

HODGKIN'S DISEASE IN ASSOCIATION WITH ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

A report on 36 patients

U. TIRELLI, E. VACCHER, G. REZZA, T. BARBUI, C. BERNASCONI, A. CAJOZZO, A. CARGNEL, F. DE LALLA, P. DESSALVI, P.G. FASSIO, M. GOBBI, F. M. G. LAMBERTENGI DELILIERI, A. LAZZARIN, G. LUZI, R. LUZZATI, F. MANDELLI, R. MASERATI, N. PIERSANTELLI, F. PUPPO, G. RAISE, E. ROSSI, G. SALIVA, A. SCANNI, A. SINICCO, R. FOÀ, F. GAVOSTO and S. MONFARDINI
for the Gruppo Italiano Cooperativo AIDS and Tumori

Abstract

In an Italian cooperative study on AIDS and cancer a diagnosis of Hodgkin's disease was established in 36 HIV-positive patients. The series was characterized by a high proportion of drug abusers, a high proportion of mixed cellularity and lymphocytic depletion subtypes and short survival. It is still unclear if HIV infection promotes the development of Hodgkin's disease or only modifies the course of the disease. According to the authors, however, patients who are HIV seropositive and have biopsy-proven Hodgkin's disease should be considered as fulfilling the criteria for AIDS.

Key words: Hodgkin's disease, AIDS.

Hodgkin's disease (HD) in patients with HIV infection has been reported to have unusual and aggressive features (1, 2) but it is not in itself considered as a criterion for the diagnosis of AIDS. In several reports from the USA (1-14) HD in patients with HIV infection has been described as being atypical with unusual sites of involvement, such as central nervous system (CNS), skin and ano-rectum. Mixed cellularity has been the most frequent subtype reported. Advanced stage, opportunistic infections by pneumocystis carinii, unusual intolerance to the commonly used cytotoxic drugs, overall poor response to treatment and very short survival have been common characteristics of these patients. Moreover, as HD is a typical disease of the young, it is not clear whether HD is truly more common in HIV infected patients than in the general population. HD has not apparently increased in the San Francisco area (9), whereas it seems to have

increased among i.v. drug abusers in the New York prisons (3) and among homosexual men in New Orleans (2). The aim of this report is to update the experience of the Gruppo Italiano Cooperativo AIDS & Tumori (GICAT) on the incidence of HD in HIV-infected persons in Italy. A previous report on the incidence of malignant lymphoma in this population has been published in letter form (13).

Material and Methods

In November 1985 a cooperative study group was established in Aviano and Turin, Italy in an attempt to assess the incidence and subtypes of malignant lymphomas in persons with HIV infection in Italy. Questionnaires were sent to members of the Italian Societies for Medical Oncology, Haematology, Pathology, Immunology and to selected specialists in infectious diseases. The investigators were asked to report all known patients treated for AIDS in whom HD had developed between January 1980 and November 1987. In addition the Italian Ministry of Health in Rome (Istituto Superiore di Sanità) reported all cases of AIDS with a diagnosis of HD.

The criteria used for diagnosis of persistent generalized lymphadenopathy (PGL) and AIDS conformed to those established by the Centers for Disease Control in the USA.

Presented at ECCO-4, Madrid, November 1-4, 1987.

Table
Hodgkin's disease in persons at risk for AIDS. Literature review

Author	No. of patients	Risk group	Clinico-pathological characteristics
Joachim et al., 1985 (8)	3	Homosex.	Stage IV 2/3 Unfavourable subtypes: MC 2/3 Rapidly progressive
Scheib & Siegal, 1985 (1)	1	Homosex.	Atypical and aggressive stage IV with lung parenchymal involvement without mediastinal adenopathy
Moore & Cook, 1986 (15)	1	I.v. drug abuser + homosex.	Association with malignant melanoma
Temple & Abe Andes, 1986 (2)	3	Homosex. (n=2) I.v. drug abuser + homosex. (n=1)	Stage III-IV 3/3 Extranodal sites 2/3 Aggressive disease Severe cytopenia after usual doses of chemotherapy
Schoeppel et al., 1986 (12)	19	Homosex.	Stage III-IV 74 % Extranodal sites 37 % (CNS, skin, endobronchial) Association with PGL 32 % Short survival (1-6 months)
Unger & Strauchen, 1986 (14)	4	Homosex.	Stage III-IV 3/4 Unfavourable subtypes: MC 3/4 Aggressive course Severe depletion of T ₄ and predominance of T ₈ in HD tissue
Baer et al., 1986 (4)	3	Homosex.	Stage III-IV 3/3 Unfavourable subtypes: MC 2/3 Association with PGL 2/3 Fatal opportunistic infection and/or Kaposi's sarcoma
Raphael et al., 1986 (16)	5		None special
De Luca et al., 1987 (6)	4	I.v. drug abuser (n=3) Homosex. (n=1)	Stage IV 4/4 Poor prognostic histology: MC-DL 4/4
Gongora-Bianchi et al., 1987 (7)	1	Homosex.	Stage IV with liver and lung involvement Aggressive disease complicated by opportunistic infection
Bello et al., 1987 (5)	1	Haemophil.	Aggressive atypical disease
Kaplan et al., 1987 (9)	13	Homosex.	Stage III-IV 75 % Unfavourable subtypes: MC 70 % Aggressive clinical course Short survival

Results

By November 1987, 36 patients with HIV-associated HD had been diagnosed in 21 Italian institutes. One case was diagnosed in 1983, 2 cases in 1984, 6 cases in 1985, 12 cases in 1986 and 11 cases in the first 11 months of 1987. The ratio observed/expected cases of HD in HIV infected population in Italy was 1.3 and thus not significantly increased. The median age was 26 years (range 20-45). Clinical information was not available for all patients and so data will be reported with numbers observed and numbers with available information within parentheses. Eighty-eight per cent (30/34) of the patients were i.v. drug

abusers, 9% (3/34) i.v. drug abusers plus homosexual men and 3% (1/34) homosexual. HIV infection was documented in 97% (33/34) of the patients (2 patients with HIV test not performed were diagnosed in 1984, and presented clinical AIDS), 9% (3/33) of the patients were diagnosed as being affected by full-blown AIDS or AIDS related complex. PGL was associated with HD diagnosis in 76% (26/34) and preceded the diagnosis of HD in 76% (16/21) of the cases with a median latency of 14 months (range 1-52). The histological subtype was as follows: nodular sclerosis in 32% (10/31), mixed cellularity in 52% (16/31) and lymphocyte depletion in 16% (5/31) of the cases.

Concerning stage, 31% (10/32) had stage III and 47% (15/32) stage IV, 19% (6/32) stage II and 3% (1/32) stage I. With regard to the initial sites of the disease, involvement of lymph nodes alone was described in 42% (14/33), of spleen in 48% (16/33), of liver in 36% (12/33), of bone marrow in 18% (6/33) and of CNS in 3% (1/33). Sixty-two per cent (16/26) of the patients could be evaluated concerning therapy. They were treated with MOPP alternately with ABVD± radiotherapy (n=4), MOPP followed by ABVD± RT (n=5), MOPP alone ±RT (n=4), ABV (n=1), POB (prednisone, vincristine, bleomycin; (n=1), and radiotherapy alone (n=1). Complete remission was observed in 50% (8/16) and 50% (8/16) achieved partial remission.

The median survival was 15 months; 41% (13/32) of the patients died, 7 of opportunistic infections, 3 of tumour progression and 2 of disseminated intravascular coagulation; in one patient the cause of death could not be ascertained.

Discussion

Several investigators have described the development of HD in male homosexuals (1, 2, 4, 7, 8, 10-12, 14). The Table shows the reports as they appear in the literature. Since HD is expected to occur in young men and since there is no epidemiologic evidence that the incidence of HD in HIV infected persons has increased, it remains doubtful whether HD should be considered as a criterion for diagnosis of full-blown AIDS. Some investigators, however, have claimed that the often unusual characteristics of HD in HIV infected patients justify the inclusion of this disease among the diagnostic features of full-blown AIDS. However, it is also possible that the HIV infection only modifies the clinical pictures of HD. The present study contains the largest series of patients with HIV associated HD so far reported. The series revealed: 1) a rise in the number of cases since 1983; 2) a high percentage of i.v. drug abusers in agreement with the epidemiology of HIV infection in Italy; 3) a high percentage of PGL associated with HD; 4) high percentages of mixed cellularity and lymphocytic depletion subtypes (68%) and of stage III and IV (78%); 5) extra-nodal disease in 58% of the cases with rare involvement such as CNS and 6) short median survival with 41% of the patients dying within 2 years from diagnosis, mainly due to opportunistic infections. We agree with Scheib & Siegal (1) and Temple & Abe Andes (2) that patients who are HIV seropositive and have biopsy proven HD should be considered as fulfilling the criteria for AIDS. However, since no epidemiological evidence currently exists that would prove that HD is in fact a part of the spectrum of AIDS, further studies are needed.

ACKNOWLEDGEMENTS

This work was supported by a grant from the Associazione Italiana per la Ricerca sul Cancro (A.I.R.C.), contract No. 1004/700/84 No. 6/86 and by a grant from the Friuli-Venezia Giulia region.

Request for reprints: Dr Umberto Tirelli, Division of Medical Oncology, Centro di Riferimento Oncologico, Via Pedemontana Occidentale, I-33081 Aviano (PN), Italy.

REFERENCES

1. Scheib RB, Siegal RS. Atypical Hodgkin's disease and the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; 102: 554.
2. Temple JJ, Abe Andes W. AIDS and Hodgkin's disease. *Lancet* 1986; 2: 454.
3. Ahmed T, Worsler G, Stahl R, et al. Increased risk for Hodgkin's disease (HD) and non-Hodgkin's lymphomas (NHL) in a population at risk for AIDS. (Abstract.) The Annual Meeting of the American Society of Clinical Oncology. Houston, Texas 1985.
4. Baer DM, Anderson ET, Wilkinson LS. Acquired immunodeficiency syndrome in homosexual men with Hodgkin's disease. *Am J Med* 1986; 80: 738.
5. Bello JL, Magallon M, Villar JM. Hodgkin disease in hemophilia. *Ann Intern Med* 1987; 107: 257.
6. De Luca RR, Needleman SW, Schiffer CA. Hodgkin's disease in HTLV-III positive patients. (Abstract.) *Proc ASCO*. Washington, 1987.
7. Gongora-Bianchi RA, Gonzalez-Martinez P, Bastarrachea-Ortiz J. Hodgkin's disease as the initial manifestation of acquired immunodeficiency syndrome. *Ann Intern Med* 1987; 107: 112.
8. Joachim HL, Cooper MC, Hellman GC. Lymphomas in men at high risk for acquired immune deficiency syndrome (AIDS). *Cancer* 1985; 56: 2831.
9. Kaplan LD, Abrams D, Volberding PA. Clinical course and epidemiology of Hodgkin's disease (HD) in homosexual men in San Francisco. (Abstract.) III International Conference on AIDS, Washington, 1987.
10. Picard O, de Gramont A, Krulik M, et al. Rectal Hodgkin's disease and the acquired immunodeficiency syndrome. *Ann Intern Med* 1982; 106: 775.
11. Robert NJ, Schneidermann H. Hodgkin's disease and the acquired immunodeficiency syndrome. *Ann Intern Med* 1984; 101: 142.
12. Schoepfel S, Hoppe R, Abrams D, et al. Hodgkin's disease (HD) in homosexual men: the San Francisco Bay area experience. (Abstract.) The annual meeting of the American Society of Clinical Oncology, Los Angeles, 1986; 9: 3.
13. Tirelli U, Rezza G, Lazzarin A. Malignant lymphoma related to HIV infection in Italy: a report of 46 cases. *JAMA* 1987; 258: 2064.
14. Unger PD, Strauchen JA. Hodgkin's disease in AIDS complex patients: report of four cases and tissue immunologic marker studies. *Cancer* 1986; 58: 821.
15. Moore GE, Cook DD. AIDS in association with malignant melanoma and Hodgkin's disease. *J Clin Oncol* 1985; 3: 1437.
16. Raphael M, Tulliez M, Bellefigh S, et al. Les lymphomes et le SIDA. *Ann Pathol* 1986; 6: 278.