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Comparing the First and Second Hundred AIDS Cases in Hong Kong

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ABSTRACT

Objectives: To study the clinical and epidemiological features of the first 200 AIDS patients in Hong Kong.

Method: A retrospective analysis of the data reported to the Department of Health. The patients were divided into two groups of first 100 and second 100 cases for comparison so as to discern the temporal changes.

Results: The first 100 AIDS cases were reported from February 1985 through to March 1994 (122 months) while the second 100 in the following 26 months. For both groups, they were predominantly male (94%, 89%), Chinese (66%, 74%) who acquired HIV via sex (83%, 91%). The proportion of Caucasians and homo/bi-sexual contacts in first and second 100 cases have fallen from 26% to 12% (p=0.012), and from 53% to 31% (p=0.006) respectively. For primary AIDS-defining illness (ADI), the frequency of *Pneumocystis carinii* pneumonia (PCP) has decreased (46% to 30%, p=0.03) while that of tuberculosis (10%, 19%) and *Penicillium marneffei* (5%, 14%) infection have increased. *Mycobacterium avium intracellualare* and cytomegalovirus infection have become commoner subsequent ADIs. Frequency of PCP (22%, 9.5%) as the cause of death have dropped while that of tuberculosis has risen (4.8%, 14.3%). Median survival probability had improved from 7.3 months for the first half of patients to 11.9 months for the second half.

Conclusion: Incidence of PCP has declined among local AIDS patients whereas tuberculosis, penicilliosis, MAI, and CMV diseases have increased. Survival chance of AIDS patients has improved over the years.

Keywords: AIDS, Chinese, tuberculosis, *penicillium marneffei*, Hong Kong

INTRODUCTION

It is not an exaggeration to describe HIV infection as one of the most important disease entities that has emerged in the last two decades. Basically an infectious disease, HIV/AIDS and its related complications have nevertheless involved many different medical specialities, eg. immunology, ophthalmology, and clinical epidemiology. Needless to say, the psychosocial impact that it brings along is definitely no less than its medical consequences. Though HIV/AIDS is a relatively new disease in the history of human medical science, dedicated research efforts have enhanced greatly the understanding of its pathogenesis and clinical manifestations, which in turn allowed improved care and management. As a result of these interactions, the disease course of HIV infection is ever changing. For example, many countries have reported a change in disease presentation and outcome of their HIV/AIDS patients[1,2].

In Hong Kong, the start of HIV epidemic lagged a few years behind the Western countries. Despite the relatively low HIV prevalence locally, Hong Kong has been proactive in taking early actions for this devastating disease. Among the components of the AIDS programme, surveillance obviously plays a crucial role. HIV/AIDS are not notifiable diseases in Hong Kong. However, as a central component of the surveillance mechanism of the infection, a voluntary reporting system has been adopted since 1985 to document the demographic features, clinical manifestations and outcome of the local patients. The first AIDS case in Hong Kong was reported in February 1985, when a Caucasian presented with cytomegalovirus disease and was subsequently diagnosed to be HIV positive[3]. More than 11 years into the local HIV/AIDS epidemic, it is our intention to study whether, like other countries, there were also changes in the profile of our AIDS patients. This study summarises the findings of the first 200 AIDS patients in Hong Kong.

METHODS

Case records of the first 200 consecutive AIDS patients reported to the Department of Health were retrieved and studied. These reports were made by medical practitioners under strictly confidential setting. In Hong Kong, HIV infection is diagnosed by a positive screening test (usually enzyme-linked immunosorbent assay – ELISA) followed with the Western Blot confirmatory test. AIDS is diagnosed only when an HIV-infected person develops clinical complications due to the underlying immunosuppression. The 1987 AIDS surveillance definitions laid down by the US Centers for Disease Control (CDC) was adopted locally in early years[4] except that disseminated *Penicillium marneffei* infection was also considered an AIDS-defining illness (ADI) in our setting[5]. Following the modification of the CDC definition in 1994[6], Hong Kong also officially established its own surveillance case definition for AIDS in June 1995[7], with the following differences from that of CDC's: (i) pulmonary

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tuberculosis was only regarded as an AIDS event in the presence of a CD4 count < 200/uL; (ii) disseminated *Penicillium marneffei* infection was an ADI locally, and (iii) a CD4 level of < 200/uL alone was not regarded as an AIDS-defining criterion.

The following parameters of the patients were analysed: demography (sex, age, ethnicity, transmission route, age), interval from HIV diagnosis to AIDS progression, clinical presentation regarding first and subsequent ADIs, immunologic status of CD4 level, survival and causes of death. The 200 AIDS patients were arbitrarily divided into first 100 and second 100. Emphasis was made on the comparison of the characteristics of these two halves, to discern any temporal changes clinically or epidemiologically. Status of the patients as at the end of June 1996 was used for analysis on subsequent ADI and outcome. Significance testing of the data was performed using the chi-square test or Fisher's exact test for categorical variables, Log Rank test for comparison of survival probability and Wilcoxon (rank sum) test for comparison of CD4 count. A p value of < 0.05 was taken to be significant.

RESULTS

The first 100 AIDS cases were reported from February 1985 through to March 1994 (122 months) while the second 100 in the following 26 months up till May 1996. All of them except one were infected by HIV-1. During these same two periods, the number of HIV infections reported were 435 and 243 respectively.

Demographic features

As shown in Table I, both groups of patients were predominantly male, Chinese, and acquired HIV via sexual contact. There were more female AIDS cases in the second 100 patients but still significantly fewer than males. The proportion of Chinese and Asian, non-Chinese had increased while that for Caucasians fell significantly from 26% in the first half to 12% in the second group (p = 0.012). Cases arising from heterosexual contact has increased from 29% to 60% (p < 0.001) while the importance of homosexual transmission had dropped (41% vs 24%, p = 0.006). Mean age at HIV and also AIDS diagnosis presentation were similar for both groups of patients.

Table I – Demographic charactersitics of the first 200 AIDS patients in Hong Kong (February 1985 – May 1996)

	1st 100	2nd 100
Sex		
male : female	94 : 6	89 : 11
Ethnicity		
Chinese	66	74
Caucasian	26	12
Asian, non-Chinese	7	13
African	1	1
Age (mean ± SD in yr)		
HIV diagnosis	37.4 ± 12.4	35.2 ± 11.3
AIDS diagnosis	38.6 ± 12	36.6 ± 10.7
Risk factor (No.)		
heterosexual	29	60
homosexual	41	24
bisexual	12	7
injecting drug user	2	1
transfusion	10	3
perinatal	0	2
undetermined	6	3

Progression to AIDS & immunologic status

Two-thirds of the first 100 AIDS patients had a late HIV diagnosis with less than 6 months from HIV detection to progression to AIDS. The same phenomenon was observed for the second half of patients. Median HIV-to-AIDS intervals were 1 month for both groups while the mean value were 12 months (range, 0 – 80 months) and 15 months (range, 0 – 133 months) respectively.

CD4 counts at HIV detection and AIDS diagnosis are depicted in Table II. For the two halves, there was significant difference between the proportion of patients with CD4 < 50/uL at time of AIDS diagnosis whereas the differences between the two groups were significant for those patients with CD4 from 51 – 200/uL both at times of AIDS and HIV diagnosis. Median counts at HIV detection were similar at 137/uL (n = 52) and 130/uL (n = 44) for the two groups. However, median counts at AIDS diagnosis were 90/uL (n = 76) vs 50/uL (n = 55), and the difference was statistically significant (p = 0.0006).

Table II – Distribution of CD4 count at HIV and AIDS diagnosis of the first 200 AIDS patients

	% of 1st 100 AIDS	% of 2nd 100 AIDS	p value
CD4 at HIV (/uL)			
< 50	21.2	38.6	0.06
51 – 200	46.1	18.2	0.004
> 200	32.7	43.2	0.29
CD4 at AIDS (u/L)			
< 50	32.9	56.4	0.007
51 – 200	53.9	34.5	0.028
> 200	13.2	9.1	0.47

AIDS-defining diseases

Although *Pneumocystis carinii* pneumonia (PCP) remained the most common presenting ADI for both halves of patients (Table III), its frequency has decreased from 46% to 30% (p = 0.03). While *Mycobacterium tuberculosis* (MTB) infection was the second most frequent primary ADI for all patients, its growing importance has become apparent. The increase in the number of disseminated *Penicillium marneffei* infections was especially marked (5% vs 14%, p = 0.03). There were no significant changes in incidence of other opportunistic infections and Kaposi's sarcoma as the first AIDS indicator disease.

Eighty-two and 39 episodes of subsequent AIDS-defining diseases were recorded for the first 100 and second 100 AIDS patients respectively (Table IV). Cytomegalovirus (CMV) infection was observed to have become a commoner subsequent ADI in the second group of patients: 33% vs 23%. However, this did not reach statistical significance (p = 0.24). Similarly, *Mycobacterium avium intracellulare* (MAI)

Table III – Profile of primary AIDS-defining illnesses among the first 200 reported AIDS cases

	1st 100	2nd 100
Pneumocystis carinii pneumonia	46	30
Mycobacterium tuberculosis	10	19
Penicillium marneffei	5	14
Oesophageal candidiasis	5	7
Extrapulmonary cryptococcosis	6	6
CMV diseases	6	4
Kaposi's sarcoma	7	7
Cryptosporidiosis	2	6
Mycobacterium avium infection	4	1
Toxoplasmosis	4	0
Lymphoma	2	1
HIV encephalopathy	1	3
Isosporiasis	1	0
HIV wasting syndrome	1	1
Recurrent pneumonia	0	1
Total	**100**	**100**

Table IV – Profile of subsequent AIDS-defining illnesses among the first 100 (82 episodes) and second 100 (39 episodes) AIDS patients

	1st 100 AIDS	2nd 100 AIDS
Pneumocystis carinii pneumonia	7	2
Mycobacterium tuberculosis	4	3
Fungal infections	16	8
CMV diseases	19	13
Kaposi's sarcoma	6	1
*Others	17	4
Total	**82**	**39**

*include cerebral toxoplasmosis, cryptosporidiosis, HIV encephalopathy, chronic herpes simplex infection, recurrent salmonella septicaemia and lymphoma

arose more frequently in the second 100 AIDS patients (20.5% vs 15.8%, p = 0.57).

Mortality & survival

Seventy-seven patients of the first group were known to have died, compared with 38 of the second hundred patients. Another 16 and 10 of the two groups respectively were lost to follow-up. The others are alive and receiving treatment. Sixty-three and 21 of the deceased patients in the two groups had the cause of death identified and the vast majority – 97% and 86% respectively – were due to HIV-related complications. Frequency of PCP leading to death dropped from 22% to 9.5% among the cases with known causes of death (Fig 1). MAI as the cause of death has also decreased from 15.9% to 4.8%. On the other hand, tuberculosis (4.8% vs 14.3%), and septicaemia (6.3% vs 14.3%) had become more important killer conditions for the second group of patients, compared with that for the first group. However, all these differences did not reach statistical significance.

Median survival of the deceased patients after AIDS diagnosis was 6 months for the first 100 patients and 3 months for the second 100. Nevertheless, overall survival chance was better for the second 100 AIDS patients as most of them were still alive and they had a much shorter duration of follow-up. The median survival probability after progression to AIDS (Fig 2) was 7.3 months for the first half of patients and 11.9 months for the second half (p = 0.10).

DISCUSSION

Despite an early beginning for the AIDS epidemic in Hong Kong compared to the HIV/AIDS epidemic in South-East Asia, Hong Kong strove to maintain a low HIV seroprevalence, as evidenced by the surveillance statistics[8]. Besides having a relatively small number of reported HIV infections, data from HIV testing of selected community groups and unlinked anonymous screening (UAS) confirmed the low prevalence. In the past ten years, screening for over 1.7 million donated blood has found a HIV detection rate among blood donors of 0.0016% for years 1985 – 1990 and 0.0029% for years 1991 – 1995. HIV detection rate for attendants of sexually transmitted diseases clinics was 0.017% for years 1985 – 1990 and 0.06% for years 1991 – 1996. HIV prevalence among selected target groups, though seemingly rising, has remained low. Continual UAS for drug users of the methadone clinics since 1990 had found a HIV positivity rate of 0.0003% without rising trend observed.

Albeit bound by its many limitations, the voluntary reporting system has yielded useful information on the epidemiological and clinical pattern of our HIV/AIDS patients. The adoption of a consistent method for collection of reported data forms a base for its validity. From February 1985 to May 1996, a cumulative total of 678 HIV infections were reported, giving a HIV/AIDS ratio of 3.39. It was not surprising to find that the HIV/AIDS ratio was much smaller for the second 100 AIDS patients (2.43) than the first 100 (4.35). The second half of AIDS cases were reported in only 26 months – one-fifth of the duration of the first 100 cases – which was compatible with the maturing local HIV epidemic as more and more infected people progressed to the stage of AIDS. The trend of seeing more AIDS patients is expected to persist in the coming few years.

In Hong Kong, HIV/AIDS has more often than not been mistaken as a foreigner's disease by the lay population. This may be due to the fact that the first few cases were reported among Caucasian patients back in 1985. From this study, however, it is indisputable that HIV disease has taken root and its incidence has been ever growing in the local Chinese community. The contribution of Caucasians to the overall HIV/AIDS toll has become significantly less important nowadays. This was in parallel with the trend of heterosexual transmission far surpassing that of homosexual

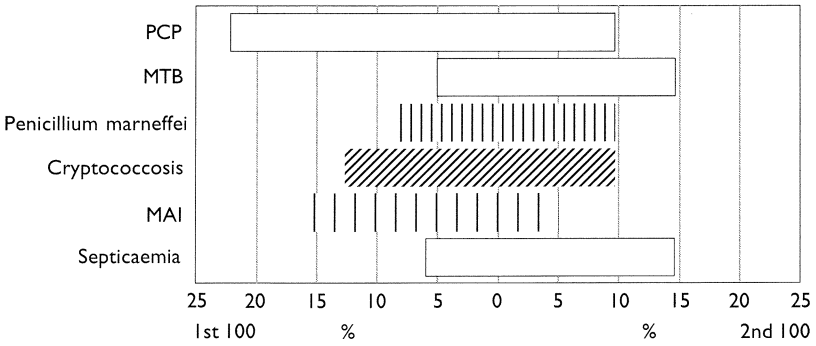

Fig 1 – Frequency of major killer condition for the AIDS patients who had known causes of death: 63 and 21 for the first 100 and second 100 cases respectively

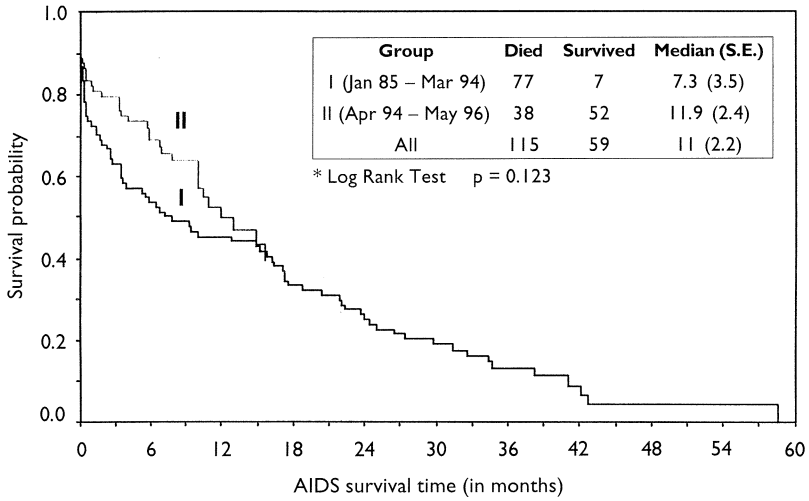

Fig 2 – Survival probability of the first 200 AIDS patients reported in Hong Kong

contact which was the main risk factor for the HIV positive Caucasians in early years. The importance of sexual transmission, especially heterosexual, among our HIV/AIDS patients has to be stressed again.

A majority of the AIDS patients were still diagnosed late regarding their HIV infection, as two-thirds of them had a HIV-to-AIDS interval of < 6 months. Not uncommonly they were known to be HIV positive only when they presented with AIDS indicator diseases. The phenomenon of late diagnosis of the underlying HIV infection did not improve over the years, and may have actually worsened. This was possibly related to the fact that HIV/AIDS is still a stigmatised disease in Hong Kong and the infected people might be reluctant to come out for HIV testing even if they were aware of their risk. Also, the cultural factor of low awareness about health in Chinese might have been another contributing factor. Though their median CD4 count at HIV diagnosis were similar, more of the second 100 AIDS patients had a CD4 count of < 50/uL compared with the first 100. This may however be partially explained by the switch locally in early 1994 from manual method to flow cytometry for enumeration of T-lymphocyte subset and the latter test gives a corresponding lower value for the same blood specimen (Kam KM, unpublished data). Furthermore, as the improved management should have lengthened the time to development of AIDS, the observation that the two halves had similar HIV-to-AIDS interval again pointed to a later HIV diagnosis of the second group of patients. It has been shown that a short interval from HIV detection to AIDS correlated with a poorer survival of local AIDS patients[9]. Efforts to enhance an earlier diagnosis of the HIV positive patients need to be strengthened. Activities, eg. via media and targeted group publicity and education, to promote acceptance and positive attitudes towards HIV-infected people are as important as prevention messages. In addition to building up a supportive social environment, more training for health care workers to facilitate the diagnosis and treatment of infected patients is obviously crucial. Recent improvements in anti-retroviral therapy may also be an incentive for at-risk/infected patients to seek medical consultation early.

Besides changes in the epidemiological pattern of local AIDS patients, there were changes in their clinical manifestations and outcome. Even though *Pneumocystis carinii* pneumonia remained the most common presenting AIDS indicator illness, its incidence has dropped significantly in the second half. Prophylaxis for PCP has become a crucial standard care for HIV/AIDS patients as it is very effective. Nowadays, patients on preventive drug for PCP are rarely complicated by this ADI.

The increasing trend of tuberculosis and penicilliosis as the primary ADI demands awareness for these complications and the underlying HIV infection in at-risk people. Inclusion of pulmonary tuberculosis with a low CD4 count as an ADI since mid-1995 partially accounted for the rise in *Mycobacterium tuberculosis* infection as an AIDS event in Hong Kong. Nonetheless, there are definitely more local HIV-infected subjects being complicated by MTB infection and subsequent disease development. As tuberculosis has been prevalent among the general population for many years in Hong Kong, the reason behind the recent surge of the infection in HIV-positive patients remains unclear. Dual infection with tuberculosis and HIV can lead to an atypical presentation of the former[10]. Treatment with standard anti-TB drugs for a longer duration of 9 – 12 months is the recommended management. However, they still tended to have a higher mortality rate than HIV-negative patients[11]. The occurrence of multi-drug resistant tuberculosis (MDRTB) is often an area of concern as outbreaks in healthcare institutions in USA have led to significant morbidity and mortality[12]. This is however often related to prior poor drug compliance. Fortunately in Hong Kong, the incidence of MDRTB has been rare.

The rise in cases of *Penicillium marneffei* infection as a primary ADI was marked. Our patients usually presented with a variable combination of fever, weight loss, anaemia, cervical lymphadenopathy, skin lesions and lung shadows[13]. Diagnosis is often confirmed by a blood culture or histological evidence from bone marrow[14] or lymph node examination. Recently, an antigen test for penicillium was found to be useful for diagnosis and treatment monitoring[15]. In our experience, some of the patients with penicilliosis ran

a rapidly downhill and fatal course. However, the majority responded satisfactorily to anti-fungal treatment and maintenance if diagnosis can be made and treatment initiated promptly. Healthcare workers should thus be on the look out for this emerging and potentially treatable complication in HIV-positive patients.

The increasing incidence of cytomegalovirus and *Mycobacterium avium intracellulare* disease as subsequent ADI reflects the trend towards more advanced immunosuppression for our patients. These two opportunistic infections often occur at a CD4 level of < 50/uL. As the second 100 AIDS patients had a lower median CD4 counts at the time of AIDS diagnosis, some of them survived to the state of even greater immunosuppression, becoming susceptible to these late-occurring complications. It is believed that this progressively chronic course of HIV disease will be the typical manifestation of patients in the years to come. Advances in anti-retroviral therapy and management of opportunistic diseases played a role in this cause.

The exact situation of survival and mortality in AIDS are difficult to ascertain as not uncommonly the outcome of some patients are unknown because they are lost to follow-up or other reasons. Nevertheless, we have demonstrated that the premature death in our AIDS patients were frequently related to its complicating illnesses. Again there has been changes, though not found to be significant, in the pattern of mortality.

It is not unexpected to witness a lowered mortality rate from PCP in our patients. The increased frequency of death due to tuberculosis may be due to increased incidence or late diagnosis of severe cases. Globally, tuberculosis is an important cause of death for HIV/AIDS patients[16]. We should try our best to prevent this from happening in Hong Kong. The trend that our patients were having a higher chance of lengthened survival is encouraging. Many studies had found an improved survival of AIDS patients shortly after the beginning of the epidemic, eg. from 1986 – 1987, but not thereafter[17]. In contrast, we have observed that our second 100 patients who were diagnosed after 1994 had better survival probability than their predecessors. However, the difference was not statistically significant. Sixty-five and 59 of the patients respectively in the two groups were known to have received some form of anti-retroviral therapy.

In conclusion, this comparative study of the first and second hundred AIDS cases in Hong Kong sheds light on the evolving epidemic in the territory. This not only enables healthcare workers to have a better understanding of the changing features and, hopefully, enhanced preparation for the care of patients with this devastating disease but may also add to the overall knowledge base of HIV infection in a global perspective. It will be worthwhile to continually keep track of the changing epidemiological and disease patterns of local HIV/AIDS patients in the future.

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