidioides braziliensis*.[1] Paracoccidioidomycosis is a disease prevalent in most of the country, with greater frequency in the states of the southeast and midwest regions, affecting mainly rural workers.[1] Contagion occurs through inhalation and it is admitted that the majority of the infected do not develop the disease, which remains in a latent state, with quiescent foci sheltering viable fungi. The clinical manifestations are grouped in forms denominated acute-subacute (juvenile type) and chronic.[2] The acute-subacute forms affect young patients, have monocyte-macrophage system tropism and are clinically manifested by lymph node adenomegaly and hepatosplenomegaly.[2,3] The chronic form is typical of adults and is characterized by integumentary-pulmonary involvement. Immunosuppressed patients and those suffering from neglected disease or who received a late diagnosis, the trend is for the illness to spread.[2,3] Classically, the involvement of the genitourinary tract occurs in patients with the chronic adult disease form and has rarely been reported.[4]

Fava Netto & Del Negro (1954) published what would be the first report of *in vivo* diagnosis of testicular and epididymal paracoccidioidomycosis, as the few existing reports were part of necropsy findings.[5] In the reported case, the tumoral testicular lesion formed a fistula in the scrotum, externalizing as a cutaneous ulcer, 3 cm in diameter. The patient presented associated pulmonary disease and the authors concluded that the testicular localization was rare, a product of the hematogenous dissemination of the illness. Brito & Caprini (1958) reported what would be the first case of prostatic localization, diagnosed from biopsy of tumoral lesion suspected as neoplasm.[6] The authors included an interesting parallel between the rarity of prostate involvement in paracoccidioidomycosis, in contrast with the relative frequency of involvement in blastomycosis, prevalent in North America. In 1966, Londero & Fabrício published the first report on a case of penile lesion, described as an ulcerated lesion of moriform aspect similar to the commonly observed in oral mucosa lesion.[7] The second publication on prostate involvement in paracoccidioidomycosis occurred in 1969 and was also diagnosed during investigation of a possible neoplasm by biopsy.[8] In the following years, few reports of testicular or prostatic localization of lesions were published in the national or international literature.[9-15]

Cechella and cols. (1982) reported a total of seven cases of paracoccidioidomycosis of the genitourinary tract affecting male patients, six with testicular and/or epididymal lesion and one case with prostate lesion.[16] All of the patients presented systemic disease and in only one of the cases a complaint of testicular pain and scrotum edema was the primary reason for the appointment. In the other patients the specific involvement was identified by secondary complaint or by finding in tests.

Campos and cols. (1986) published what would be the first case of paracoccidioidomycosis of the female genital tract, with a specific lesion in the ovary and endometrium, while the patient also presented a specific pulmonary lesion.[17] The involvement by the *P. braziliensis* was found in anatomopathological exam, in material obtained during surgical intervention in acute abdomen, in patient already diagnosed as having paracoccidioidomycosis. Another report of female genital tract lesion was published in Venezuela by Guarnizo and cols. (1987), with the patient presenting a pulmonary symptom complex diagnosed as paracoccidioidomycosis and a concomitant specific lesion on the cervix and external genitalia.[18]

Tomimori-Yamashita and cols. (1997) published a case of a patient with vegetating verrucous lesions by paracoccidioidomycosis, inguinal and scrotal localization, apparently associated only with specific nasal mucosa lesion.[19]

Severo and cols. (2000) reported the majority of the series of cases of genitourinary tract involvement in paracoccidioidomycosis, with eleven cases, all in male patients.[4] The authors included the testicular, epididymal and prostatic localizations in the sample. Only two cases were described as specifically involving the external genitalia, in the penile localization. In every case there was associated systemic involvement, all of them with images suggestive of pulmonary compromise. In the same publication, the authors revised cases already published and mentioned as previously published only one case of penile lesion and two cases of scrotum lesion with cutaneous manifestation. The other localizations cited in the mentioned study were testicular and epididymal, with a total of 14 cases, and seven previously described cases of prostate involvement. The authors do not mention nor cite any case of female genital tract involvement.

In face of the rarity of reports of genitourinary tract paracoccidioidomycosis and particularly of the extreme rarity of cases involving the external genitalia, the authors have the objective of identifying those specifically involving the external genitalia, in a historical series of cases of paracoccidioidomycosis diagnosed at a Dermatology service in a tertiary referral teaching hospital.

CASE STUDY AND METHODS

This is a descriptive, cross-sectional study of

paracoccidioidomycosis cases diagnosed at the Dermatology service of the School of Medicine of São Paulo State University (Universidade Estadual Paulista - FMB-Unesp), in the period between 1967 and 2009. The cases were confirmed by the visualization of the agent by means of direct, culture or anatomopathological exam. All of the cases filled out a specific protocol at the time of diagnosis, which includes a comprehensive clinical examination and identification of the affected organs and systems. Only the cases located on external genitalia will be object of this publication. In cases of interest, the clinical classification, which organs and systems were affected, which therapy was chosen and disease progression were studied

RESULTS

A total of 483 protocols of cases diagnosed in the period were revised. Six (1.2%) patients met the inclusion criteria, with specific paracoccidioidomycosis of external genitalia lesions. Five patients were male and only one was female. The ages of male patients ranged between 38 and 60 years, with an average of 47.2 years. The female patient was 15 years old. All of the male patients presented the chronic adult form, with associated pulmonary lesion, according to the thorax radiographic image. The female patient presented the subacute juvenile form, with hepatosplenic lesion and a lymph node mass of the hepatic hilus. Lesion localizations and other data are described in chart 1. The predominant clinical pattern was a shallow ulcerated lesion, with or without hemorrhagic dots evident and of different sizes (Figures 1, 2 and 3). Only one patient (case 3) presented a tumoral-ulcerated lesion (Figures 4 and 5). The histological image of case 3 is reproduced in figure 6.

In only one case the genital lesion (case 3) was the reason that led the patient to make an appointment for the first time, The clinical diagnosis when he presented at the Urology clinic was penile squamous cell carcinoma. The female patient was first admitted to the Gastrosurgery clinic with the diagnosis of jaundice, etiology to be clarified. When she was admitted and a vesical probe was inserted, a nodular and ulcerated lesion was detected on the vulva, at first suspected as being a syphilitic lesion. A joint consultation with the Dermatology clinic allowed a correct diagnosis by direct exam, confirmed by the histological exam of a lesion biopsy; The jaundice, later confirmed, was a consequence of lymph node paracoccidioidomycosis obstructing the hepatic hilus.

The demographic, clinical and progression data for all of the patients included in the present study are shown in chart 1.

Figure 1: Genital paracoccidioidomycosis: ulcer with seropurulent secreting bottom, with infiltrated borders compromising the frenulum and the glans. Histopathological diagnosis

Figure 2: Genital paracoccidioidomycosis: shallow ulcer with rare hemorrhage dots and erythematous halo, located on the glans

Figure 3: Genital paracoccidioidomycosis: shallow ulcer with rare hemorrhage dots and infiltrated base, located on the mucosal prepuce side

Figure 4: Genital paracoccidioidomycosis: tumoral lesion with ulcerated area on the mucosal side of the prepuce and glans. Hemorrhage dots can be observed in the ulcer bed

Figure 5: Genital paracoccidioidomycosis: same patient of figure 4 after relapse, presenting tumoral lesion, infiltrated and swollen, compromising the entire prepuce. There are also shallow ulcerated lesions, with hemorrhage dots located on the prepuce and glans

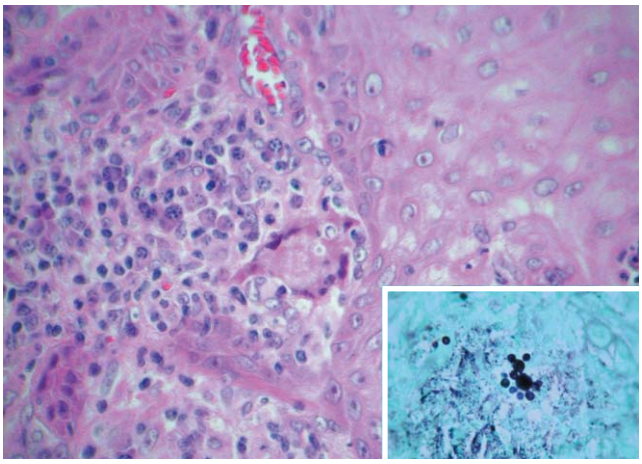

Figure 6: Paracoccidioidomycosis: same patient of figure 4. Hyperplasia of the epidermis, inflammatory pyogranulomatous infiltrate with giant cell and fungal structures in the cytoplasm (HE X 400). In the detail, image of the *Paracoccidioides braziliensis* in typical budding (Prata X 200)

DISCUSSION

The genital tract involvement in paracoccidioidomycosis is very rare,[4] but the scarcity of reports may be connected with the absence of systematic investigation of cases when paracoccidioidomycosis is diagnosed. One example of the importance of protocols that routinely systematize the detection of affected organs and systems is the variability regarding the frequency of cutaneous involvement by paracoccidioidomycosis, which fluctuate widely even in publications from university services.[20] Such disparity of results is fruit of the emphasis or not on the comprehensive clinical and imaging examination of diagnosed cases. Anyway, several inferences may be outlined based on this study and data in the literature: i- the genital tract involvement is associated with the manifestation of the disease at a distant point, usually pulmonary involvement. The lesions occur, therefore, in a context of dissemination of the disease from a systemic focus. ii- the majority of reports suggest that the identification of the involvement resulted from secondary complaints in the context of paracoccidioidomycosis, already diagnosed. Or, as a consequence of the investigation with another diagnostic suspicion in mind, and that only rarely the genital tract lesion motivated the first medical appointment. iii- testicular, epididymal and prostatic lesions are expressed, in the majority of cases, by tumoral lesions, leading to the initial diagnosis of neoplasm. iv- the external genitalia lesions were manifested as ulcers or vegetating lesion, as if reproducing the observed in cutaneous-mucosal lesions in other localizations. However, the ulcerated lesions in the present case study did not always present the same typical characteristics of moriform aspect usually seen in the oral mucosa. The differential diagnosis should be made with sexually transmitted diseases, mainly syphilis, if there is compatible history time, and with donovanosis, given certain clinical similarity. But the differential diagnosis should include penile squamous cell carcinoma, considering the aggressive aspect of the lesion, compatibility with how long the disease has been present, and differential diagnosis with vegetating lesion as well. In the immunosuppressed patient with HIV/AIDS the differential diagnosis includes histoplasmosis, disseminated sporotrichosis, syphilis and even chronic mucocutaneous herpes.

The diagnosis, as in the classical paracoccidioidomycosis, should be demonstrated by visualization

CHART 1: Demographic and clinical data of external genitalia paracoccidioidomycosis patients diagnosed between 1967 and 2009 at the Dermatology Service, FMB-Unesp

Case	Age	Genital localization	Diagnosis	Serology	Other localizations	Progression
1	47	Penis-frenulum	Histological	ELISA +	Pulmonary, mucosal, cutaneous, intestinal	Death by PCM
2	15	Vulva (labia majora)	MD, Histological	ELISA +	Hepatosplenic, lymph nodes, intestinal	Death by sepsis
3	38	Penis – balanopreputial fold Prepuce, glans	MD, Histological	ID +	Pulmonary, mucosal, lymph nodes	Cured with itraconazol
3	51	Penis-frenulum	Histological	ID +	Pulmonary, mucosal	Cured with itraconazol
4	60	Penis - glans	Histological	ID +	Pulmonary, suprarenal, mucosal, cutaneous	Cured with itraconazol
5	40	Penis - glans	Histological	ID +	Pulmonary, mucosal	Cured with sulfamidics

of the agent, according to indisputable identity characteristics and, when possible, corroborated by culture. Molecular methods present good sensibility and high specificity and may constitute an extremely useful tool to clear any doubts. The treatment will be the one recommended for systemic disease, with adequate options for each case according to the established consensus.[21]

The reasons why the female sex is little represented in this case study reflect, in part, the greater prevalence of the illness in the male sex, emphasized by the lack of knowledge that the female genital tract may be prone to specific involvement and also by the nonexistence of routine genital examination, unless a specific complaint is made by the patient.

CONCLUSIONS

The authors report a series of paracoccidioidomycosis cases affecting the genitourinary tract, with focus on external genitalia lesions. The six cases reported (five male patients) corresponded to 1.2% of a 483-patient sample diagnosed in the 42-year period in a Dermatology Service of the Teaching Hospital of the State of São Paulo, Brazil. The clinical aspect was of ulcerated lesions or ulcerated vegetating lesion, with the main localization on the glans and frenulum. In every case, the diagnostic confirmation resulted from visualization of the agent, in anatomopathological examination. ❑

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