



Paracoccidioidomycosis in women

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Summary A retrospective review of paracoccidioidomycosis cases seen between January 1966 to January 1997 revealed 27 of the 627 cases occurred in women (male to female ratio 27.3:1). Data for 23 of these 27 cases demonstrated the protective effect of female hormones

Key words Paracoccidioidomycosis, Women, Estrogen

Paracoccidioidomycosis en mujeres

Resumen Una revisión retrospectiva de los casos de paracoccidioidomycosis vistos entre enero de 1966 y enero de 1997 reveló que 27 de los 627 casos ocurrieron en mujeres (relación hombre/mujer 27,3:1). Los datos de 23 de estos 27 casos demostraron el efecto protector de las hormonas femeninas.

Palabras clave Paracoccidioidomycosis, Mujer, Estrógeno

Epidemiologic surveys using paracoccidioidin skin testing has shown that the infection by *Paracoccidioides brasiliensis* occurs at an early age. The incidence of infection increases with age, initially no sexual differences. Overt-disease has been observed since early in life, regardless of the sex of the individuals [1]. However, later on, males are more frequently infected than women with a mean ratio of 15 to 22.1:1. The difference in the incidence of the disease has been explained by the protection of females because of the sex hormones they produce that are protective against progression of infection by *P. brasiliensis* [2,3,4]. This report presents some data regarding paracoccidioidomycosis in women. It focuses upon their hormonal states at the time of diagnosis.

Six hundred and twenty seven patients with paracoccidioidomycosis were seen between January 1966 and January 1997. Twenty seven of them were females. Medical records of these women were reviewed. Diagnosis was based on the finding of the characteristic yeast-like forms of *P. brasiliensis* in clinical specimens by direct microscopic examination or in tissue sections stained by the Gomori-Grocott technique. Culture and immunodiffusion testing complemented the diagnosis.

With the exception of four patients whose protocols were incomplete, data on the remaining 23 women are shown in Table 1. Ten patients (43.5%) presented with the chronic pulmonary form, 12 (52.2%) had the dis-

seminated chronic form with lung involvement and one patient (4.3%) had skin lesions resulting from hematogenous dissemination. Three patients (cases 1, 4, and 17) had received corticosteroids prior to diagnosis, two patients (cases 21 and 22) had concomitantly AIDS, and one patient (case 16) had tuberculosis.

Menopausal signs and symptoms, usually hot flashes, were the complaints in 19 patients (82.6%). In two patients (cases 4 and 7) their past histories were remarkable for hysterectomy and bilateral oophorectomy; another one (case 16) presented no symptoms of menopause with normal estrogen levels, had a hysterectomy. Estradiol levels were determined in eight patients, five of them (62.5%) presented levels indicative of menopause (<20 pg/ml).

The chronic pulmonary form of paracoccidioidomycosis occurs more frequently in women (43.5%) than men (25.9%). Involvement of lymph nodes and skin are rare, contrast to what has been observed in men [5]. The diagnosis of paracoccidioidomycosis in mature women is rare. Unfortunately, it is not always considered in the differential diagnosis. The association with tuberculosis (case 16), the presentation of the mycosis as a breast abscess (case 23), the unusual histopathological finding of small forms of *P. brasiliensis* resembling *Histoplasma capsulatum* var. *capsulatum*, or even capsule deficient isolates of *Cryptococcus neoformans* (case 2), and generalized erythematous maculo-papular lesions as seen in AIDS (case 22) can cause confusion.

The evidence of post puberty male predominance of paracoccidioidomycosis suggested the importance of hormonal factors in the pathogenesis of the disease. *in vitro* studies have shown that estradiol inhibits the mycelial-to-yeast and conidium-to-yeast transition of the fungus [3,4]. This effect was thought to be related to the regulation by a protein expression mediated specific protein-ligand complexes [2]. Our data support the protective role of female hormones against tissue invasion by *P. brasiliensis*.

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Table 1. Paracoccidioidomycosis in women: general characteristics of 23 patients.

No.	Age	Sites of involvement	ID ^a	Gynecological state/ Associated conditions
1	40	Lungs	+	Menopause; estradiol 10 pg/ml/Prednisone 60 mg/day
2	64	Lungs	+	Menopause
3	44	Lungs	+	Menopause; estradiol 12 pg/ml
4	44	Lungs, tongue	+	Previous (8yrs) hysterectomy and bilateral oophorectomy; estradiol 10 pg/ml /Prednisone 20mg/day
5	66	Lung	+	Menopause
6	62	Lungs, esophagus	+	Menopause
7	55	Lungs	+	Previous (12yrs) hysterectomy and bilateral oophorectomy; estradiol 10 pg/ml
8	59	Lungs, gums, lymph node	ND ^b	Menopause
9	44	Lungs	ND	Menopause; estradiol 12 pg/ml
10	35	Lungs	+	Regular menstrual cycle; estradiol 50 pg/ml
11	36	Lungs	+	Regular menstrual cycle
12	60	Lungs, gums	+	Menopause/ Alcoholism
13	63	Lungs, larynx	+	Menopause
14	54	Lungs, skin	-	Menopause
15	61	Lungs	+	Menopause
16	56	Lungs	+	Menopause/Tuberculosis
17	55	Lungs, lips	+	Menopause/ Prednisone 20 mg/
18	55	Lungs, skin, cheek	+	Menopause
19	38	Lungs, trachea	+	Regular menstrual cycle
20	46	Lungs, larynx, tongue	+	Previous (10yrs) hysterectomy; estradiol 54 pg/ml
21	47	Lungs, skin, gums	+	Menopause/AID
22	43	Skin	+	Menopause; estradiol 25 pg/ml/AIDS
23	47	Lungs, tongue, left breast	+	Menopause

a ID = Immunodiffusion test

b ND = not done

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References

1. Londero AT, Rios-Gonçalves AJ, Terra GMF, Nogueira SA. Paracoccidioidomycosis in Brazilian children. A critical review (1911-1994). *Arq Bras Med* 1996; 70: 197-203.
2. Clemons KV, Feldman D, Stevens DA. Influence of oestradiol on protein expression and methionine utilization during morphogenesis of *Paracoccidioides brasiliensis*. *J Gen Microbiol* 1989; 135: 1607-1617.
3. Restrepo A, Salazar ME, Cano LE, Stover EP, Feldman D, Stevens DA. Estrogens inhibit mycelium-to-yeast transformation in the fungus *Paracoccidioides brasiliensis*: implications for resistance of females to paracoccidioidomycosis. *Infect Immun* 1984; 46: 346-353.
4. Salazar ME, Restrepo A, Stevens DA. Inhibition by estrogens of conidium-to-yeast conversion in the fungus *Paracoccidioides brasiliensis*. *Infect Immun* 1988; 56: 711-713.
5. Londero AT, Ramos CD. Paracoccidioidomycose. Estudo clínico e micológico de 260 casos observados no interior do Estado do Rio Grande do Sul. *J Pneumol* 1990; 16: 129-132.