

BRIEF COMMUNICATION

HISTOPLASMOSIS IN THE MUÑIZ HOSPITAL OF BUENOS AIRES

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SUMMARY

Some epidemiological and immunological characteristics and the methodology of diagnosis of 44 cases of histoplasmosis (HP); 36 (27 males and 9 women) associated with AIDS (HP+AIDS) and 8 (7 males and 1 female) with other predisposing factors (HP+non AIDS), diagnosed in the Muñiz Hospital (MH) during 1994, were retrospectively studied.

The median age (MA) of HP+AIDS patients was 28 years; 25.5 (22-40) in the women and 28.5 (20-42) in the men and 50 (22-58) years in the HP+non AIDS patients.

The more frequent risk factors for HIV infection were intravenous drug addiction (55%) and homo/bisexuality (19%). The MA of these groups were 28 (20-39) and 41 (26-42) years, respectively. Tobaccoism was a predisposing factor in 83% of HP+non AIDS patients.

The muco-cutaneous lesions scraping and blood-cultures established the initial diagnosis in 53% and 36% of HP+AIDS patients, respectively and the muco-cutaneous lesions biopsies in 75% of HP+non AIDS cases. At time of diagnosis, all HP+AIDS patients had <200 while HP+non AIDS patients had > 200 CD4 + lymphocytes/ μ l.

Seventy two per cent of HP+AIDS patients were born in Buenos Aires (Bs As) city and 62% of HP+non AIDS patients were born in provinces of Argentina other than Bs As. At moment of diagnosis, 87.5% of HP+AIDS and 62.5% of HP+non AIDS patients lived in Bs As city and Bs As outskirts.

KEYWORDS: Histoplasmosis; Histoplasmosis associated to AIDS; Epidemiology of histoplasmosis.

INTRODUCTION

Histoplasmosis (HP) is a systemic mycosis whose endemic area includes the Argentina provinces of Buenos Aires (Bs.As.), Santa Fe, Entre Ríos, southern Córdoba and eastern La Pampa. In this region (named "humid Pampa") live more than 12 millions inhabitants ⁷.

HP is the third mycosis in frequency in AIDS patients (HP+AIDS) and it is present as acute disseminated disease when the CD4+lymphocytes count is

lower than 200/ μ l ⁵. Chronic disseminated histoplasmosis is the clinical form most frequently observed in the HP associated with other predisposing factors (HP+non-AIDS) ^{7, 10, 11}. The methodology of diagnosis is also different in both clinical forms ^{2, 10}.

The aim of this work is to evaluate some immunological and epidemiological characteristics and the initial diagnosis methods of the cases of HP diagnosed in the MH in 1994.

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MATERIALS AND METHODS

Patients: all patients hospitalized in the MH during 1994 due to first episode of HP were retrospectively studied.

Diagnosis of AIDS: antibodies to HIV-1/2 were determined by an enzyme-immunoassay (Abbott Laboratories, Germany). Samples repeatedly reactive by enzyme-immunoassay were tested by Western Blot (Bio Rad, Hercules, California, USA). Results were interpreted according to the manufacturer instructions.

Diagnosis of histoplasmosis: it was based on positive microscopic examination and/or cultures for *Histoplasma capsulatum* (*H. capsulatum*) from clinical samples (scrapings and biopsies of mucocutaneous lesions, blood cultures, bone marrow aspiration and other body fluids and tissues). The blood cultures only were carried out in HP+AIDS patients and only in HP+non AIDS patients the presence of specific antibodies was investigated by counterimmunoelectrophoresis, immunodiffusion and complement fixation tests ⁷. The employed methodology was that used routinely in the laboratory of the Unit of Mycology of the MH and ⁹.

CD4+ and CD8+ count: CD4+ and CD8+ lymphocytes in peripheral blood were determined with monoclonal antibodies (Dynabeads T4-T8 Quant, DYNAL A. S., Oslo, Norway).

Analysis of the results: a data base was prepared containing demographic characteristics of the patients (age, sex, address in the moment of diagnosis and place of birth), risk factor for HIV infection, method of initial diagnosis and CD4+ lymphocytes count at the moment of the diagnosis of HP.

Statistics: the ages of HP+AIDS and HP+NON AIDS patients, of HP+AIDS males and females and of intravenous drug abusers (I.D.A.) and homo/bisexuals (H/B M) AIDS men were analyzed with the Mann-Whitney Rank Sum Test and all calculations were done with the Stat Primer program ⁶.

RESULTS

In the MH, during 1994 44 patients with HP were hospitalized; 36 associated with AIDS and 8 with other predisposing factors. The distribution of males, females, I.D.A. and H/B M HP+AIDS and HP+non AIDS patients by age groups, the MA and range are summarized in Table 1.

The ages values of the women were lower than HP+AIDS males, but the difference was not statistically significant ($p > 0.1$). The values of age were statistically lower in HP+AIDS ($p = 0.03$) and I.D.A. ($p = 0.04$) respect to HP+non AIDS and H/B M patients, respectively.

TABLE 1

Distribution by age groups, median age and range of the patients with histoplasmosis (HP) associated with AIDS (HP+AIDS): males, women, intravenous drug abusers (I.D.A.) and homo/bisexuals men (H/B M) and those with HP associated with other predisposing factors (HP+non AIDS), diagnosed in the Muñiz Hospital in 1994

age group in years	total		HP+AIDS cases				risk factor				HP+non-AIDS cases	
			sex		female		I.D.A.		H/B M			
			N°	%	N°	%	N°	%	N°	%	N°	%
28			22		6		15		5		8	
< 20	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
20-29	16	57.14	12	54.54	4	66.66	10	66.66	1	20.00	1	12.50
30-39	7	25.00	6	27.27	1	16.66	5	33.33	0	0.00	1	12.50
40-49	5	17.85	4	18.18	1	16.66	0	0.00	4	80.00	2	25.00
> 50	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	4	50.00
median:	28.00 yr		28.50 yr		25.50 yr		28.00 yr		41.00 yr		50.00 yr	
range:	(20-42)		(20-42)		(22-40)		(20-39)		(26-42)		(22-58)	

References:
yr. years

Among HP+AIDS patients, 27 (75%) were male and 9 (25%) female and among HP+NON AIDS cases 7 (85.71%) were men and 1 (14.28%) a woman. The more frequent risk factors for HIV infection were the intravenous drug addiction, present in 15 (55%) patients, homo/bisexuality in 5 (19%) and promiscuity among heterosexual men in 2 (8%). Blood transfusion, inhalatory drug addiction and HIV+ sexual partner were present in 1 (4%) case each. In 2 patients no risk factor could be determined.

Tobaccoism was referred by 5 (83.33%) HP+non AIDS patients (1 case associated with alcoholism) as predisposing factor. Other HP+non AIDS cases were observed in a girl suffering chronic mucocutanea candidiasis and in the remaining 2 cases it was probably due to psychic stress.

The initial diagnosis was achieved in 21 (58.33%) out of 36 HP+AIDS patients by scraping of mucocutaneous lesions, by blood cultures in 13 (36.11%) and by lymph node aspiration and cutaneous biopsy in 1 (2.77%) case each. The biopsies (75%) and scraping (25%) of mucocutaneous lesions established the initial diagnosis in the 8 HP+non-AIDS cases.

In 69% of 23 HP+AIDS patients, CD4+ lymphocytes count was $<50/\mu\text{l}$; in 22% ranged from 51 to $100/\mu\text{l}$ and in 9% from 101 to $200/\mu\text{l}$. All 8 HP+non-AIDS patients had more than 200 CD4+ lymphocytes/ μl ; 12.5% from 401 to $600/\mu\text{l}$ and 50% $> 600/\mu\text{l}$. In all cases the ratio CD4+/CD8+ was < 1 in HP+AIDS and > 1 in the HP+non-AIDS patients.

The places of birth of the HP+AIDS cases were: Bs As city, in 14 (56%) cases; Bs As outskirts in 2 (8%); Bs As province towns in 3 (12%) and the provinces of Chaco, Misiones, Corrientes, Formosa, Santa Fé and Santiago del Estero in 1 (4%) patient each. HP+non-AIDS patients were born in Tucumán (2 cases), Bs As outskirts (2 cases), and 1 (12.5%) each in the provinces of Entre Ríos, Córdoba and Corrientes and Bs As city.

At diagnosis of HP, 3 (37.5%) HP+non-AIDS patients lived in Bs As city, 2 (25%) each in Bs As outskirts and Córdoba and 1 (12.5%) in Entre Rios province. In that moment, 18 (56.25%) HP+AIDS patients lived in Bs As city, 10 (31.25%) in Bs As outskirts and 1 (12.5%) each in towns of Bs As and Formosa provinces.

DISCUSSION

In the MH, the annual incidence of HP in the last 10 years was heterogeneous and until 1990, the annual number of cases diagnosed was never higher than 20 %. The annual incidence of HP+AIDS in the MH can be divided in 4 periods: in the first, (1983-86) only one case was diagnosed; in the second (1987-90), 2 to 7 cases/year; in the third, (1990-93) an average of 15 annual cases and in 1994 the annual incidence was duplicated with respect to the anterior period. Probably, in the next years the number of patients diagnosed in the MH will be higher than that observed in 1994.

According to data from the Public Health Office, the incidence of HP in AIDS patients in Argentina would be 2.5% (93 cases among 3,658 AIDS patients diagnosed among 1983-93), a figure similar to those published in the literature for endemic areas ^{8, 12}.

In Argentina, the incidence of HP-infection was studied in healthy adult people by skin tests which were positive in 30% of persons living in different zones within the endemic area. The prevalence index of HP-disease has been estimated in about 0.5-1 per 1,000 infected peoples. These values are important because more than 12 millions people live in the most populous cities within the endemic area of HP, where AIDS is endemic too ⁷.

Among the 575 AIDS patients hospitalized in MH during 1994, 81% were male and 19% female; the average age was 30.2 years and the more frequent risk factors for HIV infection were intravenous addiction (51.5%) and homo or bisexuality (23%) ¹.

Demographic characteristics of AIDS and non-AIDS patients with HP were different as well as the distribution for age groups in men, women, I.D.A. and H/B M HP+AIDS patients. The masculine predominance among HP+AIDS was lower than that present in the AIDS patients hospitalized in the MH during 1994 and the number of female HP+AIDS cases observed in 1994 was higher than that diagnosed in 1983-93. The ratio I.D.A.: H/B M was similar to that observed in AIDS population of the MH in 1994 ¹.

In the HP+non-AIDS patients the predisposing factors were those commonly observed by us in HP+non-AIDS patients hospitalized in the MH and they had been present for long periods of their life ¹¹.

The visualization and isolation of *H. capsulatum* from clinical samples were sensitive enough to achieve the initial diagnosis in all studied patients. The serological tests were only employed in HP+non-AIDS patients, because in a previous report the sensitivity of similar serological techniques in our hands was less than 50% in 20 HP+AIDS patients hospitalized in the MH ¹⁰.

Lysis-centrifugation technique for blood-culture was done only in HP+AIDS patients; it increased the isolation of *H. capsulatum* with respect to the conventional method in HIV+ patients. The systematic scraping of muco-cutaneous lesions was the most effective method of diagnosis in these patients ^{1,4}. Many patients were initially diagnosed by blood culture and subsequently other studies, such as scraping of mucocutaneous lesions and/or lymph node aspiration, were positive. In 3/13 patients the blood cultures results were available when they were already dead. More sensitive methods, such as the dosage of *H. capsulatum* antigen in body fluids, not yet available in Argentina, will increase the possibility of diagnosis of HP in AIDS patients ¹².

In HP+non-AIDS patients, the traditional methodology (biopsy and scraping of muco-cutaneous lesions and specific serology), provided a reliable diagnosis ².

CD4+ lymphocytes counts of HP+AIDS patients were coincident with those known as predisposing for the clinical manifestation of the HP in HIV+ patients ⁵.

Most of HP+AIDS patients were born in the territory of Bs As province, epicenter of the endemic area of HP in Argentina. The site of birth of some HP+non-AIDS patients were other provinces than Bs As where the endemicity of HP has not been confirmed. The endemic area of HP in Argentina probably is greater than the humid Pampa, and it must be studied.

At moment of diagnosis, most of the studied patients lived within the endemic area of HP. Whether they acquired the infection with *H. capsulatum* in the first years of their life or when the immunodepression was present; while they lived or traveled across the endemic area, is difficult to establish. Probably the present episode is a reactivation of a latent infection, but we cannot rule out the recent infection of this patients because they live and are hospitalized within the endemic area of HP ¹².

CONCLUSIONS

The incidence of HP in the MH has increased in the last 4 years, due to its association with AIDS, reaching the most elevated values in the last 30 years. Between 1983-94 99 cases of HP+AIDS were diagnosed in the MH; 83% of them between 1991-94 ².

The AIDS patients are predominant in the population hospitalized in the MH and the studied non-AIDS patients with HP were not severely immunocompromised. The possibility to acquire nosocomial infections with multiresistant agents, binds the hospitalization of patients with other predisposing factors of HP (transplantation, corticosteroids and antituberculous drugs treatments, etc).

The scraping of mucocutaneous lesions, a simple, rapid and economic method of diagnosis is today an important tool for the diagnosis of HP, either in AIDS or non-AIDS patients ².

The studied demographic parameters were different in HP+AIDS and HP+non-AIDS patients and the values obtained from HP+AIDS would represent the addition of their own values for the two diseases. The statistical significance of these differences cannot be established because the information obtained about the whole AIDS population hospitalized in the MH during 1994 is poor ⁷.

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RESUMO

Histoplasmoze no Hospital Muñiz de Buenos Aires

Foram estudadas, retrospectivamente, algumas características epidemiológicas e imunológicas e a metodologia de diagnóstico de 44 casos de histoplasmoze (HP); 36 (27 homens e 9 mulheres) associados com AIDS (HP+AIDS) e 8 (7 homens e 1 mulher) com outros fatores predisponentes (HP, sem AIDS), diagnosticados no Hospital Muñiz (MH) durante 1994.

A idade média (MA) de pacientes com HP + AIDS foi 28 anos; 25,5 (22-40) nas mulheres e 28,5 (20-42)

nos homens e 50 anos (22-58) nos pacientes HP, sem AIDS.

Os fatores de risco mais frequentes para infecção pelo HIV foram uso de drogas intravenosas (55%) e homo/bissexualidade (19%). A MA destes grupos foi de 28 anos (20-39) e 41 anos (26-42), respectivamente. Tabagismo foi fator predisponente em 83% dos pacientes HP, sem AIDS.

A raspagem das lesões mucocutâneas e as culturas de sangue estabeleceram o diagnóstico inicial em 53% e 36% dos pacientes HP + AIDS, respectivamente e as biopsias de lesões mucocutâneas em 75% dos casos HP, sem AIDS. No momento do diagnóstico, todos os pacientes HP + AIDS tinham menos de 200 linfócitos CD4+/ μ l enquanto que os pacientes HP, sem AIDS tinham mais de 200.

Setenta e dois por cento dos pacientes HP + AIDS nasceram na cidade de Buenos Aires e 62% dos pacientes HP, sem AIDS nasceram em outras províncias da Argentina. No momento do diagnóstico 87,5% dos pacientes HP + AIDS e 62,5% dos pacientes HP, sem AIDS moravam na cidade de Buenos Aires e subúrbios.

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