

## PERIODONTAL ASPECTS OF THE JUVENILE FORM OF PARACOCCIDIOIDOMYCOSIS

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### SUMMARY

Three cases of the juvenile form of paracoccidiodomycosis are reported. Emphasis has been given to the oral manifestations, particularly the periodontal involvement. The main periodontal findings were: generalized and progressive alveolar bone destruction leading to gingival recession with exposure of the tooth roots, and spontaneous tooth losses. The gingival mucosa was predominantly smooth, erythematous and slightly swollen. These aspects, although rare, may be the earliest signs of the disease and sometimes its only manifestation.

**KEYWORDS:** Paracoccidiodomycosis; Oral manifestations; Periodontal infection.

### INTRODUCTION

Paracoccidiodomycosis (PCM) is an infectious disease of great importance in South America, mainly because of its high prevalence, its endemic behavior and its high potential for morbidity<sup>1,2</sup>. It is caused by the fungus *Paracoccidioides brasiliensis*, the habitat of which is believed to be the soil of endemic areas<sup>3</sup>. In Brazil these areas are mostly confined to the Central and South-East regions.

This disease has been recently classified into two forms, acute and chronic, based upon its clinical behavior<sup>8</sup>. The chronic form, also referred to as adult type, produces clinical manifestations that may vary from mild to severe involvement of the organism. In the acute or juvenile type, however, only moderate and severe involvement has been described.

The chronic form of PCM occurs almost exclusively in adult males who, in general, are of lower socioeconomic status and dwellers of rural areas. The disease may affect any organ or tissue of the organism, although the lungs are the most affected site. Oral manifestations in this form are very often present and can be easily recognized. They are typically characterized by ulcerations of mulberry-like appearance, first described by AGUIAR-PUPO in 1936<sup>11</sup>.

The acute, juvenile type, is a rare form of PCM, accounting for approximately 4% of the reported cases<sup>4, 10</sup>. It affects mostly children and young adults of both sexes. These young patients have the same background as adults: they are usually poor and

reside in endemic areas. But their clinical profile is different. The juvenile form of the disease usually produces a more aggressive clinical course involving predominantly the macrophage phagocytic system where the principal manifestations are: lymphadenopathy, hepatosplenomegaly, gastro-intestinal dysfunction and bone lesions<sup>2, 8</sup>. In contrast with adults, young patients rarely develop lung and oral mucosa lesions.

The scarcity of descriptions in the literature concerning the oral manifestations of the juvenile type of PCM prompted the authors to document three cases of this disease with emphasis on the clinical pattern of the observed periodontal lesions.

### CASE REPORTS

#### Case 1

An 18-year-old white girl was referred to the Hospital das Clínicas, Departamento de Dermatologia da Faculdade de Medicina da Universidade de São Paulo, with widespread cutaneous lesions that had been present for 45 days. On admission she reported that over the last two years she had been unsuccessfully treated for a persistent cervical lymphadenopathy, and that ninety days before the present consultation she had developed erythematous skin lesions, which turned into ulcers, and oral lesions had appeared one month before. She also complained of dizziness and dyspnea.

Physical examination showed a weak but afebrile and conscious patient. Her skin presented multiple ulcerations of

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different size and shape with a granular surface. These lesions were mainly distributed over the face, cervical, abdominal and femoral regions. The lymph nodes of the cervical, axillary and inguinal branches were swollen, painful and mobile. Abdominal palpation revealed hepatosplenomegaly. Chest radiography was normal.

The diagnosis of paracoccidioidomycosis was made by the observation of *P. brasiliensis* on histologic and direct examination of specimens obtained from skin and oral lesions. Laboratory findings were: erythrocytes (2,900,000/mm<sup>3</sup>), hemoglobin (6.3 g/dL), leukocytes (13,700/mm<sup>3</sup>), platelets (160,000/mm<sup>3</sup>), Na (132 mEq/L), K (3.6 mEq/L). Specific immunologic tests showed positive reaction for immunodiffusion; counterimmunoelectrophoresis titers were 1:8 and the complement fixation reaction was 29.5.

The patient was initially treated with slow releasing sulphonamide (400 mg/day for 35 days), but the clinical response was poor. As a replacement therapy she was given Amphotericin B (AmB), with a total dose of 1,565 mg, which proved to be effective. She was then dismissed with maintenance treatment of 200 mg/day of ketoconazole.

#### Case 2

A 12-year-old black boy was seen at the same Hospital das Clínicas, with a 1.5-year history of multiple ulcerated skin lesions. His clinical picture had begun with the simultaneous appearance of a painful nodule on his submandibular area and a proliferative lesion on his palatal gingival mucosa. Later on he developed cutaneous ulcerations and other lymphadenopathies were also noted, at which time he was treated with antibiotics without any improvement. Additionally, he developed intense anaemia for which he was given blood transfusion. Since the beginning of the disease he had lost 10 kg.

Physical examination showed a debilitated patient with generalized cutaneous ulcerations of erythematous-granular surface. He had multiple enlarged lymph nodes and some of them exhibited signs of fistulation. His abdomen was soft and painless, with no evidence of hepatomegaly or splenomegaly. Chest X-rays were normal.

Histologic examination of biopsy performed on skin and oral lesions revealed the presence of *P. brasiliensis*. Direct examination and culture of pus material secreted from lymph nodes were also positive for *P. brasiliensis*. Laboratory results at the time of admission showed erythrocytes (4,380,000/mm<sup>3</sup>), hemoglobin (10.1 g/dL), leukocytes (6,100/mm<sup>3</sup>), platelets (160,000/mm<sup>3</sup>), Na (133 mEq/L), K (4.3 mEq/L). Anti-*P. brasiliensis* serologic assays were positive for immunodiffusion; counterimmunoelectrophoresis titers were 1:32 and the complement fixation was 15.5.

With the diagnosis of paracoccidioidomycosis the patient received initially 400 mg/day for 40 days of slow releasing sulphonamide, but no improvement was noticed. Then he was

given ketoconazole (200 mg/day), but the clinical response was also poor. Finally, he was treated with AmB (320 mg as a total dose) and his recovery was satisfactory. After 5 months of hospitalization the patient was dismissed with 100 mg/day of ketoconazole and returned periodically for clinical and serological evaluations.

#### Case 3

A 16-year-old white girl was admitted to the clinic of Oral Diagnosis, Faculdade de Odontologia da Universidade de São Paulo, for evaluation of a 1.5-year history of gingival bleeding. She recalled that her symptoms had initiated with bleeding, redness and pain on the upper left side of her gingiva. Furthermore, as the process extended to the other areas of the gingiva, she started noticing that many of her teeth were loosening. Eventually, she had four of her teeth extracted and one she lost spontaneously. At that time she was treated with antibiotics and dental root scaling, but no improvement was obtained. Her medical history only revealed a single episode of iron deficiency anaemia at the age of 9.

Physical examination showed a conscious and afebrile patient. On the left side of her face there was a hard, erythematous plaque-like lesion. Oral examination showed an extensive loss of the alveolar bone with exposure of the dental roots. The gingival mucosa surface exhibited a smooth erythematous aspect. Nontender and mobile cervical lymph nodes were also present.

The diagnosis of paracoccidioidomycosis was obtained by histologic examination upon gingival biopsy, which showed the presence of *P. brasiliensis*. The patient was then referred to hospital for a more appropriate clinical and laboratory evaluation. She was free of any other lymphadenopathies; her liver and spleen were normal size. Chest X-ray and CT scanning were normal. Blood cell values were within normal ranges; anti-*P. brasiliensis* immunological tests showed positive reaction for immunodiffusion, and titers for counterimmunoelectrophoresis and complement fixation reactions were 1:64 and 1:8 respectively.

Her ongoing treatment is based on the administration of ketoconazole (400 mg/day) and the clinical response has been very satisfactory after 11 months of therapy, although her serology still indicates disease activity. She is currently receiving 200 mg/day of ketoconazole and being periodically monitored.

#### THE ORAL FINDINGS

The most striking oral aspect observed in the three reported cases was an extensive gingival recession accompanied by the exposure of the tooth roots (Figs. 1, 2 and 3). Progressive tooth mobility, which eventually caused some spontaneous tooth losses, was also an important sign found. The gingival mucosa appeared mainly smooth, erythematous, and slightly swollen. Small ulcerated areas covered by tiny granular tissue on the gingival mucosa were present in one of the patients (Fig. 2). Periodontal pockets were absent regardless of the extension of gingival recession. Intraoral radiographic examinations showed

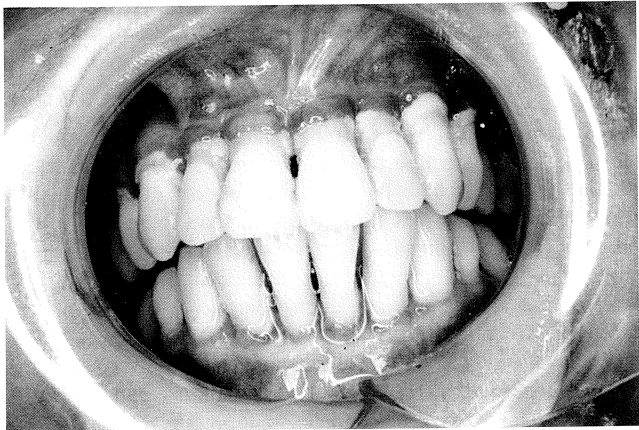


Fig. 1 – Case 1. Extensive and generalized gingival recession.

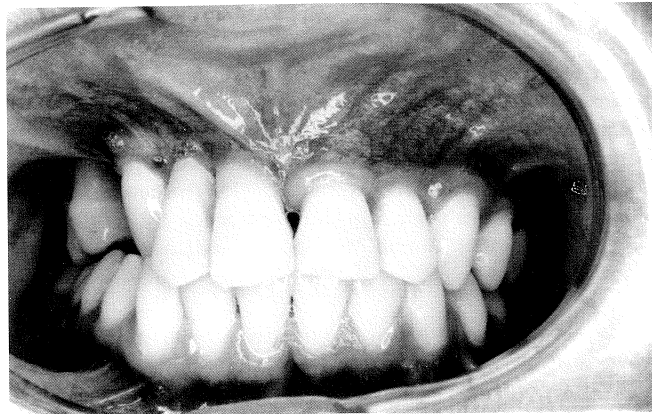


Fig. 4 – Case 2. The oral aspect after resolution of the mucosa and gingival lesions. The exposure of the tooth roots is now more visible.

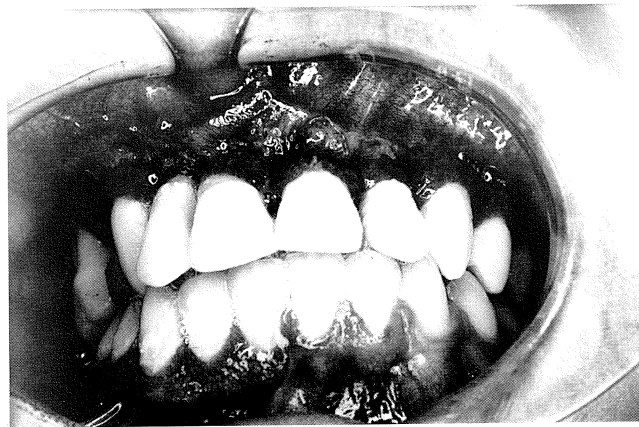
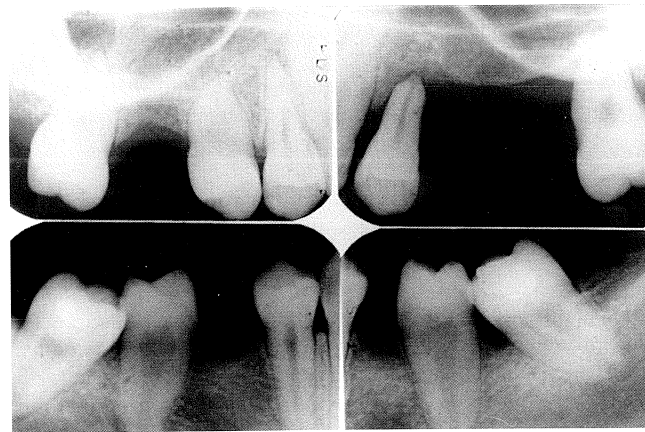


Fig. 2 – Case 2. This picture shows granular ulceration on the upper vestibular mucosa. The gingival mucosa appears erythematous with areas of recession. Small ulcerations are also seen on the mandibular gingiva.



Fig. 3 – Case 3. Erythematous aspect of gingival mucosa accompanied by gingival recession. Acrylic splinting for maintaining the teeth in position had been applied by her dentist.



Figs. 5 and 6 – Radiographic aspects of Case 3 (Fig. 3) showing an extensive loss of the alveolar bone.

varying degrees of periodontal bone destruction of the horizontal pattern (Fig. 5 and 6). Characteristic oral mucosa lesions of PCM, i.e., mulberry-like ulcers with pinpoint hemorrhages, were seen in only one patient (case 2), affecting the upper vestibular mucosa and the hard palate.

## DISCUSSION

Paracoccidioidomycosis is a complex infectious disease which occurs endemically in South America. The disease has been classified into two types: the adult form (chronic type) and the juvenile form (acute type). Adults, in particular adult males,

are the most affected individuals, while juvenile patients are much less susceptible. This has been explained by the more effective immune system of the younger patients which enables them to control the fungus proliferation and the spread of the infection<sup>1,2</sup>. The pathogenic mechanism of PCM in adult patients probably results from the reactivation of a quiescent focus, which is present since the early ages. The development of the disease in children is usually preceded by a failure or breakdown in their immune system before their exposure to *P. brasiliensis*.

Few studies have described oral manifestations of PCM in young patients, perhaps owing to the rarity of the disease in young individuals. According to a large study<sup>4</sup>, in which the medical records of 1899 PCM patients were reviewed, 52 of them fit the criteria for the juvenile form of PCM, and among these patients only 9 presented oral lesions. Unfortunately the characteristics of the oral involvement were not reported in that study.

Reports on oral manifestation of PCM are therefore mostly restricted to the adult form<sup>5,9</sup>. As it was pointed out earlier in this paper, the involvement of the oral mucosa in this form is highly frequent, and has importance for the diagnosis since its clinical oral signs are very characteristic. Ulcerations covered by a tiny granular tissue containing pinpoint hemorrhages, which characterize the mulberry-like appearance, are the chief identifying oral aspects for this disease. There seem to be no specific oral mucosa sites for its manifestation, although the periodontal tissues are significantly affected, since the fungus is frequently isolated in this location even in the absence of gingival lesions<sup>7</sup>.

In a study of 37 cases of PCM<sup>9</sup>, mostly adult patients, 26 had oral lesions showing a variable degree of involvement of the mucosa sites, which included lip, alveolar, hard and soft palate, and gingival mucosas. Of particular interest were the periodontal lesions, which were the main purpose of that paper. The author's findings included: ulcerations on the gingival mucosa, periodontal pockets, thickening of the periodontal ligament space, and loss of the alveolar cortical bone (lamina dura).

That and other articles<sup>5,6</sup> on PCM reported findings different from those given here. The pattern of the periodontal manifestations observed in our juvenile patients combined a progressive destruction of the alveolar bone with recession of gingival mucosa. No periodontal pocket was detected. Also absent, at least on the gingival mucosa, were the mulberry-like ulcerations, which were present in only one patient and on the vestibular and hard palate mucosas. Lesions exhibiting the characteristics described here, whenever they are encountered, may very well be an indicator of an underlying PCM infection. To confirm the diagnosis, histologic examination of the affected gingival tissue has proved to be an effective method for the identification of *P. brasiliensis*. Although we can not assert that these periodontal alterations are unique to juvenile PCM, due to the fact that other diseases like Langerhans cells histiocytosis and juvenile periodontitis may exhibit similar manifestations, it is important for clinicians to be acquainted with this sort of periodontal lesion, which may be helpful for an early diagnosis of PCM.

## RESUMO

### Aspectos periodontais da forma juvenil da paracoccidioidomicose

Três casos da forma juvenil da paracoccidioidomicose são relatados. Especial ênfase foi dada com relação às manifestações bucais, particularmente no que diz respeito ao envolvimento periodontal. Os principais achados periodontais foram: destruição progressiva e generalizada do osso alveolar causando acentuada retração gengival e exposição das raízes dentárias. Mobilidade dentária e perda espontânea de alguns dentes constituíram também sinais clínicos importantes. A mucosa gengival apresentava-se lisa, eritematosa e superficialmente edemaciada. Pequenas áreas de ulceração com finas granulações foram observadas na gengiva de um dos pacientes. Estes aspectos, embora raros, podem representar os primeiros sinais da paracoccidioidomicose juvenil e, às vezes, sua única manifestação.

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