Lymphoreticular Involvement in Human Immunodeficiency Virus Infection

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Abstract

Background: Although lymphadenopathy, hepatomegaly and splenomegaly are commonly seen in human immunodeficiency virus (HIV) infection, little is known about the prognostic significance of these findings.

Method: A retrospective study of lymphoreticular involvement in 612 HIV-positive patients was done.

Result: Lymphadenopathy was found in 301 (49.18%), hepatomegaly in 102 (16.66%) and splenomegaly in 58 (9.47%) patients. Sixty eight (32.54%) of the 209 patients with only lymphadenopathy had acquired immunodeficiency syndrome (AIDS), as compared to 70 (23.97%) of the 292 patients without lymphadenopathy or hepatosplenomegaly (χ^2 4.49, df-1, $p < 0.05$). There was a higher chance of having AIDS if hepatomegaly was present with lymphadenopathy. Eight (72.73%) of 11 patients with hepatomegaly alone, had AIDS. Thirty (68.18%) of 44 cases with splenomegaly, with lymphadenopathy and hepatomegaly, three (50%) of six cases having splenomegaly with lymphadenopathy and one (33.33%) of three cases with splenomegaly had AIDS. Majority of lymphoreticular involvement cases were due to *Mycobacterium tuberculosis* infection. All 29 cases with abdominal lymphadenopathy and one with hilar lymphadenopathy had AIDS. Bilateral discrete cervical, axillary and inguinal lymphadenopathy was the most common presentation. CD4 counts were significantly ($p < 0.05$) lower in those with lymphadenopathy and hepatosplenomegaly.

Conclusion: HIV cases with lymphadenopathy and hepatomegaly should be investigated for the presence of opportunistic infection.

MJAFI 2008; 64 : 04-06

Key Words: Human Immunodeficiency Virus; Lymphadenopathy; Hepatomegaly; Splenomegaly

Introduction

Lymphadenopathy is commonly seen in early human immunodeficiency virus (HIV) infection. It is associated with improved outcome while regression is seen as a sign of disease progression [1]. Cervical, axillary, and inguinal lymph nodes are usually involved. Significant enlargement of thoracic or abdominal lymph nodes usually indicates an underlying opportunistic infection, such as pulmonary or disseminated tuberculosis, mycobacterium avium complex (MAC) disease, histoplasmosis or lymphoma [2]. Hepatomegaly and splenomegaly are common findings on abdominal computerised tomography [3]. However, prognostic significance of these findings in the Indian subcontinent is unclear. We studied the pattern of lymphoreticular involvement in HIV-positive patients in armed forces.

Material and Methods

This is a retrospective, hospital record based analytic study of newly diagnosed 612 cases of HIV infection. The medical records of these patients were analysed with a view to find out the pattern of lymphoreticular involvement. Haemogram, erythrocyte sedimentation rate, platelet count, urine analysis, liver function tests, venereal disease research laboratory test (VDRL), hepatitis B surface antigen (HBsAg), radiograph of the chest, ultrasound abdomen and tuberculin

tests were carried out. CD4, CD8 and absolute lymphocyte counts (ALC) were done. Patients were classified into category A, B, C and diagnosed as having AIDS as per the revised guidelines [4].

Results

Out of 612 patients two were females. Of these 301 (49.18%) had lymphadenopathy, 102 (16.66%) hepatomegaly and 58 (9.47%) splenomegaly. Two hundred and twelve (34.64%) cases had acquired immunodeficiency syndrome (AIDS). Lymphoreticular involvement of these cases is shown in Table 1. There was significantly higher incidence of developing

Table 1

Lymphoreticular involvement and incidence of AIDS in HIV-positive patients

Group	Number	Number with AIDS (%)
Only L	209	68 (32.54)
L+H	42	32 (76.19)
L+H+S	44	30 (68.18)
L+S	6	3 (50)
Only H	11	8 (72.73)
H+S	0	0
Only S	3	1 (33.33)
Without L, H or S	292	70 (23.97)
Total	612	212

Legend: L-lymphadenopathy; H-hepatomegaly; S-splenomegaly

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AIDS in those with only lymphadenopathy than in those without lymphadenopathy or hepatosplenomegaly (χ^2 4.49, df-1, $p < 0.05$). This increased by two and half times, if hepatomegaly was also present along with lymphadenopathy (χ^2 47.24, df-1, $p < 0.001$). However presence of splenomegaly alone or in addition to lymphadenopathy and/or hepatomegaly did not further increase the incidence of AIDS..

Distribution of AIDS defining conditions in relation to lymphadenopathy and hepatosplenomegaly is shown in Table 2. Majority of lymphadenopathy, hepatomegaly and splenomegaly cases with AIDS were due to *Mycobacterium tuberculosis* infection. The diagnosis of tuberculosis was based on clinical assessment, chest radiograph, sputum examination and biopsy. Majority (96.23%) had developed category C illness and in eight (3.77%), AIDS was diagnosed with patients having CD4 counts less than 200/cmm without any associated category C condition. Three patients each with (1.00%) and without (0.96%) lymphadenopathy were

having significant VDRL titre. Eight (7.87%) and 17 (3.33%) patients with and without hepatomegaly were HBsAg positive. One (0.98%) patient each of hepatomegaly had latent syphilis, syphilitic meningitis and cirrhosis.

Average CD4, CD8, CD4:CD8 and ALC is shown in tables 3-5. It was observed that mean CD4 count was lower in those with lymphadenopathy as compared to those without it, although it was statistically not significant. The mean CD4 count was lower in patients with hepatomegaly and lymphadenopathy as compared to those without it, but it was statistically not significant, possibly due to small number of patients. The CD4 counts were significantly lower in patients with hepatosplenomegaly and lymphadenopathy than those without it. In addition, CD4 count of 106 was found in one case of hepatosplenomegaly without lymphadenopathy. CD4 count of 68 and CD8 count of 140 was seen in one case of splenomegaly with lymphadenopathy.

Cervical lymphadenopathy was commonest, seen in 214 (34.96%), followed by axillary in 211 (34.48%), inguinal in 179 (29.25%), retroperitoneal in 29 (4.74%), epitrochlear in 16 (2.61%), supraclavicular in nine (1.47%), submandibular in three (0.49%), hilar and posterior auricular in one (0.16%) each (Table 6). Lymph nodes were matted in 13 (2.12%).

All 29 cases of retroperitoneal lymphadenopathy had AIDS, 22 (75.86%) had pulmonary tuberculosis, four (13.79%)

Table 2**AIDS cases with lymphadenopathy and hepatosplenomegaly**

AIDS defining condition	Lymphadenopathy (%)	Hepatomegaly (%)	Splenomegaly (%)
Tuberculosis	122* (91.72)	71 (95.95)	36 (94.74)
PCP	2 (1.50)	2 (2.70)	0
Cryptococcosis	0	0	0
Isosporiasis	1 (0.75)	0	0
Oesophageal candidiasis	1 (0.75)	0	0
CD4 count <200/cmm	7 (5.26)	1 (1.35)	2 (5.26)
Total	133 (100)	74 (100)	38 (100)

*Two in addition had *P. carinii* pneumonia (PCP) and one each had disseminated cryptococcosis and AIDS dementia

Table 3**Lymphadenopathy and average CD4, CD8, CD4:CD8 and ALC**

	CD4 (No. tested)	CD8 (No. tested)	CD4: CD8 (No. tested)	ALC (No. tested)
With lymphadenopathy only	219.05 (20)	872.37 (18)	0.251 (18)	2051.69 (13)
Without lymphadenopathy and hepatosplenomegaly	292.14 (34)	931.54 (24)	0.314 (24)	2085.18 (17)

SD for CD4 counts- 144.07 and 238.22, SE-52.02, $p > 0.05$, * No.= number

Table 4**Hepatomegaly, lymphadenopathy and average CD4, CD8, CD4:CD8 and ALC**

	CD4 (No. tested)	CD8 (No. tested)	CD4: CD8 (No. tested)	ALC (No. tested)
With hepatomegaly and lymphadenopathy	252 (5)	692 (3)	0.212 (11)	1800 (1)
Without lymphadenopathy and hepatosplenomegaly	292.14 (34)	931.54 (24)	0.314 (24)	2085.18 (17)

SD for CD4 counts-172.63 and 238.22, SE 87.34, $p > 0.05$, * No.= number

Table 5**Hepatosplenomegaly, lymphadenopathy and average CD4, CD8, CD4:CD8 and ALC**

	CD4 (No. tested)	CD8 (No. tested)	CD4: CD8 (No. tested)	ALC (No. tested)
With lymphadenopathy and hepatosplenomegaly	184.60 (9)	1043.63 (8)	0.177 (9)	2320 (5)
Without lymphadenopathy and hepatosplenomegaly	292.14 (34)	931.54 (24)	0.314 (24)	2085.18 (17)

SD for CD4 counts-102.60 and 238.22, SE 53.33, $p < 0.05$, * No.= number

Table 6**Distribution of lymphadenopathy in HIV-positive cases**

Lymph nodes	Bilateral (%)	Left only (%)	Right only (%)	Total (%)
Cervical	190 (88.78)	11 (5.14)	13 (6.07)	214 (100)
Axillary	192 (91.00)	8 (3.79)	11 (5.21)	211 (100)
Inguinal	174 (97.21)	1 (0.56)	4 (2.23)	179 (100)

disseminated tuberculosis and one (3.45%) each had tubercular lymphadenitis and tubercular pleural effusion. Two (6.90%) patients had associated ascites. Of the 28 patients with epitrochlear, supraclavicular, submandibular and posterior auricular lymphadenopathy, five (31.25%) out of 16 had bilateral involvement as compared to nine (75%) out of 12 with unilateral involvement. The difference was statistically significant ($\chi^2 4.25$, df-1, $p < 0.05$).

Discussion

Bilateral discrete cervical, axillary and inguinal lymphadenopathy in HIV-positive patients was the commonest finding in this study, as reported by others also [2]. The HIV epidemic has been associated with a marked increase in pulmonary and extrapulmonary tuberculosis [5-8]. Involvement of retroperitoneal and hilar lymph nodes in our study was found to be a sign of opportunistic infection. All these patients had tubercular infection. In another study of lymphadenopathy in Blantyre, Malawi, 73% cases were having tuberculosis and 84% were later found to be HIV positive [9]. Asymmetrical involvement of lymph nodes (other than cervical, axillary and inguinal) and involvement of retroperitoneal and hilar lymph nodes is associated with significantly higher chance of developing AIDS. Debnath et al [10], reported a higher incidence of thoracic lymphadenopathy in HIV-positive patients as compared to HIV-negative controls.

Knollmann et al [3], in a study of 339 HIV infected patients found splenomegaly in 43.36%, hepatomegaly in 42.48% and lymphadenopathy in 32.74% as compared to 9.47%, 16.66% and 4.74% respectively observed in our study. They also concluded that these findings lack prognostic relevance except in cases with large hepatomegaly, grossly enlarged lymph nodes or ascites, which indicate immunosuppression. In contrast, we found a positive correlation between hepatomegaly and development of AIDS. Presence of retroperitoneal lymphadenopathy was found to be a sign of opportunistic infection in our study. Aubry et al [11] concluded that combination of abdominal lymphadenopathy and/or serous exudates (peritoneal, pleural or pericardial) suggested disseminated tuberculosis in AIDS cases. Two cases in our study had abdominal lymphadenopathy with ascites and one had pleural effusion.

We found an increased association of AIDS in cases with lymphadenopathy possibly due to endemicity of tuberculosis in our country. Satyanarayana et al [12], in a study of fine needle aspiration cytology (FNAC) of lymph nodes in 196 HIV-positive patients demonstrated acid fast bacilli (AFB) with equal frequency in both symptomatic and asymptomatic groups. This suggests that many of the cases of generalised lymphadenopathy

in HIV positive patients are tubercular in aetiology. We did not find any co-relation between splenomegaly and development of AIDS. Furrer [13], reported that splenomegaly was not associated with a higher risk of developing AIDS. To conclude, lymphadenopathy and hepatomegaly cases with HIV infection should be investigated for opportunistic infections.

Conflicts of Interest

None identified

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