



CYTOLOGICAL STUDY OF LYMPHADENOPATHY IN HIV POSITIVE PATIENTS WITH CLINICOPATHOLOGICAL CORRELATION

Pathology

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ABSTRACT

This is a study of 52 consecutive Human immunodeficiency virus (HIV) positive cases with lymphadenopathy undergoing Fine Needle Aspiration Cytology (FNAC) of lymph nodes, including 25 male patients and 27 female patients. Maximum number of cases were seen in fourth and fifth decades of life. Cervical lymphadenopathy was the commonest presentation. Tuberculous lymphadenitis was the most common lesion accounting for 31 cases followed by reactive lymphoid hyperplasia (eight cases). Other lesions included acute suppurative lymphadenitis (three cases), metastasis (five cases), Non Hodgkin Lymphoma (four cases) and suspicious of malignant cells (one case). Caseating granulomatous lymphadenitis was the commonest cytological pattern of tuberculosis (41.93%). AFB positivity was most commonly seen in cases of tuberculosis with caseating pattern of lymphadenitis (80%)

KEYWORDS

FNAC, Lymph node, HIV, Tuberculosis

INTRODUCTION -

Lymphadenopathy is a common manifestation of Human immunodeficiency virus (HIV) infection which may be due to persistent generalised lymphadenopathy due to HIV itself or due to infections like tuberculosis, cryptococcosis, histoplasmosis etc, malignancies like Lymphomas, Kaposi sarcoma, etc. as well as other causes like medications, sarcoidosis, etc.¹ The diagnosis of the cause of lymphadenopathy is important for proper management of the patient, to reduce morbidity as well as mortality. The fundamental goal is to exclude malignancy or serious treatable causes.¹ Although lymph node biopsy is the gold standard for the diagnosis of lymphadenopathy, it requires surgical intervention and is associated with some risk to the patient as well as to the doctor when the patient is HIV infected. Fine Needle Aspiration Cytology (FNAC) is a safe and easy procedure especially for palpable lymph nodes, which gives the diagnosis in short time, in most of the cases. In the present study, we have analysed the findings of FNAC of lymph nodes in HIV positive patients.

MATERIAL AND METHODS -

This is a study of 52 consecutive HIV positive cases with lymphadenopathy undergoing (FNAC) of lymph nodes at a tertiary care center which was performed over a period of 4 years. Ethical approval was taken for the study from the institutional ethical committee. Detail clinical history was taken from the patient followed by systemic and local examination. After explanation of procedure, informed consent was obtained. FNAC was done with 10 cc 22/23G needle under all aseptic precautions. Four or five smears were prepared from the material aspirated. One or two smears were dry fixed and remaining smears were wet fixed in ethyl alcohol. Wet fixed smears were stained with Hematoxylin – Eosin, and PAP stain. Dry fixed smears were stained with Leishman stain. Special stains like Zeihl-Neelsen stain, Gram stain, PAS stain, Methanamine silver stain were used when required. Microscopic examination was performed followed by analysis of cytological findings and clinicopathological correlation. Data was analysed with respect to frequency distribution and percentage.

RESULTS -

A total of 52 consecutive HIV positive cases with lymphadenopathy undergoing Fine Needle Aspiration Cytology (FNAC) of lymph nodes were studied.

Table 1 shows the age wise and gender wise distribution of all cases.

Table no. 1 – Age Wise And Gender Wise Distribution Of Patients

Age (in years)	Males	Females	Total
1 - 10	--	01	01
11 - 20	01	06	07
21 - 30	03	05	08
31 - 40	05	08	13
41 - 50	11	01	12
51 - 60	02	02	04
61 - 70	02	04	06
71 - 80	01	--	01
Total	25	27	52

Out of the total 52 cases, there were 25 male patients and 27 female patients (male to female ratio-1:1.08) with a wide age range from first through eighth decades. The youngest patient was four-year-old girl. Maximum cases were in fourth and fifth decades of life.

All the cases were analysed according to the cytological diagnosis as shown in Table no. 2.

The cytological findings of different lesions were as follows

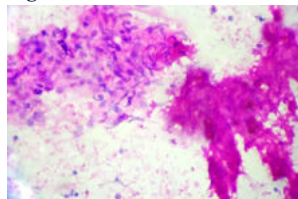
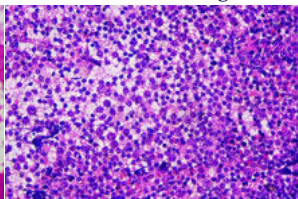
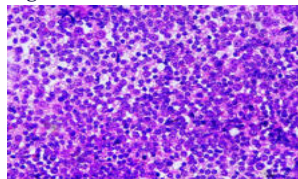
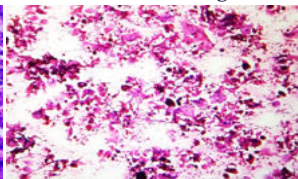
1. Reactive lymphoid hyperplasia – The smears showed mixed population of lymphoid cells at varying stages of maturation.
2. Tuberculous lymphadenitis – Smears showed varying combination of caseous necrosis, epithelioid granulomas and suppuration.
3. Acute suppurative lymphadenitis – Smears showed viable and degenerated polymorphs.

4. Non-hodgkin lymphoma – Smears showed monotonous population of neoplastic atypical lymphoid cells.
5. Metastasis – Smears of metastatic squamous cell carcinoma showed squamous cells with pleomorphic hyperchromatic nuclei. Few dyskeratotic cells were also noted.

Table no. 2 – Cytological diagnosis in HIV positive cases

Cytological diagnosis	Frequency	Percentage
I. Benign lesions		
Reactive lymphoid hyperplasia	08	15.38%
Tuberculous lymphadenitis	31	59.62%
Acute suppurative lymphadenitis	03	5.76%
II. Malignant lesions		
Metastasis	05	9.62%
Lymphomas	04	7.69%
III. Suspicious of malignant cells	01	1.93%
Total	52	100%

Tuberculous lymphadenitis (Figure 1 A) was the commonest lesion accounting for 31 cases (59.62%), followed by reactive lymphoid hyperplasia. (Figure 1 B). Malignant lesions included 5 cases of metastatic carcinoma and four cases of Non Hodgkin Lymphoma (Figure 1 C). Metastatic tumors included three cases of metastatic squamous cell carcinoma (Figure 1 D) and two cases of metastatic poorly differentiated carcinoma.

Figure 1 A**Figure 1 B****Figure 1C****Figure 1D****Figure 1. Microphotograph of cytology smear of**

- A- Tuberculous lymphadenitis showing epithelioid granuloma and caseation
- B- Reactive lymphoid hyperplasia showing mixed population of lymphoid cells
- C - Non Hodgkin Lymphoma showing monotonous population of neoplastic lymphoid cells
- D- Metastatic squamous cell carcinoma showing squamous cells with pleomorphic hyperchromatic nuclei and eosinophilic cytoplasm.

Table no. 3 – Site wise distribution of lesions in HIV positive cases

Site	RLH	Tub lym	Ac sup lym	Mets	Lym-pho	Sus of Mal	Total
Cervical	04	16	01	02	--	--	23
Submandibular	--	02	--	02	--	--	04
Inguinal	04	--	01	--	--	01	06
Axillary	--	04	--	01	02	--	07
Supraclavicular	--	05	--	--	01	--	06
Posterior auricular	--	01	--	--	--	--	01
Generalised	--	03	01	--	01	--	05
Total	08	31	03	05	04	01	52

The sitewise distribution of lesions (table no.-3) shows that the patients commonly presented as localised lymphadenopathy. Out of 52 cases, maximum cases had lymphadenopathy in the cervical region. Five cases showed generalised lymphadenopathy and the aspirate was obtained from at least two sites in these cases. For most of the lesions, cervical lymphadenopathy was the commonest presentation. Almost half of the cases of Tuberculosis had cervical lymphadenopathy.

The cases of tuberculosis were further studied according to cytology pattern and the result of Zeihl Neelsen (ZN) staining for the presence of acid fast bacilli (AFB). The cytological patterns in tuberculous lymphadenitis were classified into four categories namely Caseating granulomatous lymphadenitis, Granulomatous lymphadenitis, Caseating lymphadenitis and Necrotizing and suppurative lymphadenitis. The cases with granulomatous lymphadenitis were included under the category of tuberculosis after clinical correlation and after ruling out the other causes of granulomatous lymphadenitis. The cases with suppurative lymphadenitis were considered as tuberculosis only if the smears showed AFB positivity or admixture with caseous necrosis. Table no. 4 shows the distribution of cases of tuberculous lymphadenitis according to the cytological pattern and its correlation with AFB positivity.

Table no. 4 – Correlation of cytological patterns of tuberculous lymphadenitis in HIV positive cases with AFB positivity

Tuberculous lymphadenitis	No. of cases (Percentage of total)	AFB positive cases	Percentage of AFB positivity
Caseating granulomatous lymphadenitis	13 (41.93%)	09	69.23%
Granulomatous lymphadenitis	06 (19.36%)	--	---
Caseating lymphadenitis	05 (16.13%)	04	80%
Necrotizing and suppurative lymphadenitis	07 (22.58%)	03	42.85%
Total	31 (100%)	16	51.61%

Caseating granulomatous lymphadenitis was the commonest pattern noted. Out of 31 cases, 16 cases were AFB positive (51.61%). AFB positivity was most commonly seen in caseating lymphadenitis i.e. 80% followed by necrotizing and suppurative lymphadenitis, and no positivity was seen in granulomatous lymphadenitis.

Reactive lymphoid hyperplasia was diagnosed in eight cases showing mixed lymphoid population without any specific pathology . There were two HIV positive male patients and six HIV positive female patients showing reactive lymphoid hyperplasia. Of these, four cases were in the second decade.

Acute suppurative lymphadenitis was diagnosed in three cases showing numerous polymorphs on cytology and negative ZN staining result for AFB . These cases were in the age group of 11 – 35 years. There were two female patients and one male patient.

Of the metastatic malignancies, three cases were diagnosed as metastatic squamous cell carcinoma and two cases were diagnosed as metastatic poorly differentiated carcinoma.

The youngest patient was 48-year-old lady and the oldest patient was 68-year-old man. Among the lymphoma cases, the youngest patient was 4-year-old girl and the oldest patient was 80-year-old man. In one case (80 year old male), the diagnosis of Diffuse large B cell lymphoma was suggested on cytology.

DISCUSSION-

The maximum number of HIV positive cases with lymphadenopathy were seen in fourth and fifth decades in the present study similar to the finding of Baghel et al², corresponding to the sexually active group. Similarly, fourth decade was found to be the common age group with lymphadenopathy by Parikh UR et al³, Deshmukh AT et al⁴, Tirumalasetti N et al (21-40years)⁵, also by Laishram RS et al (30-45 years)⁶ and Thakor et al⁷.

There were 25 male patients and 27 female patients who were HIV positive with slight female predominance. The male: female ratio in the present study was 1:1.08. However, Parikh UR et al³, Deshmukh AT et al⁴, Laishram et al⁶, Tirumalasetti N et al⁵ reported male predominance with the male: female ratio being 3.44:1, 1.7:1, 1:0.35, 1.3:1 respectively.

The variation in age wise and gender wise distribution of HIV positive cases with lymphadenopathy may be due to varying incidence of HIV positive cases in the corresponding geographic areas.

In the present study, out of 52 cases, the most common site of lymphadenopathy was cervical region i.e. 23 cases (44.23%)

Similarly, Parikh UR et al³ reported 62.5% cases, Deshmukh AT et al⁴ reported 81.8% cases, Tirumalasetti N et al⁵ reported 81.04% cases, Laishram RS et al⁶ reported 54.84% cases presenting as cervical lymphadenopathy. In all the studies cervical region was found to be the commonest site of lymphadenopathy. The following table (no.5) shows the cytological diagnosis in HIV positive patients as reported by various authors in comparison with the present study.

Table no. 5 showing cytological diagnosis in HIV positive patients in various studies

Authors	Parikh UR et al ³ (2012)	Laishram RS et al ⁶ (2014)	Naveen K et al ⁸ (2015)	Patil BU et al ⁹ (2019)	Present study
Diagnosis					
React Lymph	7 (18.92%)	18 (28.12%)	37 (37%)	11 (20.4%)	8 (15.38%)
Tub Lym	15 (40.54%)	27 (42.19%)	59(59%)	24 (44.4%)	31 (59.62%)
Ac Sup Lym	10 (27.03%)	7 (10.94%)	-	6 (11.1%)	3(5.76%)
Fungal inf	-	5(7.81%)	1(1%)	1(1.8%)	
Viral inf	-	1(1.6%)	-	-	-
Chr Nonsp Lym	4(10.81)	-	-	-	-
Metastasis	--	1(1.6%)	1(1%)	3(5.5%)	5(9.62%)
Lymphomas	1(2.7%)	2(3.2%)	2(2%)	9(17.1%)	4(7.69%)
Sus of mal	--	--	-	-	1(1.93%)
Inad/ Incon	--	3(4.7%)	-	-	--
Total	37 (100%)	64(100%)	100 (100%)	54 (100%)	52 (100%)

- React Lymph- Reactive lymphoid hyperplasia/Reactive lymphadenitis
- Tub Lym – Tuberculous lymphadenitis
- Ac Sup Lym – Acute suppurative lymphadenitis
- Inf- infection * Chr. Nonsp. Lym - Chronic nonspecific lymphadenitis
- Sus of mal – Suspicious of malignant cell
- Inad/ Incon – Inadequate/ Inconclusive for opinion

All the studies reported tuberculous lymphadenitis as the commonest lesion seen in HIV positive cases similar to our study. In the present study, the cytological patterns in tuberculous lymphadenitis were classified into four categories namely Caseating granulomatous lymphadenitis, Granulomatous lymphadenitis, Caseating lymphadenitis and Necrotizing and suppurative lymphadenitis. Caseating granulomatous lymphadenitis was the commonest cytomorphological pattern (41.93%) in our study, comparable to that of Parikh UR et al³ (40%) and Deshmukh AT et al⁴ (40%). Laishram RS et al⁶ reported necrotizing lymphadenitis as the commonest cytomorphological pattern in HIV positive patients (33.33%) followed by caseating granulomatous pattern (29.6%). Tirumalasetti et al⁵ observed three cytological patterns of tuberculous lymphadenitis i.e. caseous necrosis- epithelioid cell granulomas (CN-ECG) in 28 (51.85%) of patients, caseous necrosis (CN) in 20 (37.04%) patients and epithelioid cell granulomas (ECG) in 6 (11.11%) patients.

In the present study, out of 31 cases of tuberculosis, 16 cases showed AFB positivity (51.61%). Parikh UR et al³ reported AFB positivity in 46.67% cases. In our study AFB positivity was most commonly seen in caseating lymphadenitis i.e. 80% cases and no positivity was seen in granulomatous lymphadenitis. Similarly, Tirumalasetti et al⁵ found that Acid fast bacilli (AFB) were abundant in smears with caseous necrosis and decreased in cases with granulomas. In the study by Laishram et al⁶, out of the 8 cases of caseating granulomas, 4 cases showed AFB, among the granulomatous lesion, 2 out of 5 cases showed AFB.

In our study, three out of seven cases (42.85%) of necrotizing and suppurative pattern showed AFB positivity. These cases were diagnosed as tuberculosis if the smears showed AFB positivity or admixture of caseous necrosis. Laishram et al⁶ found high positivity of AFB in all the cases of necrotizing and suppurative pattern. Patil et al⁸ also found AFB positivity in all the cases of tuberculous lymphadenitis showing tubercular abscess with predominant neutrophils along with epithelioid cells and semifluid necrosis. Thus suppuration in the absence of granulomas does not rule out tuberculosis. The difference in

the patterns of reaction as well as the variation of AFB positivity could reflect the difference in the immune status of the patients. Hence ZN staining should be done on the cytology smears of lymph node in all the cases of HIV infection. In our study the cases were labelled as Acute suppurative lymphadenitis only after a negative result of ZN stain.

Fungal infection was reported by Laishram et al⁶ (Histoplasma -2 Penicillium marneffeii- 2 Cryptococcus -1) and Patil et al⁹ (Cryptococcus-1) and Naveen et al⁸ (Cryptococcus-1). Laishram et al⁶ found one case of infectious mononucleosis. Fungal or viral infection was not observed in our study.

In the present study, out of 52 HIV positive cases, five cases (9.62%) had metastatic tumours. Patil et al⁹ reported 3 cases (5.5%). Laishram RS et al⁶ reported single case of metastatic adenocarcinoma.

Out of 52 HIV positive cases, four cases (7.69%) of lymphomas were observed in our study. All four cases were diagnosed as NHL. One case was suggestive of Diffuse Large B-cell Lymphoma (DLBCL). Most of the other studies have also reported cases of lymphoma. Patil et al⁹ in their study of 54 cases found three cases of Hodgkin Lymphoma and six cases of Non -Hodgkin Lymphoma which included five cases of Diffuse Large B-cell Lymphoma and one case of anaplastic lymphoma

CONCLUSION:

Lymphadenopathy is a very common occurrence in HIV infected patients which may be due to HIV itself or other infections like tuberculosis or malignancies like lymphomas. FNAC is a minimally invasive tool which provides diagnosis of lymphadenopathy and helps in further management in most of the cases, thus obviating the need for surgical excision.

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