



## A Study of Cytomorphological Spectrum of lymphadenopathy in HIV seropositive Patients

Authors

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### Abstract

**Background:** Lymphadenopathy in HIV/AIDS patients is the earliest and commonest manifestation of opportunistic infection and malignancies. FNAC is a simple technique which is safe and minimal traumatic to patients.

**Aims of Study:** To Evaluate the Cytomorphological spectrum of lymphadenopathy in HIV seropositive cases using FNAC technique and to co-relate cytomorphological pattern with Clinical features, CD4 count and Hematological alterations.

**Method:** The study was conducted in the department of pathology S.M.S. medical college Jaipur from Jan 2016 to end of 2017. FNAC performed on 100 cases with lymphadenopathy. Aspirates stained with H&E and giemsa in routine and special stains whenever indicated.

**Result:** Out of 100 cases, maximum cases were in age group 26-45 years in 71% with male predominance in 64%. Most common site of lymphadenopathy was cervical region in 72%. Tubercular lymphadenitis was the most common cause of lymphadenopathy in 65% with mean CD4 count 227.40 cells/ $\mu$ l, followed by reactive in 20%, mean CD4 count 546.45 cells/ $\mu$ l, suppurative in 11%, mean CD4 count 162.72 cells/ $\mu$ l, lymphoma in 2%, mean CD4 count 565.50 cells/ $\mu$ l and 2% metastatic malignancies, mean CD4 count <100 cells/ $\mu$ l. Most common pattern of tubercular lymphadenitis was epithelioid cell granuloma with caseous necrosis seen in 58.46% cases. Grade 1+ was the most common on ZN grading of AFB with mean CD4 count was 257.08 cells/ $\mu$ l.

**Conclusion:** Tuberculosis was the most common cause of lymphadenopathy. FNAC is a rapid easily performed technique in HIV seropositive cases for early and appropriate diagnosis.

**Keywords:** HIV, Lymphadenopathy, FNAC, CD4 count.

### Introduction

Human immunodeficiency virus (HIV) Infection is one of the most important public health Problem worldwide.<sup>1</sup> According to UNAIDS report 2016, there are over 2 million HIV positive people

living in India and ranked as third largest HIV epidemic in the world.<sup>8</sup> It is a causative agent of AIDS. HIV belongs to the lenti-virus genus of retro-viridae family.<sup>2, 10</sup> AIDS is a fatal illness that breakdowns the body's immunity and leaves the

patient vulnerable to life threatening infection.<sup>5, 6,</sup>

<sup>14</sup>It is a lymphotropic virus, lymphadenopathy is a very common and the earliest finding in HIV positive cases.<sup>1, 5,8,13,14,21</sup> Lymph node enlargement is found almost in all stages of HIV infection, may be due to multiplication of HIV or may be due to manifestation of opportunistic infections, malignant or non-malignant conditions developing in immune-deficient individuals.<sup>5,11,14</sup> CD4 count is an important indicator of immunity, as the CD4 count decreases severity of disease increases and opportunistic infection supervene. FNAC is an easy, rapid, safe, cost effective and less traumatic technique

### Material and Method

The present study was conducted at the Department of Pathology, S.M.S. Medical College and Hospital, Jaipur, Rajasthan during the study period starting from January 2016 to November 2017, after approval by ethical committee. This was the prospective observational study. All the cases referred from ART center, of any age group, were included in the study. Patients detailed history and clinical examination after taking informed consent. FNAC was performed on HIV seropositive patients who presented with lymphadenopathy. During procedure, all aseptic precautions were taken. Prepare the smears with the aspirate. Two smears fixed immediately in 95% ethyl alcohol for H&E staining and three were air-dried for giemsa stain and special stain like AFB, PAS, and Grams stain.

### Observation and Result

**Table No.1** Distribution of cases according to age and Gender

	Age (Years)	Male		Female	
		N	%	Nr	%
1	5-15	8	12.50	2	5.56
2	16-25	7	10.94	4	11.11
3	26-35	21	32.81	14	38.89
4	36-45	22	34.38	14	38.89
5	46-55	5	7.81	2	5.56
6	>56	1	1.56	0	0.00
	Total	64	100.00	36	100.00

A total of 100 HIV Seropositive cases with lymphadenopathy were aspirated and results noted In the present study age of patients ranged from 6-63years. Maximum numbers of cases 36% were between age of 36-45years and 35% cases between 26-35 years. Lymphadenopathies in extremes of ages were less (as in Table no.1). Out of 100 cases 64 were males and 36 were female with Male to female ratio of 1.8:1.

**Table No. 2** Distribution of the cases according to site of lymphadenopathy

Site	N	%
Cervical	72	72
Supraclavicular	9	9
Submandibular	5	5
Axillary	5	5
Inguinal	5	5
Submental	1	1
Post-auricular	1	1
Sub-occipital	1	1
Generalized	1	1

In our study most common site of involvement was cervical in 72% cases, followed by supraclavicular 9%, Submandibular, Axillary and Inguinal lymphadenopathy were 5% each. Sub-mental, Post-auricular and Sub-occipital were 1% each. One case showed generalized lymphadenopathy.

Out of 100 cases, Fever was the most common symptom seen in 71% of cases, followed by Weight-loss in 51% cases, cough in 17% of cases, diarrhea, joint pain and jaundice in 3%, 2% and 1% cases respectively.

The cytological diagnosis offered were tuberculous lymphadenitis most common in 65% cases. Diagnosis of tuberculosis was based on AFB positivity on ZN stained smears, mean CD4 count was 227.40cells/ $\mu$ l. The Cytological patterns of tuberculous lymphadenitis were further subdivided into the caseous necrosis only (27.69%), caseous necrosis with epithelioid cell granulomas (58.46%) and epithelioid cells granulomas only in (13.84%).

Reactive lymphadenopathy (20%) was the second most common diagnosis, these Cases showed

varying proportion of centroblast, centrocytes, tingible body macrophages, plasma cells and histiocytes and mean CD4 count was 546.45 cells/μl.

Suppurative lymphadenitis was seen in 11% cases with features of dense acute inflammatory infiltrate with predominant neutrophils, few lymphocytes and fibrillary necrotic background and Acid-fast bacilli were not seen on ZN stain. In 6 cases Gram positive bacteria were seen on Grams staining.

Two percent cases of Lymphoma (NHL) noted with mean CD4 count of 565.50cells/μl. Metastatic carcinomas (metastatic squamous cell

carcinoma) noted in 2% cases and mean CD4 count was <100cells/μl.

**Table No. 3** Distribution of the cases according to Cytodiagnosis

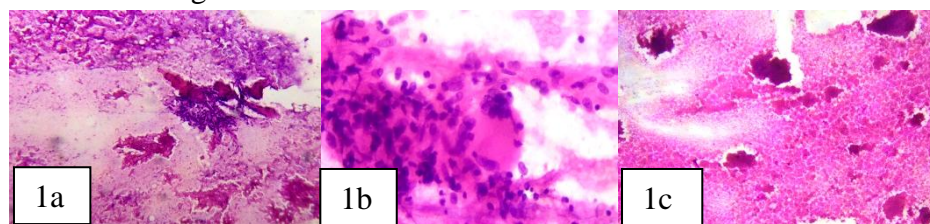
Cytodiagnosis	Number	Percentage %
Tuberculosis	65	65
Reactive	20	20
Suppurative	11	11
Lymphoma	2	2
Metastasis	2	2
<b>Tuberculosis (Patterns)</b>		
Caseous Necrosis only	18	27.69
Epithelioid cell granuloma	9	13.84
Necrosis+Epithelioid cell granuloma	38	58.46

**Table No. 4** Correlation of FNAC finding with CD4 count

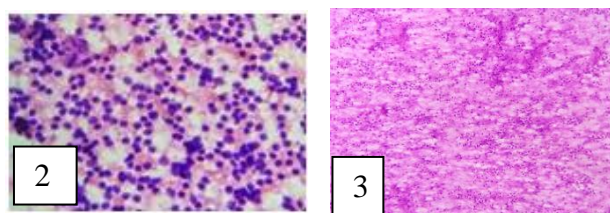
Cytodiagnosis	N	Mean	SD	Minimum	Maximum
TB	65	227.40	187.24	30	1021
Reactive	20	546.45	413.60	62	1662
Suppurative	11	162.27	118.97	51	425
Lymphoma	2	565.50	33.23	542	589
Metastasis	2	67.50	13.44	58	77

Grading of AFB was done on ZN stained smears as proposed by Kumar et al.<sup>46</sup> grade 1+ = AFB found after a careful search, 2+ = AFB were singly scattered, grade 3+ = AFB were found in large number (singly, clustered) bacilli could be detected even under 10 x magnification. Mean

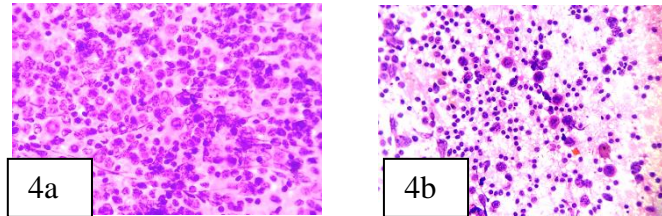
CD4 count was maximum in grade 1+, 257.08 cells/μl (48 cases), lowest in 3+, 78 cells/μl (10 cases) and in grade 2+ mean CD4 count was 121.14 cells/μl (7 cases).



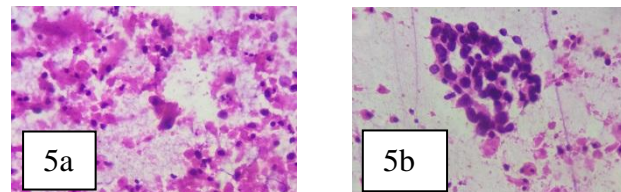
1a. H&E stained smear (100 X) showing epithelioid cell granuloma, langhans giant cells and caseous necrotic material 1b. H&E stained smear (400 X) showing epithelioid cell granuloma, langhans giant cell 1c. H&E stained (100 X) smear showing caseous necrosis - Tuberculous lymphadenitis



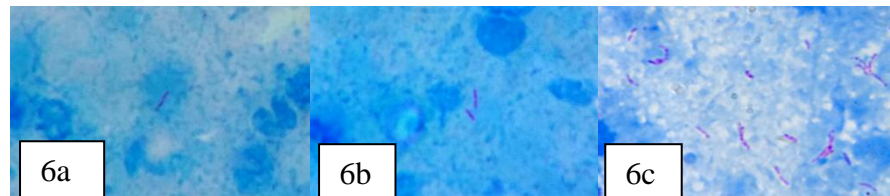
2. H&E stained smear (400 X) showing polymorphous lymphocytes, histiocytes and tingible body macrophage- Reactive lymphadenitis 3. H&E stained smear (100 X) showing degenerated neutrophils and necrosis - Suppurative lymphadenitis



4a.& 4b. H&E stained smear (400 X) showing relatively monomorphic lymphoid cells 4b. H&E stained smear (400 X) showing relatively monomorphic lymphoid cells and large cells having hyperchromatic nuclei with coarse chromatin and irregular nuclear membrane- Lymphoma (NHL)



5a.H&E stained smear (100X) showing numerous squamous cells with hyperchromatic and pyknotic nuclei- Metastatic squamous cell carcinoma 5b. H&E stained smear (400X) showing cluster of malignant squamous cells and tadpole cells- Metastatic squamous cell carcinoma



6a. ZN stained smear showing (1000 X) Acid Fast Bacilli (grade 1+) 6b. ZN stained smear showing (1000 X) Acid Fast Bacilli (grade 2+) 6c. ZN stained smear showing (1000 X) Acid Fast Bacilli (grade 3+)

## Discussion

Lymph node is the usual target organ affected in HIV-AIDS patients. Great advances in investigation techniques and treatment protocol, providing HIV positive patient an opportunity to live symptom free prolong life, despite the presence of disease. FNAC was performed on 100 HIV seropositive patients who presented with lymphadenopathy for early diagnosis.

Lymphadenopathy in HIV seropositive cases was studied with respect to age distribution, sex distribution, site of lymphadenopathy, CD4 count, and cytological findings.

In our study, age of Patient ranged from 6- 63 years, maximum number of cases were seen in age group of 26-35 years (36%) and 36-44 years (35%). Similar findings were reported by others.<sup>3, 5,10,15,16,17.</sup>

The present study revealed male predominance 64% cases, with male to female ratio of 1.8:1. The

finding of our study correlated with others.<sup>3, 5, 10, 13, 14, 17</sup>

While Jayshree Khiste et al.<sup>9</sup> noted female preponderance.

Most common site of lymphadenopathy was cervical region (72 %), which is comparable with others.<sup>4,5,7,9,13,14,17,11,21,22,23</sup>

While Satyanayaranet al.<sup>16</sup> noted higher number of axillary Lymphadenopathy cases than cervical.

Most common symptom was fever seen in 71% of cases followed by weight loss, cough. Jaundice was seen in one case similar findings were noted by Naveen K et al.<sup>24</sup>

Most Common Cytomorphological pattern in our study was tubercular lymphadenitis (65%), followed by reactive lymphadenopathy (20 %). These findings were concordant with other studies.<sup>3,5,7,13,17,18</sup>

While P. Baghelet al.<sup>15</sup> and Ratan K. et al.<sup>10</sup> did not support our Study. They noted reactive

Lymphadenitis more than the tubercular lymphadenitis.<sup>10, 15</sup>

We found 11% cases of acute suppurative Lymphadenitis. Similar finding noted by Neelima Tirumalasetti et al.<sup>3</sup> While Jayshree Khiste et al.<sup>9</sup> noted higher number of suppurative lymphadenitis cases (Table no.5)

**Table No. 5** Comparison of FNAC (Non-Neoplastic) finding with various studies

Diagnosis	Tuberculosis	Reactive	Suppurative
NeelimaT. et al. <sup>3</sup>	41.8	35.6	12.4
Vanisri et al. <sup>5</sup>	58.3	36.1	0
P.Baghel et al. <sup>15</sup>	18	22	2
JayshreeKhiste et al. <sup>9</sup>	50	15.6	25
Ratan K. et al. <sup>10</sup>	38.9	42.1	5.6
Naveen K. et al. <sup>24</sup>	59	37	0
AmruthaGorva et al. <sup>7</sup>	56	25	4
Deshmukh et al. <sup>14</sup>	58.3	29.5	0
Present Study	65	20	11

Tuberculous lymphadenitis cases with CN+ECG (58.46%) was most common pattern followed by caseous necrosis only (27.69%) and then epithelioid cell granuloma only (13.84%). Studies corroborated with others.<sup>3,17</sup>

While Jayshree Khiste et al.<sup>9</sup> did not support our finding and noted maximum number of Epithelioid cell granuloma pattern.

In our study Lymphoma cases were 2%, this finding was supported by others.<sup>17</sup>, Deshmukh et al.<sup>5,14,15,16,24</sup> Where as some western studies noted higher number of lymphoma cases- Bates et al.<sup>22</sup> 7.8%, Reid et al.<sup>19</sup> 9%, Bottles et al.<sup>23</sup> 20%.

Present study noted 2% cases of metastatic carcinoma (Metastatic SCC). Similar finding were also noted by others.<sup>3, 9, 17</sup>

No any case of Kaposi sarcoma was seen, like other studies.<sup>3,5,14,16</sup> Some studies conducted in western countries noted cases of Kaposi sarcoma. (Reid et al.<sup>19</sup>, Bates et al.<sup>22</sup> and Bottles et al.<sup>23</sup>).

The tuberculosis patterns were correlated with mean CD4 count as CN+ECG 236.58 cells/ $\mu$ l, CN 201.83 cells/ $\mu$ l, ECG only 239.78 cells/ $\mu$ l, these findings of our Study corroborated well with study of Guru et al.<sup>21</sup>

Mean CD4 count in reactive lymphadenitis was 546.45cells/ $\mu$ l, which was higher than tuberculous

lymphadenitis. Our finding were supported by other studies.<sup>1,9,10,14,17,21</sup>

In Acute suppurative lymphadenitis cases, mean CD4 count was 162.27cells/ $\mu$ l. Our study was supported by Neelima Tirumalasetti et al.<sup>3</sup>

The CD4 counts in 2 cases of NHL were 525 and 585 cells/ $\mu$ l. Similarly higher count were also noted by Naveen K et al.<sup>24</sup> (400 & 267 cells/ $\mu$ l).

In metastatic lymphadenopathy cases (metastatic SCC), CD4 counts were <100 cells/ $\mu$ l (58,77cells/ $\mu$ l). These finding were supported by other studies.<sup>26,3</sup> Study that did not support our finding was of Amit Agravat et al. (257.7cells/ $\mu$ l).<sup>17</sup>

### Conclusion

We concluded that the most common opportunistic infection in our center is tuberculous lymphadenitis. FNAC helps in early diagnosis of neoplastic and non-neoplastic cases for planning further management and gives disease free long survival to the patient. We found higher CD4 count in lymphoma cases. AFB positivity increase as mean CD4 count decreased.

It is concluded that FNAC is a reliable, rapid, easily performed, low risk technique, cost effective and minimally traumatic for HIV seropositive patients with lymphadenopathy.

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