

DISSEMINATED AMERICAN MUCO-CUTANEOUS LEISHMANIASIS CAUSED BY
LEISHMANIA BRAZILIENSIS BRAZILIENSIS IN A PATIENT WITH AIDS:
A CASE REPORT

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The authors report a case of culture-proven disseminated American muco-cutaneous leishmaniasis caused by Leishmania braziliensis braziliensis in an HIV positive patient. Lesions began in the oropharynx and nasal mucosa eventually spreading to much of the skin surface. The response to a short course of glucantime therapy was good.

Key words: muco-cutaneous leishmaniasis – HIV infection

CASE REPORT

A 36-year-old male from the state of Pernambuco, Brazil was referred to the Infectious Diseases outpatient unit on 16 October 1990 by the otolaryngologist due to a one month ulcerative lesion involving the pharynx and soft palate. He denied any other complaint, except soreness at the site of a previous biopsy which suggested paracoccidioidomycosis. He was already taking sulfamethoxazole-trimethoprim (SMZ + TMP) since 30 September. He looked healthy except for an ulcerative lesion on his soft palate, a slight infiltration on the edge of the nostrils and a few palpable lymph nodes in the cervical region. The hematocrit was 36.6% and the white cell count 4.300/mm³ with 46% lymphocytes and a erythrocyte sedimentation rate (ESR) of 85 mm. Skin tests showed a depressed cell mediated immunity (PPD 2UT – zero, candida 2 mm, trichophyton 3 mm, SK – zero). His sputum disclosed *Candida* sp. and no acid fast bacilli.

On 16 November he felt better but oropharyngeal candidiasis was noticed. On 21 December he complained of having caught a

“cold” that began two weeks before with a low grade fever on the first two days. He also complained of nasal obstruction and redness and soreness inside his nose and throat.

On physical examination the nose appeared enlarged and red with small papules on the edge of the left nostril. The left maxillary sinus was tender on pressure and the oropharyngeal candidiasis had increased. Mycostatin was started.

On 7 January all the symptoms had worsened, the fever had returned, nasal lesions were more prominent and there were papules on the upper limbs. Maxillary sinusitis was diagnosed on X Ray.

Biopsies of skin and pharyngeal lesions were done. The previous biopsy was also revised and amastigotes were seen in all histological sections.

The patient was admitted to hospital on 24 January 1991. On physical examination he was found to have papules and nodules scattered over the face, body and limbs. The nose was swollen and of purplish red color. The nasal mucosa was erythematous and the nasal septum was involved. Papules and nodules, of varying size showing central necrosis (pustules) were seen on the ears, hands and penis giving the patient a striking varicelliform appearance. (Figs 1, 2). The oral mucosa showed an

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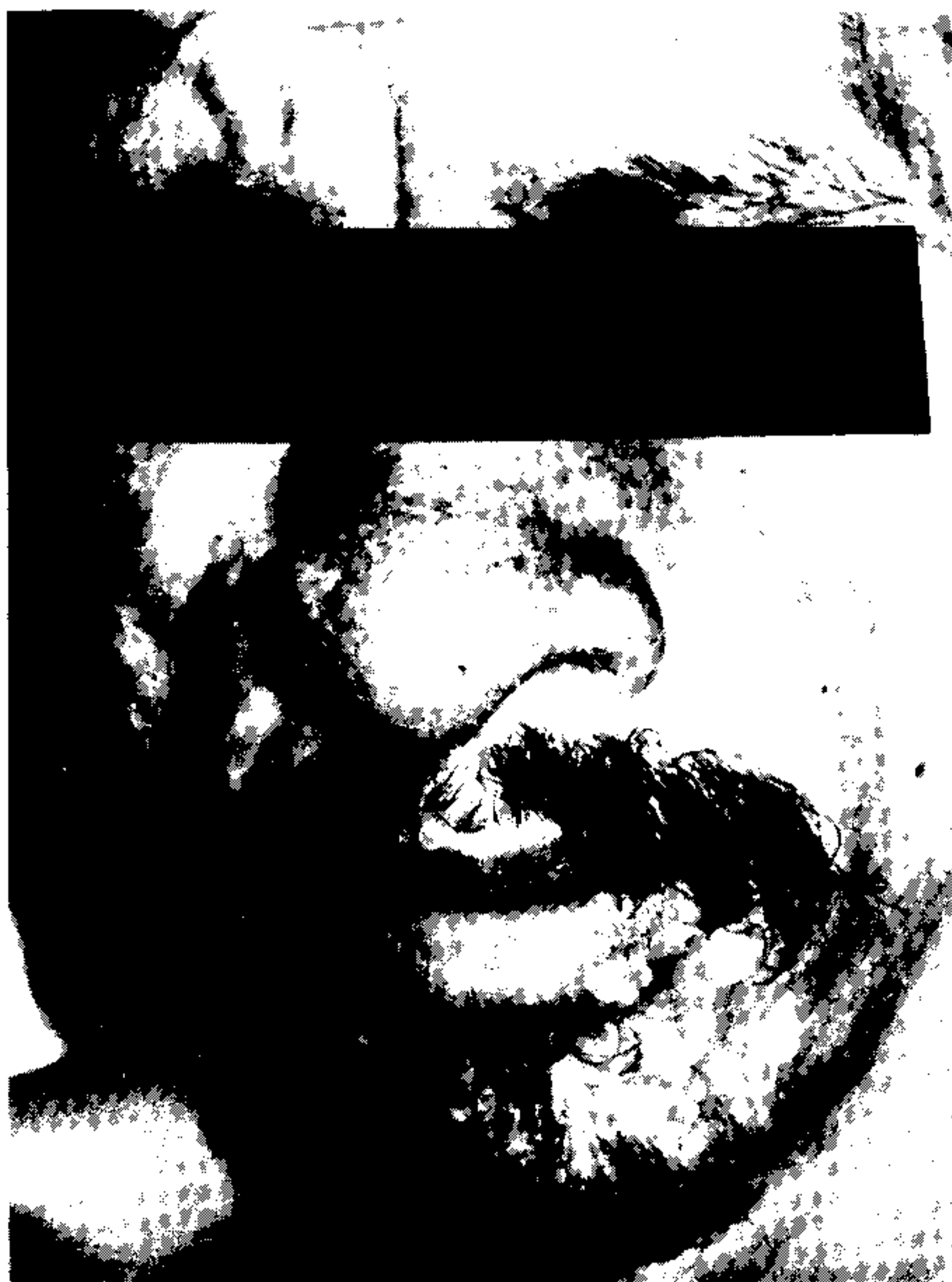


Fig. 1: patient's face. The nose is swollen and papules are scattered mostly on the forehead, chin and around the mouth and nostrils.

erythematous palate with a whitish exudate covering the whole tongue. The glans penis was red with a white mucoid secretion. Visceral involvement was not observed as revealed by ultrasonography which showed no enlargement of the liver, spleen or lymph nodes.

Laboratory examination revealed a white blood cell count of $4,400 \text{ mm}^3$ (with 76% neutrophils, 6% eosinophils, and 17% mononuclear lymphocytes), ESR 110 mm, albumin 3.4 g% and globulin 5 g%. A VDRL reaction was negative as well as the leishmanin skin test, but IG anti-leishmania antibody titer was 1/180 using an indirect immunofluorescence technique (IFAT).

Anti-HIV antibody titers were detected using both the Elisa and IFAT tests (Elisa: 2.000; cut off: 0.299).

Cultivation of a skin lesion in blood agar yielded numerous promastigotes that were further identified as *Leishmania (Viannaia) braziliensis* (Lvb). The parasite isolate was characterized by radioimmune binding assay using specific monoclonal antibodies, as well as by enzyme electrophoresis analysis (Grimaldi et al., 1991).

Cellular immune response of the patient was depressed as shown by a CD4/CD8 inversion and a diminished *in vitro* response to mitogens and specific antigen as described elsewhere (Da-Cruz et al., 1992).

Histopathological examination of the cutaneous lesions displayed an intermediate type lymphoplasmocytic infiltrate with giant cells as well as neutrophils. Amastigotes were easily visualized in H & E sections from the bi-

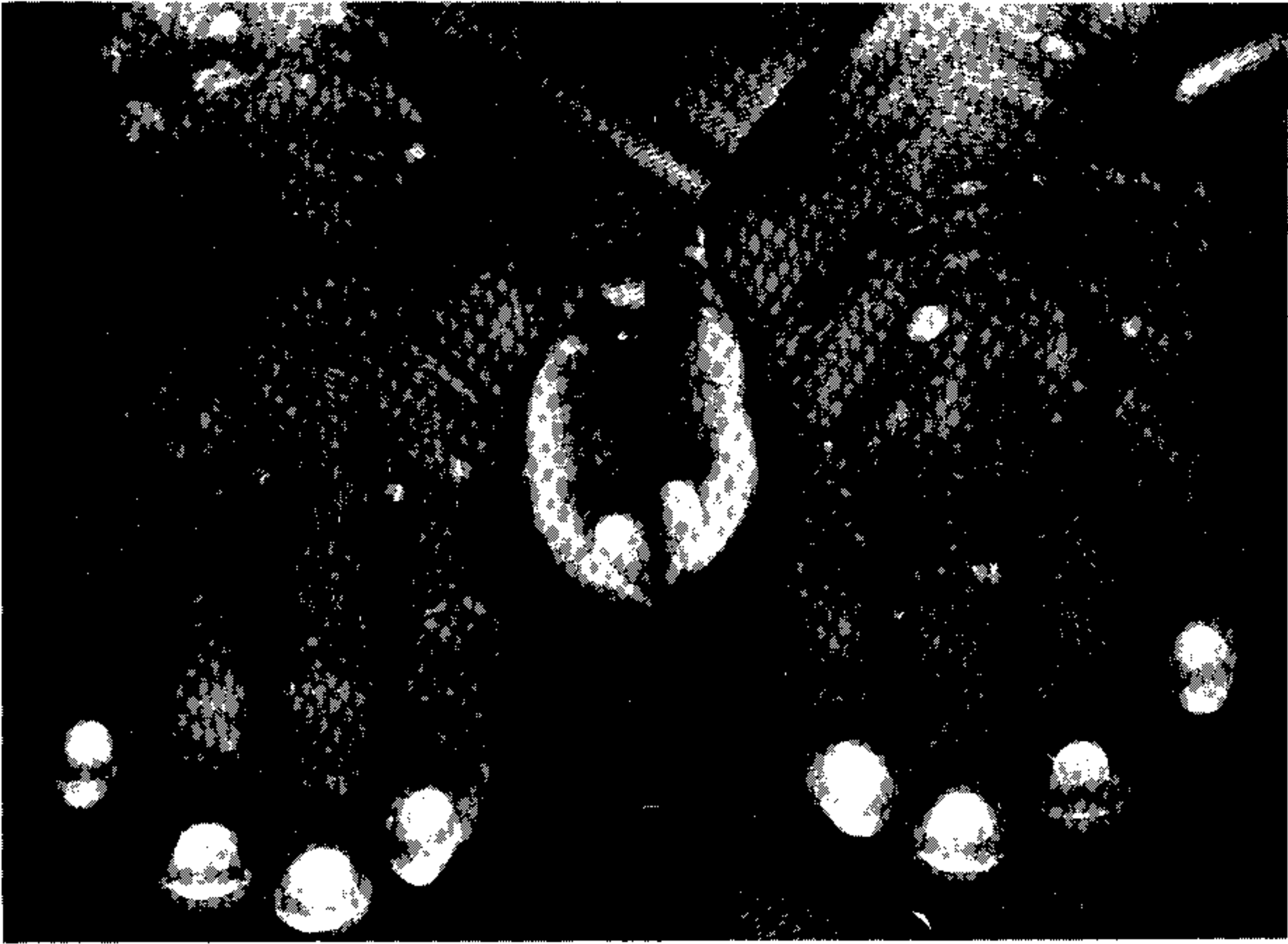


Fig. 2: papular and pustular lesions were scattered on trunk and limbs with a varicelliform appearance.

opsies of cutaneous and mucosal granuloma as well as with the immunoperoxidase technique with polyclonal antibody anti-*Leishmania braziliensis* (Figs 3A, 3B).

The patient had no history of a previous skin lesion or sign of a scar suggesting leishmaniasis. However one of his sisters had an ulcerated lesion on her leg about 25 years ago when they were living in Pernambuco.

In relation to HIV infection, the patient denied any risk factor. He was married with children and his wife had a negative anti-HIV Elisa test.

The patient was given glucantime, 15 mg/kg of Sb^v in a daily dose with a rapid improvement. He abandoned treatment after the 20th injection. In a short time lesions became flat, hypopigmented, slightly atrophic and scaly (Fig. 4).

The patient was examined once again in August 1991; skin lesions were completely healed and he was in a regular state of general health, but with slight dyspnoea. At this time he was taking sulfamethoxazole-trimethoprim for a "pneumonia" diagnosed clinically at a local health unit. He was readmitted to hospital on October 91 with dyspnoea and a high

fever. A lung abscess was detected on X ray examination; a blood culture yielded *Escherichia coli* and a lumbar puncture was positive for *Cryptococcus neoformans*. He was already disoriented, cachectic but the skin and mucosal lesions of leishmaniasis had not recurred. He died on the 7th day of admission and autopsy was not performed.

DISCUSSION

Coura et al. (1987), reported the first case of American cutaneous leishmaniasis in a patient with AIDS. Skin lesions and histological features were similar to the above case but a congested nasal mucosa and a small ulcer on the soft palate where the only noticeable mucosal lesions. The parasite was not isolated and the patient died one week later with *Pneumocystis carinii* pneumonia.

Scaglia et al. (1989) isolated *L. infantum* from a single ulcerative lesion on the wrist of a intravenous drug user (IVDU) HIV-positive who also had oral candidiasis, genital herpes and deep-sited tuberculous lymphadenopathy. The ulcer healed slowly after two 14-day courses of meglumine antimoniate (100 mg/kg daily) but parasitological cure was achieved in a short time.

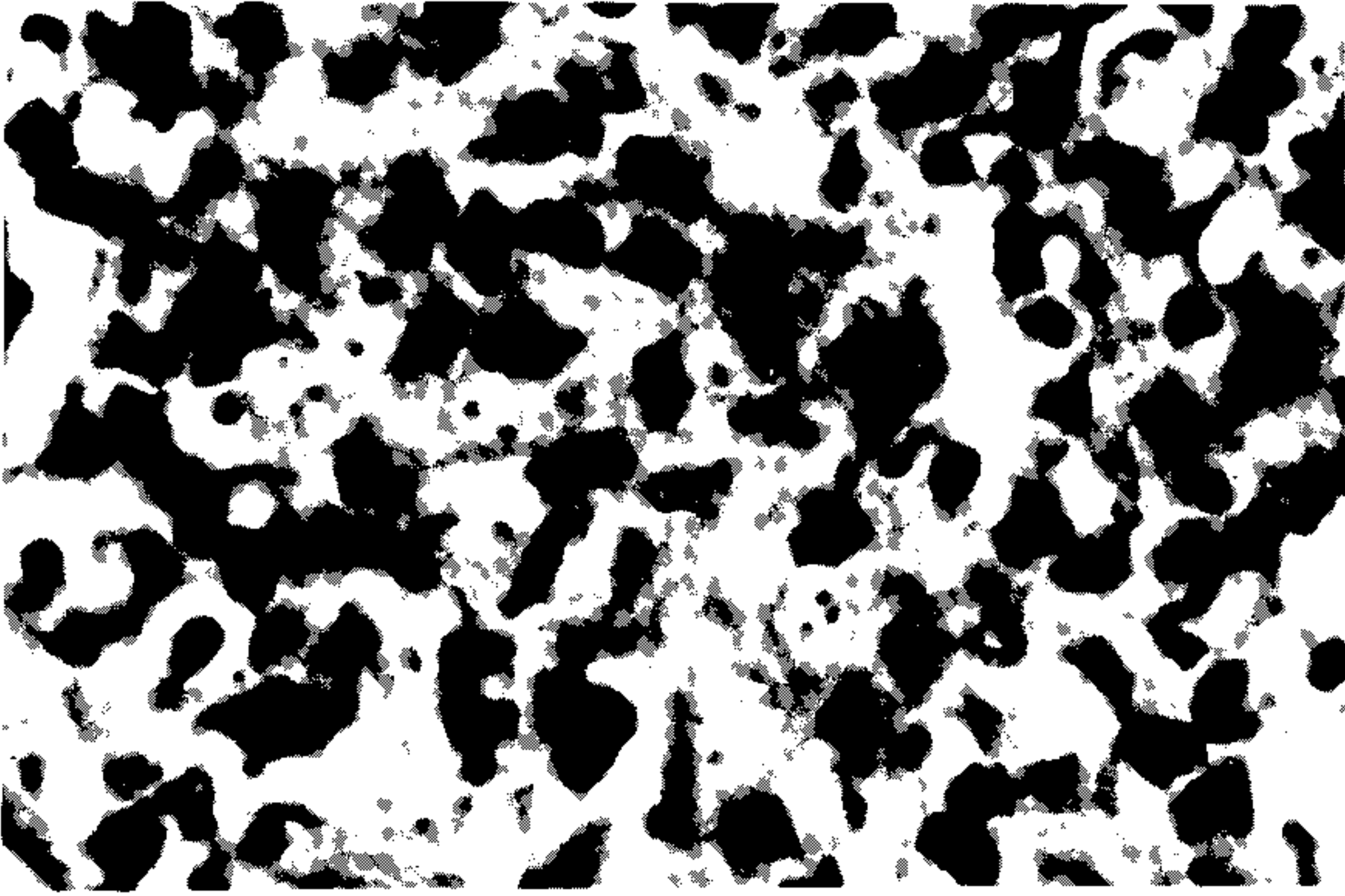
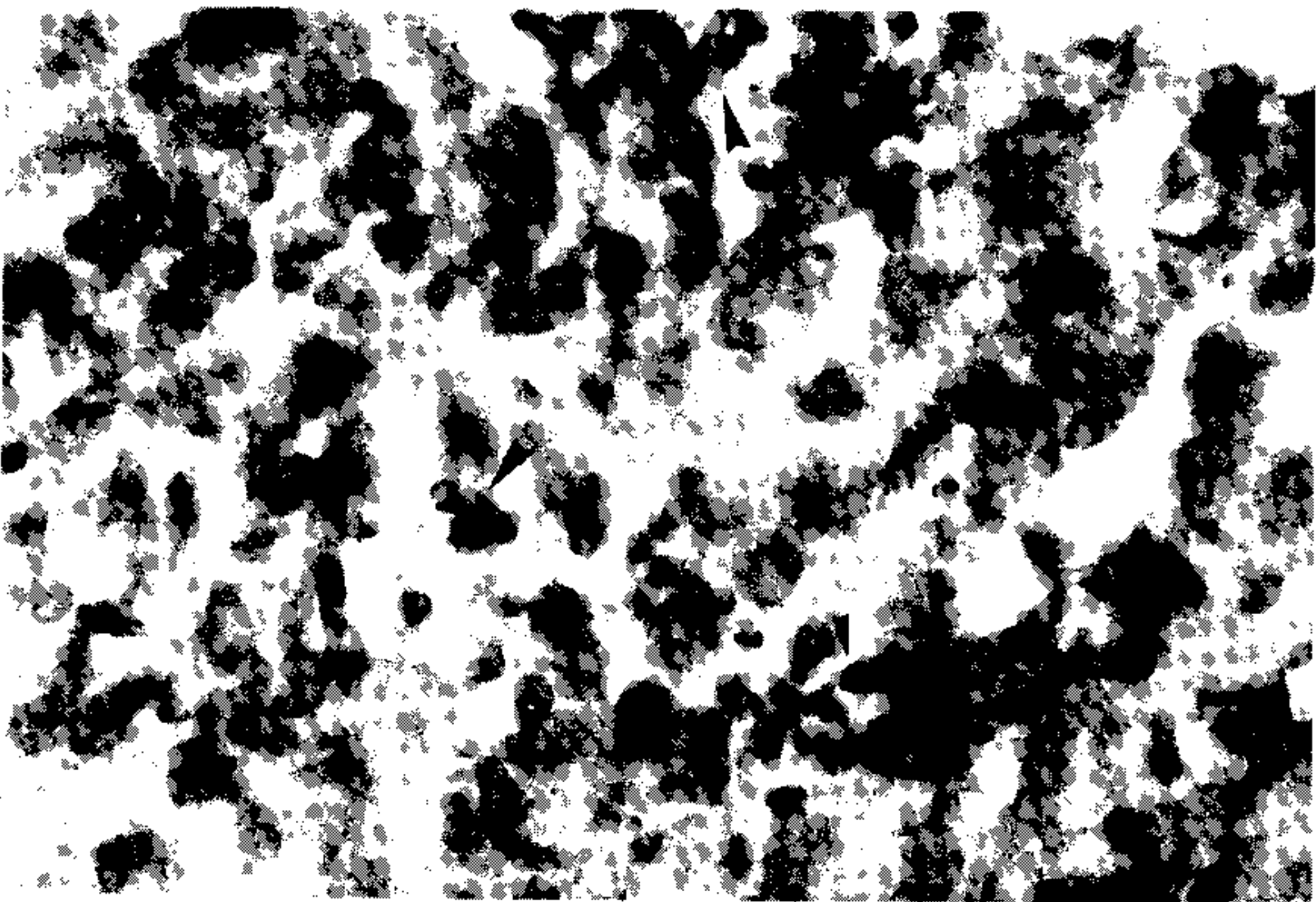
**A****B**

Fig. 3A: cutaneous lesion amastigotes inside vacuoles (Hematoxylin and Eosin) objective 100x. 3B: immunoperoxidase technique with polyclonal antibody anti-*Leishmania braziliensis*. Amastigotes (100x).

Pialoux et al. (1990) described an HIV positive case who developed two skin lesions in which amastigotes were demonstrated. The patient responded to a 3-month treatment

with 400 mg/day itraconazole, remaining well after 18 months in spite of a CD4 count of $65/\text{mm}^3$ by the time treatment was started.



Fig. 4: after antimonial therapy the lesions are flattened, hypopigmented and slightly scaly.

Cunha et al. (1991) described a case of a CDC-group IV HIV-patient with multiple skin lesions, suggestive of leishmaniasis with positive leishmanin skin test, but no parasite could be demonstrated. The lesions had healed after glucantime therapy but relapsed when the drug was discontinued. Similar to the case described by Coura et al. (1987) this patient developed other clinical features (such as multiple skin lesions rich in amastigotes) characteristic of the anergic, non-ulcerative form (DCL) which is accompanied by defective cellular immune responses. However differing from these and the present cases extensive and aggressive mucosal involvement are not features of DCL, only slight or limited lesions of mucous membranes can occasionally be observed in DCL patients (Menezes et al., 1978).

The case is also remarkable because the disease began in the oropharynx, affected the nose in a two month period and only after four months did the lesion disseminate throughout

the skin. The usual mucosal involvement in American muco-cutaneous leishmaniasis occurs either simultaneously or a short time (12 to 24 months) after the initial skin lesion. However the primary skin lesion may never exist and the mucosal aggression can appear after decades (Coutinho et al., 1981; Marsden et al., 1984). In the present case the patient denied any previous skin lesion and had no typical scar but his sister had probably suffered from cutaneous leishmaniasis in the past. It is possible that a dormant infection with few parasites was reactivated as a result of an acquired depressed cell-mediated immunity. Response to treatment was surprisingly good and there were no relapses even when the patient was dying in a state of advanced immunosuppression. Unfortunately neither skin biopsies nor necropsy were then performed. A favorable therapeutic response was also described in other cases of cutaneous leishmaniasis in AIDS patients (Scaglia et al., 1989; Pialoux et al., 1990). In contrast, a high AIDS-associated relapse rate

and resistance to treatment were observed in visceral leishmaniasis (Antunes et al., 1987; Alvar et al., 1989). This fact has been explained by the association of two highly immunosuppressive diseases. In view of the high endemicity of American cutaneous leishmaniasis in Brazil it should not be too surprising to detect more often the disseminated form of the disease in humans suffering from AIDS. However, only very few cases of this association have been described in the country (Coura et al., 1987; Cunha et al., 1991). In contrast, worldwide, the number of cases of visceral leishmaniasis associated with AIDS patients is much higher than with cutaneous cases (Clauvel et al., 1986; Berenger et al., 1989).

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