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Original Research Article

Cytology's New Frontier: The Sydney System's Innovative Approach to Lymph Node Diagnosis

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ABSTRACT

Background: FNAC is the first diagnostic step in patients with lymphadenopathy because of its simplicity and minimal invasive nature which helps to confirm the clinical suspicion. A definite specific diagnosis may not be possible in a few cases but a categorization of disease and differential diagnosis can help suggest the most efficient further investigations, saving time and resources.
The aim of this study was to ascertain the system's applicability and precision in the diagnosis of lymph node cytology.

Material and methods: A retrospective cross-sectional study on lymph node cytology samples collected between January 2024 and June 2024, categorizing results into five groups (L1-L5) according to the Sydney System. Cytological findings were validated against histopathological results and relevant clinical data that prompted FNA procedures. Diagnostic performance was evaluated using metrics such as sensitivity, specificity, predictive values, and malignancy risk estimates.

Results: 60 cases were evaluated by FNAC. Out of this 44 were benign cases, 16 cases were of Reactive lymphadenitis, 24 cases of Granulomatous/Tuberculous lymphadenitis and 4 cases were of Acute suppurative lymphadenitis. Out of 16 malignant cases, 1 case was of Non Hodgkins lymphoma, 2 case was of Hodgkins lymphoma and 13 cases were of metastatic carcinoma.

Conclusion: The Sydney system was used for clinicopathological diagnosis of patients presenting with lymphadenopathy and was found to be a reliable tool for evaluation of risk of malignancy and its subsequent management of the patient.

Keywords: fine needle cytology, lymph node, Sydney system, risk of malignancy

INTRODUCTION

Fine needle aspiration dates back to 1950[1]. Fine needle aspiration cytology is most common method for evaluation of lymphadenopathy. The clinical value of FNAC is not limited to neoplastic conditions. FNAC's versatility extends to diagnosing inflammatory, infectious, and degenerative conditions, enabling microbiological, biochemical, and cytological analysis. This is particularly valuable for immunocompromised patients, such as those with AIDS. Additionally, FNAC aids in monitoring graft rejection in transplant patients. While a definitive diagnosis may not always be possible, categorization

and differential diagnosis can guide further investigation, optimizing resource utilization. Used effectively, FNAC has become a crucial diagnostic tool, complementing surgical histopathology.[1]

The Sydney System, introduced at the 20th International Congress of Cytology in 2020, provides a standardized framework for lymph node cytopathology reporting and classification (Table-1). Developed from extensive international research and expert experience, this system enables categorization of LN-FNA diagnoses and offers practical guidelines. Endorsed by prominent cytology organizations, the Sydney System has been validated for clinical use.[2]

The main purpose of this system was to provide consensus guidelines and a framework to facilitate system-based practice.[3,4]

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted on lymph node cytology samples from January 2024 to June 2024, with results categorized into five groups (L1-L5) using the Sydney System. Cytological diagnoses were validated against histological diagnoses and clinical findings justifying FNA. Statistical analysis included true and false positives (TP, FP), true and false negatives (TN, FN), and ROM calculations.

Exclusion criteria:

1. Cases without corresponding histopathological correlation: Patients for whom there is no additional tissue analysis (histopathological examination) available criteria or comparison were excluded. This step ensures that there is a way to verify or validate the FNAC results against more conclusive diagnostic methods.
2. Loss to follow-up cases: Patients for whom subsequent clinical follow-up data could not be obtained were excluded. This is to prevent bias caused by missing data and ensure that the study is based on comprehensive information.
3. Exclusion of Inadequate or Non-diagnostic FNAC Samples (L1): Samples with inadequate or non-diagnostic material (classified as L1) were excluded from specific calculations, likely to ensure the accuracy and reliability of the study's findings.

Inclusion criteria:

1. Patients with Lymphadenopathy: The study focuses on individuals who have enlarged lymph nodes (lymphadenopathy).
2. Histopathological Examination Reports: For some patients, the extracted tissue samples obtained through FNAC were subjected to histopathological examination.This involves a detailed microscopic analysis of the tissue to determine the nature of any abnormalities or diseases.
3. Clinical Follow-Up Data: For other patients, histopathological examination might not have been performed. Instead, their condition was monitored through clinical follow-up, which involves tracking their medical history, symptoms, and any changes in their health over time.

Table-1: Sydney System of Classification of Lymph node Cytology

CATEGORY		FEATURES
L1	Inadequate/ Insufficient	• Scant cellularity • Extensive necrosis • Technical limitations that cannot be overcome
L2	Benign	• Suppurative and granulomatous inflammation • Reactive lymphoid population
L3	Atypical (Cells) Undetermined significance/ Atypical lymphoid (cells) of Uncertain significance (ALUS/AUS)	• Heterogeneous lymphoid population, features suggest a reactive process, follicular lymphoma cannot be excluded • Excess of large cells (centroblasts or immunoblasts) or immature small lymphoid
L4	Suspicious	• suspicious of lymphoma, but the cytomorphology alone is not sufficient • Polymorphous lymphoid smears, few Hodgkin- or Reed-Sternberg-like cells are detected • Large cell or Burkitt lymphomas scantly cellular • atypical cells suspicious for metastasis present, but are too scant to be diagnostic
L5	Malignant	• NHL; HL • Metastatic neoplasms

Study procedure:

FNAC procedures were performed after obtaining informed consent from patients. Rapid Onsite Evaluation (ROSE) using toluidine blue stain was done for assessing specimen adequacy. An explanation of the procedure to the patient along with its possible risks and benefits was given and consent was taken. The FNAC procedure involved using a 23G needle to collect samples, with direct smears prepared from the first pass. For superficial and palpable lymph nodes, aspirations were taken blindly, while non-palpable and deep lymph nodes were aspirated under image guidance, mostly using ultrasonography. At least two air dried and three wet fixed smears were made and stained with Papanicolaou, Haematoxylin and Eosin (H&E) as well as May Grunwald Giemsa (MGG) stain. Additional smears were stained with Ziehl-Nelsen stain in suspected cases of tuberculosis. The smears were reported and classified into five diagnostic categories based on the proposed Sydney system of reporting, with immunohistochemical markers used for subtyping in suspected lymphoma cases.

Statistical analysis:

The statistical analysis was done with the help of software International Business Management (IBM) SPSS version 26.0.

ROM in each category was calculated by dividing the number of cases with a confirmed malignant diagnosis by the total number of cases in each diagnostic category as shown in Table-4.

Among the 36 cytologically benign cases, 14 cases were proved to be histopathologic ally benign, TNs. 1 case was diagnosed histopathologically as malignant, FN. Among the 21 Cytologically malignant/suspicious cases, 14 cases were proved to be malignant histopathologically were TP, and 2 cases was diagnosed as benign, FP on cytology. The true and FPs and negatives in comparison to gold standard shown in Table-2.

Table-2: Comparison of Cytological And Histopathological Diagnoses with Diagnostic Accuracy Parameters

		Histopathology Diagnosis		
Cytology		Malignant	Benign	Total
	Malignant	14(TP)	1(FN)	16
	Benign	2(FP)	14(TN)	15
Total		16	15	31

The True and False Positives (FP) and negatives in comparison to gold standard.

*L1-non-diagnostic category (1 cases) excluded;

TP: True positive; TN: True negative; FP: False positive; FN: False negative

Table-3: Correlation of Cytological and Histopathological Diagnoses According to Diagnostic Categories (L1-L5)

CATEGORY	**CYTOLOGICAL DIAGNOSIS**	**HISTOPATHOLOGICAL DIAGNOSIS**
L1	Caseous necrosis (n=1)	•Granulomatous lymphadenitis •N=1
L2	• Suppurative lymphadenitis (n=4) • Reactive lymphadenitis (n=10) • Granulomatous lymphadenitis (n=22)	•Reactive lymphadenitis (n=4) •Granulomatous lymphadenitis (n=10) •Hodgkins lymphoma (n=1)
L3	•Reactive lymphadenitis (n=6) •Atypical lymphocytes (n=2)	•Hodgkins lymphoma (n=1) •Reactive lymphadenitis (n=2)
L4	•Mets (n=7) •Non Hodgkin lymphoma (n=1)	•PTC (n=4) •SCC from the oral cavity(n=3) •Diffuse large B cell lymphoma (n=1)
L5	•Mets (n=7)	•IDC of breast (n=3) •Melanoma of foot (n=2) •Adenocarcinoma of lung (n=2)

Table-4: Risk of malignancy (ROM) in each cytological diagnostic category (L1-L5)

CATEGORY	ROM
L1	-
L2	2.7%
L3	12.5%
L4	100%
L5	100%

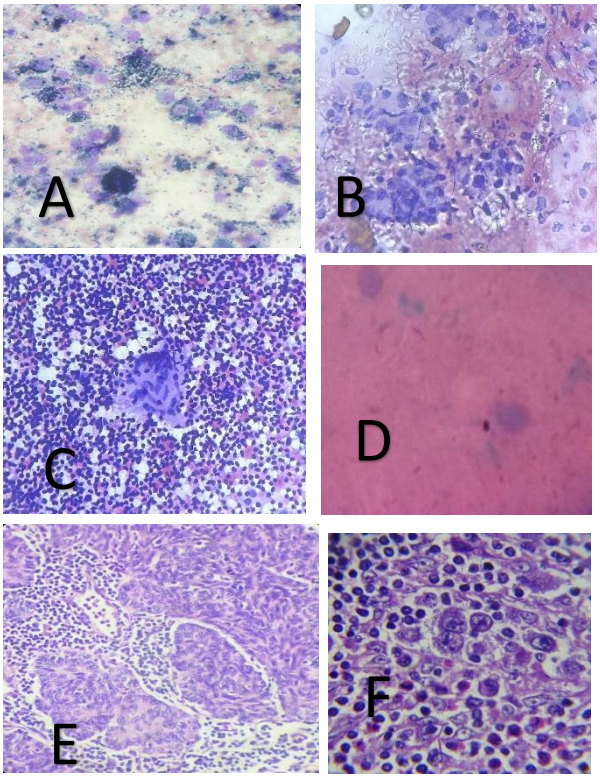

Figure-1: Photomicrographs of Lymph node aspiration cytology (A-D) & Biopsy-(E-F) ; (A) L5-Malignant melanoma metastasis with pigment in lymph node (Pap stain 40X); (B)L3-Atypical lymphoid cells (Pap 40X); (C) L2-Granulomatous lymphadenitis (Pap stain 40X); (D) AFB bacilli (ZN stain 100X); (E); L4-Squamous cell carcinoma of oral cavity; (F) Hodgkin's Lymphoma histopathology (H&E 40X).

RESULTS

This study examined 60 lymphadenopathy aspirates, with corresponding lymph node histopathology diagnoses available for 34 cases (56.6%). Patient ages ranged from 6 months to 65 years, averaging 30.64 years. The sample consisted of 38 males (63.33%) and 22 females (36.66%), resulting in a male-to-female ratio of approximately 1.72:1.

60 cases were evaluated by FNAC. Out of this 44 were benign cases, 16 cases were of Reactive lymphadenitis, 24 cases of Granulomatous/Tuberculous lymphadenitis and 4 cases were of Acute suppurative lymphadenitis. Out of 16 malignant cases, 1 case was of Non-Hodgkin's lymphoma, 2 cases were of Hodgkin's lymphoma and 14 cases were of metastatic carcinoma. (Table-3)

Category L1-There were 1 was scanty material with what looked like necrosis. Cytologically it was diagnosed as Caseous necrosis. Repeat aspirate was suggested.

Category L2-Out of 36 cases in L2, there were 10 reactive lymphadenitis granulomatous lymphadenitis in 22 and 4 suppurative lymphadenitis cases. Diagnosis of reactive background with histiocytes, to rule out toxoplasmosis by serology was given in 4 cases. Epithelioid granulomas were seen in all 10 cases of granulomatous lymphadenitis (Fig 1-A). Acid-Fast Bacilli (AFB) positivity was seen in 1 case (Fig 1-D). AFB positivity was confirmed later with a sputum positive test.

Category L3-There were 8 cytology diagnosis. Atypical cells in a reactive background, large cells and immunoblasts were found. Biopsy and IHC were recommended.

Category L4-There were 8 cases. 7 were suspicious of metastasis, where granuloma, necrosis and atypical cells found. Cases suspicious of lympho- proliferative lesions in 1 case were advised biopsy with recommendation for ancillary studies (Fig 1-F).

Category L5-Included 6 malignant lesions, all 6 were metastatic malignancy (Fig 1-A.1-B,1-E).

DISCUSSION

The use of ancillary techniques and clinical data ensures satisfactory diagnostic accuracy in lymph node fine-needle cytology (LN-FNC). However, despite its benefits, LN-FNC is not uniformly accepted by clinicians, mainly due to the lack of guidelines and standardized reporting systems[3]. The Sydney System addresses this issue by providing a comprehensive approach to categorizing lymph node cytopathology, thereby enhancing diagnostic accuracy and reproducibility. The Sydney System is a comprehensive approach to categorizing lymph node fine-needle aspiration (LN-FNA) diagnoses, combining both broad diagnostic categories and more specific diagnostic entities using ancillary techniques[5,6,7]. In this system, the first level of diagnostic categorization (L1-L5) likely allows for a general classification of lesions based on their characteristics, which include categories such as inadequate (L1), benign (L2), and suspicious/malignant (L3-L5). This initial classification provides a broad understanding of the nature of the lesion. The second diagnostic level involves utilizing additional techniques, such as immunocytochemistry (ICC), fluorescent in situ hybridization (FISH), and cell block preparations, to further refine the diagnosis and identify specific diagnostic entities. These ancillary techniques can provide more precise information about the cellular and molecular characteristics of the sample, aiding in distinguishing between different types of malignancies or other pathologies. By incorporating these two diagnostic levels and utilizing advanced techniques for more accurate characterization, this system seems to be designed to enhance the reliability and specificity of lymph node cytopathology diagnoses[7]. This could be particularly valuable for guiding patient management and treatment decisions.

In the present series, we showed the ability of the Sydney system to secernate lymph node. The proposed system for reporting LN-FNAC cytopathology has the following aims.

1.Develop Consensus Guidelines and Framework:

Establish a set of agreed-upon guidelines and a framework to improve communication between various medical professionals involved in lymph node FNAC, including cytopathologists, hematopathologists, clinicians, and surgeons. This collaboration ensures a shared understanding and approach to diagnosis and management.[6,7]

2.Obtain Key Diagnostic Cytopathological Features:

Identify and establish the essential diagnostic features that are commonly observed in different categories of lymph node FNAC samples[8.] Understanding these features enables accurate categorization and diagnosis of various types of lesions.

3.Make Recommendations on Standardized Diagnostic Reports:

Propose a standardized format for diagnostic reports to enhance communication between cytopathologists and clinicians. Clear, uniform reporting helps healthcare providers better understand the diagnosis, which in turn can lead to more effective patient management.[7,8,9]

4.Provide Management Recommendations Linked to Reporting Categories:

Offer management suggestions based on the reported diagnostic categories. Recommendations could encompass clinical and imaging follow-up, additional ancillary testing, and the consideration of potentially excising the lymph node if necessary.[10]

5.Encourage Cyto-Histopathological Correlations, Cell Storage, and Research:

Promote the correlation between cytopathological findings and histopathological results for further validation. Encourage the storage of cellular material for future reference and research purposes, focusing on both neoplastic (cancerous) and non-neoplastic (non-cancerous) lymph node specimens.

6.Increase LN-FNAC Reliability and Clinician Awareness:

Improve the reliability of LN-FNAC results through standardized guidelines and practices. Also, enhance clinicians' awareness of the diagnostic potential outcomes.[11,12]

Limitations:

Small sample size, less histopathological follow-up and lack of adequate ancillary techniques were the main limitations of this study.

The study lacked access to ancillary tests like flow cytometry or molecular studies, which are often crucial for confirming lymphoid malignancies, potentially limiting the diagnostic accuracy of the lymph node cytology results.

CONCLUSIONS

Lymph node fine needle aspiration cytology helps in the primary diagnosis of lymphadenopathy which is very useful for further management according to the lesions. The Sydney System for lymph node reporting is a valuable classification system that enables effective risk stratification and management. Its high sensitivity and specificity make it a reliable tool for diagnostic purposes, enhancing patient care and treatment planning. However, multicentric studies with a larger sample size along with advanced ancillary techniques are required for more accurate results.

The main objective of the study is to determine how effective the Sydney reporting system is when applied to fine needle aspiration cytology (FNAC) for diagnosing lymph node lesions. The Sydney reporting system provides a structured framework for reporting cytological and histological findings in lymph node lesions. It emphasizes including essential clinical data, radiological findings, and site information. The core of the system involves categorizing findings into five basic diagnostic categories (L1-L5), along with additional details like microscopic descriptions, ancillary techniques used, and any secondary diagnoses provided. However, the Sydney system remains underutilized and there is limited data in literature to date. Therefore, the present study was aimed to assimilate the diagnostic utility of Sydney reporting system in fine needle aspiration cytology for lymph node lesions.

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