HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN SINGAPORE - THE FIRST 50 CASES

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ABSTRACT

As at 31 May 1990, fifty Singaporeans with the Human Immunodeficiency Virus (HIV) infection had been detected. Of these, nineteen had the Acquired Immunodeficiency Syndrome (AIDS). The majority of infected persons had been infected through sexual contact (homosexual 52%; bisexual 24%; heterosexual 20%) with men and women from countries where HIV infection was prevalent. The majority of infected patients (88%) were in the age range 20-39 years. There was one case of blood transfusion-associated AIDS. There were no infected paediatric or haemophiliac cases or intravenous drug use in any of the patients. A spectrum of AIDS-related opportunistic infections and cancers was observed, and *Pneumocystis carinii* pneumonia was the most frequent presentation. Thirteen patients with AIDS had died and the median survival time was about seven months.

Keywords: AIDS, HIV, Clinical, Epidemiology, Singapore

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INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a human retrovirus discovered in 1983 (1,2). It is now widely accepted that infection by HIV is the cause of the epidemic of the Acquired Immunodeficiency Syndrome (AIDS) and related illnesses, first reported in the United States in 1981 (3), and now evident in all parts of the world, including Singapore.

A comprehensive programme was established in early 1985 to control and limit the spread of HIV infection in Singapore (4). The programme included health care delivery, education of health care workers and the community, surveillance and counselling of high-risk individuals, as well as screening of blood donors for HIV.

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The strategy was a multi-pronged approach. HIV infection was made a notifiable disease under the Infectious Diseases Act on 17 April 1985 to empower the Ministry of Health to control the spread of the disease (5).

A Health Plan to deal with all aspects of clinical management of HIV infection was formulated. This included the formation of an Advisory Committee on AIDS, which was later replaced by an AIDS Task Force in November 1987 to enable swifter action in the control of the disease. The functions of this Task Force were related to management of HIV infected persons, epidemiology of the disease, development of services and support for infected individuals, and provide information on the latest development of the disease (6). The Plan also included the provision of an AIDS ward at the Communicable Disease Centre (CDC) to admit and manage infected patients. The ward was commissioned in April 1986 and admitted the first patient with AIDS in September that year. In addition, upgraded outpatient and surgical facilities were made available in 1989.

All medical and paramedical personnel were issued guidelines on precautions to be taken in handling infected patients and laboratory specimens. Training at established overseas centres for clinical management and counselling of patients with HIV infection were made available to medical and nursing staff. An important facet in the clinical strategy was the surveillance and counselling of infected persons and their sex contacts. In this context, the monitoring and evaluation of the extent of disease penetration was provided by the Epidemiology Department of the Health Ministry.

METHODS

A descriptive study was conducted using data from case records and interviewing patients at the CDC. All reported patients with HIV infection, including AIDS, were notified to the Ministry of Health and subsequently managed at the CDC. All patients had a positive ELISA screening

test and a confirmatory Western Blot test. Diagnosis of AIDS was made in accordance with established classification systems (7,8). The period of study was from 1 January 1985 to 31 May 1990 and a total of 50 patients were reviewed. Basic demographic data, including sex, age and ethnic origin, and socioeconomic background were obtained using a questionnaire. The patients were also asked about their sexual practices, recreational drug usage, and travel patterns. Clinical perspectives on presenting features and HIV-related illnesses were studied. Surveillance data was incomplete in the sense that one patient who had AIDS received treatment and died abroad, and another had refused cooperation. The sample statistics were analysed using the computer programme "Epistat". Significance testing was carried out with Fisher's exact test. Survival analysis of patients with AIDS was carried out using the product-limit method of estimating survivorship function developed by Kaplan and Meier (9,10).

RESULTS

The first case of HIV infection in Singapore was detected on 16 May 1985 in a young homosexual man, and the first case of AIDS was diagnosed in a 55-year-old heterosexual male in September 1986 when he was admitted to the CDC with *Isospora belli* infection and malignant high grade immunoblastic lymphoma. Since the first case of HIV infection was detected, the number of cases identified had increased (Table I). As at 31 May 1990, there were 50 Singaporeans with HIV infection. Of these, 19 had AIDS, one had the AIDS-Related Complex (ARC) and the remainder were asymptomatic. A clinico-epidemiological review of the first 22 patients was published elsewhere by the author (11).

Table I

Frequency distribution of HIV/ AIDS patients (reported) by year

Year	No. of patients				Cumulative frequency	
	HIV		AIDS		HIV	AIDS
1985	2	(0.8)	-		2	-
1986	7	(2.7)	1	(0.4)	9	1
1987	10	(3.8)	3	(1.1)	19	4
1988	15	(5.7)	6	(2.3)	34	10
1989	10	(3.8)	6	(2.3)	44	16
1990*	6	-	3	-	50	19

Parentheses : rate (reported cases per million population)
* till 31 May 1990

Mode of Transmission

Sexual transmission, both homosexual (52%) and bisexual (24%) as a means of HIV infection accounted for 76% of all reported cases, while heterosexual transmission accounted for 20% (Table II). One man had transfusion-associated AIDS after receiving contaminated blood overseas in 1981, and his wife had been infected heterosexually. No paediatric or haemophiliac cases were seen and there was no history of intravenous drug use in any of the patients.

Table II

Distribution of patients with HIV infection by sex and risk factors

Risk factors	No. of patients			
	Male	Female	Total	(%)
Homosexual	26	-	26	(52)
Bisexual	12	-	12	(24)
Heterosexual	8	2	10	(20)
Blood Transfusion	1	-	1	(2)
Unknown	1	-	1	(2)
Total	48	2	50	(100)

Patient Characteristics

All, except two, patients were male; the male-to-female case ratio was 24:1. The age of patients was measured as "age last birthday" at the time of diagnosis. A large proportion of them were in the most sexually active age groups of 20-29 years (48%) and 30 - 39 years (40%). The median age was 29 years (range:17 - 55). One female patient was 51 and the other 35 years old. The majority of the patients were Chinese (66%), while 10% were Malays, 22% were Indians and 2% Eurasian. Although the proportion of the different races in this study tend to approximate that of the population of Singapore (12), with the exception of that of the Indian race which was comparatively higher, cautious interpretation should be exercised in view of the small sample of patients.

Patients who were single and never married accounted for 80% of the total, and all were male. Nine patients (18%) were married, and the remaining one had a non-consummated marriage which was annulled. All, except two, spouses of the married patients were tested seronegative. In an analysis of the occupational group distribution (13) of the infected, 48% of the patients were employed in the service industry, mainly in the catering and lodging industry as waiters, hotel room stewards, and as airline stewards. The categories of "professionals" and "managerial workers" each accounted for 16% of the total, while "production workers" formed 14%. Travel histories were obtained in 49 patients (98%), and 72% of them had sexual exposures with homosexual men and female prostitutes in the countries they visited.

Presentation

The source of referral of the patients to the CDC was reviewed. Fourteen (28%) patients were diagnosed to have HIV infection following admission to acute-care hospitals for HIV-related illnesses. Thirty-six (72%) patients

were detected in the asymptomatic stage when blood was sent for HIV antibody testing. Of these 36 patients, 12 (24%) were detected through blood donor screening, 6 (12%) had voluntary testing, and 5 (10%) each were detected through contact tracing and by tests initiated by doctors. Four (8%) patients were detected through life insurance agencies.

Opportunistic infections and cancers

The clinical pattern of opportunistic infections and cancers in patients with AIDS are summarised in Table III. The commonest infection was *Pneumocystis carinii* pneumonia (PCP) (52.6%). PCP was diagnosed definitively in five patients while the remainder were diagnosed on presumptive evidence. The median CD4 count in these patients at diagnosis of PCP was 105 cells/mm^3 (range: 16 – 255). These patients were treated with sulphamethoxazole-trimethoprim and they were subsequently maintained on suppressive therapy with the same or pyrimethamine-sulfadoxine. Three patients had received intravenous pentamidine and continued subsequent maintenance on the aerosolised drug.

Table III

Frequency distribution of patients with AIDS according to opportunistic infections and cancers

Infections/ cancers	No. of patients (%)
OPPORTUNISTIC INFECTIONS	
Pneumocystis carinii pneumonia	10 (52.6)
Cytomegalovirus retinitis	4 (21.1)
Cryptococcal meningitis	2 (10.5)
Disseminated tuberculosis	1 (5.3)
Isospora belli enteritis	1 (5.3)
Cryptosporidosis	1 (5.3)
Salmonella septicaemia	1 (5.3)
Klebsiella pneumonia	1 (5.3)
Pneumococcal pneumonia	1 (5.3)
CANCERS	
Kaposi's sarcoma	4 (21.1)
Malignant lymphoma	2 (10.5)
Chronic lymphatic leukemia	1 (5.3)

The first AIDS patient (a heterosexual) who acquired the disease through blood transfusion presented with chronic lymphatic leukemia, salmonellosis and *Isospora belli* enteritis. The voluminous diarrhoea resulting from the coccidial enteritis responded to treatment with furazolidone (14). He perished from fulminant Klebsiella septicaemia. At autopsy, malignant high grade immunoblastic lymphoma was identified in multiple organs.

Malignant lymphoma was also diagnosed in a homosexual patient. The patient with cryptosporidium enteritis presented with weight loss and profuse diarrhoea which responded partially to treatment with spiramycin.

Oral candidiasis was present in all patients with AIDS. They were treated either with oral nystatin or ketoconazole. Two patients with dysphagia had oesophageal candidiasis diagnosed by barium meal studies. *Cryptococcus neoformans* meningitis was seen in two homosexual patients who did not respond to treatment with intravenous amphotericin. Another homosexual patient had disseminated mycobacterium tuberculosis with pulmonary and gastrointestinal involvement; he succumbed after developing the adult respiratory distress syndrome.

Retinitis due to cytomegalovirus (CMV) infection was present in four (21.1%) homosexual patients. Their median CD4 cell count at diagnosis of CMV retinitis was 137 cell/mm^3 (range:50-255). Ganciclovir was administered to these patients to control progression of infection. Four (21.1%) homosexual patients developed Kaposi's sarcoma (KS); two had the cutaneous form while the remainder the visceral form which was confirmed histologically. The median CD4 cell count in patients with KS at diagnosis was 155 cells/mm^3 (range: 84-284).

Other related illnesses

The HIV wasting syndrome was observed in a homosexual patient who later developed CMV retinitis. Painful peripheral neuropathy was seen in one patient. Six patients had a past history of herpes zoster infection. Seborrhoeic dermatitis was present in 11 patients. Of the sexually transmitted diseases, 6 patients had gonorrhea, 3 had syphilis, 3 had genital herpes, and one had non-specific urethritis. Three homosexual patients who practised anal intercourse had perianal herpes and four had perianal sinus, fistula or abscess.

Immunological studies

T-lymphocyte subsets were available in 46 (92%) of the patients studied. The median CD4 cell counts in patients with AIDS and asymptomatic HIV carriers at diagnosis were 217 cells/mm^3 (range: 8-560) and 492 cells/mm^3 (range:145-1225), respectively. The normal range for CD4 cells is 600 to 2400 cells/mm^3. In the group of patients with CD4 cell count of 400 cells/mm^3 or less at diagnosis, 46% had died, while in those with cell count above this level had a significantly better prognosis with 95% of them still alive ($p < 0.01$).

Survival

Thirteen patients with AIDS had died. The case fatality rate for AIDS was 68.4%. The median survival time was 7 months. The entry point for these patients was at the time of diagnosis of AIDS and the end point was death. Ten patients (52.6%) with AIDS had received azidothymidine (Zidovudine) of whom six were alive as at 31 May 1990. As the number of patients is small, it would not be meaningful at this stage to assess the impact of the drug on survival.

DISCUSSION

The incidence of AIDS in Asia is low compared to that in

the Americas, Europe or Africa. As at 31 January 1990, only 511 cases were reported from countries in Asia, compared with 215,144 worldwide (15). While there had been an abundance of literature and knowledge of HIV infection worldwide, there was a noticeable paucity of information on epidemiological and clinical patterns of the disease in Asia. Infection had occurred among persons who had travelled to areas where HIV infection was prevalent, or who had sexual contact with homosexual men and prostitutes from these areas. HIV infections were now increasingly recognised among intravenous drug users, prostitutes, and the heterosexual population (16-24).

The epidemiological characteristics of patients with HIV infection in Singapore were similar to those reported in pattern 1 countries and most other countries in Asia (16). The predominant route of infection was through sexual contact, primarily homosexual. There was only one case of transfusion-associated AIDS in a heterosexual man who received contaminated blood overseas. Heterosexual transmission accounted for 20% of the total number of patients and there has been concern over the increase in the proportion of heterosexuals who were infected since June 1988 (13.2%) (25). There were no cases of HIV infection in haemophiliacs, children or intravenous drug users.

The local pattern of opportunistic infections and neoplasms in patients with AIDS resembled that reported in western countries with pattern 1 transmission (26). PCP was the most frequent presentation in our patients with AIDS (52.6%), and 31.5% had died. PCP had been reported to develop ultimately on one or more occasions in at least 80% of patients with AIDS and was the major cause of death in 25% of these patients (27). KS was present in four homosexual men (21.1%), and this cancer has been described to be common among male homosexuals in western countries (28, 29). HIV infection has also been described to be an important risk factor for tuberculosis, and an increasing number of persons with disease caused by mycobacterium tuberculosis had been reported in the United States (30). There was only one case of disseminated tuberculosis in our study.

The median length of survival of the local patients with AIDS was seven months. This was poor in contrast to studies elsewhere of median survivals of about one year (31-33), and was related to the larger proportion of patients (74%) presenting at a late stage. The earlier detection of HIV infection allows close monitoring of the immune status and earlier diagnosis and treatment of opportunistic infections. Although it has not been possible to provide specific treatment for HIV infection despite intensive research, azidothymidine (Zidovudine) had been shown to decrease the incidence of opportunistic infections and to prolong survival (34-36).

With Singapore at the cross-roads of international travel, there is ample opportunity for introduction of the HIV virus into the country. The buoyant tourism sector resulted in double-digit growth annually since 1986, and had attracted more than 4 million visitors in 1988 (37). In the same year, 813,819 nationals travelled overseas, and 96% of them had embarked from the Asian region, mainly from the ASEAN countries. In this group, 62% were male, and 53% of them were in the age group 20 - 39 years. In this study, 98% of the patients had foreign travel and 72% of them had sexual exposure with natives in the countries of destination. It had also been observed that 82% of the patients travelled to Asian countries, including ASEAN (25). This high flow of visitor traffic between Singapore and Asia, and vice versa, will have an impact on virus transmission, particularly when some Asian countries have recently reported an increase in the number of infected cases (17-23). This is compounded by the fact that people from countries where HIV infection is prevalent will continue to visit Singapore.

While the world is at a dilemma on how best to reduce virus spread, Singapore has been faced with the visible end-product of HIV infection: an increasing number of reported AIDS cases and deaths. Soon, many will know, or know of, an infected friend, acquaintance, or family member dying of AIDS. This has already produced fear, which is a motivating factor in preventing infection by changing behaviour to prevent transmission. Educational approaches, including counselling, peer group support, condom advocacy programmes, and information dissemination to the community, have been shown to bring about sustained changes in sexual behaviour (38,39). With the number of cases expected to increase, the cost of treatment must be balanced against the cost of education and prevention programmes. Investments in such programmes could dampen future social and care costs of an even larger epidemic.

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