Acute HIV infection in Singapore: predominance of men who have sex with men

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ABSTRACT

Introduction: The incidence of human immunodeficiency virus (HIV) infection in Singapore is on the rise. We aimed to study the clinical epidemiology of acute HIV infection in Singapore.

Methods: All patients that fulfilled the criteria for definite and probable acute HIV infection were prospectively identified from January 1, 2003 to June 30, 2006. Demographic, clinical and laboratory data were recorded.

Results: A total of 16 out of 34 patients had definite acute HIV infection, and 68 percent of the entire cohort comprised men who have sex with men (MSM). Ten percent of the patients were co-infected with hepatitis B and C viruses, while 27 percent were infected with syphilis. Signs and symptoms were nonspecific, with fever, rash and diarrhoea being the three most common symptoms. Only 35 percent of the patients required hospitalisation.

Conclusion: Men who have sex with men account for the majority of patients with acute HIV infections in Singapore, many of them also being co-infected with syphilis. Safer sex campaign among MSM should be implemented or intensified.

Keywords: acute HIV infection, HIV transmission, men who have sex with men, seroconversion, Singapore

Singapore Med J 2011; 52(12): 860-863

INTRODUCTION

The first case of human immunodeficiency virus (HIV) infection in Singapore was reported in 1985, and as of December 31, 2006, 3,060 cases had been notified to the Ministry of Health, Singapore.[1] The incidence of HIV infection among Singaporeans is on the rise, with rates of 91.4, 101.3 and 118.1 per million population in 2005, 2006 and 2007, respectively.[1] Thus far, 53% of the notified cases presented with acquired immune deficiency syndrome (AIDS) at diagnosis. However, while AIDS cases comprised 59% and 56% of all notified HIV/AIDS cases in 2003 and 2004, respectively, the number decreased to 32% and 35%, in 2005 and 2006 respectively. Increasing acute or early HIV cases may represent a change in the epidemiology of HIV transmission in Singapore, and warrants further investigation and public health intervention.

We aimed to study the clinical features and epidemiology of acute HIV infection among patients who were referred to the Communicable Disease Centre or hospitalised at Tan Tock Seng Hospital under the Department of Infectious Diseases. Communicable Disease Centre is the national referral centre for HIV/AIDS in Singapore and a part of the Department of Infectious Diseases at Tan Tock Seng Hospital, a 1,200-bed tertiary referral university teaching hospital in Singapore.

METHODS

From January 1, 2003 to June 30, 2006, acute HIV patients were identified prospectively from the weekly departmental meeting, where all HIV/AIDS patients seen for the first time as outpatients at the Communicable Disease Centre as well as newly diagnosed HIV-infected patients admitted as inpatients to the Department of Infectious Diseases, Tan Tock Seng Hospital were discussed.

Definite acute HIV infection is defined as an initial negative HIV enzyme-linked immunosorbent assay (ELISA) or an indeterminate HIV Western blot, followed by positive HIV ELISA and Western blot tests within the next six weeks to three months, with compatible acute clinical illness. Probable acute HIV infection is defined as compatible acute clinical illness and positive HIV ELISA and Western blot within three months of a recent high-risk exposure to HIV infection, without an initial negative HIV ELISA or indeterminate Western blot.

Institutional Review Board approval was obtained to retrospectively review the patients' medical records in this study. The patients' demographic, clinical and

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Table I. Demographic, clinical and selected laboratory data of acute HIV-infected patients in Singapore (n = 34).

Demographic	No. (%)
Age; range (yrs)	32; 21–61
Ethnicity	
Chinese	30 (88)
Malay	2 (6)
Indian	1 (3)
Others	1 (3)
Sexual orientation	
Heterosexual	11 (32)
Homosexual	20 (59)
Bisexual	3 (9)
Injecting drug use	1 (3)
Requiring hospitalisation	12 (35)
Co-infection	
Hepatitis B carrier	3/30 (10)
Hepatitis C-infected	3/30 (10)
RPR-reactive	7/30 (23)
TPPA-reactive	8/30 (27)
CD4 count at diagnosis (× 10^6/L)	
< 200	3/22 (14)
≥ 200 and < 350	10/22 (45)
≥ 350 and < 500	6/22 (27)
≥ 500	3/22 (14)

RPR: rapid plasma reagin; TPPA: treponemal pallidum particle agglutination assay

Table II. Clinical features of acute HIV-infected patients in Singapore (n = 34).

Clinical feature	No. (%)
Symptom	
Fever	31 (91)
Rash	19 (56)
Diarrhoea	18 (53)
Headache	8 (24)
Myalgia	15 (44)
Arthralgia	10 (29)
Weight loss	9 (26)
Anorexia	7 (21)
Pharyngitis	9 (26)
Cough	8 (24)
Nausea/vomiting	6 (18)
Swollen glands	4 (12)
Mouth ulcers	3 (9)
Genital ulcers	1 (3)
Neck stiffness	2 (6)
Sign	
Lymphadenopathy	14 (41)
Rash	10 (29)
Tonsilitis	4 (12)
Oral thrush	3 (9)
Oral ulcers	2 (6)
Genital ulcers	2 (6)
Meningism	2 (6)

laboratory data, risk factors for HIV infection and need for hospitalisation were extracted using a standardised data form. Descriptive statistics were used to report the data. Categorical variables were compared using Fisher's exact test. A p-value < 0.05 was considered statistically significant.

RESULTS

During the study period, a total of 1,140 patients were referred to the Communicable Disease Centre or admitted to the Department of Infectious Diseases, Tan Tock Seng Hospital. Overall, 16 patients had definite acute HIV infection while 18 had probable acute HIV infection. They represented 3% of all HIV patients seen at our institution over the study period. There were eight HIV patients in 2003, 13 in 2004, ten in 2005 and three in the first six months of 2006.

Table I shows the demographic, clinical and laboratory data of the cohort. The median age of the patients was 32 years, and all but one were male. Men who have sex with men (MSM) comprised 68% of the cohort. Hepatitis B carrier status and hepatitis C infection were present in 10% of the patients each, while 27% of the patients had serologic evidence of recent or previous syphilis. Ten patients reported prior sexually transmitted infections; syphilis (n = 5), gonorrhoea (n = 1) and genital herpes (n = 1); combinations of gonorrhoea and syphilis (n = 1), syphilis and nonspecific urethritis (n = 1), and syphilis and genital herpes (n = 1). Table II shows the symptoms and signs experienced by patients with acute HIV infection. Fever, rash and diarrhoea occurred in more than 50% of patients, while myalgia was noted in 44%, arthralgia in 29%, weight loss and pharyngitis in 26% each and headache in 24% of patients.

The most common clinical sign was lymphadenopathy, which affected the cervical region in all patients (41%), followed by concomitant axillary (n = 4) and inguinal lymphadenopathy (n = 2). Erythematous maculopapular rash was seen in all ten patients. Leukocytosis was noted in one (3%) patient, while leukopenia was noted in six (19%) patients. Lymphocytosis and lymphopenia occurred in five (16%) patients each, while anaemia was noted in one (3%) patient. Thrombocytosis occurred in one (3%) patient and thrombocytopenia in four (13%) patients. Elevated levels of alanine and aspartate transaminases were noted in 16 (62%) and 11 (42%) patients, respectively. Serologic evidence of prior cytomegalovirus and toxoplasma infection was seen in 28 (93%) and five (17%) patients, respectively. There were more MSM with syphilis than heterosexuals (30% vs. 9%); however, the difference was not statistically significant.

Hospitalisation was required in 35% of the patients due to symptomatic illness, which lasted for more than a week in half of the patients; in 26% of the patients, the acute illness exceeded three weeks. Up to three

symptoms were reported by 29% of the patients, 4–6 symptoms by 38% and more than six symptoms by 32% of patients. Although it was a small cohort, 14% of acute HIV infections resulted in CD4 count < 200 × 10^6/L.

DISCUSSION

Acute HIV infection represents a very small percentage of newly diagnosed HIV infections in Singapore. This is likely due to a lack of recognition of its nonspecific symptoms and signs. Doctors in primary care settings, where patients with acute HIV are likely to present, should be alert to this differential diagnosis in a patient with fever exceeding one week and in whom there is no clear-cut alternative diagnosis. Further history-taking to determine sexual risk factors should be undertaken before proceeding to offer HIV serological testing on at least two occasions (three months apart), should the initial HIV serology be negative. It is noteworthy that in our local population, fever, rash and diarrhoea are the three most common symptoms. In addition, myalgia, arthralgia, pharyngitis, weight loss and headache are relatively common. Oral and genital ulcers are relatively uncommon, although with maculopapular rash, this triad was reported as fairly specific for acute HIV infection.[2,3]

Consistent with most large studies on acute HIV infection, the majority of patients were young MSM.[4-6] Our series comprised 68% MSM, compared with 72%–93% in the aforementioned three series. Overall, MSM comprised only 30% of notified cases in 2006 in Singapore. This may indicate a new epidemic of HIV among MSM in Singapore and warrants urgent public health interventions, including education and access to safer sex measures. It is interesting to note that while the proportion of men diagnosed with HIV and AIDS in Singapore increased slightly from 86% in 2001 to 93% in 2007, the proportion of MSM among males nearly doubled from 19% in 2001 to 37% in 2007, which represents a disproportionate increase in the incidence of HIV in this group.[7] A possible confounder is detection bias, i.e. MSM are more aware of HIV risk and seek medical attention when they become sick. If so, this potential awareness of HIV risk has not reduced high-risk sexual behaviour, i.e. unprotected sexual intercourse resulting in acute HIV infection. These social and behavioural aspects merit further study.

It is interesting that 14% (three out of 22 cases) of the patients in our cohort had CD4 < 200 × 10^6/L during acute HIV infection, in contrast to 3%–4% in one series of 102 patients[5] and none in three other series (comprising 67, 395 and 148 patients, respectively).[4,6,8] Two patients had definite acute HIV infection, with initially negative or indeterminate Western blot, which tested positive on follow-up. The third patient had probable acute HIV infection with a history of negative HIV serology a year ago. Two of these three patients did not experience CD4 rebound after six months and commenced highly active antiretroviral therapy (HAART), one of whom had persistently low CD4 (< 200 × 10^6/L) despite having repeatedly undetectable HIV viral load. The third patient had to commence HAART due to symptomatic illness, and apart from cutaneous Kaposi's sarcoma, there was no other opportunistic infection or AIDS-defining conditions after extensive microbiological and radiological evaluations.[9]

Of note, 27% of patients with acute HIV infection in our cohort were co-infected with syphilis, a trend that was also seen in the USA.[10] There have been increasing rates of infection with syphilis[11] and gonorrhoea[12] among MSM in the USA. This has been linked to an increase in high-risk sexual behaviour among MSM[13] and the influence of methamphetamine.[14] Local research in this area is required in order to better understand the sexual risk factors that perpetuate new HIV infections among MSM so as to design effective intervention strategies.

In conclusion, the clinical features of acute HIV infection are nonspecific. Thus, doctors should be alert when determining sexual risk factors and should offer HIV serology testing in patients with prolonged viral fever. Although this was a small study, we have documented that MSM account for a large proportion of acute HIV infections in Singapore. This is an area that warrants more public health research in order to guide effective preventive measures.

REFERENCES

1. Ministry of Health. Communicable Diseases Surveillance in Singapore 2006 [online]. Available at: www.moh.gov. sg/mohcorp/publicationsreports.aspx?id=17516. Accessed August 11, 2008.
2. Cooper DA, Gold J, Maclean P, et al. Acute AIDS retrovirus infection. Definition of a clinical illness associated with seroconversion. Lancet 1985; 1:537-40.
3. Kinloch-de Loës S, de Saussure P, Saurat JH, et al. Symptomatic primary infection due to human immunodeficiency virus type I: review of 31 cases. Clin Infect Dis 1993; 17:59-65.
4. Berrey MM, Schacker T, Collier AC, et al. Treatment of primary human immunodeficiency virus type 1 infection with potent antiretroviral therapy reduces frequency of rapid progression to AIDS. J Infect Dis 2001; 183:1466-75.
5. Kassutto S, Maghsoudi K, Johnston MN, et al. Longitudinal analysis of clinical markers following antiretroviral therapy initiated during acute or early HIV type 1 infection. Clin Infect Dis 2006; 42:1024-31.
6. Hoen B, Cooper DA, Lampe FC, et al. Predictors of virological

outcome and safety in primary HIV type 1-infected patients initiating quadruple antiretroviral therapy: QUEST GW PROB3005. Clin Infect Dis 2007; 45:381-90.
7. Ministry of Health. HIV Statistics [online]. Available at: http://www.moh.gov.sg/content/moh_web/home/diseases_and_conditions/h/hiv_aids.html. Accessed August 11, 2008.
8. Hecht FM, Wang L, Collier A, et al. A multicenter observational study of the potential benefits of initiating combination antiretroviral therapy during acute HIV infection. J Infect Dis 2006; 194:725-33.
9. Lye D, Lee CC, Leo YS. Acquired immune deficiency syndrome at acute seroconversion. Abstract. 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention, 2007; Sydney, Australia.
10. Chesson HW, Heffelfinger JD, Voigt RF, Collins D. Estimates of primary and secondary syphilis rates in persons with HIV in the United States, 2002. Sex Transm Dis 2005; 32:265-9.
11. Buchacz K, Klausner JD, Kerndt P, et al. HIV incidence among men diagnosed with early syphilis in Atlanta, San Franscisco, and Los Angeles, 2004 to 2005. J Acquir Immune Defic Syndr 2008; 47:234-40.
12. Fox KK, del Rio C, Holmes KK, et al. Gonorrhea in the HIV era: a reversal in trends among men who have sex with men. Am J Public Health 2001; 91:959-64.
13. Stall RD, Hays RB, Waldo CR, Ekstrand M, McFarland W. The Gay 90s: a review of research in the 1990s on sexual behaviour and HIV risk among men who have sex with men. AIDS 2000; 14 suppl 3: S101-14.
14. Frosch D, Shoptaw S, Huber A, Rawson RA, Ling W. Sexual HIV risk among gay and bisexual male methamphetamine abusers. J Subst Abuse Treat 1996; 13:483-6