

## Immunological Features of Chronic Adult Paracoccidioidomycosis: Report of a Case Treated with Fluconazole

Sir,

Imported paracoccidioidomycosis constitutes an interesting diagnostic problem. First, it may not occur to the patient (unless otherwise prompted) to report a stay in endemic areas many years previously. Second, the clinical picture of the mucosal lesions caused by *Paracoccidioides brasiliensis* may be confused with lesions due to other disorders (1). Here, we report a case of paracoccidioidomycosis which had been latent for over 50 years. We discuss the clinical and immunological aspects of this case.

### CASE REPORT

A 72-year-old male was referred to the Maxillofacial Surgery Service of our hospital for extirpation of a tumoral mass of the upper jaw, following clinical diagnosis of epidermoid carcinoma. At the age of 22 the patient had had a stomach ulcer surgically removed. At the age of 65, he had undergone surgery for polyploid carcinoma of the colon. He presented an ulcerated lesion in the upper left jaw, extended to the lip mucosa and the nasal grave. The lesion had first been noted 6 months previously and had turned very painful, affixed to deep planes, infiltrated and with dirty bottom. Histological examination revealed a chronic granulomatous reaction, with epithelioid cells and giant cells. PAS staining revealed PAS-positive elements, suggesting a

mycotic aetiology. The patient was thus referred to our Dermatology Service.

A complete mycological study was carried out. Giemsa staining of a smear revealed the presence of yeast-like structures. Histological examination in our laboratory confirmed the previous findings, showing PAS-positive yeast-like structures with multiple buddings characteristic of *P. brasiliensis*. Cultures were performed on Sabouraud agar, developing filamentous colonies at 25°C and yeast-like colonies at 37°C. Immunodiffusion test results were positive for a *P. brasiliensis* antigen up to the dilution 1/1024.

Routine tests were normal. Standard multitest for cellular immunity (tetanus, diphtheria; streptococcus, proteus, tuberculin, glycerol, candidin, trichophylin) gave negative results. The paracoccidioidin skin test was not carried out. Peripheral lymphocyte counts revealed an abnormally high CD4/CD8 ratio, though NK cell numbers were within the normal range.

The X-ray examination revealed a diffuse interstitial pulmonary disorder, with basal bronchiectasis. In addition, the frontal and maxillary sinuses showed a thickened soft tissue, particularly on the left side. Computer tomography of the upper jaw revealed a mass of soft tissue on the left sinus.

Oral treatment with fluconazole (200 mg/day) was commenced, and marked improvement was observed within 15 days. Within 2 months we obtained the whole clinical cure. The treatment was continued for another 4 months. By the end of treatment, radiographic findings

were normal, though immunodiffusion testing gave a positive result at sample dilutions of up to 1/512. Two years after the end of treatment, clinical appearance and radiographic findings remain unchanged. Multitest results have remained negative throughout the entire period.

## DISCUSSION

Paracoccidioidomycosis is a common disease in a number of South American countries, most notably Venezuela, Brazil and Colombia. In these countries it generally begins as a respiratory disorder, often with mucocutaneous manifestations. Usually it is separated into five clinical pictures: (a) primary benign disease with self-limiting and asymptomatic pulmonary involvement, (b) acute and chronic progressive pulmonary form, (c) disseminated form with mucocutaneous manifestations, (d) chronic disseminated form with extracutaneous foci, and (e) disseminated infantile form (1, 2). Most cases of imported paracoccidioidomycosis reported in the literature appear to be of forms (a) and (d), both of which may unroll latencies for long periods with a delayed endogenous activation many years later (1).

The length of the latency period (up to 60 years) and the rarity of this disease in non-endemic areas make diagnosis difficult; indeed, many of the cases reported in the literature were initially misdiagnosed as tuberculosis, blastomycosis, epidermoid carcinoma, Wegener's granulomatosis, syphilis, sarcoidosis or leishmaniasis (1, 3).

Full immunological studies of patients with paracoccidioidomycosis have only recently appeared in the literature, and most of these studies deal with patients in endemic areas. In such studies, chronic mucocutaneous forms of the disorder have generally been reported to have latencies of 1–8 years (4). Most reported cases of imported paracoccidioidomycosis are likewise of the chronic mucocutaneous form, but in such cases the period of latency tends to be longer than 7 years and may be up to 60 years (1). Cases previously reported in our region (Galicia, northwest Spain, a region with large numbers of emigrants returned from South America) have had latency periods of between 7 and 32 years (1, 5). In the case reported here, the latency period was 50 years. We consider that the differences in immunological findings between this case and the cases reported previously (4) may be attributable to differences in the latency period: the immune status of patients in which the disease has remained quiescent for a very long period (over 10 years) must necessarily differ from that of patients with a shorter quiescent period.

A number of triazole compounds (including itraconazole, fluconazole and SCH 39304) have previously been used for treatment of paracoccidioidomycosis (6, 7). In most cases in which treatment with these drugs is successful, cell-mediated immunity appears to improve (5, 6, 8). However, anti-*P. brasiliensis* antibodies may remain detectable even after prolonged treatment (9). In the present case, treatment led to rapid clinical and radiological improvement and to reduced anti-*P. brasiliensis* serum antibody levels. Despite this, the results of the multitest continued to indicate anergy.

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Accepted July 31, 1995.

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