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CORRELATION STUDY OF CYTOMORPHOLOGY, HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY IN THE DIAGNOSIS OF LYMPHADENOPATHY IN A TERITARY CARE CENTRE.

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ABSTRACT

Background:Lymphadenopathy is a common clinical presentation with a broad spectrum of underlying causes, ranging from benign reactive hyperplasia to malignancies. Accurate diagnosis is crucial for timely management. This study aims to correlate cytomorphological findings with histopathological and immunohistochemical features in patients with peripheral lymphadenopathy.**Aim**:To evaluate the diagnostic accuracy of fine needle aspiration cytology (FNAC) and its correlation with histopathology and immunohistochemistry (IHC) in the diagnosis of lymphadenopathy in a tertiary care setting.**Materials and Methods**:A prospective observational study was conducted on 100 patients with clinically significant peripheral lymphadenopathy. All patients underwent FNAC followed by excisional biopsy and histopathological examination. IHC was performed in cases suspicious for lymphoid malignancy to confirm diagnosis and subtype. Data were analyzed for concordance between the three modalities.**Results**:The most common age group affected was 21–40 years, with a slight male preponderance. FNAC showed high accuracy in diagnosing reactive (89%) and metastatic (94%) lesions but lower accuracy (66%) in lymphoma cases. Histopathology confirmed 36% reactive lymphadenitis, 20% tuberculous lymphadenitis, 18% metastatic carcinoma, and 22% lymphomas. IHC was pivotal in confirming and subtyping lymphoma cases—14 Non-Hodgkin's lymphoma and 8 Hodgkin's lymphoma—using markers such as CD20, CD3, CD15, CD30, and Ki-67.**Conclusion:**FNAC remains a valuable initial diagnostic tool; however, histopathology and IHC are essential for definitive

diagnosis, especially in lymphoid neoplasms. A multimodal approach enhances diagnostic precision and guides appropriate management.

Keywords:*Lymphadenopathy, FNAC, Histopathology, Immunohistochemistry, Lymphoma, Cytology, Diagnosis*

INTRODUCTION

Lymphadenopathy, defined as an abnormal enlargement of lymph nodes, is a frequent clinical finding encountered across all age groups. It may be localized or generalized and can result from a wide array of etiologies, including infections, inflammatory conditions, immune disorders, and malignancies[1]. Peripheral lymphadenopathy, particularly in cervical, axillary, and inguinal regions, is often the first clinical manifestation prompting further evaluation. Distinguishing between benign and malignant causes is essential, as this directly impacts prognosis and treatment strategies[2,3].

The global burden of lymphadenopathy is significant, with infectious causes such as tuberculosis being more prevalent in developing countries, while neoplastic causes, including lymphomas and metastatic carcinomas, are more frequently diagnosed in older populations[4]. In India, tuberculous lymphadenitis continues to be a leading cause of peripheral lymphadenopathy, accounting for up to 60% of cervical lymph node enlargements in some regional studies[5]. On the other hand, lymphomas contribute substantially to the burden of malignant lymphadenopathy, with non-Hodgkin's lymphoma being more common than Hodgkin's lymphoma[6,7].

Fine Needle Aspiration Cytology (FNAC) is widely used as a first-line, minimally invasive, cost-effective technique for evaluating lymphadenopathy. It provides rapid preliminary diagnosis but has limitations in distinguishing between reactive hyperplasia and low-grade lymphomas. Histopathological examination of excised lymph nodes remains the gold standard for definitive diagnosis. However, it may not always suffice for subtyping lymphomas, which require immunohistochemical (IHC) analysis for accurate classification based on cell lineage and proliferative index[8,9].

Previous studies have reported varied diagnostic concordance rates between FNAC and histopathology. While FNAC shows high sensitivity in metastatic and granulomatous lesions, it is less reliable in diagnosing and subclassifying lymphomas.

Immunohistochemistry has emerged as an indispensable adjunct to histopathology, especially in the diagnosis and subclassification of lymphoid malignancies based on WHO guidelines[10].

This study is justified by the need for a comprehensive approach that integrates cytomorphology, histopathology, and immunohistochemistry to improve diagnostic accuracy in lymphadenopathy. Given the wide spectrum of differential diagnoses and the clinical implications of misdiagnosis, a multimodal diagnostic strategy can facilitate timely and appropriate management, particularly in resource-limited tertiary care settings.

AIM AND OBJECTIVES

AIM:

To correlate cytomorphological, histopathological, and immunohistochemical findings in the diagnosis of lymphadenopathy in patients presenting to a tertiary care center.

OBJECTIVES:

1. To evaluate the diagnostic accuracy of fine needle aspiration cytology (FNAC) in differentiating benign and malignant causes of lymphadenopathy by comparing it with histopathology.
2. To assess the utility of immunohistochemistry (IHC) in confirming and subtyping lymphoid malignancies diagnosed on histopathology.

MATERIALS AND METHODS

STUDY DESIGN:

A prospective observational study conducted over a period of 18 months (december 2022 to may 2024) in the Department of Pathology, in collaboration with the Departments of Surgery and Medicine, at a tertiary care teaching hospital in India.

STUDY DURATION:18 months

STUDY POPULATION:

Patients of all age groups presenting with clinically significant peripheral lymphadenopathy (cervical, axillary, inguinal, or supraclavicular) were included.

SAMPLE SIZE:

A total of 100 patients were included based on convenience sampling and availability of complete cytological, histopathological, and immunohistochemical data.

INCLUSION CRITERIA:

- Patients presenting with peripheral lymphadenopathy ≥1 cm in size.
- Patients who underwent fine needle aspiration cytology (FNAC) followed by excisional lymph node biopsy.
- Availability of sufficient tissue for immunohistochemical (IHC) analysis where required.
- Informed consent obtained for procedures and use of data for research.

EXCLUSION CRITERIA:

- Patients with deep-seated lymphadenopathy not amenable to excision.
- Inadequate cytological or histological material.
- Lymph nodes showing only non-specific inflammation or necrosis with no definitive diagnosis on biopsy.

Procedure:

1. Clinical Evaluation:

All patients were evaluated clinically for duration, site, consistency, and associated systemic features (fever, weight loss, night sweats, etc.).

2. Fine Needle Aspiration Cytology (FNAC):

- Performed using a 22–23gauge needle and 10 mL disposable syringe.
- Smears were prepared on clean glass slides and stained with:
    - May-Grünwald-Giemsa (MGG) stain.
    - Hematoxylin and Eosin (H&E) stain.

- Ziehl-Neelsen stain in suspected tuberculosis cases.

3. Excision Biopsy and Histopathological Examination:

- Excision of lymph node done under local/general anesthesia.
- Tissues fixed in 10% buffered formalin, processed, and embedded in paraffin.
- Sections stained with Hematoxylin and Eosin (H&E) for routine histopathological diagnosis.

4. Immunohistochemistry (IHC):

- IHC performed for cases suggestive of lymphoid neoplasms on histopathology.
- Panels included markers based on WHO classification:
  - B-cell markers: CD20, CD79a, PAX5.
  - T-cell markers: CD3.
  - Other markers: CD15, CD30, CD45, Ki-67, BCL2, BCL6, ALK-1 depending on differential diagnosis.
- IHC interpreted by experienced pathologists for confirmation and subtyping.

Data Analysis:

- Data were recorded in Microsoft Excel and analyzed using SPSS version 25.
- Diagnostic accuracy, sensitivity, specificity, and positive predictive value (PPV) of FNAC were calculated using histopathology as the gold standard.
- The concordance between FNAC, histopathology, and IHC was analyzed.
- Results were presented in tables and charts.

Ethical Considerations:

- The study was approved by the Institutional Ethics Committee.
- Written informed consent was obtained from all patients (or guardians in case of minors).

RESULTS

Table 1: Demographic Distribution of Patients with Lymphadenopathy (n = 100)

Age Group (years)	Male (n)	Female (n)	Total (%)
0–20	10	12	22%
21–40	18	15	33%
41–60	12	10	22%
>60	13	10	23%
Total	53	47	100%

Table 2: FNAC Diagnosis Distribution

FNAC Diagnosis	Number of Cases	Percentage (%)
Reactive lymphadenitis	38	38%
Granulomatous lymphadenitis (TB)	22	22%
Metastatic carcinoma	18	18%
Suspicious for lymphoma	12	12%
Non-diagnostic/inconclusive	10	10%

Table 3: Correlation Between FNAC and Histopathology (n = 100)

FNAC Diagnosis	Histopathology Correlated	Discrepant	Diagnostic Accuracy (%)
Reactive	34	4	89%
Granulomatous (TB)	20	2	91%

FNAC Diagnosis	Histopathology Correlated	Discrepant	Diagnostic Accuracy (%)
Metastatic	17	1	94%
Lymphoma (Suspicious)	8	4	66%
Non-diagnostic	-	-	-

Table 4: Final Histopathological Diagnosis Distribution

Histopathological Diagnosis	Number of Cases	Percentage (%)
Reactive lymphadenitis	36	36%
Tuberculous lymphadenitis	20	20%
Metastatic carcinoma	18	18%
Non-Hodgkin’s lymphoma	14	14%
Hodgkin’s lymphoma	8	8%
Other (e.g., sarcoidosis)	4	4%

Table 5: Role of IHC in Lymphoma Cases (n = 22)

Histopathology Suggestion	Confirmed by IHC	Subtype Identified	IHC Markers Used
Non-Hodgkin's Lymphoma	14	DLBCL (10), SLL (4)	CD20, CD3, BCL2, Ki-67
Hodgkin’s Lymphoma	8	NSHL (5), MCHL (3)	CD15, CD30, PAX5, CD45

DISCUSSION

The present study aimed to evaluate and correlate cytomorphological, histopathological, and immunohistochemical findings in cases of peripheral lymphadenopathy. Among the 100 cases included, the most common age group affected was 21–40 years, with a slight male predominance. These demographic trends are consistent with previous studies by Priya et al.[11] (2021) and Pandit et al.[12] (1987), which also reported a higher prevalence of lymphadenopathy in the young adult population, particularly in males, reflecting the higher exposure of this age group to infectious and environmental agents.

In our study, reactive lymphadenitis was the most frequently diagnosed benign condition, followed by tuberculous lymphadenitis. This aligns with the findings of Prashant et al.[13] (2017), who reported reactive hyperplasia in 40% and tubercular lymphadenitis in 30% of cases evaluated by FNAC in North India. The persistence of tuberculosis as a significant cause of lymphadenopathy in our setting underscores the continued public health burden of TB in India.

FNAC showed excellent diagnostic correlation with histopathology in cases of reactive lymphadenitis (89%), tuberculous lymphadenitis (86%), and metastatic carcinoma (94%), findings that are in line with the work of Dhingra et al.[14] (2010), who reported similar concordance rates, highlighting the high sensitivity and specificity of FNAC in these conditions. However, lymphomas showed lower diagnostic accuracy (66%) on FNAC alone, which is consistent with the study by Khajuria et al.[15] (2012), where cytological diagnosis of lymphomas was often inconclusive or misclassified due to overlapping features with reactive hyperplasia.

Histopathological examination confirmed the presence of lymphoma in 22% of cases in our study, including 14 cases of Non-Hodgkin's Lymphoma (NHL) and 8 cases of Hodgkin's Lymphoma (HL). This finding is supported by the study of Nischitha et al.[16] (2019), which reported a similar predominance of NHL over HL in their cohort. The diagnosis and subtyping of lymphomas were definitively established only after IHC, which utilized lineage-specific markers such as CD20, CD3, CD15, CD30, and Ki-67. These markers played a crucial role in differentiating between B-cell and T-cell

lymphomas and identifying the classical subtype of Hodgkin's lymphoma, in agreement with the observations of Satish et al.[17] (2010).

Our study highlights the limitation of FNAC in classifying lymphomas, emphasizing the indispensable role of immunohistochemistry. Similar conclusions were drawn by Ozlem et al., (2021)[18], who emphasized that while FNAC is valuable for screening and preliminary diagnosis, histopathology with IHC is necessary for definitive diagnosis and classification according to the WHO lymphoma classification guidelines.

Furthermore, we found 100% concordance between histopathology and IHC in the subtyping of lymphomas, reaffirming the importance of IHC in guiding management. The work by Swerdlow et al.[10] (2017) on the revised WHO classification supports this approach, as accurate classification not onlyhas diagnostic implications but also prognostic and therapeutic relevance.

CONCLUSION

The study emphasizes the importance of cytomorphology, histopathology, and immunohistochemistry in diagnosing lymphadenopathy. Fine Needle Aspiration Cytology (FNAC) is a useful first-line diagnostic tool, but it has limitations in definitive diagnosis and subtyping lymphomas. Histopathological examination confirms diagnosis in most cases, while immunohistochemistry enhances diagnostic precision, especially in lymphoid malignancies. An integrated approach using all three modalities improves diagnostic accuracy, enables early therapy initiation, and enhances patient outcomes in lymphadenopathy cases.

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