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ORIGINAL ARTICLE

# Aspiration Biopsy Cytology of Non Neoplastic Lymphadenopathies Accompanied by Necrosis

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## ABSTRACT

***Background:*** Necrosis in lymph node biopsy is relatively common observation. It may be seen in wide range of neoplastic and non-neoplastic lesions. However, the pattern and extent of necrosis are often distinctive for certain entities, or at least may suggest a limited number of possibilities in the differential diagnosis. This emphasizes the need for assessing the diagnostic utility of aspiration biopsy cytology of non neoplastic lymphadenopathies accompanied by necrosis.

***Objectives:*** 1) To study the cytological features in non neoplastic lymph node aspiration accompanied by necrosis. 2) To correlate with histopathology wherever possible.

***Material:*** A total of 193 patients with lymphadenopathy were included in the study. This is a prospective study, undertaken in the Department of Pathology, J.J.M. Medical College, Davangere, during the period of July 2014 to June 2016.

***Result:*** Our study included 193 patients with lymphadenopathy accompanied by necrosis. Age group ranged from four months to 82 years. Among the 193 patients, most common non neoplastic lesions with necrosis encountered were tubercular lymphadenitis in 134 cases and acute suppurative lymphadenitis in 52 cases.

***Conclusion:*** Fine needle aspiration cytology of the lesions in lymph node was proved to be useful technique for the evaluation of patients having lymphadenopathies with necrosis. The pattern and extent of necrosis suggests a limited number of possibilities in differential diagnosis.

## KEYWORDS

• Biopsy • Fine-Needle • Lymph Nodes • Lymphadenitis • Diagnosis • Differential

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## INTRODUCTION

Lymph nodes are an integral component of the immune system and are a common presentation in the clinical practice. Fine needle aspiration cytology (FNAC) has been a simple, safe, reliable, and inexpensive method of establishing the diagnosis of lesions and masses in various sites and organs and is the most convenient bedside diagnostic aid.[1] As a minimally invasive technique, it also helps in early direction of appropriate investigations. Necrosis in lymph node biopsy is relatively common observation seen in wide range of neoplastic and non-neoplastic lesions. However, the pattern and extent of necrosis are often distinctive for certain entities, or at least may suggest a limited number of possibilities in the differential diagnosis. [2]

## MATERIAL METHOD

The present study "Aspiration Biopsy Cytology of Lymphadenopathies Accompanied By Necrosis" is a retrospective study, undertaken in the Department of Pathology, J.J.M. Medical College Davangere during the period from July 2014 to June 2016. A total 193 cases with lymph node aspirates with necrosis. Lymph node aspirates without necrosis and non cooperative patients were not included in present study. All the patients having peripheral lymphadenopathy were subjected to detailed clinical examination. After obtaining an informed consent, under aseptic precautions FNAC was performed using 22 or 23 gauges, 30- 40 mm long needle fitted to a 5 ml syringe. Smears were prepared by evenly spreading the material. Both air dried and alcohol fixed smears (smears were immediately fixed in 95% ethyl alcohol) were prepared. Alcohol fixed smears were stained with Papanicolaou stain, Hematoxylin and Eosin stain. Air dried smears were stained with Giemsa stain and Ziehl-Neelsen stain.Smears were examined microscopically for presence of necrosis. 193 aspirates from 193 patients were selected and assessed for amount and nature of the aspirated material.

## RESULT

This study include 193 patients, who underwent aspiration of lymph node at different sites.

Majority of the patients were in the age group of 20-29 years (25.99%). Out of 193 patients 90 were males and 103 were females.

Clinically patients presented with history of swelling (lymphadenopathy) in all cases. Fever and generalised weakness were most common constitutional symptoms followed by loss of weight, appetite and cough. Few patients also presented withhistory of change of voice, growth in laryngopharynx, growth over tongue, palpable breast lesions, hepatosplenomegaly,enlarged thyroid, malar skin rash and black lesion over foot.

Generalised lymphadenopathy was seen in 16 patients (5.77%), while the remaining 177 (94.22%) had localised lymphadenopathy. Cervical region was the most common site of lymphadenopathy in 118 (66.66%) patients followed by axillary in 22 (12.42%) patients, supraclavicular in 17 (9.60%), inguinal in 10 (5.64%),submandibular in 6 (3.38%), and pre-auricular in 4 (2.25%) patients.

**Table 1:** Localized lymphadenopathies site

| Site | Number of cases (Percentage) |
|---|---|
| Cervical lymph node | 118 (66.66%) |
| Axillary lymph node | 22 (12.42%) |
| Supraclavicular lymph node | 17 (9.60%) |
| Inguinal lymph node | 10 (5.64%) |
| Submandibular lymph node | 6 (3.38%) |
| Pre-auricular lymph node | 4 (2.25%) |

Among 193 aspirations, the most common cytological diagnosis, tubercular lymphadenitis was done on 134 aspirations and acute suppurative lymphadenitis in 52 cases. The cytological diagnosis of Kikuchi-Fujimoto disease and BCG lymphadenitis in two cases each.

Diagnosis of Cryptococcosis of lymph node, Lymphogranuloma venereum (LGV) and Systemic Lupus Erythematosus (SLE) lymphadenopathy was made in one aspirate each.

**Table 2:** Distribution of various non neoplastic lesions on cytological smears

| Lymph node lesions | Total number of cases (Percentages) |
|---|---|
| Tubercular lymphadenitis | 134 (69.43%) |
| Acute suppurative lymphadenitis | 52 (26.94%) |
| Kikuchi-Fujimoto disease | 2 (1.03%) |

| Lymph node lesions | Total number of cases (Percentages) |
|---|---|
| BCG lymphadenitis | 2 (1.03%) |
| Cryptococcosis | 1 (0.5%) |
| LGV | 1 (0.5%) |
| SLE lymphadenopathy | 1 (0.5%) |

The aspirates from lymph nodes were diagnosed as tubercular lymphadenitis based on the presence of epitheloid cell granulomas and caseous necrosis with or without Langhans giant cells in a background lymphoid cells.

In 134 aspirations, cytologically diagnosed as tuberculous lymphadenitis, 98 aspirates were moderately cellular and 36 aspirates were sparsely cellular. Diagnostic clusters of epitheloid cells and caseous necrosis were seen in all aspirates, whereas 24 aspirates showed presence of multinucleated giant cells, possibly Langhans' giant cells. Ziehl-Neelsen stain demonstrated acid fast bacilli in 44 (32.83%) aspirates.

Histopathological correlation was possible in 23 cases which confirmed the cytological diagnosis of caseating granulomatous lymphadenitis.

10 cases of tubercular lymphadenitis were associated with HIV. Seven patients were male and four patients were female. Cervical group of lymph node was the most common affected site. Smears showed epitheloid cell clusters with focal and largeconfluent areas of caseous necrosis. AFB positivity was seen in five patients.This observation was assumed to be due to compromised immunity in HIV infected individuals.

One case of Cryptococcosis of lymph node was reported. This patient was a 14 year female child presenting with bilateral cervical lymphadenopathy and splenomegaly since 2 weeks.

Aspirate showed extracellular and intracellular cryptococci, macrophages and few neutrophils in a dirty necrotic background. Splenic aspirate was also done which showed histiocytes, foamy macrophages with background and intracytoplasmic cryptococci. A diagnosis of systemic Cryptococcosis (immunocompromised state) was offered, following which Human Immunodeficiency Virus test-1 (ELISA) done showed positivity.

Cytological diagnosis of BCG lymphadenitis was made in two cases. Both were female babies of six months and four months of age presenting with enlargement of isolated axillary lymph node ipsilateral to site of BCG vaccination. Lymph nodes aspirated were discrete ranging from two cm to three cm in diameter, mobile, firm to cystic and nontender.

Aspirates were grey white necrotic and scant turbid fluid. Both aspirates showed clusters of epitheloid cells, lymphocytes, neutrophils, histiocytes and giantcells with foci and background of caseous necrosis. AFB positivity was seen in one case.

Lymph node biopsy was available in both cases which confirmed the cytological diagnosis of BCG lymphadenitis.

Cytological diagnosis of Kikuchi-Fujimoto disease was done in two cases. Aspirates were haemorrhagic and grey white. Both aspirates showed mixed population of lymphoid cells and focal aggregates of histiocytes with crescent-shaped, peripherally placed nucleus, nuclear debris with focal areas of coagulative and apoptotic type of necrosis. Neutrophils were absent. Lymph node biopsy was available in both cases which confirmed the cytological diagnosis of Kikuchi-Fujimoto disease.

Cytological diagnosis of SLE lymphadenopathy in one female patients. Aspirate was grey white necrotic. Smears showed polymorphous population of lymphoid cells composed of mature lymphocytes, centrocytes, centroblasts and numerous plasma cells with fibrinoid necrosis in the background. Hematoxylin bodies were not seen. Antinuclear antibody test was positive.

Cytological diagnosis of acute suppurative lymphadenitis was made in 52 aspirates in age group of two years to 70 years. Thirty patients were males and twenty two were females. All the patients presented with localised lymphadenopathy. Size of lymph node varied from two cm to five cm and they were tender and soft in consistency.

Aspirate was purulent in all cases. All the aspirates were moderately cellular and predominantly consisted of neutrophils, macrophages, lymphocytes and cellular debris. Proteinaceous necrotic material was seen in the background.

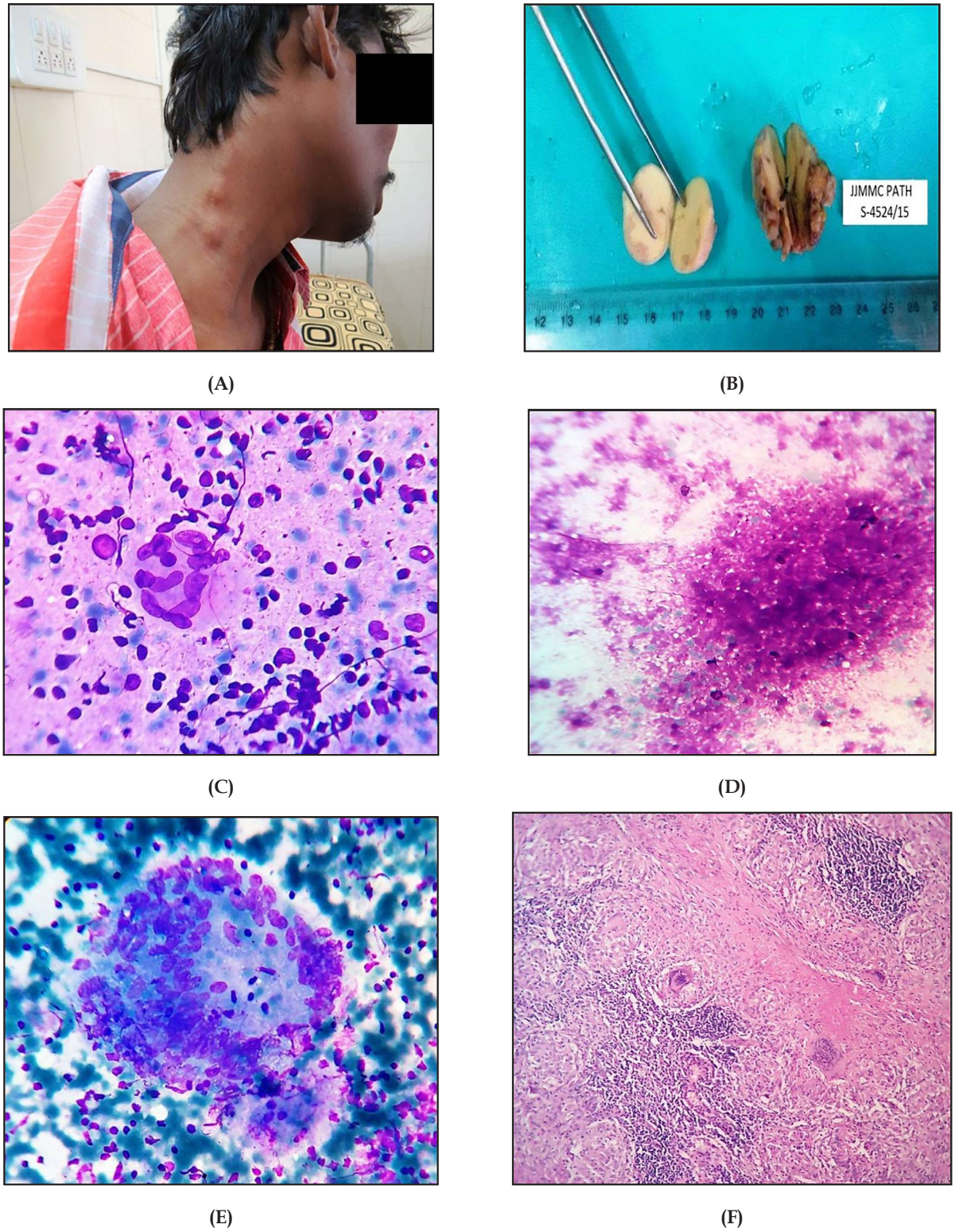
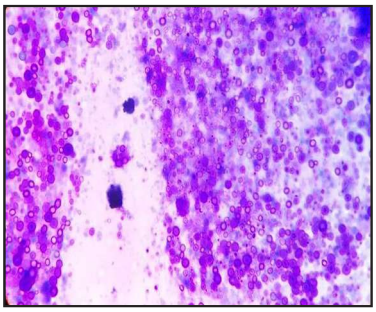



**Figure 1: (a)** Clinical photograph of a patient with tubercular lymphadenitis showing multiple matted lymph nodes in cervical region **(b)** Photograph of lymph node biopsy tubercular lymphadenitis showing confluent areas of necrosis **(c)** FNAC smear of tubercular lymphadenitis showing Epitheloid cell cluster with slipper shaped nuclei in background of necrosis and lymphocytes (Giemsa x 400) **(d)** FNAC smear of tubercular lymphadenitis showing large confluent areas of caseous necrosis (Giemsa x 400) **(e)** FNAC smear of tubercular lymphadenitis showing focal caseous necrosis (Giemsa x 400) **(f)** Histopathological section of tubercular lymphadenitis (H&E x 100) Inset showing Langhans' giant cell with caseous necrosis (H&E x 400)



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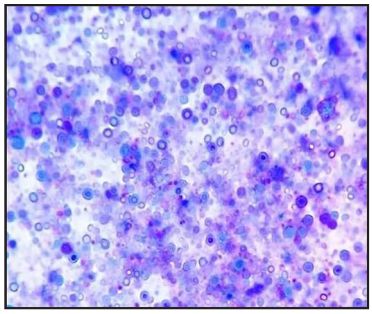

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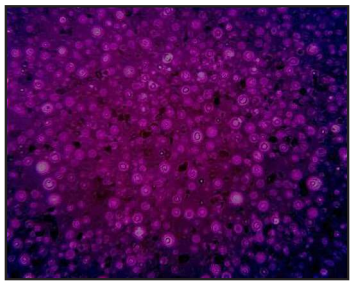
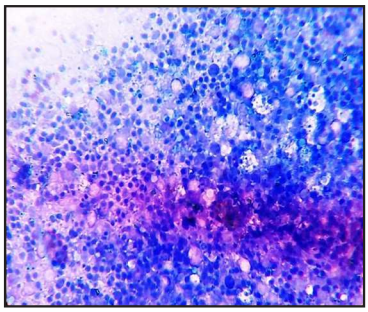


(C)

**Figure 2: (a)** FNAC smear of Cryptococcosis lymph node showing cryptococci in a dirty necrotic background (Giemsa x 400) **(b)** FNAC smear of tubercular lymphadenitis showing focal caseous necrosis (Giemsa x 400) **(c)** FNAC smear of tubercular lymphadenitis showing ill formed granuloma (Giemsa x 400).

(A)



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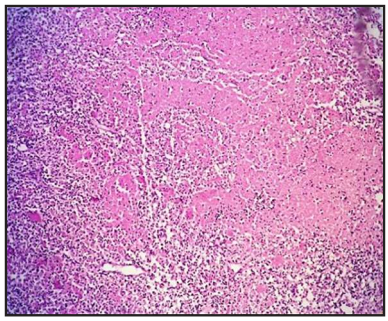

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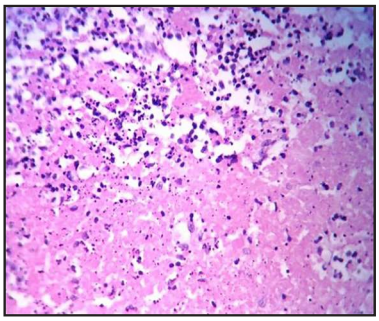
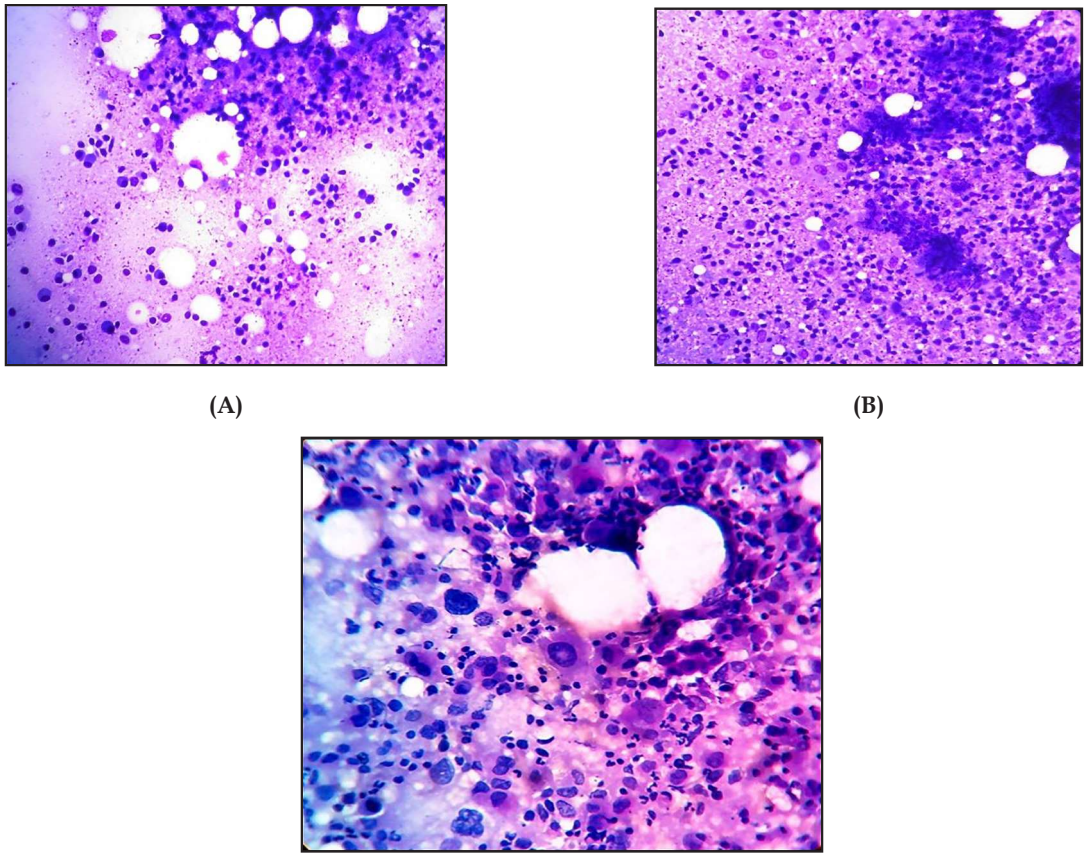


(D)

**Figure 3: (a)** Clinical photograph of young female patient of Kikuchi-Fujimoto disease with cervical lymph node enlargement **(b)** FNAC aspirate of lymph node of Kikuchi-Fugimoto disease showing karyorrhectic debris and histiocytes with phagocytosis of apoptotic debris. Neutrophils are absent (Giemsa x 400) **(c)** Histopathological section of lymph node of Kikuchi-Fugimoto disease showing effacement of architecture with areas of apoptotic necrosis, abundant karyorrhectic debris and histiocytes (H&E x 100) **(d)** Histological section of Kikuchi-Fujimoto showing apoptotic necrosis surrounded by karyorrhectic debris and histiocytes (H & E x 400).



**(A)** **(B)**

**(C)**

**Figure 4: (a)** FNAC smear of SLE lymphadenopathy showing centrocytes and immunoblasts and numerous plasma cells with fibrinoid necrosis in the background (Giemsa x 400). **(b)** FNAC smear of SLE lymphadenopathy showing fibrinoid necrosis, centrocytes and immunoblasts and plasma cells (Giemsa x400). **(c)** FNAC smear of SLE lymphadenopathy showing fibrinoid necrosis, centrocytes and immunoblasts and numerous plasma cells (Giemsa x 400).

Of the 193 cases, 62 surgical specimens of lymph node biopsy were available for histopathological examination. In all 62 cases, histopathology and cytological diagnoses remained same.

The overall diagnostic accuracy of fine needle aspiration cytology is 100%.

**Table 3:** Age and sex distribution of all cases

| Lesions | Sex | Age group (Yrs) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | >70 |
| Tubercular lymphadenitis | M | 2 | 9 | 19 | 10 | 6 | 2 | 2 | 1 |
| | F | 3 | 16 | 35 | 16 | 7 | 5 | 0 | 1 |
| Acute suppurative lymphadenitis | M | 2 | 4 | 11 | 4 | 8 | 0 | 1 | 3 |
| | F | 1 | 4 | 8 | 1 | 0 | 2 | 2 | 1 |
| Kikuchi-Fujimoto disease | M | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | F | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| BCG lymphadenitis | M | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | F | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Lesions | Sex | Age group (Yrs) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | >70 |
| Cryptococcosis | M | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | F | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LGV | M | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | F | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SLE lymphadenopathy | M | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | F | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

**Table 4:** Clinical features associated with non neoplastic lymphadenopathies

| Cytological diagnosis | Most common site | Number of lymph nodes involve | Mean size |
|---|---|---|---|
| Tubercular lymphadenitis | Cervical | Single/multiple | 5 cm |
| Acute suppurative lymphadenitis | Cervical | Single/multiple | 6 cm |
| Kikuchi-Fujimoto disease | Cervical | Single | 4cm |
| BCG lymphadenitis | Axillary | Single | 3 cm |
| Cryptococcosis | Cervical | Multiple | 4 cm |
| LGV | Inguinal | Single | 2 cm |
| SLE lymphadenopathy | Cervical | Single | 2 cm |

**Table 5:** Histopathology and cytological correlation of non neoplastic lesion

| Lesions | Histopathological examination | Correlation |
|---|---|---|
| Tuberculer lymphadenities | 23 | 100 % |
| Acute suppurative lymphadenities | 35 | 100 % |
| Kikuchi lymphadenities | 2 | 100 % |
| BCG lymphadenities | 2 | 100 % |

## DISCUSSION

Various entities should be considered in the differential diagnosis when necrosis is identified in lymph node aspiration biopsy. Numerous benign conditions cause necrosis in lymph nodes, and presence or absence of granulomatous inflammation along with clinical features are helpful in suggesting various possibilities.

During the present study, lymph node aspiration was done in all ages. All the aspirates were satisfactory. Majority of the patients were in the age group of 20-29 years (25.99%). Similar observation was made by Vimal S. *et al* in which maximum cases were between 20-30 years.[3]

Tubercular lymphadenitis is the most common extra pulmonary form of tuberculosis. Tubercular lymphadenitis constituted commonest group of benign lymphadenopathies showing necrosis diagnosed by fine needle aspiration. The cytological diagnosis of tubercular lymphadenitis was made in 134 aspirates. Cytologic criteria for the diagnosis of tuberculosis are epitheloid cell granulomas and caseation necrosis with or without giant cells.

In the present study most common age group affected by tubercular lymphadenitis was 21-30 years with 54(40.3%) cases. Similar results were observed by Laishram R.S. *et al* and Paliwal N. *et al* where the most common

age group affected was 21-30 years. This study also showed that no age was exempted and tubercular lymphadenitis was not limited to younger age groups. A female preponderance was noted in this study.[4,5]

In the present study the most common group involved in tubercular lymphadenitis was cervical 97 (72.38%), similar to study of Chand P *et al* 385(70%).[77] Axillary and inguinal lymph nodes were also involved in tuberculosis.

Similar to a study done by Ayesha sarwar *et al,* the morphological features were studied in all cases to observe the spectrum of morphological changes seen on cytological smears of tubercular lymphadenitis. The detailed study of cytomorphological features in smears of tubercular lymphadenitis showed that tuberculous infection of lymph node follows a spectrum as the disease progresses with early and late stages. More than one lymph node is known to be characteristically involved in tuberculosis. So, variable number of lymph nodes with variable stages of disease is seen.[6]

Early stages show suppuration, caseation necrosis with epitheloid cells in singles or ill-defined granulomas. As immune response is mounted, which is type-IV hypersensitivity usually after 2-4 weeks after primary infection, well defined granulomas with scattered epitheloid cells appears. In late lesions, well defined granulomas seen and caseation necrosis disappears with chronicity. Lymphocytes are more in late granulomas phase and in intense caseous phases they are few or absent. Neutrophils with suppuration are present in early lesion and they are absent in late lesion when granulomas are well defined. Plasma cells are seen with well-defined granulomas.

The overall Acid Fast Bacilli positivity in tubercular lymphadenitis in the present study was 44/134 (32.83%). Varying AFB positivity has been described by many authors ranging from 29.8% to 55.8% to as low as 19.3%. [7-9]

In the present study majority of smears showing large confluent areas of caseous necrosis with epitheloid cells in singles were positive for acid fast bacilli. Similar observation was made by Das D.K. *et al* and Mistry Y *et al* showing maximum AFB positivity in smears showing necrosis with epitheloid cells in singles. [8, 9]

In their study of correlation of cellular components and necrosis in lymph node aspirates of tubercular lymphadenitis Das D.K. *et al* showed that AFB positivity was lower in presence of lymphocytes, epitheloid cells and Langhans giant cells while picture was reverse in presence of necrosis and neutrophil infiltration.[8]

The diagnostic accuracy of tubercular lymphadenitis was 100%. FNA is a useful tool for routine cytodiagnosis with diagnostic accuracy ranging from 84.2% to 100%.[10]

In the present study, cytological diagnosis of tubercular lymphadenitis was offered in 134 (60%) cases. Out of 134, ten (7.4%) cases were found to be HIV-1 Positive. In a study of 85 cases of tuberculosis lymphadenitis, Rajasekaran S. *et al* observed HIV seropositivity in 16 (18.8%) and 9 (56.2%) had demonstrable AFB. During the present study we found males are predominantly affected by HIV infection. Similar observation was made by Damor P. *et al*.[11, 12]

One case of Cryptococcosis of lymph node was reported. This patient was a 14 year female child presenting with bilateral cervical lymphadenopathy and splenomegaly. Aspirate showed extracellular and intracellular Cryptococci, macrophages and few neutrophils. Splenic aspirate was also done which showed histiocytes, foamy macrophages with background and intracytoplasmic Cryptococci. In addition to these cytological findings, Srinivasan R. *et al* also found few granulomas in few of the cases, which were not seen in our case.[13]

Cytological diagnosis of BCG lymphadenitis was made in two cases. Both were female babies of 6 months and 4 months of age presenting with enlargement of isolated axillary lymph node ipsilateral to site of BCG vaccination. Both aspirates showed clusters of epitheloid cells, lymphocytes, neutrophils, histiocytes and giant cells with foci and background of caseous necrosis. AFB positivity was seen in one case. Similar cytological findings were noted by Guptha N *et al*.[14]

Cytological diagnosis of Kikuchi-Fujimoto disease was done in two cases. Both aspirates showed mixed population of lymphoid cells and focal aggregates of histiocytes with crescent-shaped, peripherally placed nucleus, nuclear debris and apoptotic necrotic areas and karyorrhectic debris. Neutrophils were absent. Similar observation was made by Taghvaei MR *et al*.[15]

In their report of four cases, Basu D *et al* concluded that diagnosis of KFD merits consideration in a lymph node showing necrosis, karyorrhectic debris and paucity of neutrophils, especially in young woman with cervical lymphadenopathy and also observed spontaneous recovery and regression of lymphadenopathy within months of presentation.[16]

Cytological diagnosis of systemic lupus erythematosus lymphadenopathy was made in one female patient aged 30 years. Aspirate from cervical lymph node showed polymorphous population of lymphoid cells composed of mature lymphocytes, centrocytes, occasional centroblasts, and numerous plasma cells with fibrinoid necrosis. Hematoxylin bodies were not seen, however Antinuclear Antibody test (ANA) was positive in this patient.

The morphologic changes of lymph nodes in SLE have been shown as extremely variable. Except for lymph node necrosis, the histological findings are usually nonspecific and consist of moderate follicular hyperplasia associated with increased vascularity and scattered immunoblasts and plasma cells. The most characteristic lymph node lesion in SLE is characterized by several degrees of coagulative necrosis with hematoxylin bodies or reactive follicular hyperplasia.[17]

The morphological features of lymph nodes in patients with SLE may be identical to those in Kikuchi's necrotizing lymphadenitis, hematoxylin bodies and presence of numerous plasma cells favours the diagnosis of SLE over Kikuchi's lymphadenitis.[2]

In the present study cytological diagnosis of acute suppurative lymphadenitis was made in 52 patients. In the initial phase of acute infection a mixture of lymphocytes and neutrophils may be seen in smear. This phase is followed by a florid state in which frank purulent material will be seen and smear will contain both well preserved and degenerated neutrophils and cell debris. In the present study the cytological findings correlated with above mentioned features.

Forensic pathology aspects of fine needle aspiration cytology (FNAC) of lymph nodes involve considerations relevant to the postmortem examination and legal investigations. FNAC can help identify the cause of death by revealing underlying pathological conditions such as infections or malignancies affecting the lymph nodes. Detection of infectious agents in lymph nodes through FNAC can be crucial in cases involving suspected infectious diseases or epidemics. FNAC findings contribute to the overall documentation of an autopsy, providing microscopic details about lymph node pathology.

FNAC can identify malignant cells in lymph nodes, contributing to the determination of whether cancer played a role in the individual's death. In cases where a clinical diagnosis exists, FNAC can serve to confirm or refute the preliminary findings, offering additional insights for forensic pathologists.

## CONCLUSION

Fine needle aspiration cytology of the lesions in lymph node was proved to be useful technique for the evaluation of patients having lymphadenopathies with necrosis. It was a sensitive and specific diagnostic tool in our institution. Particular attention to subtle morphologic changes may aid in avoiding pitfalls and arriving at the right diagnosis.

Fine needle aspiration cytology is quick, reliable as well as conclusive for diagnosis of tuberculous lymphadenitis when done along with Z-N staining for Acid Fast Bacilli.

The statistical values indicating high degree of sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy, accompanied by zero false positive error rate and false negative error rate indicates that further management of patient can be undertaken following initial cytological diagnosis.

The pattern and extent of necrosis suggests a limited number of possibilities in differential diagnosis.

***Conflict of Interest:*** None

***Funding:*** none

***Ethics Declaration:*** Done

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