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Spectrum of lesions in HIV patients: an Indian scenario

Minal Wasnik^{1*}, Nitin Kashyap², P.M. Roplekar³

^{1*} Department of Pathology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

² All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

³ Department of Pathology, Grant Medical College and Sir J.J. Group of Hospitals, Mumbai, India

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Abstract

India has been referred to as the new hot bed of HIV with Mumbai being the capital of HIV/AIDS. HIV has remarkable ability to cripple host defenses with development of complications having peculiar natural histories. It is this realization that prompted us to study HIV/AIDS associated lesions which continue to spread and cause significant threats to life. A prospective study of 380 HIV patients was done in a tertiary care teaching hospital for two years. Samples received for cytopathology and histopathology were studied. 72.3% were in the age group of 21-40 years with 256 males and 124 females. Tuberculosis was seen in 200 cases, reactive lymphadenitis in 65 cases, lymphoid malignancies in 32 cases and genital tract malignancies in 18 cases. The commonest presentation was weight loss in 362 cases, followed by lymphadenopathy in 324 and fever in 196 cases. Of the 32 lymphoid malignancies, 27 were non-Hodgkin's lymphoma and 5 were Hodgkin's disease. The most common type of genital malignancy encountered was carcinoma cervix seen in 72.22%, followed by carcinoma vulva in 22.22% and carcinoma penis in 2.56%. In India, large-scale studies need to be done to evaluate the exact burden of HIV-related lesions with urgent need to increase the awareness of various aspects of AIDS, gathering of epidemiological data and to direct the research efforts in Indian subjects.

Keywords : Spectrum of HIV, HIV in India, Seropositive, HIV associated lesions

Introduction

A remarkable and tragic fact is that although acquired immunodeficiency syndrome (AIDS) was recognized as a distinct disease entity as recently as the 1980s, in this brief period of time, it has become one of the most devastating afflictions in the history of mankind. According to UNAIDS 2008 report on the global AIDS epidemic, there is estimated 33 million people living with HIV and overall 2 million people died of AIDS in 2007, globally [1]. India has been referred to as the new hot bed of HIV infection. The prevalence of HIV infection has been increasing every year and by July 2006, 2.5 million cases of HIV infection had been reported by National AIDS Control Organization (NACO), New Delhi [2]. The first case in India was found in 1986 in Chennai, Tamil Nadu [3], whereas, the first case in Mumbai was detected in 1985-86.

Geographically, higher prevalence occurs in south-central and north-eastern India. Maharashtra is amongst the high prevalence state in India and Mumbai is considered the capital of HIV/AIDS. In the developed countries, 34% of AIDS patients suffer from cancer. On the other hand, the incidence of cancer in patients infected with HIV is only 3-4% in the Indian population [4]. Nearly all patients with AIDS in India are victims of tuberculosis and opportunistic infections. Various autopsy studies showed tuberculosis and other opportunistic infections to be the most common pathology seen in HIV/AIDS [5, 6, 7]. However, with improving care of HIV and better management of infections, especially tuberculosis, the longer survival of patients with HIV/AIDS will likely increase the importance of cancer as a clinical problem. The challenge of knowing various lesions in the setting of HIV infection does not merely involve knowing the potential for development of its complications but to understand their peculiar natural histories and strategies for management. It is this realization that has urged us to make an attempt to study various lesions associated

*Corresponding Author

E-mail: minal8681@rediffmail.com

with HIV/AIDS which continues to spread and cause significant threats to life.

Materials and Methods

A study of 380 HIV seropositive patients was done in prospective manner for two years in a tertiary care teaching hospital. The HIV seropositive status of the patients was carried by ELISA test. The tests were done at the HIV testing centre of our institution. All HIV positive patients irrespective of their CD4+ counts were included. Cases referred, either for cytology or histopathology, were studied. The specimen/biopsy material for histopathological examination was received from various specialities of our institution. The specimen ranged from completely resected organs to small biopsies. A properly completed surgical pathology requisition form containing the patient's identification, age, sex, essential clinical data, operation, surgical findings, and tissue submitted was received with every specimen.

The specimen received was placed on the cutting board in an anatomic position and examined grossly. Specimen was sectioned and tissue bits were submitted for processing and paraffin blocks were prepared. Slides were prepared and were examined microscopically. Fine needle aspiration cytology (FNAC) was done in patients who presented with palpable swelling. Procedure was described in detail to the patient for his cooperation during the actual procedure. A formal written consent was taken in all patients. After obtaining the detailed clinical history and complete clinical examination, the FNAC was done in an outpatient setting without any anaesthesia. The 22 to 25 gauge needles attached to the plastic syringe were used for aspiration. Smears were prepared and stained appropriately followed by microscopic examination. The patients were subjected to various diagnostic investigations, blood tests and bone marrow aspiration as and when necessary. The data of 380 patients were collected and the results were carefully analyzed.

Results

We studied a total of 380 HIV cases in a period of two years. Majority of the patients were in the reproductive age group of 21-40 years. Out of the 380 cases studied, most of the patients were in the age group of 31-40 years (50.26%) followed by 41-50 years age group (22.37%) (Table 1) and 256 (67.37%) were males and 124

(32.63%) were females (Table 2). Majority of the cases, i.e. 200, were that of tuberculosis (52.63%) followed by reactive lymphadenopathy in 65 cases (17.10%). Lymphoid neoplasms were seen in 8.32% and genital tract malignancies were seen in 4.74% of cases (Table 3 & Figure 1). Weight loss/ anorexia was the most common presenting feature in 362 cases followed by lymph node swelling in 324 and fever in 196 cases (Table 4). Of the 50 neoplastic cases, majority were in the age group of 31-40 years, i.e. 27 cases (54%) followed by 13 cases in 41-50 years age group (26%) (Table 5).

Age-group	No. of cases	Percentage (%)
0-10 years	5	1.32
11-20 years	10	2.63
21-30 years	84	22.11
31-40 years	191	50.26
41-50 years	85	22.36
51-60 years	5	1.32
Total	380	100

Table 1. Age distribution of HIV cases

Sex	No. of cases	Percentage (%)
Male	256	67.37
Female	124	32.63
Total	380	100

Table 2. Sex distribution of HIV cases

Diagnosis	No. of cases	Percentage (%)
Tuberculosis	200	52.63
Reactive LN	65	17.10
Suppurative	40	10.53
Lymphoid neoplasms	32	8.42
Ca genital tract	18	4.74
Others	12	3.16
Inconclusive	13	3.42
Total	380	100

Table 3. Distribution of lesions encountered in HIV

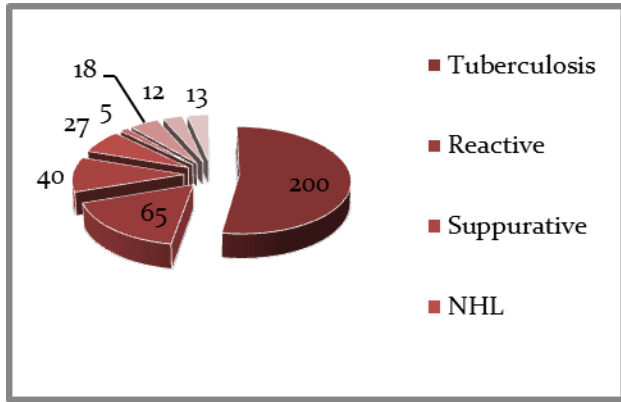


Figure. 1. Pie chart showing distribution of lesions in HIV

Presenting features	No. of cases
Weight loss/ Anorexia	362
Lymph node swelling	324
Fever	196
Cough	114
Diarrhoea	20
Others	168

Table. 4. Presenting features of HIV cases

Age group	No. of cases	Percentage (%)
0-10 years	3	6
11-20 years	1	2
21-30 years	6	12
31-40 years	27	54
41-50 years	13	26
51-60 years	-	-
Total	50	100

Table.5. Age distribution of neoplastic cases

Most of the neoplastic cases i.e. 29 cases (58%), were seen involving the lymph nodes, of which the cervical groups of lymph nodes were most commonly involved followed by axillary group of lymph nodes. Genital tract neoplasms were also found in majority i.e. 18 cases (36%) (Table 6). Of the 27 cases of NHL studied by FNAC and histopathology, majority of the patients were in the age group of 31-40 years (48.15%) followed by 41-50 years age group (29.63%) (Table 7) and male patients (85.18%) outnumbered the females (14.82%) (Table 8). Based on Working Formulation, most of the NHL belonged to intermediate grade i.e. 15 cases

(55.55%), followed by 11 cases (40.75%) of high grade and 1 case (3.7%) of low grade lymphoma (Table 9).

Site	No. of cases	Percentage (%)
Cervical lymph nodes	18	36
Axillary lymph nodes	6	12
Inguinal lymph nodes	5	10
Gastro-intestinal tract	3	6
Male & Female genital organs	18	36
Total	50	100

Table. 6. Site-wise distribution of neoplastic cases

Age group	No. of cases	Percentage (%)
0-10 years	2	7.41
11-20 years	-	-
21-30 years	4	14.81
31-40 years	13	48.15
41-50 years	8	29.63
Total	27	100

Table.7. Age distribution of Non-Hodgkin's Lymphoma

Sex	No. of cases	Percentage (%)
Male	23	85.18
Female	4	14.82
Total	27	100

Table. 8. Sex distribution of NHL

Grades	No. of cases	Percentage (%)
Low grade	1	3.7
Intermediate grade	15	55.55
High grade	11	40.75
Total	27	100

Table.9. Grading of NHL based on working formulation

Of the 5 cases of HD, 2 cases (40%) were in the age group of 31-40 years, whereas 1 case each was seen in 0-10 years, 11-20 years and 41-50 years age group (Table 10) and 3 were females (60%) and 2 were males (40%) (Table 11). Mixed cellularity was the most common type, seen in 4 cases (80%), followed by a single case of lymphocyte depletion type (20%) (Table 12).

Age group	No. of cases	Percentage (%)
0-10 years	1	20
11-20 years	1	20
21-30 years	-	-
31-40 years	2	40
41-50 years	1	20
Total	5	100

Table.10. Age distribution of Hodgkin's disease

Sex	No. of cases	Percentage (%)
Male	2	40
Female	3	60
Total	5	100

Table.11. Sex distribution of Hodgkin's disease

Types	No. of cases	Percentage (%)
Nodular sclerosis	-	-
Mixed cellularity	4	80
Lymphocyte depletion	1	20
Lymphocyte rich	-	-
Lymphocyte predominant	-	-
Total	5	100

Table.12. Histo/Cytomorphological types of Hodgkin's disease

Of the 18 cases of genital tract malignancies, majority were in the age group of 31-40 years i.e. 12 cases (66.67%), followed by 4 cases (22.22%) in 41-50 years age group (Table 13). Carcinoma cervix was the most common seen in 13 cases (72.22%), followed by 4 cases (22.22%) of carcinoma vulva and a single case (5.56%) of carcinoma penis (Table 14).

Age group	No. of cases	Percentage (%)
0-10 years	-	-
11-20 years	-	-
21-30 years	2	11.11
31-40 years	12	66.67
41-50 years	4	22.22
Total	18	100

Table.13. Age distribution of Genital Tract Malignancies

Site	No. of cases	Percentage (%)
Cervix	13	72.22
Vulva	4	22.22
Penis	1	5.56
Total	18	100

Table.14. Site-wise distribution Genital Tract Malignancies

Discussion

Ever since its recognition in 1981, HIV/AIDS continues to ravage all countries of the world. Currently in India an estimated number of 2.5 million people are living with this virus. HIV infection produces a panorama of opportunistic infection and neoplasms which may be the presenting features of the disease. The current study was done for a period of two years and a total of 380 HIV cases were studied.

In the present study, among total number of 380 HIV patients, 256 (67.37%) were males and 124 (32.63%) were females. Hira *et al.*, 2003 [8] found out in their study that 76.8% males and 23.2% of females were affected. In a study done by Silverberg *et al.*, 2008 [9] there were 90.2% males. Age distribution of the HIV patients in the present study is comparable with that of Fontanet *et al.*, 1998 [10] (Table 15) showing maximum number of HIV patients in the age group of 21-40 years i.e. reproductive age group. In the present study, we found out that, maximum neoplastic cases were seen in the age group of 21-40 years. It follows the age distribution trend of HIV [11].

Age groups	Fontanet et al., (1998) n=172	Present study (2009) n=380
0-20 years	17.44%	3.95%
21-40 years	72.67%	72.37%
41-60 years	9.88%	23.68%

Table. 15. Comparison of Age wise distribution of HIV cases

HIV associated non-neoplastic lesions

Infections with opportunistic pathogens have been one of the hallmarks of acquired immunodeficiency syndrome since the beginning of the epidemic. Bacterial infections have emerged as an important cause of morbidity and mortality in individuals with HIV. Pulmonary tuberculosis with extra-pulmonary widespread organ involvement by tuberculosis is commonly observed. Patients with AIDS are prone to develop recurrent and reactivated viral infections like *Herpes simplex* and *Varicella zoster*. Other viruses include Epstein-Barr virus (EBV), pox virus associated with *Molluscum contagiosum*, and human papilloma virus. In the present study, 200 cases (52.63%) were that of tuberculosis, followed by 65 cases (17.10%) of reactive lymphadenitis, 40 cases (10.53%) of suppurative lymphadenitis, 32 cases (8.42%) of lymphoid malignancies and 18 cases (4.74%) of malignancies of male and female genital tracts. Similar studies have been done in other regions of the world as well [12, 13, 14, 15] (Table 16). The present study compared to other studies [15, 16], showed weight loss as the most common symptom seen in 362 cases followed by lymphadenopathy in 324 and fever in 196 cases (Table 16).

HIV associated neoplastic lesions

Lymphomas

Out of 32 cases of lymphomas, 29 (90.6%) were found out to be involving the lymph nodes, mainly cervical group (56.3%), followed by axillary (18.8%) and inguinal (15.5%). However 3 cases (9.4%) of extranodal involvement (gastrointestinal tract) were seen. Raphael et al., 1991 [17] studied 113 cases of lymphoid neoplasms and got 27.5% cases with nodal and 72.5% with extranodal involvement. Ioachim et al., 1991 [18] found out 39% cases in lymph nodes, with maximum cases in cervical followed by axillary and inguinal group, whereas

61% cases in extranodal sites. According to the study done by Carbone et al., 1991 [19], gastrointestinal tract is the most common extranodal site. In our study also we found gastrointestinal tract to be the most common extranodal site of involvement.

Non-hodgkin's lymphoma (NHL)

In the present study, the age distribution trend of NHL follows that of age distribution trend of HIV. Maximum number of cases were seen in the age group of 21-40 years (62.96%). Several other studies have shown similar results [18, 19]. In the present study, out of the 27 cases of NHL, 23 were males (85.18%) and 4 were females (14.82%) which is comparable with other studies [18, 19] (Table 18). In the present study, the NHL cases were grouped according to the Working Formulation, as low, intermediate and high grade lymphomas. Out of the 27 cases of NHL, 15 were intermediate grade (55.55%), 11 were high grade (40.75%) and 1 was low grade (3.7%). Similar to other studies [17, 18, 19], maximum cases were of intermediate or high grade lymphomas (Table 19). Immunohistochemical markers were used for further confirmation. Immunohistochemical markers used commonly included CD 3, CD 20, CD 15, CD 30, CD 45 (leukocyte common antigen), immunoglobulins, etc. Immunohistochemistry is a useful and necessary diagnostic modality and helps subdivide different types of NHL [20].

Hodgkin's disease (HD)

The age distribution of HD follows that of HIV, with most of the cases in the age group of 21-40 years (40%) and 3 were females (60%) and 2 were males (40%). In the present study, out of the 5 cases, 4 were of mixed cellularity (80%) whereas 1 case was that of lymphocyte depletion type (20%) (Table 20) [18, 19, 21, 22]. Thus like other studies, we also got maximum cases of mixed cellularity type of Hodgkin's disease. Although morphology remains the gold standard in the diagnosis of Hodgkin's disease, immunophenotyping is a useful adjunct in differentiating distinct subtypes. The panel of antibodies used included CD 15, CD 30, CD 3, CD 20, CD 45 [23].

Authors	TB	Reactive LN	Lymphoma	Kaposi's sarcoma	Genital malignancies	Other
Reid et al., 1998 [12] n=65	15%	51%	9%	2%	-	23%
Pezzotti et al., 1999 [13] n=41,722	8.1%	-	3%	4.9%	0.2%	83.8%
Shenoy et al., 2002 [14] n=56	48.2%	35.7%	8.9%	-	-	7.2%
Sharma et al., 2004 [15] n=135	71%	-	1.5%	-	-	27.5%
Present study, 2009 n=380	52.63%	17.10%	8.42%	-	4.74%	25.53%

Table. 16. Comparison of distribution of different lesions encountered in HIV patients

Clinical features	Sharma et al., 2004 [15]	Chakravarty et al., 2006 [16]	Present study, 2009
Weight loss	88	234	362
Lymphadenopathy	126	-	324
Fever	95	310	196
Cough	95	177	114
Diarrhoea	32	189	20
Others	319	79	168

Table. 17. Comparison of presenting symptoms of HIV

Authors	No. of cases	Male	Female
Carbone et al., 1991 [19]	35	28 (80%)	7 (20%)
Ioachim et al., 1991 [18]	100	97 (97%)	3 (3%)
Present study, 2009	27	23 (85.2%)	4 (14.8%)

Table. 18. Comparison of sex wise distribution of NHL

Authors	No. of Cases	Low grade	Intermediate grade	High grade
Raphael et al., 1991 [17]	113	-	35 (31%)	78 (69%)
Carbone et al., 1991 [19]	35	-	5 (14.3%)	30 (85.7%)
Ioachim et al., 1991 [18]	100	1 (1%)	44 (44%)	55 (55%)
Present study, 2009	27	1 (3.7%)	15 (55.5%)	11 (40.8%)

Table. 19. Comparison of grades of NHL

Authors	No. of Cases	Nodular sclerosis	Mixed cellularity	Lymphocyte depletion	Others/not classified
Ioachim et al., 1991 [18]	11	5 (45.5%)	5 (45.5%)	1 (9%)	-
Carbone et al., 1991 [19]	10	1 (10%)	3 (30%)	4 (40%)	2 (20%)
Agarwal et al., 2002 [21]	7	1 (14.3%)	5 (71.4%)	-	1 (14.3%)
Biggar et al., 2006 [22]	774	285 (36.8%)	414 (53.7%)	54 (7%)	19 (2.5%)
Present study, 2009	5	-	4 (80%)	1 (20%)	-

Table. 20. Comparison of subtypes of HD

Genital tract malignancies

In the present study, we got maximum cases in the age group of 21-40 years as seen in other malignancies. It also follows the age distribution trend of HIV. The range of age distribution of carcinoma cervix was from 25-46 years, which is comparable with the study done by Feingold *et al.*, 1990 [24]. In the present study, out of the 18 cases of genital tract malignancies, 13 were of carcinoma cervix (72.2%), 4 cases were of carcinoma vulva (22.2%) and 1 case of carcinoma penis (5.6%) which is comparable with the study by Frisch *et al.*, 2000 [25] (Table 21).

Authors	No. of cases	Carcinoma cervix	Carcinoma vulva	Carcinoma penis
Frisch <i>et al.</i> , 2000 [25]	1187	1122 (94.5%)	24 (2.02%)	41 (3.45%)
Present study, 2009	18	13 (72.2%)	4 (22.2%)	1 (5.6%)

Table.21. Comparison of genital tract malignancies

HIV seropositive women have a high rate of persistent HPV infections with the types of HPV (16, 18) that are strongly associated with the development of high grade squamous intraepithelial lesions (HSILs) and invasive cervical cancer [26]. The increasing relative risks for in-situ and advanced cancers reflect the gradual loss of control over HPV-infected keratinocytes with advanced immunosuppression. HPV DNA should therefore be studied in the patients with genital tract malignancies. As this facility was not available in our set up, these studies were not done.

Although the study provides some insight on the distribution of various lesions in HIV/AIDS patients, it is not free of limitations. As the study included those patients only who approached the centre for treatment/management, the results cannot be generalized. As there was no follow up of patients done by us, the prognosis of these lesions cannot be determined in the study. Nevertheless, it is a small contribution from authors' side to add to the data of HIV-related lesions.

Conclusion

Currently, the load of HIV-infected patients is increasing world-wide. A similar trend is being observed in India as well. As India is a large country and geographically and culturally diverse, large-scale studies need to be done by various HIV/AIDS centres across the country to evaluate the exact burden of HIV-related lesions. In India, majority of HIV patients have tuberculosis and other opportunistic infections. However with improving care of HIV and better management of infections, especially tuberculosis, the longer survival of HIV/AIDS patients will increase the importance of malignancies as a clinical problem. There is absence of Kaposi's sarcoma in this region. The raised incidence for cervical cancer emphasizes the urgent need for screening programs in India and HPV DNA studies in all patients of malignancies of anogenital region in HIV. The genetic, molecular and phenotypic studies should be done in patients having AIDS-related lymphomas.

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