Spectrum of cytology findings in patients presenting with lymphadenopathy at tertiary health care centre in north Maharashtra region- A 2 year study

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Abstract
Introduction: Fine needle aspiration cytology (FNAC) was thought as a means to confirm a clinical suspicion of local recurrence or metastasis of known cancer without subjecting the patient to further surgical intervention. The role of FNAC is not limited to neoplastic conditions. The aim of present study is to evaluate various pattern of lymph lesion & various causes of lymphadenopathy.

Materials and Methods: This is retrospective study of 380 patients with complaint of lymph node swellings of all age and sex. FNAC was done in all cases after maintaining aseptic precaution using 22-24 G needle attached to 05-20 ml syringe. Slides were stained with H&E stain and every slide of all the cases of lymphadenopathies were examined. Finally cytological diagnosis made according to the cytomorphology of cells, etiology & clinical findings.

Results: Out of 308 cases most common etiology of lymphadenopathy was found to be Tuberculous Lymphadenitis 37.37%, followed by reactive hyperplasia of lymph node 26.58%, Cold Abscess 13.16%, Malignancy 8.15%, Lympho-proliferative disorder 1.32% and least common was Necrotizing lymphadenitis 0.53%.

Conclusion: Tuberculous Lymphadenitis is common in this region of Maharashtra, which can be effectively diagnosed by combination of FNAC, Ziehl-Neelsen stain and Cartridge Based Nucleic Acid Amplification Test. FNAC has high accuracy rate to differentiate infective, non neoplastic conditions from neoplastic conditions. FNAC is a simple, safe, reliable, and inexpensive method in early detection of lymph node lesions, which has been proven in this study.

Keywords: Fine needle aspiration cytology, Lymphoproliferative disorder, Reactive lymphadenitis, Tuberculous lymphadenitis.

Introduction
Lymphadenopathy is the enlargement of a lymph node and lymphadenitis is the inflammation in a lymph node. Lymphadenopathy is one of the most common clinical presentations of patients of all age group attending the outdoor department of a hospital. Lymph nodes become enlarged in a wide spectrum of diseases, including infection and malignancy. Overall, infective conditions (reactive and tuberculous) are responsible for the majority of lesions. Mycobacterium tuberculosis is the most common cause of granulomatous lymphadenitis in India. Diagnosing these lesions poses a major challenge to the clinicians. Fine needle aspiration cytology (FNAC) has become a veritable tool for assessment and diagnosis of superficial lymph node enlargements.

The knowledge of the pattern of lymphadenopathy in a given geographical region is essential for making a confident diagnosis or suspecting a disease. FNAC is a reliable, simple, safe, rapid and inexpensive method of establishing the diagnosis of lesions and masses at various sites and organs. The technique is minimally invasive and gives a speedy result. Lymph node aspiration is of great value for the diagnosis of lymphadenitis, lymphomas and metastatic carcinoma. In last few decades Fine Needle Aspiration Cytology become an important, reliable, safe, first line diagnostic tool. SAFE (Simple Accurate Fast & Economical) an attractive abbreviation introduced for FNAC by DeMay. A rapid and accurate diagnosis of lymphadenopathy through FNAC followed by confirmation by histopathology helps in reducing morbidity and mortality by starting specific therapy. The purpose of the study was to evaluate the usefulness of FNAC as a diagnostic tool in etiological causes of lymphadenopathy and study the cytomorphological and histopathological features associated with lymphadenopathy with respect to age, sex and anatomical site.

Materials and Methods
This is the two years retrospective study at tertiary health centre in north Maharashtra. Total 380 patients with lymph node swelling were referred to cytology section of pathology department from either OPD or IPD. All the patients were examined and necessary clinical data obtained from outpatient department/in patient department case papers and noted in prescribed proforma. Under all aseptic precautions FNAC procedure performed by pathologist using 22-24 G needle attached to 05-20 mL syringe. Aspirated material was smeared on the slides in each case. Slides were immediately put into the fixative 95% ethyl alcohol solution and air-dried. Alcohol-fixed smears were stained by Haematoxylin and eosin (H&E) and Papanicolaou (PAP) method. Special stains like Ziehl Neelson (ZN) stain for acid-fast bacilli and Periodic Acid Schiff (PAS) stain were used, whenever required. The cytological diagnosis for each case was based on cytomorphology and available clinical information.

Result
Total 380 patients were studied, out of which 143 (37.63%) were male and 237 (62.37%) were female. Among these patient maximum number of patient diagnosed are tuberculosis lymphadenitis 37.37%, followed by reactive hyperplasia of lymph node 26.58%, cold abscess 13.16%,...
malignancy 8.15%, suspicious for malignancy 1.58%, lympho-proliferative disorder 1.32% and least common was necrotizing lymphadenitis 0.53%. (Table 1) Most of the lymph node swelling was found on cervical region, followed by axillary, supraclavicular and less common site was inguinal region. (Table 2) Tuberculous lymphadenitis was found to be the most common cytological diagnosis of all cases. Maximum number of cases 29, (11 male and 18 female) were found 30-39 years age group. Whereas 20 cases (4 male and 14 female) of cold abscess was found in 20-29 years age group. (Table 3)

Out of 380 patients, 31 patients (23 male and 8 female) were diagnosed as malignancy. Total 6 cases, 4 male & 2 female were labeled as suspicious for malignancy. Both malignancy and suspicious for malignancy were found to have maximum incidence in 60-69 year age group. (Table 3) Total 05 patients were diagnosed as lymphoproliferative disorder, 1 male & 4 female patient. Twenty nine patients, 13 male & 16 female were diagnosed as abscess 4 male cases were < 9 yrs of age, the maximum number of cases were found in 20-29 yrs age group. (Table 3)

**Table 1**: Cytological diagnosis of all cases (n=380) in present study

| S. No. | Diagnosis                      | Male (%) | Female (%) | Total No. of cases (%) |
|--------|-------------------------------|----------|------------|-----------------------|
| 1      | Tuberculous Lymphadenitis     | 39 (10.26%) | 103 (27.11%) | 142 (37.37%)          |
| 2      | Reactive lymph node           | 31 (8.16%) | 70 (18.42%) | 101 (26.58%)          |
| 3      | Cold Abscess                  | 20 (5.26%) | 30 (7.89%)  | 50 (13.16%)           |
| 4      | Malignancy                    | 23 (6.05%) | 8 (2.11%)   | 31 (8.15%)            |
| 5      | Abscess                       | 13 (3.42%) | 16 (4.21%)  | 29 (7.63%)            |
| 6      | Chronic non specific lymphadenitis | 8 (2.11%) | 6 (1.58%) | 14 (3.68%) |
| 7      | Suspicious for malignancy     | 4 (1.05%) | 2 (0.53%)   | 06 (1.58%)            |
| 8      | Lymphoproliferative disorder  | 4 (1.05%) | 1 (0.26%)   | 05 (1.32%)            |
| 9      | Necrotizing lymphadenitis      | 1 (0.26%) | 1 (0.26%)   | 02 (0.53%)            |
|        | **Total**                     | 143 (37.63%) | 237 (62.37%) | 380 (100%)          |

**Table 2**: Sites of lymph node involvement (n=380)

|                      | Male (%) | Female (%) | Total No. of cases (%) |
|----------------------|----------|------------|-----------------------|
| Cervical             | 312 (82%) |            |                       |
| Axillary             | 13 (3.4%) |            |                       |
| Supraclavicular      | 35 (9.2%) |            |                       |
| Submental            | 15 (3.95%) |            |                       |
| Inguinal             | 05 (1.32%) |            |                       |
| **Total**            | 380 (100%) |            |                       |

**Table 3**: Age and sex wise distribution of cases in present study

| Diagnosis                  | Tuberculous Lymphadenitis (n=142) | Cold abscess (n=50) | Malignancy (n=31) | Suspicious for malignancy (n=6) | Abscess (n=29) | Lymphoproliferative disorder (n=5) |
|---------------------------|-----------------------------------|---------------------|------------------|---------------------------------|---------------|----------------------------------|
| Age group (years)         | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| <9                        | 2    | 4      | 3    | -      | -    | -      | 4    | -      | -    | -      | -    | -      |
| 10-19                     | 8    | 20     | 5    | 7      | -    | -      | -    | -      | 2    | 3      | -    | -      |
| 20-29                     | 5    | 33     | 6    | 14     | -    | -      | 1    | 5      | -    | -      | -    | -      |
| 30-39                     | 11   | 18     | 4    | 3      | 1    | -      | -    | 4      | -    | -      | -    | -      |
| 40-49                     | 7    | 12     | -    | 5      | 4    | 1      | -    | 2      | -    | 2      | -    | 2      |
| 50-59                     | 2    | 8      | -    | 3      | 2    | 1      | 1    | 3      | 1    | 1      | -    | -      |
| 60-69                     | 4    | 5      | 1    | 1      | 10   | 4      | 3    | 1      | -    | 1      | -    | 2      |
| 70-79                     | -    | 3      | 1    | -      | 5    | 1      | -    | 1      | -    | -      | -    | -      |
| **Total**                 | 39   | 103    | 20   | 30     | 23   | 8      | 4    | 2      | 13   | 16     | 1    | 4      |
Discussion
Enlarged lymph nodes are easily accessible for FNAC in the diagnosis of malignant and benign lesion. It also helps to know the sensitivity and specificity of diagnosis made by FNAC for different primary organ involved in the diseases. In cases of lymphoid malignancies, FNAC is used mainly to assess the staging and to recognize the residual and recurrent lymphoproliferative disorder.

In this study 380 cases were studied, 37.63% male & 62.37% female and age ranges from 10 month to 78 yrs of age. Cervical lymph node is the major site to aspirate. Patro et al1 reported 206(62.42%) patients were female and 124(37.57%) were male patients age of the patients ranged from 1 year to 75 years. Cervical lymph nodes were the most commonly affected group of lymph nodes (74.24%). Sharma et al5 studied 678 cases of neck lesions. The age ranging from 3 years to 70 years, out of which 65.6% were females and 34.4% were males. Kochhar et al11 revealed there were 84(46.15%) female and 98(53.84%) male patients with an age range of 1–70 years. Sharma et al10 studied 736 FNACs and found that the ages of the patients ranged from 21days to 80 years with the male to female ratio of 0.87:1. Cervical lymph nodes were enlarged in 630 of 736 cases (85.59%) followed by axillary lymph nodes in 59 cases (8.01%). Shameema et al13 in their study reported cervical lymph node enlargement in 124 cases (86.72%) followed by axillary 6(4.19%), supraclavicular 4(2.79%) least common site is submental 1(0.70%). Gaur et al12 reported cervical lymph node (90.15%) is the most common superficial lymphadenopathy followed by axillary (6.98%) and lastly inguinal (2.3%). Biradar et al.3 found that, out of 160 cases, 82(51.25%) patients were male and 78(48.75%) were female patients. The age of the patients ranged from 3months to 80 years. Cervical lymph nodes were enlarged in 111(69.37%). Nikethan et al4 revealed Out of 322 patients with palpable lymphadenopathy, 142(44.37%) female and 178 (55.63%) male patients with age of the patients ranged from 1 to 70 years. The various site wise FNAC was done in cervical 256(80%), axillary 20(6.25%), submandibular 18(5.6%), supraclavicular 14(4.4%) and inguinal lymph nodes 12(3.75%). Hence findings are in accordance with studies by Patro et al8 Sharma et al,9 and Sharma et al.10

In India and other developing countries, Mycobacterium tuberculosis infection is most common compared to other granulomatous diseases hence the presence of granulomas is highly suggestive of tuberculous. In present study, it is observed that the most common lesion diagnosed in FNAC of cervical lymphadenopathy is tuberculous lymphadenitis 37.37%, of these 26 cases were AFB positive, followed by reactive hyperplasia of lymph node 26.58%. Maximum numbers of cases were seen in 20-39yrs age group with female predominance. Cold abscess was diagnosed on the basis of presence of necrosis and epithelioid cells without granuloma which contributed 7.63% in our study. Most of the tuberculous lymphadenopathy is granuloma with caseous necrosis showing epithelioid cells & lymphocytes (Fig. 1). Maximum number of patients belongs to Muslim community, this may due to geographical variation. Also 12 patients were HIV positive on anti retroviral treatment. Reactive lymph node hyperplasia was diagnosed by the presence of a polymorphous population of lymphoid cells and tingible body macrophages. Kochhar et al1 observed tuberculous lymphadenitis and reactive hyperplasia were the most common lesions seen (35.7% and 31.3% respectively), tuberculous lymphadenitis showed female predominance. Florence et al13 reported tuberculosis as most common disease found in 165(35.9%) patients followed by reactive non-specific lymphadenitis in 152(33.1%). Patro et al8 observed tuberculous lymphadenitis as the most frequent cause of lymphadenopathy with 106 cases (32.12%). The next frequent diagnosis was reactive with 84 cases. Sharma et al.10 revealed tuberculosis lymphadenitis as most frequent diagnosis with 419 cases (56.92%), maximum number of cases were recorded in the age group 10-19 years with AFB positive in 22.67% of cases. Shameema et al11 in their study reported granulomatosus lymphadenitis in 143(34.04%) cases with 88 male & 55 female, chronic reactive lymphadenitis 149(35.47%), 87 male & 62 female. Nikethan et al4 revealed, tubercular lymphadenitis 146 cases (45.34%) followed by reactive hyperplasia 58 cases (18.01%). Malhotra et al2 found tubercular lymphadenitis (44.02%) was the single most common cause of lymphadenopathy followed by reactive lymphadenitis (42.64%). Gaur et al12 reported tuberculous lymphadenitis 54.4% and reactive lymph node 29.1%. However other studies by Farooq, et al.14 found that reactive hyperplasia 37%, tuberculous lymphadenitis 32% each male & female 16%, 4% of suppurative lymphadenitis and found that the overall most common cause of lymphadenopathy in female is tuberculous lymphadenitis. Biradar et al.3 observed reactive lymphadenitis with 89 cases (55.62%) & tuberculosis 38 cases (23.75%). Duraiswami et al.15 found that the reactive lymph node hyperplasia was diagnosed in 126 aspirates out of 253(49.8% of cases) and was the most common diagnosis offered. Granulomatous lymphadenitis, caseating or non - caseating, was diagnosed in 94 aspirates out of 253(37.15%) and was the second most common diagnosis offered. In study by Natchimuthu et al16 the most common pathological lesion was reactive lesions 34%, followed by tuberculous lymphadenitis 30% with 45% of cases had granuloma and caseous necrosis with granulomas 28%. Vimal, et al17 studied 168 cases, of which 63 cases (33.69%) were diagnosed as reactive hyperplasia, followed by 54 cases (28.88%) of tubercular lymphadenitis, of these 22 cases (40.74%) were positive for acid-fast bacilli (AFB). Necrosis was seen in 16 cases (29.62%). Granulomas were seen in a total of 23 cases. Thus the present study is similar to studies by Kochhar et al.1 Florence et al.13 Patro et al8 Sharma et al10 Shameema et al11 Nikethan et al4 and Malhotra, et al2.
In present study, out of 380 cases, 31 (8.15%), cases show metastatic deposits and most of them are from Squamous cell carcinoma which varies according to degree of differentiation (Fig. 2). Most of the cases were found in age group 50-69 yrs, with male predominance. Maximum number of cases presented with history of chronic smoking, tobacco chewing and dysphasia, some of them have complaint of change of voice. Also 6 cases (1.58%) reported as suspicious for malignancy. Other study by Ipsita et al\(^7\) reported 119 cases (7.72%) were suggestive of metastatic deposits and Malhotra et al\(^2\) metastatic lesions (9.40%) cases. Natchimuthu et al\(^{16}\) revealed 7.14% metastatic deposits in their study; Sharma et al\(^{10}\) revealed metastatic lymphadenopathy 47/736 (6.38%). Maximum cases were seen in age groups 50-69 years and predominant deposits were of squamous cell carcinoma.\(^{16}\) Motiwala et al\(^{18}\) reported Metastatic deposits in 7.83% cases. However some of studies by Vimal et al\(^{17}\), Gaur et al\(^{12}\), Nikethan et al\(^2\) & Shameema et al\(^{11}\) revealed high > 12% of mets in lymph nodes all showed most common deposit from Squamous cell carcinoma and Biradar et al\(^3\), Duraismami et al\(^{15}\) & Patro et al\(^8\) showed less than 3%. So this study follows observation in studies of Ipsita et al\(^7\) and Natchimuthu et al\(^{16}\). The present study revealed 29 cases 7.63% of acute inflammatory lesion- abscess, 13 cases were male and 16 cases were female, cytology shows plenty of degenerated polymorphs on necrotic background (Fig. 3). Other studies by Kochhar et al\(^4\) showed suppurative lymphadenitis in 9.8%, Vimal, et al\(^{17}\) found 12 cases (6.42%) of acute suppurative lymphadenitis, Sharma et al\(^{10}\) revealed acute suppurative lymphadenopathy was seen in 45 out of 736 cases (6.11%). Our study is similar to all above studies. But Patro et al\(^8\) observed Acute suppurative lymphadenitis was seen in 12 cases (3.63%), Biradar et al\(^3\) observed acute suppurative lymphadenitis was seen in 7 cases (4.37%) and Shameema et al\(^{11}\) reported acute suppurative lymphadenitis 6(1.43%) which are less than present study and Urmila et al\(^{19}\) found acute suppurative lymphadenitis in 12.43% cases, Florence, et al\(^{13}\) acute suppurative lesions in 50 (10.8%) are higher than this study.
Many of the patients presented with lymph node swelling since > 3yrs with history of medication and change of size of swelling. We have reported 14(3.68%) of such cases as Chronic non specific lymphadenitis. Nikethan et al. \(^4\) revealed, non-specific lymphadenitis 12(3.72%), Patro et al. \(^8\) found 8.78%. Motiwala et al.\(^{18}\) showed 12.17% and Ipsita et al.\(^{17}\) reported 639 cases (41.4%) as chronic non-specific lymphadenitis. In present study total 05 (1.32%) patients were diagnosed as lympho-proliferative disorder. 1 male and 4 female. Cytomorphology of cells are monomorphic with scanty cytoplasm (Fig. 4). Duraiswami et al.\(^{3}\) found that lymphoproliferative disorder in 4 out of 253 cases (1.6%) and Shameema et al.\(^{11}\) 12 cases (2.86%). Ipsita et al.\(^{17}\) reported 62 cases (4.02%) as lymphoproliferative disorder; Natchimuthu et al.\(^{16}\) observed 3.57% lymphoproliferative disorder. Vimal et al.\(^{12}\) found total of four cases of non Hodgkin’s lymphoma (NHL) (2.14%) and a single case of Hodgkin’s lymphoma. Thus our study is similar with the study by Duraiswami et al.\(^{15}\) but not with other studies. Only two cases (0.53%) each one male & female was diagnosed as necrotizing lymphadenitis, which shows only non caseating necrosis. Duraiswami et al.\(^{15}\) and Sharma et al.\(^{10}\) found necrotic lymphadenitis in 3 (1.1%) & 18/419 (4.29%) aspirates respectively.

Conclusion

FNAC is fairly reliable for the diagnosis of lymph node swelling and reduces the chances of unwanted surgery. It is useful in differentiating infective from malignant lesions and guides further management. TB lymph node which is endemic in our region can be effectively diagnosed. FNAC can be used as screening tool for all elderly patients presenting with lymphadenopathy because all metastatic swellings were found in 60-69yrs of age.

Conflict of Interest: None.

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