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Cytological Evaluation of Lymphadenopathy in HIV Seropositive Patients

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Abstract

Background: Lymphadenopathy accounts for one of the most common lesions encountered in HIV positive patients. The cytopathology of these masses encompass a variety of changes that provide insight into the underlying condition associated with HIV. Aim of the present study was to analyze the cytological patterns of lymph node lesions in HIV/AIDS patients by Fine Needle Aspiration Cytology (FNAC) and correlate its findings with serum CD4 counts.

Method: A total 75 cases of all genders and age, already diagnosed as seropositive by ELISA and presented with lymphadenopathy of ≥1 cm were studied in the Department of Pathology by FNAC during the period of 1 and half year. Smears were fixed in 95% ethyl alcohol for PAP staining. Air dried smears were kept for MGG and AFB. The serum CD4 count was assessed by BD FACS Count System.

Results: Male predominance observed with male to female ratio of 1.3: 1. Maximum cases (80%) had involvement of cervical lymph nodes followed by axillary 6 (8%). The commonest cytological diagnosis was chronic granulomatous lymphadenitis 30 cases (40%), followed by tuberculous lymphadenitis 27 (36%). Most common cytomorphological pattern in cases of tuberculous lymphadenitis was caseous necrosis with epithelioid cells (55.5%). Most of the cases (20 cases) of chronic granulomatous had a serum CD4 count between 200-499 cells/μL with a mean of 330.2. The least mean value of serum CD4 count was seen in tuberculous lymphadenitis and it was 118.29 cells/μL.

Conclusion: FNAC is the simple and very effective diagnostic modality for HIV lymphadenopathy patients. It guides identification of majority of the granulomatous, reactive, and opportunistic infections. It therefore, helps in guiding subsequent management of these patients.

Keywords: Lymphadenopathy; Cytopathology; FNAC; Smear; Seropositive; Lymphadenitis; Necrosis; Granulomatous; Opportunistic

Introduction

Human immunodeficiency virus (HIV) infection and its resultant acquired immune deficiency syndrome (AIDS) have become a global pandemic [1]. AIDS was first recognized in United States in 1981. In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated to be the causative agent of AIDS [2]. HIV disease can be divided on the basis of immunodeficiency into an early stage [cluster of differentiation (CD)4 > 500/μL], an intermediate stage (CD4=200-500/μL), and an advanced stage (CD4<200/μL), [3,4].

Lymph nodes, which form the bulk of lymphoid tissue, are the major anatomic site for establishing and propagation of HIV infection. Lymphadenopathy is one of the earliest manifestations of HIV [5]. It may also be a manifestation of opportunistic infections, lymphoid malignancy developing in an immunodeficient individual [6]. The most useful diagnostic procedures for HIV patients with lymphadenopathy are lymph node biopsy (Gold standard), but the method has several drawbacks [7].

FNAC can serve as an alternative method and may be practiced for the diagnosis of opportunist infection in HIV/AIDS, e.g. Tuberculosis, Histoplasmosis, Toxoplasmosis and malignant condition such as Kaposi's sarcoma and lymphoma [8]. FNAC has become the primary investigative procedure for mass lesions on HIV-positive patients, particularly in the assessment of lymphadenopathy. The procedure is rapid, easily performed and in many cases obviates excision while guiding subsequent therapy or observation [9]. The use of a simple investigative tool to rapidly identify the cytomorphological patterns in lymphadenopathy of seropositive cases, and in turn initiate therapy directed specifically towards the disease can help reduce the already excessive burden on HIV patients.

The present study was undertaken to evaluate the role of FNAC as a cytological investigative tool in the diagnosis of various lesions in HIV lymphadenopathy and correlate its findings with serum CD4 counts.

Materials and Methods

After obtaining Institutional Ethical Committee approval and written informed consent from the patients, this hospital based cross sectional study was conducted in the Department of Pathology, at Tertiary Health Care Centre, over a period of one and half year. A total 75 cases of all genders and age, already diagnosed as seropositive by ELISA and presented with lymphadenopathy of ≥ 1 cm were included in the study. Patients not willing to participate in the study were excluded from the study.

A detailed clinical history of patient was recorded in a set proforma including the demographic data, history of acquiring and first diagnosis of HIV/AIDS. A detailed and thorough clinical examination including the general examination and specific examination of palpable lymph nodes was done. Sites for lymph node aspiration were Cervical, Axillary, Inguinal and any other.

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All HIV positive cases with lymphadenopathy were subjected to FNAC in the cytology OPD of the Pathology department. The swelling was localized by careful palpation and site was cleared with spirit and fixed in a favorable position with one hand. A 23 or 24 gauge needle was attached to a 20cc syringe fitted on to a comeco syringe pistol. The needle was inserted through the skin with quick motion and advanced into the swelling. By noting the resistance encountered on puncture, it was ensured the needle was in lymph node. After puncturing swelling negative pressure was created by retracting the plunger of pistol. The needle was moved to and fro within node maintaining negative pressure. Once aspirate was observed at the junction of needle and hub, aspiration was stopped by releasing vacuum in syringe. The needle was withdrawn from the lymph node, content of needle carefully expressed on to the glass slide. Smears were prepared with use of flat surface of another slide by applying pressure. Smears were immediately fixed in 95% ethyl alcohol for PAP staining [10]. Air dried smears were kept for MGG [10] and AFB [10]. The serum CD4 count of the patient was assessed by BD FACS Count System (immunocytometry system) [11].

Data Analysis

Data collected was entered simultaneously into "Statistical Package for Social Scientists" (SPSS) software version 17.0 and coded appropriately. Results are presented in the form of tables, pie chart and bar diagrams. Findings were compared against findings from similar studies and discussed.

Observations and Results

Total 75 HIV positive patients were included in the study, amongst them 43 (57.3%) were male and 32 (42.7%) were female suggesting a male predominance. The ratio of male: female comes out to be 1.3: 1. Majority of the male patients were between the age group of 31-40 years (17.33%) and females were between 21-30 years (20%), as shown in Table 1. Most of the cases had involvement of cervical lymph nodes i.e. 60 (80%) followed by axillary 6 (8%) and others [(12%) (Supraclavicular 4%, Sub mandibular 2.7%, Inguinal 1.3%, Post auricular 1.3%, Pre auricular 1.3%, Submental 1.3%)].

Commonest cytological diagnosis was chronic granulomatous lymphadenitis seen in 30 cases (40%), followed by tuberculous lymphadenitis 27 (36%). The reactive lymphadenitis is reaction to any foreign antigen while non-specific lymphadenitis is a type of reactive which may be long standing. In present study reactive lymphadenitis was seen in 14 cases (18.6%). Non-specific lymphadenitis and acute suppurative lymphadenitis accounted for 2.7% each, as shown in Figure 1. Amongst tubercular lymphadenitis the most common cytomorphological pattern diagnosed was smears showing caseous necrosis with epithelioid cells with total 15 cases (55.5%) out of 27 as shown in Figures 2 and 3. Seven cases (26%) had smears showing caseous necrosis only and 2 (7.4%) had epithelioid cells only. Suppurative features were found in 3 cases (11.1%).

Age (Years)	Male	Female	Total (%)
1-10	03	00	03 (04)
11-20	11	06	17 (22.7)
21-30	08	15	23 (30.7)
31-40	13	07	20 (26.7)
41-50	05	03	08 (10.7)
51-60	02	00	02 (2.6)
>60	01	01	02 (2.6)
Total	43	32	75 (100)

Table 1: Distribution of cases according to age and sex.

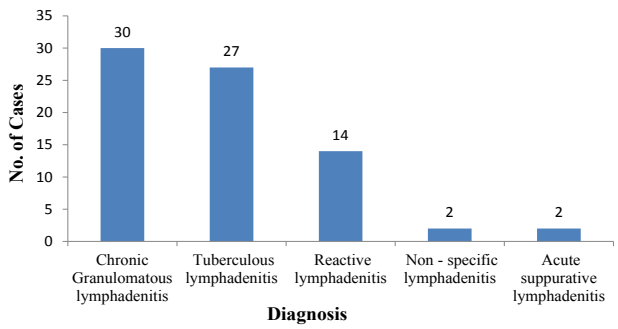

Figure 1: Distribution of cases according to cytological diagnosis.

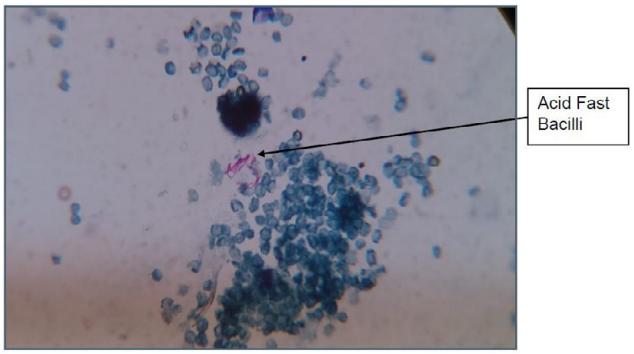

Figure 2: Photomicrograph showing Tubercle bacilli (OI, ZN) (Tubercular lymphadenitis).

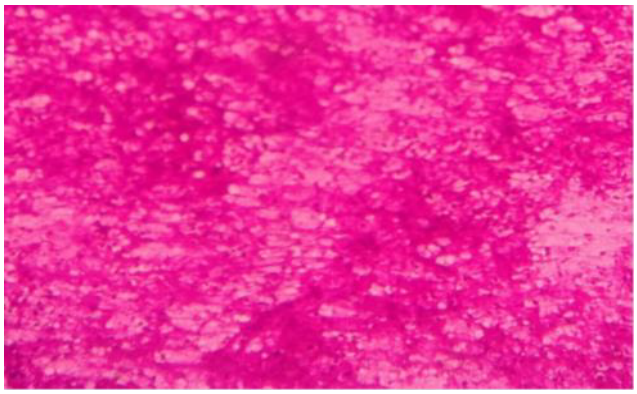

Figure 3: Photomicrograph showing caseous necrosis (H&E).

In all the patients serum CD4 cell count was carried out and compared with the cytological pattern as shown in Table 2. Serum CD4 count of >500 cells/μL was seen in 6 (8%) cases of reactive lymphadenitis and 2 (2.6%) cases of chronic granulomatous lymphadenitis. Patients with tubercular infection had serum CD4 count of 200-499 cells/μL in 10 (13.3%) cases and <200 cells/μL in 17 (22.6%) cases. Twenty cases of chronic granulomatous lymphadenitis had a serum CD4 count of 200-499 cells/μL and 8 cases had serum CD4 count < 200 cells/μL as shown in Figures 4-6.

Discussion

In the present study, the incidence of HIV lymphadenopathy was more common in males in the 4th decade of life and majority of

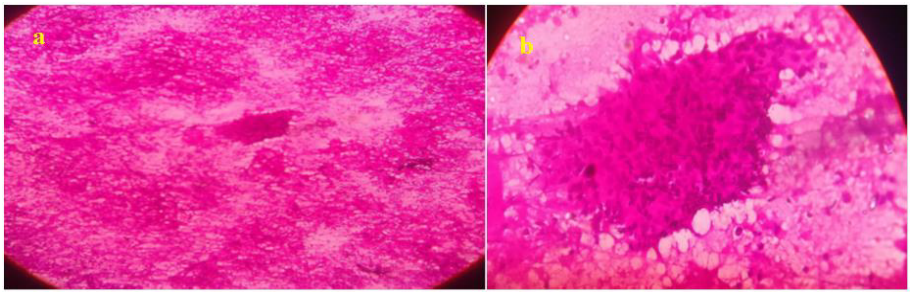

Figure 4: Photomicrograph showing group of a) epitheloid cells (LP, H&E) and b) epithelioid cells (HP).

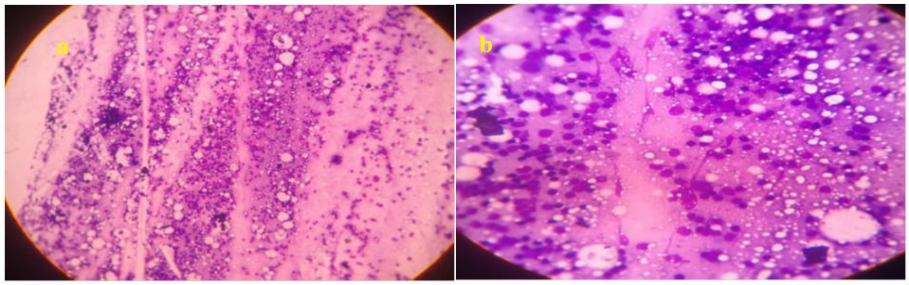

Figure 5: Photomicrograph showing mixed population of lymphoid cells, centroblasts, and centrocytes, small and large lymphocytes a)- (LP, MGG) and b) -(HP, MGG) (Reactive lymphadenitis).

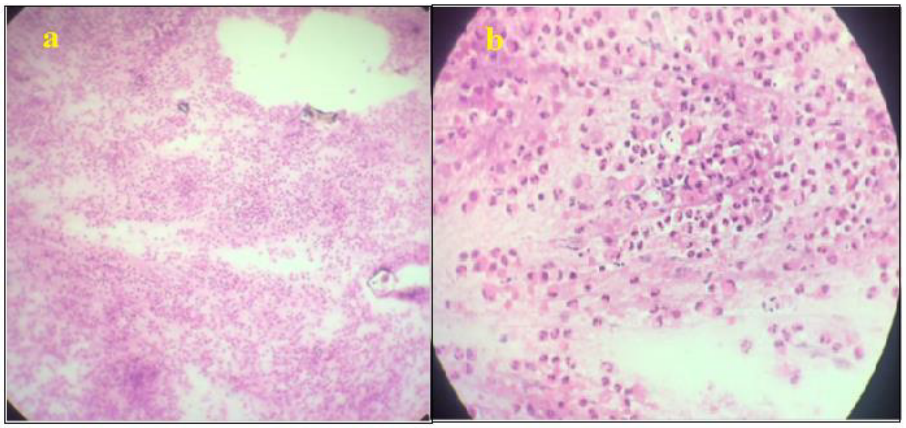

Figure 6: Photomicrograph showing dense infiltration of neutrophils a) - (LP, H&E) and b) - (HP, H&E) (Acute suppurative lymphadenitis).

CD4 Count (cells/µL)	Tubercular lymphadenitis	Reactive	Chronic granulomatous lymphadenitis	Non-specific lymphadenitis	Acute suppurative
>500	0	6	2	1	0
200-499	10	8	20	0	2
<200	17	0	8	1	0
Total	27	14	30	02	02

Table 2: Comparison of CD4 Count with various cytological diagnoses.

females in age group of 21-30 years. Most of the HIV patients had involvement of cervical lymphadenopathy followed by axillary. Our study correlated well with the previous studies [5-7,12,13]. Chronic granulomatous lymphadenitis is the most common cytological diagnosis which is quite in contrast to other studies conducted in the Indian subcontinent [14-17], where the main contributor was mycobacterial infection. This could suggest an increased incidence of HIV positive patients already on HAART and Anti Tubercular drugs before presenting with lymphadenopathy in cytology OPD, therefore showing paucity of AFB on smears. However, Reid et al. [18] also had a lesser incidence of mycobacterial cases which may be due to less overall incidence of tuberculosis as an opportune pathogen. This study had reactive lymphadenitis as the most common diagnosis (51%), whereas the present study had only 18.6% cases with reactive findings. No cases of lymphoma were found in the current study.

The most common cytomorphological pattern in cases of

tuberculous lymphadenitis was caseous necrosis with epithelioid cells and second most common pattern was caseous necrosis only with the only exception of Surase et al. [16] where the second most common was epithelioid cells only. 3 of the total 27 tuberculous lymphadenitis cases showed features of acute suppuration with positive Ziehl Neelson staining. Similar findings were seen in study done by Kumarguru et al. [5] and Gorva et al. [13].

Serum CD4 cell count was available for all the participating patients on whom FNAC was performed. Most of the cases of chronic granulomatous had a serum CD4 count between 200-499 cells/μL with a mean of 330.2, this finding was quite similar to that of Agravat et al. [14]; while 8 cases had a serum CD4 count of <200 cells/μL. Tubercular lymphadenitis cases did not show serum CD4 count of above 500 cells/μL, which may suggest a depression in the immune system and the presence of an opportune infection, this is correlated well with finding of Deshmukh et al. [17]. The least mean value of serum CD4 count was seen in this particular category was 118.29 cells/μL, which was close to a study by Kumar et al. [19] where necrotizing suppurative lymphadenitis accounted for the most common cytomorphological finding amongst the tubercular group with a mean serum CD4 count of only 92 cells/μL. Those patients with a reactive lymphadenitis did not show a serum CD4 value of less than 200. Out of 14 cases, 6 (42.8%) had a serum CD4 count of >500 cells/μL (mean=633 cells/μL) and 8 (57.14%) had a value between 200-499 with a mean of 323.3 cells/μL. Reactive lymphadenitis was the only cytological diagnosis which showed such a high mean value of serum CD4 count. These results are comparable with the study done by Deshmukh et al. [17] and Pista et al. [20].

Only two cases of acute suppurative lymphadenitis were identified, both having a serum CD4 cell count between 200-499 cells/μL (mean=220.5). Similarly, only two cases of non-specific lymphadenitis were diagnosed with extremes of serum CD4 value. One had a value of 52 cells/μL and the other with a value of 551 cells/μL. Hence, no definitive interpretation of this finding could be established.

Conclusion

Fine Needle Aspiration Cytology (FNAC) of lymph node is very helpful in segregating cases that need further evaluation. One of the major opportunistic infections detected in both symptomatic as well as asymptomatic patients was Tuberculosis. Therefore, ZN staining should always be done for detection of AFB in spite of the cytological picture not suggesting it. Correlation of cytological diagnosis with serum CD4 T lymphocyte count gives invaluable information regarding immune status and stage of the disease.

Hence, FNAC is the simple and very effective diagnostic modality for HIV lymphadenopathy patients. It guides identification of majority of the granulomatous, reactive, and opportunistic infections. It therefore, helps in guiding subsequent management of these patients.

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