

AIDS in India : A report of three cases with review of literatures

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Human Immuno-deficiency Virus (HIV) is beginning to play havoc in all corners of the world.¹⁻⁷ It has also encroached the South East Asia Region.⁸⁻¹⁰ India had been free of the disease until 1½ years ago when a patient having undergone bypass surgery in USA was identified to be HIV positive. The India Council of Medical Research (ICMR) set up 35 screening centers all over the country during 1986-87 covering a population of more than 700 million. Out of these 35 centers, 4 are reference centers. Up to the present 14 cases have been recognised and in each case a contact outside India could be traced. The present report describes the antibody reaction patterns on Western blots in 3 patients of AIDS seen at one center in North India.

PATIENTS AND METHODS

An ICMR reference center was set up at the Postgraduate Institute of Medical Education and Research, Chandigarh in September, 1986 and as of February, 1988, 3500 samples had been screened. These included patients of non-Hodgkin's lymphoma, patients with sexually transmitted diseases, leprosy, jail inmates, healthy laboratory workers

SUMMARY Sera from 3500 individuals including patients of non-Hodgkin's lymphoma, patients with sexually transmitted diseases, leprosy, jail inmates, healthy laboratory workers and patients on hemodialysis were screened for antibodies against human immunodeficiency virus (HIV) as a sero surveillance exercise of one of the centers set up by the India Council of Medical Research at the Postgraduate Institute of Medical Education & Research, Chandigarh. Three individuals were found to be strongly positive by ELISA using the Wellcozyme kit, with no background noise in the population studies. These three patients were also evaluated by the Western blot technique and showed strong antibody reaction to all the major gene products. It was also possible to ascertain the approximate incubation period of infection in a case who rapidly developed full blown AIDS and died of wasting syndrome. Comprehensive data of 14 cases was also collected from all the centers in India and in every case one could trace the contact outside India. None of the 3 cases studied at our center had Kaposi's sarcoma. These observations could be important landmarks in the epidemiology of AIDS in India.

and patients on hemodialysis.

In suspected cases, a detailed history was elicited and patients subjected to routine examination, including hemoglobin estimation, total and differential lymphocyte count, estimation of serum immunoglobulins, total T cells, T helper/T suppressor ratio, lymphocyte transformation test, VDRL test, test for hepatitis B surface antigen, *etc.* On serum, ELISA for HIV infection was performed using a Wellcozyme kit and a Western blot test was done using a Du Pont kit.

Lymph node aspiration was

done in a patient with lymphadenopathy. The contacts were also screened for HIV antibodies both by ELISA and Western blot assays and reaction patterns with different peptide antigens of HIV were evaluated.

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RESULTS

All patients of various diseases, *e.g.*, non-Hodgkin's lymphoma, systemic lupus erythematosus, and patients with renal failure on hemodialysis were negative. Similarly, samples from blood donors, jail inmates, laboratory staff, *etc.* were completely negative by ELISA. All patients referred from the STD clinics were also negative except one patient who was referred because of peculiar genital sores (? possibly syphilitic). The genital lesions were later diagnosed as herpetic. Earlier he was suspected to be suffering from esophageal cancer because of dysphagia and severe weight loss (more than 10 kg in 3 months). His VDRL was negative. His ELISA was strongly positive and Western blot revealed antibodies to GP 160, 120 and P64, 55, GP 41, P31, P24 and faint reaction with P15/17 (Figure 1, lanes I and IV). He had worked as a blacksmith in Uganda for 7 years, came to India in February, 1987 and was found to be positive in May, 1987 and by that time his spouse aged 35 years was already strongly positive. She had, however, never been to Uganda. Their 3 children aged between 7-12 years were negative. The patient developed neurological symptoms, behavioral changes, severe debility and died at the end of June, 1987 while under observation.

Case II was the spouse of case I, also developed genital herpes, severe leucopenia and lymphopenia, disturbed T4/T8 ratio and mild dysphagia. There was no significant finding *viz*: lymphadenopathy, respiratory distress, hepatosplenomegaly, *etc.* The serum IgA values in both the cases were raised. The most prominent feature was rapidly developing cachexia and wasting syndrome. Her X-ray chest was normal. She died after 5 months of diagnosis. Her Western blot was strongly positive for all the major peptide fragments of HIV and in fact the reactions were stronger than those of case I

(Figure 1, land II). The time interval between arrival of case I to India and symptoms of his spouse was hardly 3½ months and the time between his arrival and death of the spouse was thus only 8½ months.

Case III was an Indian referred from Kenya with a camouflaged diagnosis of blood cancer. He presented with bilateral cervical and axillary lymphadenopathy, extensive oral candidiasis and more than 10 kg weight loss during the past 5 weeks. He had intermittent fever and anorexia. His ELISA value

was 0.2 against a normal control value of 1.8 and Western blot revealed a strongly positive reaction (Figure 1, land III). His spouse aged 35 and children aged 2½ years and 5 years were negative both by ELISA and Western blot assays.

His total leucocyte count was 8500/mm³, with 90% polymorphs. Serum IgA was markedly raised. There was a marked lymphopenia and it was difficult to ascertain the T4/T8 ratio with precision. His VDRL and HBsAg were negative. The chest X-ray was normal 2 weeks

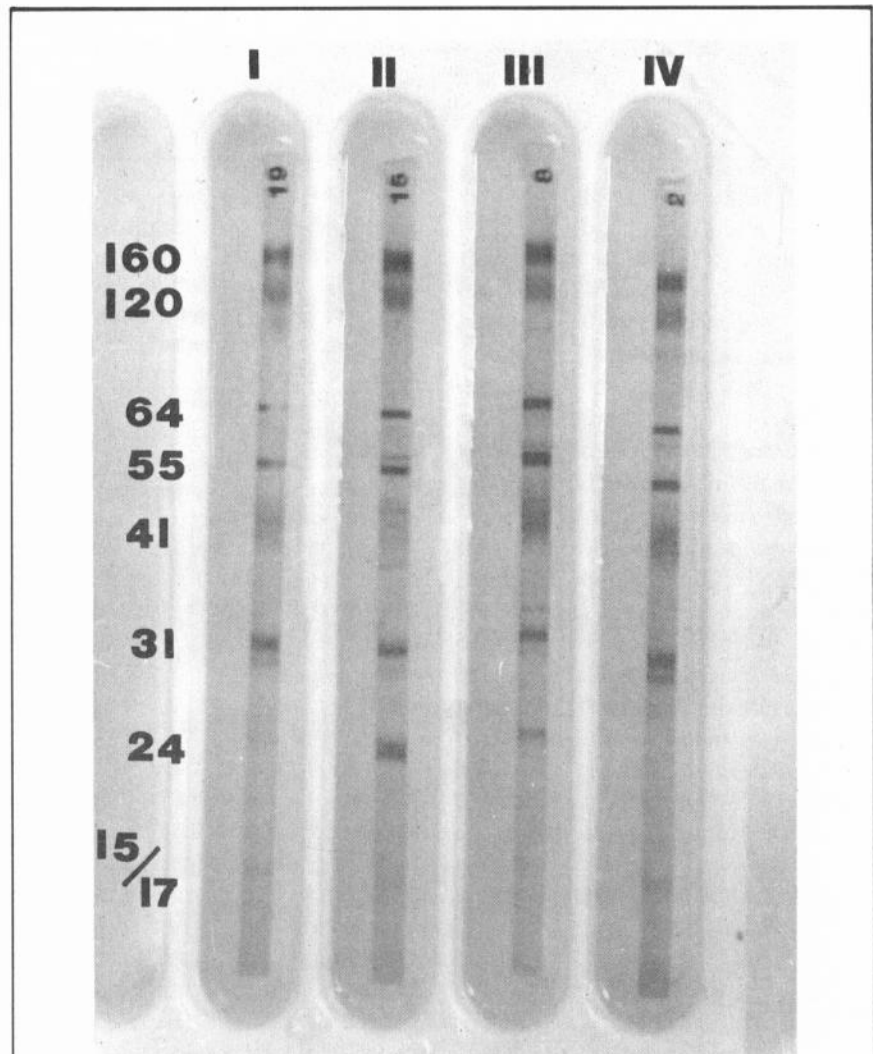


Fig. 1 Western blot using Du Pont strips. I and IV serum of case no. I; II serum of case no. II; III serum of case no. III.

before death. The lymph node aspiration revealed reactive changes only.

DISCUSSION

From the ELISA patterns (Table 1), it is clear that the North Indian population is free from infection and there is no background noise whatsoever. Patients of lymphoma also do not show low values.

The most striking observation is that all the three patients documented in this report and 11 others documented from all over India¹¹⁻¹³ have had a history of contact in a foreign country. Secondly, the incubation period of the disease could be judged from case number two, who had never been outside India. Her husband came to India in February, 1987 and she was found to be seropositive and already and features suggestive of AIDS by the end of May; she died in October, 1987.

The total time lapsed between onset of infection and death was approximately 5 months. The maximum incubation period in this case could thus be 3½ months. The relatively short incubation period could be due to two reasons. Firstly, the spouse was exposed to a heavy and repeated inoculation of the virus and secondly the pattern of sex practiced by the couple could possibly be more frequently anal than vaginal, which could result in a shortening of the incubation period. It has been argued that some areas of South East Asia where prostitution is practised regularly, have not shown the expected rise in the incidence of AIDS cases. It is possible that the pattern of sexual behaviour is more conventional, and the vaginal epithelium being a stratified squamous epithelium, is more resistant to invasion while rectal mucosa can offer ready access to the virus. It is now well recognised that in patients with sexually transmitted diseases different types of cells are passed in

Table 1. Competitive ELISA for anti-HIV (Wellcozyme) in specific diseases/conditions

Disease	Number tested	Optical density (mean ± SD)
Non-Hodgkin's Lymphoma	33	1.43 ± 0.30
Leprosy	85	1.60 ± 0.41
Systemic Lupus Erythematosus	25	1.50 ± 0.29
Cord blood	30	1.59 ± 0.38
Monkey sera	20	1.52 ± 0.39
Jail inmates	45	1.68 ± 0.23
Laboratory workers	50	1.70 ± 0.30
STD clinic	457	1.53 ± 0.31
Blood donors	454	1.75 ± 0.28
Miscellaneous diseases	801	1.62 ± 0.28

seminal fluid including lymphocytes¹⁴ which can either trigger an allogenic effect or directly transfer the virus. The incubation period and the extent of infection can thus differ depending both on the size and the route of the inoculum.

The antibody pattern is similar in all the three cases studied. The strong reaction patterns with envelope gene products GP 160, 120 are characteristic and major targets for protective antibodies.¹⁵ The reference strip of Du Pont showed a very faint reaction with these two glycoproteins while all the three patients revealed clear and strong reactions. Similar findings of faint reactions with 120/160 have been reported from Taiwan and Thailand.^{8,10} Only case II showed a very strong reaction with P24. The reaction pattern with P15/17 were weak in all the patients. It has been documented that antibodies to P24 wane off as the infection progresses but in case II it was very strong at the time of death.

According to the reports of ICMR, a total of 48,421 cases had been screened by mid August, 1987 out of which 184 were ELISA positive and 115 were Western blot positive; only 14 suffered from the disease. In a tropical country like India, the Western blot patterns need to be interpreted with great

caution. S. Sinha and coworkers at the Central JALMA Research Institute, Agra, have found that patients of leprosy reveal 4-5 bands on Western blot assays but these patients do not show an ELISA positivity (personal communication). Therefore, if an ELISA negative serum shows bands on Western blot, extreme care is needed in labelling the case as positive. Most authors feel that antibodies to 2 out of 3 gene products should be positive before a final diagnosis of HIV infection is made.

Table II summarizes data of 14 Indian cases of AIDS with risk factors and country of origin. Three cases had contacted disease from USA, one from Germany, one from Kampala, three from Uganda, one from Kenya and in one, the source could not be identified as he had visited several countries.

None of the three patients studied at our Center had Kaposi's sarcoma (Ks) or pneumocystis pneumonia (PCP) judged by the clinical examination, chest X-ray or respiratory symptoms. All the three patients studied at our Center had severe HIV wasting syndrome.

Even in the absence of KS and PCP there was no difficulty in diagnosing these patients except in case

Table 2. Summary of AIDS cases in India

	Age/Sex	Risk group	Native country	Probable source of virus	References
1.	50M	CBSG	India (Bombay)	U.S.A.	Lele <i>et al.</i> (1986)
2.	30M	PRHT	India (Delhi)	U.S.A.	Udwadia <i>et al.</i> (1987)
3.	23F	Transfused	India (Bombay)	Middle East	Udwadia <i>et al.</i> (1987)
4.	29M	PRHT	Malawi	Malawi	Malaviya <i>et al.</i> (1987)
5.	40M	IVD	U.S.A.	U.S.A.	"
6.	42M	PRHT	India	Uganda	"
7.	M	Bisexual	India	West Germany	"
8.	28M	PRHT	Kenya	Kenya	"
9.	*26M	PRHT	"	"	"
10.	*25M	Bisexual	"	"	"
11.	*26M	PRHT	"	"	"
12.	38M ^o	Bisexual ?	India (Chandigarh)	Uganda	Present report
13.	35F ^o	Spouse of no. 12	"	"	"
14.	38M ^o	PRHT	"	"	"

CBSG — Coronary bypass surgery graft

PRHT — Promiscuous heterosexual

IVD — Intravenous drug user

*no. 9,10,11 were asymptomatic

^o12,13,14 are referred as cases I,II and III in the text.

no. 12 (Table II) who was transiently suspected to be suffering from cancer of oesophagus. It is possible that ethnic and environmental differences are responsible for varying clinical features. As the case number increases the presenting features will become more crystallised in this region.

ADDENDUM

Recently virologists working at the All India Institute of Medical Sciences, New Delhi have been able to isolate HIV virus from samples of four women from Madras who were earlier Western blot positive.

REFERENCES

- Barre-Sinoussi F, Chermann JC, Rey F, *et al.* Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983; 220 : 868-71.
- Gallo RC, Salahuddin SZ, Popovic M, *et al.* Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 1984, 224 : 500-3.
- Haverkos HW. Epidemiology of acquired immune deficiency syndrome. *Antibiotics and Chemotherapy*, Vol. 32. Basal : Karper, 1984 : 18-26.
- Smith NP. Kaposi's sarcoma and acquired immune deficiency syndrome - The British Experience. *Antibiotics and Chemotherapy*, Vol. 32. Basal : Karger, 1984 : 71-5.
- Marche C, Neguesse Y, Bouton C, Kernbaum S, Regnier B, Saimot AG. Histopathological studies of lymphadenopathy in AIDS : Tentative classification. *Antibiotics and Chemotherapy*, Vol 32. Basal : Karger, 1984 : 76-86.
- Schupbach J, Haller O, Vogt M, *et al.* Antibodies to HTLV-III in Swiss patients with AIDS and pre-AIDS in groups at risk of AIDS. *N Engl J Med* 1985; 312 : 265-9.
- Kreiss JK, Koeh D, Plummer FA, *et al.* AIDS virus infection in Nairobi prostitutes : spread of the epidemic to East Africa. *N Engl J Med* 1986; 314 : 414-8.
- Wangroongsarb Y, Weinger BG, Wasi C, *et al.* Prevalence of HTLV-III/LAV antibody in selected populations in Thailand. *Southeast Asian J Trop Med Pub Hlth* 1985; 16 : 517-20.
- Ubol S, Phanuphak P, Traisupa A. Anti-HIV positivity in Thailand : The usefulness of another ELISA test kit and Western blot as confirmatory tests. *Asian pacific J Allergy Immunol* 1987; 5 : 5-12.
- Lin KT, Huang SH, Kao CL, *et al.* An autopsy-proved case of AIDS in Taiwan. *Asian Pacific J Allergy Immunol* 1987; 5 : 25-31.
- Malaviya AN, Singh PR, Khera SD, *et al.* AIDS screening in North India : Clinical spectrum of HIV infection. *J Assoc Phys India* 1987; 35 : 405-10.
- Lele RD, Parekh SJ, Wadia NH. Transfusion associated AIDS (TA-AIDS) and AIDS Dementia. *J Assoc Phys India* 1986; 34 : 549-53.
- Udwadia FE, Advani S, Jain M, Gupta R. Acquired immunodeficiency syndrome : A study of two case reports with reports manifest HIV infection. *J Assoc Phys India* 1987; 35 : 454-7.
- Coats RA, Soskolne CI, Read SE, *et al.* Abstracts, International Conference on AIDS. Paris : 1986.
- Barin FF, McLane, JF, Allan JS, *et al.* Virus envelope protein of HTLV-III represents major target antigen for antibodies in AIDS patients. *Science* 1985; 228 : 10946.