HIV positive patients first presenting with an AIDS defining illness: characteristics and survival

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Abstract

Objectives—To study the presentation and survival of patients who present with their first diagnosis of being HIV positive at the same time as their AIDS defining illness.

Design—Retrospective study of patients presenting with AIDS between 1991 and 1993.

Setting—Department of genitourinary medicine, St Mary's Hospital, London.

Main outcome measures—AIDS defining illness at presentation and survival after diagnosis of AIDS.

Results—Between January 1991 and December 1993, 97 out of 436 patients (22%) presented with their first AIDS defining illness coincident with their first positive result of an HIV test (group B). The remaining 339 patients (78%) had tested positive for HIV-1 infection within the previous eight years and had consequently been followed up in clinics before developing their first AIDS defining illness (group A). The two groups of patients did not differ in age and sex distribution, risk factors for HIV-1 infection, nationality, country of origin, or haematological variables determined at the time of the AIDS defining illness. However, the defining illnesses differed between the two groups. Illnesses associated with severe immunodeficiency (the wasting syndrome, cryptosporidiosis, and cytomegalovirus infection) were seen almost exclusively in group A whereas extrapulmonary tuberculosis and *Pneumocystis carinii* pneumonia were more common in group B. The survival of patients in group B after the onset of AIDS was significantly longer than that of patients in group A as determined by Kaplan-Meier log rank analysis ($P=0.0026$).

Conclusions—Subjects who are HIV positive and present late are a challenge to the control of the spread of HIV infection because they progress from asymptomatic HIV infection to AIDS without receiving health care. The finding that presentation with an AIDS defining illness coincident with a positive result in an HIV test did not have a detrimental effect on survival gives insights into the effects of medical intervention on disease progression after a diagnosis of AIDS.

Introduction

Previous studies have shown that the early detection of asymptomatic HIV-1 infection may lead to opportunities for the control of the spread of the infection and to interventions that may improve the prognosis for infected people.¹⁻⁴ We identified a group of patients who presented with an AIDS defining illness who did not know that they were HIV positive and therefore had not received medical intervention in relation to HIV infection. We studied these patients to gain further insights into the effect of early medical intervention on the outcome of an AIDS defining illness.

Patients and methods

We retrospectively studied 436 patients who had presented to this hospital with an AIDS defining illness between 1 January 1991 and 31 December 1993. The

patients were divided into two groups. In group A (339 patients) the time between the diagnosis of HIV seropositivity and the AIDS defining illness was greater than two months (range 2.1-120.2 months, median 46.1 months). In group B (97 patients) the time between a positive result in an HIV test and the AIDS defining illness was less than two months (range 0.0-2.0 months, median 0.0 months). Patients in group B had not been tested for HIV before developing their illness; seven of them received a clinical diagnosis of AIDS before an HIV test gave positive results, but the diagnosis was not confirmed for up to two months as a result of a delay in the completion of diagnostic tests such as culture of *Mycobacterium tuberculosis* in alveolar lavage specimens. One illness had precipitated the diagnosis of AIDS in all patients. Twelve patients had secondary AIDS defining illnesses, predominantly Kaposi's sarcoma.

The age at diagnosis of the first AIDS defining illness, sex, ethnic origin, country of origin, risk factors for HIV-1 infection, and the time between being diagnosed HIV positive and presentation with the AIDS defining illness was determined for each patient.⁵ The survival of patients until 31 December 1994 or death before this date was determined. Eight patients in group A and three patients in group B were lost to follow up after their AIDS defining illness. In addition, the following details were noted for the 305 patients presenting with their first AIDS defining illness during 1992 and 1993: the use of zidovudine or prophylaxis against *Pneumocystis carinii* pneumonia before the illness and haemoglobin concentration, mean red cell volume, neutrophil count, and CD4 positive T lymphocyte count at the time of the illness.

STATISTICAL METHODS

All categorical variables were compared between the two groups by Fisher's exact test. The survival time from the AIDS defining illness until death was compared between the two groups by Kaplan-Meier log rank analysis. The Mann-Whitney U test was used for comparison of all other continuous variables.

Results

Patients in group A did not differ significantly from patients in group B with respect to their age at presentation with their AIDS defining illness, sex, ethnic origin, the ratio of British citizens to non-British citizens, or risk factors for HIV infection (table I). Patients in group A did not differ from those in group B with respect to their haemoglobin concentration, neutrophil count, or CD4 positive T lymphocyte count (table II).

Extrapulmonary *M. tuberculosis* infection was diagnosed in 23 of the 339 (7%) patients in group A and in 15 of the 97 (15%) patients in group B ($P=0.019$, Fisher's exact test) (table III). The wasting syndrome, cytomegalovirus infection, and cryptosporidiosis were diagnosed in only three (3%) patients in group B but in 21 (6%), 31 (9%), and 17 (5%) patients, respectively, in group A (table III).

A total of 305 patients presented with their first AIDS defining illness in 1992 and 1993 (236 patients in

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TABLE I—Patient characteristics. Values are numbers (percentages) of patients unless stated otherwise

	Group A (n=339)	Group B (n=97)
Sex:		
Male	316 (93)	88 (91)
Female	23 (7)	9 (9)
Mean (SD) age (years):	37.8 (8.5)	38.3 (7.9)
Citizenship:		
British	243 (72)	65 (67)
Non-British	96 (28)	32 (33)
Ethnic origin:		
White	306 (90)	84 (87)
Afro-Caribbean	29 (9)	12 (12)
Other	4 (1)	1 (1)
Risk factors for HIV-1 infection:		
Homosexual/bisexual	261 (77)	77 (79)
Heterosexual	36 (11)	22 (22)
Partner HIV positive	22 (6)	3 (3)
Prostitute	4 (1)	0
Intravenous drug misuser	15 (4)	0
Haemophilia	1 (0.3)	0

Group A=patients unaware of HIV status at presentation with AIDS defining illness; group B=patients knowing HIV status at development of AIDS defining illness.

TABLE II—Haematological variables in patients at time of first AIDS defining illness in 1991, 1992, and 1993. Values are medians (ranges)

	Group A (n=236)	Group B (n=69)
Haemoglobin (g/l)	121 (60-166)	118 (71-169)
Mean cell volume (fl)	95 (77-135)	90 (82-106)
Neutrophils ($\times 10^9/l$)	1.9 (0.2-7.8)	2.1 (0.6-16.4)
CD4 positive T lymphocytes ($\times 10^9/l$)	68 (0-460)	58 (20-410)

Group A=patients unaware of HIV status at presentation with AIDS defining illness; group B=patients knowing HIV status at development of AIDS defining illness.

TABLE III—AIDS defining illness in patients. Values are numbers (percentages) of patients

	Group A (n=339)	Group B (n=97)
<i>Pneumocystis carinii</i> pneumonia	89 (26)	37 (38)
Kaposi's sarcoma	44 (13)	20 (21)
Oesophageal candidiasis	38 (11)	7 (7)
Cytomegalovirus infection	31 (9)	2 (2)
Wasting syndrome	21 (6)	1 (1)
Non-Hodgkinson's lymphoma	14 (4)	5 (5)
<i>Mycobacterium tuberculosis</i> infection	23 (7)	15 (15)
Cryptosporidiosis	17 (5)	0
Toxoplasmosis	14 (4)	4 (4)
<i>Mycobacterium avium</i> infection	8 (2)	2 (2)
Other	40 (12)	4 (4)

Group A=patients unaware of HIV status at presentation with AIDS defining illness; group B=patients knowing HIV status at development of AIDS defining illness.

Kaplan-Meier survival curves for patients with AIDS presenting early (group A) and late (group B)

group A and 69 patients in group B). In group A, 115 (49%) patients were taking zidovudine and 147 (62%) were receiving prophylaxis against *P carinii* pneumonia before their illness. No patients in group B were receiving either treatment before their defining illness.

A Kaplan-Meier survival analysis was performed for patients presenting with new AIDS diagnoses between 1991 and 1993 (figure). Patients in group B survived longer with AIDS than patients in group A ($P=0.0026$, log rank analysis). The observed number of deaths

during follow up was 209 in group A and 41 in group B. The expected number of deaths under the null hypothesis and with the size of the groups taken into account was 194 and 56 respectively.

Discussion

We identified a group of patients who presented with an AIDS defining illness at the same time as being found to be HIV positive; such patients thus develop AIDS before receiving health advice and medical intervention. Over one fifth of patients presenting with new AIDS diagnoses fell into this category between January 1991 and December 1993 despite there being a high profile HIV centre based in the Jefferiss Wing at St Mary's Hospital. A recent study reported that patients who were unaware of whether they were HIV positive up to nine months before being diagnosed as having AIDS were predominantly heterosexual, non-white, and aged between 15 and 24.⁶ In our study the two groups of patients did not differ in these respects. However, the criteria used to define late presenters were different in the two studies.

The pattern of AIDS defining illnesses differed between the two groups of patients. The incidence of *P carinii* pneumonia as the defining illness in patients in group A fell from 32% in 1991 to 16% in 1993, probably as a result of changing local prophylaxis guidelines from dapsone and pyrimethamine to co-trimoxazole.^{7,8} This is in contrast to the finding that the incidence of *P carinii* pneumonia in group B remained between 38% and 39% from 1991 to 1993. AIDS defining illnesses associated with severe immune deficiency such as the wasting syndrome, cryptosporidiosis, and cytomegalovirus infection were almost exclusively seen in group A.⁹ Conversely, there was an excess of AIDS defining illnesses associated with lesser degrees of immune deficiency in group B (particularly extrapulmonary *M tuberculosis* infection.) This may be because patients in group A presented with AIDS at a later stage in the decline of the function of their immune system than did those in group B. This is borne out by the finding that patients in group A who died within six months of presenting with an AIDS defining illness had lower CD4 positive T lymphocyte counts than patients in group A as a whole ($P=0.007$, Mann-Whitney U test). Paradoxically, the CD4 count at presentation with the others was higher, although not significantly, in patients in group A than in patients in group B (table III). The Concorde study suggested that a higher CD4 count attributable to the use of zidovudine during asymptomatic HIV infection was not associated with a clinical benefit.¹⁰

Key messages

- An appreciable minority of patients present with AIDS while being unaware of their HIV seropositivity
- Patients who present in this way are a challenge to the control of the spread of HIV infection
- Presentation with AIDS coincident with the first positive result of an HIV test does not seem to have a detrimental effect on survival after development of an AIDS defining illness
- The study of patients who progress from primary HIV infection to AIDS without receiving medical intervention gives insights into the effects of medical intervention on presentation and survival after developing an AIDS defining illness

The survival of patients in group B, who presented late, was found to be significantly better than the survival of patients in group A, who presented early. This finding is consistent with the view that the onset of AIDS is delayed in patients who receive early medical intervention in HIV infection.¹⁰⁻¹² However, the finding suggests that the subsequent survival of these patients when they develop AIDS may be commensurately decreased. We believe that our data are compatible with the results of the Concorde and other studies, in which early intervention with zidovudine delayed the development of AIDS but did not affect survival overall.^{10-12,13}

In conclusion, this study highlights the scale of the public health problem posed by patients presenting with AIDS coincidental with their first positive result in an HIV test. It also contributes to the debate on the effects of medical intervention on survival after an AIDS defining illness has developed.

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Waist circumference as a measure for indicating need for weight management

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Abstract

Objective—To test the hypothesis that a single measurement, waist circumference, might be used to identify people at health risk both from being overweight and from having a central fat distribution.

Design—A community derived random sample of men and women and a second, validation sample.

Setting—North Glasgow.

Subjects—904 men and 1014 women (first sample); 86 men and 202 women (validation sample).

Main outcome measures—Waist circumference, body mass index, waist:hip ratio.

Results—Waist circumference ≥ 94 cm for men and ≥ 80 cm for women identified subjects with high body mass index (≥ 25 kg/m²) and those with lower body mass index but high waist:hip ratio (≥ 0.95 for men, ≥ 0.80 women) with a sensitivity of $>96\%$ and specificity $>97.5\%$. Waist circumference ≥ 102 cm for men or ≥ 88 cm for women identified subjects with body mass index ≥ 30 and those with lower body mass index but high waist:hip ratio with a sensitivity of $>96\%$ and specificity $>98\%$, with only about 2% of the sample being misclassified.

Conclusions—Waist circumference could be used in health promotion programmes to identify individuals who should seek and be offered weight management. Men with waist circumference ≥ 94 cm and women with waist circumference ≥ 80 cm should gain no further weight; men with waist circumference ≥ 102 cm and women with waist circumference ≥ 88 cm should reduce their weight.

Introduction

About half of all British adults have a body mass index (weight (kg)/(height (m)²) of >25 , while almost 15% have an index of >30 , and these proportions are

rising.^{1,2} Given the lack of success in the management of obesity and increasing associated health costs,^{3,4} greater emphasis on prevention is needed, particularly in young people, who often have little contact with health services. While many health professionals are now familiar with the acceptable range for body mass index (20-25),^{2,5} most members of the public cannot readily calculate their index to establish their own risk or need for weight management. Charts developed by the Health Education Authority are helpful but are still not understood by many.⁶ Height must be measured accurately as small errors in the denominator are exaggerated by squaring.

The major metabolic cardiovascular risk factors (high blood pressure, plasma lipids, insulin resistance) all aggregate independently with both body mass index and waist:hip ratio^{7,8} and improve with weight loss.⁹⁻¹³ The circumference of the waist relates closely to body mass index and is also the dominant measurement in the waist:hip ratio, which reflects the proportion of body fat located intra-abdominally, as opposed to subcutaneously,⁷ and waist circumference is the best indicator of changes in intra-abdominal fat during weight loss.¹⁴

We evaluated waist circumference as a simple predictor of health risk from being overweight and through the central distribution of fat to indicate levels at which individuals should take action.

Methods

SUBJECTS

Determination study

We randomly recruited 904 men and 1014 women, aged 25 to 74 years, from the general population of north Glasgow between January and August 1992, excluding only those who were chair bound.

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