

Fine Needle Aspiration Cytology in Evaluation of Lymph Node Lesions

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Abstract

Background: Lymphadenopathy is a common clinical presentation with causes ranging from reactive and infectious processes to primary and metastatic malignancies. Fine needle aspiration cytology (FNAC) provides a rapid and minimally invasive method for initial evaluation of lymph node lesions. The aim is to study the cytomorphological spectrum of lymph node lesions diagnosed by FNAC and to assess cytohistopathological correlation wherever biopsy findings were available. **Material and Methods:** This prospective study included 208 patients who underwent FNAC of palpable lymph node lesions in the Department of Pathology from January 2020 to December 2021. Smears were examined using routine cytological stains and special stains wherever indicated. Histopathological correlation was available in 22 cases. **Results:** Of the 208 patients, 114 (54.8%) were males and 94 (45.2%) were females. The 21–30-year age group was most commonly affected. Cervical lymph nodes were the predominant site, accounting for 172 (82.7%) cases. Non-neoplastic lesions constituted 169 (81.3%) cases, while 39 (18.8%) were malignant. Reactive lymphadenitis was the most frequent diagnosis with 86 (41.3%) cases, followed by granulomatous lymphadenitis in 40 (19.2%) and tuberculous lymphadenitis in 33 (15.9%) cases. Among malignant lesions, metastatic carcinoma accounted for 33 (84.6%) cases and primary lymphoma for 6 (15.4%). Squamous cell carcinoma was the most common metastatic tumor, comprising 22 of 33 metastatic lesions. Histopathological correlation was available in 22 cases, and all demonstrated concordant cytological and histological diagnoses. **Conclusion:** FNAC is an effective first-line diagnostic modality for lymphadenopathy and provides useful differentiation between non-neoplastic and malignant lesions. It is particularly valuable in diagnosing reactive, tuberculous, and metastatic lesions. Histopathological examination and ancillary techniques remain essential in selected cases, especially for lymphoma subclassification and cytologically indeterminate lesions.

Keywords: Fine needle aspiration cytology, lymphadenopathy, lymph node, reactive lymphadenitis, tuberculous lymphadenitis, metastatic carcinoma, lymphoma cytopathology.

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INTRODUCTION

Lymphadenopathy is a common clinical presentation encountered in patients with a wide spectrum of inflammatory, infectious, and neoplastic disorders. Accurate evaluation of an enlarged lymph node is important for establishing an early diagnosis and guiding further management. Fine needle aspiration cytology (FNAC) is a simple, minimally invasive, rapid, and cost-effective technique that can provide useful diagnostic information in patients presenting with palpable lymphadenopathy.^[1] FNAC has an important role in differentiating reactive and infective lymphadenitis from primary and metastatic malignancies. It is particularly useful as an initial investigation because it can often establish a diagnosis without the need for immediate surgical biopsy. When correlated with clinical findings and supported by histopathology or ancillary investigations, FNAC demonstrates good diagnostic performance in the evaluation of lymph node lesions.^[2]

The cytological spectrum of lymphadenopathy varies according to age, geographical region, infectious disease burden, and referral patterns. Granulomatous lymphadenitis,

particularly that associated with tuberculosis, remains an important cause of lymph node enlargement in countries with a high burden of tuberculosis.^[3,4] The addition of special stains, microbiological investigations, cell-block preparation, and immunocytochemical techniques may further improve diagnostic accuracy, particularly in granulomatous and malignant lesions.^[5] Cytomorphological examination of lymph node aspirates can identify a broad spectrum of non-neoplastic and neoplastic conditions, including reactive lymphadenitis, granulomatous lymphadenitis, suppurative lesions, metastatic malignancies, and lymphomas.^[6] However, cytological distinction between reactive lymphoid proliferations and lymphomas may occasionally be

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challenging, requiring histopathological examination and ancillary techniques for definitive classification. Recent advances in lymph node cytopathology have also emphasized standardized interpretation and reporting. Such approaches may improve communication between cytopathologists and clinicians and assist in determining the need for further investigations or tissue biopsy.^[7] Therefore, the present study was undertaken to evaluate the cytomorphological spectrum of lymph node lesions diagnosed by FNAC and to assess its diagnostic performance using histopathology, cell-block findings, or demonstration of infective etiological factors wherever available.

MATERIALS AND METHODS

Study Design and Setting: This was a prospective observational study conducted in the Department of Pathology, SDM College of Medical Sciences and Hospital, Dharwad. Patients referred to the Department of Pathology for FNAC of palpable lymph node swellings during the study period were considered for inclusion.

Study Period: The study was conducted from 1 January 2020 to 31 December 2021.

Study Population and Sample Size: A total of 208 patients with palpable lymph node lesions who fulfilled the eligibility criteria were included in the study. Histopathological correlation was available in 22 cases.

Inclusion Criteria

All patients referred to the Department of Pathology for FNAC of palpable lymph node lesions during the study period were included.

Exclusion Criteria

1. Aspirates obtained from non-lymphoid lesions were excluded.
2. Inadequate or non-representative aspirates were excluded from the final cytomorphological assessment.

Materials Used: The materials required for FNAC included 5-mL or 10-mL disposable syringes, 22–26-gauge needles, clean grease-free glass slides, spirit swabs, 85% isopropyl alcohol, Coplin jars, staining reagents for hematoxylin and eosin (H&E) and May-Grünwald-Giemsa (MGG), coverslips, DPX mounting medium, and a light microscope. Additional slides were prepared for special stains, including acid-fast bacillus (AFB) staining, whenever clinically or cytologically indicated.

FNAC Procedure: After obtaining informed consent, relevant clinical details were recorded and the lymph node swelling was examined for its site, size, consistency, mobility, and other clinically relevant characteristics. The overlying skin was cleaned using an antiseptic solution.

The lymph node was stabilized between the thumb and index finger. A 22–26-gauge needle attached to a disposable syringe was introduced into the lesion. Negative pressure was created by withdrawing the syringe plunger, and the needle was moved gently in different directions within the lesion to obtain representative cellular material. Once adequate material was obtained, suction was released before withdrawing the needle.

The aspirated material was immediately expressed onto clean

glass slides and smears were prepared. Two to three wet smears were fixed in 85% isopropyl alcohol and subsequently stained with H&E. Additional smears were air-dried and stained with MGG. When tuberculosis or another infective etiology was suspected, additional smears were subjected to appropriate special staining, including AFB staining.

Cytomorphological Evaluation: All stained smears were examined systematically under a light microscope. Initially, smear adequacy and representativeness were assessed. The overall cellularity, predominant cellular population, background material, and architectural pattern were evaluated under low-power magnification. Individual cellular morphology, nuclear characteristics, cytoplasmic features, inflammatory components, granulomas, necrosis, and malignant cellular features were subsequently evaluated under higher magnification.

Based on the overall cytomorphological findings, the lymph node lesions were categorized into non-neoplastic and neoplastic lesions. Non-neoplastic lesions included reactive, granulomatous, tuberculous, and other inflammatory lymphadenitis, whereas neoplastic lesions included metastatic malignancies and lymphomas wherever identified.

Histopathological and Ancillary Correlation:

Histopathological correlation was performed in the 22 cases for which subsequent biopsy specimens were available. Cytological diagnoses were compared with the corresponding histopathological findings. Cell-block findings and demonstration of infective etiological factors were also considered for diagnostic correlation wherever available.

Outcome Measures: The primary outcome was the distribution and cytomorphological spectrum of lymph node lesions diagnosed by FNAC. Secondary outcomes included age- and sex-wise distribution of lesions, frequency of individual cytological diagnoses, cytohistopathological concordance, and diagnostic performance of FNAC. Sensitivity and specificity were calculated in cases for which an appropriate reference standard was available.

Statistical Analysis: The collected data were entered into a spreadsheet and analyzed using appropriate statistical software. Categorical variables were summarized as frequencies and percentages. Age distribution and other relevant continuous variables were summarized using appropriate descriptive statistics. Cytohistopathological correlation was assessed in cases with available biopsy findings. Where an adequate reference standard permitted construction of a diagnostic 2 × 2 table, the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of FNAC were calculated. A p-value <0.05 was considered statistically significant wherever inferential statistical testing was applicable.

RESULTS

During the study period from January 2020 to December 2021, a total of 208 patients with lymphadenopathy underwent fine needle aspiration cytology (FNAC). Of these, 114 (54.8%) were males and 94 (45.2%) were females, giving a male-to-female ratio of approximately 1.2:1. The most frequently affected age group was 21–30 years, comprising 57 (27.4%) cases, followed by 11–20 years with 41 (19.7%) cases. Cervical lymph nodes

were the most frequently aspirated nodes, accounting for 172 (82.7%) cases.

Table 1: Demographic and site-wise distribution of patients undergoing lymph node FNAC

Characteristic	Number of cases (n)	Percentage (%)
Gender		
Male	114	54.8
Female	94	45.2
Age group (years)		
0–10	27	13.0
11–20	41	19.7
21–30	57	27.4
31–40	24	11.5
41–50	25	12.0
51–60	17	8.2
61–70	12	5.8
>70	5	2.4
Site of lymph node		
Cervical	172	82.7
Submandibular	6	2.9
Submental	2	1.0
Preauricular	1	0.5
Occipital	1	0.5
Supraclavicular	5	2.4
Infraclavicular	1	0.5
Axillary	14	6.7
Inguinal	6	2.9
Total	208	100.0

The majority of lymph node lesions were non-neoplastic, accounting for 169 (81.3%) cases, while 39 (18.8%) were malignant. Reactive lymphadenitis was the most frequent cytological diagnosis, observed in 86 (41.3%) cases. This was followed by granulomatous lymphadenitis in 40 (19.2%) and tuberculous lymphadenitis in 33 (15.9%) cases.

Among malignant lesions, metastatic carcinoma was markedly more frequent than primary lymphomas. Metastatic malignancy was identified in 33 cases, while Hodgkin lymphoma and non-Hodgkin lymphoma accounted for one and five cases, respectively.

Table 2: Cytological spectrum of lymph node lesions diagnosed by FNAC

Cytological diagnosis	Number of cases (n)	Percentage of total (%)
Non-neoplastic lesions	169	81.3
Reactive lymphadenitis	86	41.3
Granulomatous lymphadenitis	40	19.2
Tuberculous lymphadenitis	33	15.9
Other non-neoplastic lesions	10	4.8
Malignant lesions	39	18.8
Hodgkin lymphoma	1	0.5
Non-Hodgkin lymphoma	5	2.4
Metastatic carcinoma	33	15.9
Total	208	100.0

Among the 39 malignant lymph node lesions, metastatic carcinoma constituted 33 (84.6%), while primary lymphomas accounted for 6 (15.4%). Of the metastatic lesions, squamous cell carcinoma was the predominant type, comprising 22 of 33 cases (66.7%). Adenocarcinoma was diagnosed in 6 (18.2%), undifferentiated carcinoma in 4

(12.1%), and metastatic papillary thyroid carcinoma in 1 (3.0%) case.

Among metastatic squamous cell carcinomas, the oral cavity was the most frequently identified primary site. Adenocarcinoma metastases arose predominantly from gastrointestinal and pulmonary primary tumors.

Table 3: Distribution of malignant lymph node lesions and metastatic tumor types

Malignant lesion/type	Number of cases (n)	Percentage within group (%)
Malignant lesions (n=39)		
Primary lymphoma	6	15.4
Metastatic carcinoma	33	84.6
Primary lymphomas (n=6)		
Hodgkin lymphoma	1	16.7
Non-Hodgkin lymphoma	5	83.3
Metastatic carcinomas (n=33)		
Squamous cell carcinoma	22	66.7

Adenocarcinoma	6	18.2
Papillary thyroid carcinoma	1	3.0
Undifferentiated carcinoma	4	12.1
Total metastatic carcinomas	33	100.0

Histopathological correlation was available for 22 cases. These comprised nine cases of tuberculous lymphadenitis, one case of Hodgkin lymphoma, two cases of non-Hodgkin lymphoma, and ten cases of metastatic carcinoma. All 22 cytological diagnoses were concordant with the corresponding histopathological diagnoses, giving an

observed cytohistopathological concordance of 100% in the verified subset.

Among the 33 cases diagnosed cytologically as tuberculous lymphadenitis, 14 (42.4%) were positive for acid-fast bacilli on Ziehl-Neelsen staining, while 5 (15.2%) showed a positive tuberculosis PCR result.

Table 4: Cytohistopathological correlation and ancillary findings

Diagnostic category / Investigation	Cases evaluated (n)	Positive/Concordant cases (n)	Percentage (%)
A. Cytohistopathological correlation			
Tuberculous lymphadenitis	9	9	100.0
Hodgkin lymphoma	1	1	100.0
Non-Hodgkin lymphoma	2	2	100.0
Metastatic carcinoma	10	10	100.0
Total cases with histopathological correlation	22	22	100.0
B. Ancillary investigations in tuberculous lymphadenitis			
Ziehl-Neelsen stain for AFB	33	14	42.4
Tuberculosis PCR	33	5	15.2

Interpretation: Histopathological correlation was available in 22 cases, and all 22 showed concordance between FNAC and histopathological diagnosis, giving an observed concordance of 100% among the verified cases. Among 33 cases of tuberculous lymphadenitis, 14 (42.4%) were positive for AFB on Ziehl-Neelsen staining and 5 (15.2%) were positive by tuberculosis PCR. Because histopathological verification was available for only a selected subset of the total 208 cases, the finding should be reported as 100% cytohistopathological concordance in verified cases, rather than as 100% overall sensitivity and specificity.

DISCUSSION

Fine needle aspiration cytology is widely used as an initial diagnostic investigation for patients presenting with lymphadenopathy because it is rapid, minimally invasive, economical, and capable of differentiating a broad spectrum of reactive, infective, and malignant conditions. Standardized reporting approaches have further strengthened the role of lymph node cytology by improving diagnostic categorization and facilitating appropriate clinical management. Radhakrishnan et al. emphasized the value of structured reporting of lymph node aspirates using the Sydney System and demonstrated its usefulness in routine cytopathology practice.^[8]

In the present study, 208 lymph node FNACs were evaluated. A slight male predominance was observed, with 114 (54.8%) males and 94 (45.2%) females. The most commonly affected age group was 21–30 years, indicating that lymphadenopathy was frequently encountered in younger adults. Robert and Saldanha also highlighted the usefulness of systematic cytological categorization in evaluating lymph node lesions across different age groups and clinical presentations.^[9]

Cervical lymph nodes were the most commonly involved site in the present study, accounting for 82.7% of all aspirated lymph nodes. This predominance is clinically expected

because cervical lymphadenopathy is frequently associated with infections, tuberculosis, head-and-neck malignancies, and lymphoproliferative disorders. Nga emphasized that lymph node FNAC is particularly valuable for reactive and infectious conditions and for metastatic malignancies, although careful attention to cytomorphological pitfalls is required.^[10]

Non-neoplastic lesions constituted the majority of cases in the present study, accounting for 169 (81.3%), whereas malignant lesions constituted 39 (18.8%). Reactive lymphadenitis was the most common individual diagnosis, followed by granulomatous and tuberculous lymphadenitis. The predominance of benign and inflammatory conditions highlights the usefulness of FNAC in avoiding unnecessary excisional biopsy in a substantial proportion of patients.

Among malignant lesions, metastatic carcinoma was substantially more frequent than primary lymphoma, accounting for 33 of 39 malignant cases (84.6%). Squamous cell carcinoma was the most common metastatic malignancy, comprising 22 of 33 metastatic lesions. This finding probably reflects the high frequency of head-and-neck primary tumors presenting with cervical lymph node metastasis. Ahuja et al., in their systematic review and meta-analysis, demonstrated high diagnostic performance of standardized lymph node FNAC reporting for identifying malignancy, particularly in suspicious and malignant categories.^[11]

The distinction between benign, atypical, suspicious, and malignant aspirates has become increasingly important in contemporary lymph node cytopathology. Liang et al. demonstrated that the Sydney System provides clinically meaningful categories with progressively increasing risk of malignancy, while also emphasizing the need for appropriate clinical, imaging, and ancillary correlation.^[12] The introduction of the WHO Reporting System for lymph node cytopathology has similarly encouraged standardized terminology and risk-based patient management.^[13]

Recent literature has also emphasized that FNAC should not be considered an isolated diagnostic procedure but rather part of an

integrated diagnostic pathway incorporating clinical findings, imaging, cell-block preparation, immunocytochemistry, microbiological studies, molecular investigations, and histopathology whenever required. Maffei et al. highlighted the continuing impact of lymph node FNAC on patient care, particularly when ancillary investigations are appropriately utilized.^[14]

In the present study, 33 cases were diagnosed as metastatic malignancy and six as primary lymphoma. Vesnic et al. likewise reported the clinical utility of FNAC in both metastatic carcinoma and lymphoma, while emphasizing the importance of further tissue-based evaluation where definitive subclassification is necessary.^[15] In suspected hematology lymphoid lesions, the addition of flow cytometry can considerably improve diagnostic characterization, as demonstrated by Murugan et al.^[16]

Histopathological correlation was available in 22 cases, comprising nine cases of tuberculous lymphadenitis, one Hodgkin lymphoma, two non-Hodgkin lymphomas, and ten metastatic carcinomas. All 22 cases showed concordant cytological and histopathological diagnoses. Recent studies applying standardized reporting systems have similarly demonstrated high diagnostic concordance between cytology and definitive diagnosis when adequate material and appropriate ancillary testing are available.^[17,18]

However, the apparent 100% concordance in the present study should be interpreted cautiously, because histopathological verification was available for only a limited and selectively investigated subset of the total cases. Accordingly, the findings support excellent diagnostic agreement in the verified cases rather than establishing an overall sensitivity and specificity of 100% for the entire study population. Contemporary analyses have also warned that partial verification and case-selection bias can substantially influence reported estimates of sensitivity, specificity, and risk of malignancy in lymph node FNAC studies.

Overall, the present findings support FNAC as an effective first-line investigation for lymphadenopathy, particularly for reactive and infectious lesions and metastatic malignancy. Nevertheless, histopathology and ancillary techniques remain important in doubtful cases and particularly in the diagnosis and subclassification of lymphomas.

CONCLUSION

Fine needle aspiration cytology is a simple, rapid, minimally invasive, and cost-effective first-line investigation for evaluating patients with lymphadenopathy. In the present study, non-neoplastic lesions predominated, with reactive lymphadenitis being the most frequent diagnosis, followed by granulomatous and tuberculous lymphadenitis. Cervical lymph nodes were the most commonly involved site.

Among malignant lesions, metastatic carcinoma was considerably more frequent than primary lymphoma, and squamous cell carcinoma was the most common metastatic tumor. Histopathological correlation in the available 22 cases showed complete diagnostic concordance with FNAC. However, because histopathology was available in only a selected subset, this finding should be interpreted as 100%

concordance among verified cases rather than overall 100% sensitivity and specificity.

FNAC can therefore effectively distinguish a large proportion of non-neoplastic from malignant lymph node lesions and guide further patient management. Histopathology, cell-block examination, immunocytochemistry, flow cytometry, microbiological investigations, and molecular testing should be employed whenever cytological findings are inconclusive or definitive classification is required.

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Conflicts of interest

There are no conflicts of interest.

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