ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Application Of The Proposed Sydney System In Classification And Reporting Of Lymph Node Fine Needle Aspiration Cytology: An Experience Of One Year In Tertiary Care Centre Of North India.

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ABSTRACT

Fine needle aspiration cytology has been routinely used technique for initial diagnosis of lymphadenopathy. Lymph Node FNA can assess whether lymphadenopathy is benign or malignant and provide staging information in patients with an established diagnosis of malignancy. Conventional system of reporting lymph node smears lack standardized diagnostic classification, common language of reporting among cytopathologists and clear communication to clinician for risk of malignancy and further management. Hence, the Sydney System for Classification and Reporting of lymph node cytology has been proposed for assessing the performance, classification and reporting of LN cytopathology. The present study was conducted to apply the proposed Sydney system in the diagnosis of lymph node cytology**.** This was a one year retrospective study of LN-FNA comprising of a total 3752 FNA's out of which 1250 were on LN's. Cytological diagnosis was categorized by the proposed Sydney System in following categories- L1: Non-diagnostic/Inadequate, L2: Benign, L3: Atypical cells of undermined significance, L4: Suspicious of malignancy, L5: Malignant. Out of total FNA's done for lymphadenopathy during the study period, 1250 (33.3%) were on LN's. Of these 102 (8.1%), 467 (37.3%), 106 (8.4%), 92 (7.3%) and 483 (38.6%) was categorized in the L1, L2, L3, L4 and L5 categories respectively. FNAC has high diagnostic accuracy for the diagnosis of various LN pathologies. Application of the proposed Sydney System can help in achieving uniformity and reproducibility in cytological diagnosis.

Keywords: Cytology, Fine Needle Aspiration, Lymph node, Sydney System Reporting.

https://doi.org/10.33887/rjpbcs/2025.16.4.10

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ISSN: 0975-8585

INTRODUCTION

Lymphadenopathy is a common manifestation of both reactive and malignant conditions. Fine-needle aspiration (FNA) remains an effective and cost-efficient method for screening, and to a lesser extent diagnosing lymphadenopathy [1–3]. Although tissue biopsies are often required for definitive lymphoma diagnosis, FNA can be valuable for obtaining samples for ancillary studies, including flow cytometry, microbiological cultures, and molecular testing [4]. While its diagnostic role in lymphoma remains debated, FNA is a useful initial screening tool, particularly in cases of benign lymphadenopathy with a low suspicion of malignancy. In such instances, FNA can help avoid unnecessary invasive procedures, including excisional biopsies [2].

Lymph node-Fine Needle Aspiration Cytology (LN-FNAC) can thus play a key role in the evaluation of lymphadenopathies as it can provide cytomorphological information and material for ancillary testing that is diagnostic. The traditional approach to reporting lymph node smears often suffers from the absence of a standardized diagnostic framework, a shared terminology among cytopathologists, and effective communication with clinicians regarding malignancy risk and subsequent management strategies [5, 6]. The Bethesda system for thyroid cytopathology, the Milan system for reporting salivary gland cytopathology, and the Yokohama system for reporting breast cytopathology have been validated to be useful and are in routine practice in many institutions. In line with these, the Sydney system was proposed for the reporting of lymph node cytopathology [9]. There are five diagnostic categories, namely, L1 to L5, denoting nondiagnostic, benign, atypical cells of undetermined significance, suspicious of malignancy, and malignant, respectively. It also provides recommendations for management in each category. There are studies in the literature that had analysed the utility of this system in routine reporting [10]. the Sydney System for lymph node cytology reporting was introduced in 2020 by a panel of experts, establishing five distinct diagnostic categories [7] (Table 1).

Despite its potential, the Sydney System remains underutilized, and limited published research has contributed to a gap in understanding its practical implementation and diagnostic value [8]. Conventional system of reporting lymph node smears lack standardized diagnostic classification, common language of reporting among cytopathologists and clear communication to clinician for risk of malignancy and further management.[8]

Hence, the Sydney System for Classification and Reporting of lymph node cytology has been proposed for assessing the performance, classification and reporting of LN cytopathology. The present study was conducted to apply the proposed Sydney system in the diagnosis of lymph node cytology and to evaluate the system's effectiveness in interpreting lymph node cytology.

MATERIALS AND METHOD

This was a one year retrospective study of LN-FNA comprising of a total 3752 FNA's out of which 1250 were on LN's. Total of 1250 cases of lymph node FNA over a period of one year i.e from January to December 2021 were included and reviewed for the study in the Department of Pathology, Pt. B.D. Sharma PGIMS, Rohtak.

Inclusion and exclusion criteria: Lymph node aspirates from both sexes and all age groups were included. Non lymph node aspirates were excluded. For cases that were included, the available clinical and radiologic details were retrieved from the patient requisition forms. Cytological diagnosis was categorized by the proposed Sydney System in following categories- L1: Non-diagnostic/Inadequate, L2: Benign, L3: Atypical cells of undermined significance, L4: Suspicious of malignancy, L5: Malignant (Table- 2).

Lymph node aspirates included in this study were from individuals of all ages and both genders. Clinical follow-up data and cytological glass slides were reviewed for all included cases. Pathology records were examined to extract relevant information, including patient age, gender, lymph node location, clinical history, further investigations, and final diagnosis. Fine-needle aspiration (FNA) was performed under strict aseptic conditions in all cases. For superficial lymph nodes, percutaneous FNA was conducted using a 22-gauge hypodermic needle. For deep-seated lymph nodes, radiologic guidance was employed, either via ultrasonography or computed tomography (CT). All the FNA smears were subjected to rapid on-site evaluation (ROSE) by using toluidine stain to evaluate for adequacy. In case of smears that yielded scant material, a second pass was performed. The smears were stained by using both May Grünwald and Giemsa.

Immunophenotyping and cell block preparation were carried out for selected cases as recommended. At least two smears were prepared per case, including both air-dried and wet-fixed slides. Wet fixed smears were stained with Papanicolaou (PAP) stain. Additional smears were prepared depending on the clinical suspicion and nature of the aspirate, such as in cases where pus was aspirated; air-dried smears for Ziehl-Neelsen staining were also prepared.

Cell blocks and immunocytochemistry

Cell blocks were prepared from samples collected in 10% formalin, using the modified plasma-thrombin clot method. This was then embedded in paraffin; blocks were prepared and 3- µm sections were cut and stained with H & E. These sections were assessed for cellularity and wherever required ICC was performed on the sections obtained on precoated slides. Cell blocks were prepared from all the EBUS-guided FNAB samples, and immunohistochemistry was performed wherever necessary. The antibodies used were TTF1, napsin, CK5/6, p40, CD 56 and synaptophysin. All the smears prepared were retrieved and reviewed along with special cytochemical and immunocytochemical stains whenever available. Flow cytometry plots, whenever available, were reviewed.

RESULTS

Of the 3752 fine-needle aspirations performed during the study period, there were 1250 (33.3%) aspirations from the lymph nodes. The majority of the aspirations were performed percutaneously (n = 1062; 84.96%), and 188 (15.04%) were performed under radiologic guidance. The mean age of the patients was 35.9 ± 19.1 years (range, 3 months- 85 years). The male- to- female ratio was 1.5:1. Most commonly aspirated lymph nodes were the cervical lymph nodes (70.2%) , axillary lymph nodes (12%) , intra-abdominal lymph nodes (10.8%) , inguinal lymph nodes (6.8%) followed by mediastinal lymph nodes (0.2 %).

A total of 102 (8.1%) samples were deemed as nondiagnostic/inadequate (L1) for interpretation. The majority (n = 90) of these showed predominantly blood or fluid and minimal to no lymphoid and/or atypical cells could be identified; 12 cases showed extensive necrosis with no viable cells.

Benign (L2) cytologic diagnoses were rendered in 467 (37.3%) cases and included reactive lymphoid hyperplasia (RLH; n = 210; 44.90%) (FIG 4), acute lymphadenitis (n = 11; 2.4 %), chronic lymphadenitis (n = 9 ; 1.9 %), granulomatous lymphadenitis (n = 233; 49.80%)(FIG 3), Rosai- Dorfman disease (n = 4; 1.0%). (FIG- 1)

Table 1: Cytomorphological features of each category of Sydney System for reporting 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; Heterogeneous lymphoid population with small lymphocytes predominating, and often germinal centers with dendritic cells and tingible body macrophages
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 cells or cases where the atypical cells are not lymphoid cells.

ISSN: 0975-8585

L4: Suspicious.	Small and/or medium-sized, monomorphic atypical lymphoid cells 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; Smears in which atypical cells suspicious for metastasis are detected, but are too scant to be diagnostic
L5: Malignant	NHL; HL: Appropriate cellular background and diagnostic Hodgkin and Reed-Sternberg cells; Metastatic neoplasms.

Table 2: Categorization of smears based on Sydney System.

Sr. No.	Category	Number of FNA (out of 1250)	Percentage
1.	L1:Nondiagnostic/ Inadequate	102	8.1%
2.	L2: Benign	467	37.3%
3.	L3 : ALUS/AUS	106	8.4%
4.	L4: Suspicious	92	7.3%
5.	L5: Malignant	483	38.6%

Figure 1

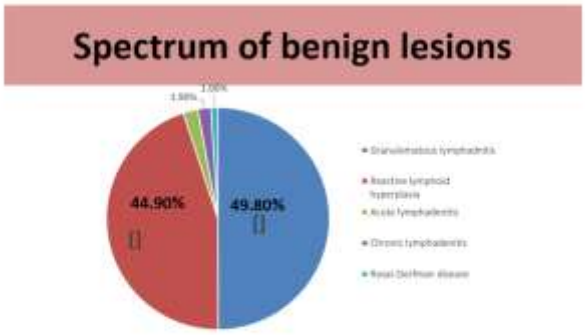
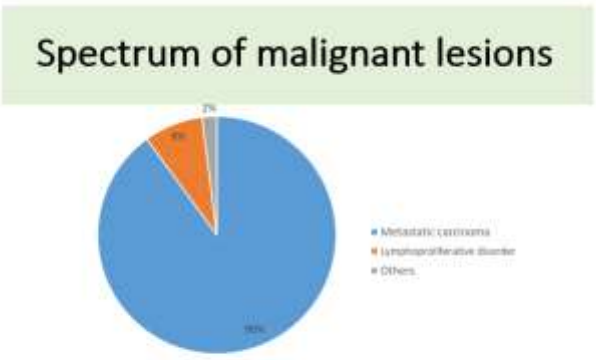


Figure 2



Metastatic carcinoma spectrum- Metastatic SCC > Metastatic PDC > Metastatic adenocarcinoma > Metastatic small cell carcinoma

ISSN: 0975-8585

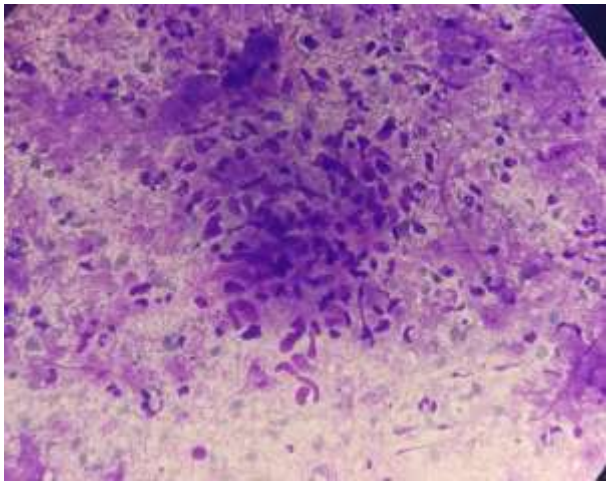


Figure 3: Necrotising granulomatous lymphadenitis (MGG;40X)

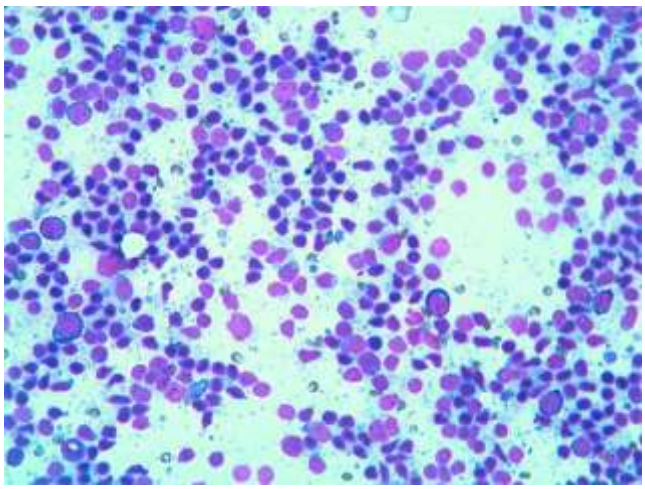


Figure 4: Reactive hyperplasia of lymph node (MGG;40X)

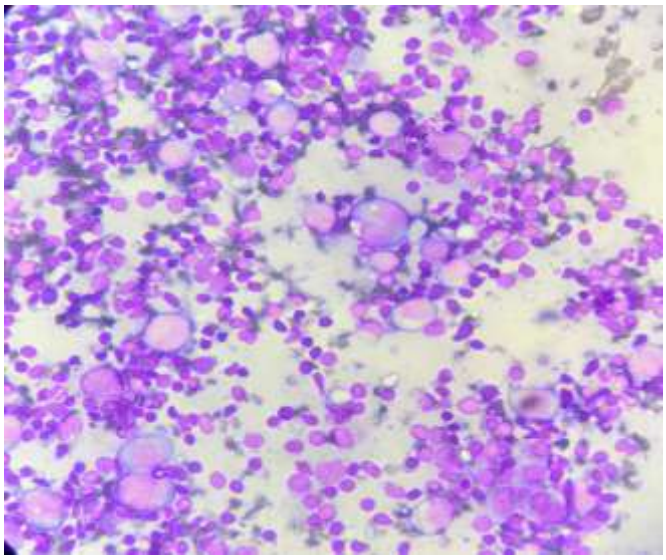


Figure 5: Hodgkin's lymphoma (MGG;40X)

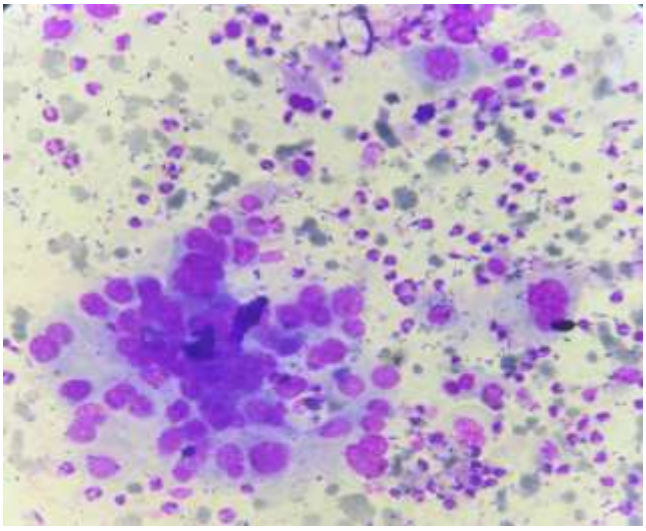


Figure 6: Squamous cell carcinoma (MGG;40X)

Category AUS/ALS (L3) included 106 (8.4%) cases; L4 had 92 cases (7.3%). Malignant (L5) cytologic diagnoses were rendered in 483 (38.6 %) aspirates. Among these, 55 (8%) cases were reported as lymphomas and other lymphoreticular malignancies (LRM) and 613 (90%) as metastatic malignancies. (FIG 2)

A majority of the LRMs (n = 55) were non- Hodgkin's lymphomas (NHLs; n = 22; 40.1%) followed by Hodgkin's lymphoma (HL; n = 11; 20.0 %)(FIG 5). There were 9 (15.6 %) aspirates reported as lymphoma, NOS with differential diagnoses of HL, and anaplastic large- cell lymphoma. A total of 13 (23.6 %) aspirates showed infiltration by various leukemias.

Among the metastatic malignancies (n = 613), the most frequently encountered were the metastatic carcinomas (n = 582; 95.0 %), followed by malignant small round- cell tumors (n = 6; 0.9%), melanoma (n = 4 ; 0.7%), germ cell tumors (n = 1; 0.2%). Additionally, there were 18 (3.0 %) cases wherein the exact differentiation of the malignant cells could not be determined, and these were reported as metastatic malignancy, NOS. The commonest cytologic diagnoses included metastatic squamous cell carcinoma(FIG 6), metastatic poorly differentiated carcinoma, metastatic adenocarcinoma, and metastatic small- cell carcinoma (Fig. 3).

DISCUSSION

Although some practitioners prefer surgical excision for lymph node diagnosis, many others have reported favourable experiences with lymph node fine-needle aspiration cytology (LN-FNAC). LN-FNAC is widely recognized as a safe, cost-effective, simple, and time-efficient diagnostic method. Its diagnostic performance is sufficiently high to support its continued use as a primary diagnostic tool[12,13], including in pediatric populations [2,14-19]. This minimally invasive technique is particularly valuable, as FNA specimens are often superior to needle core biopsies for flow cytometry (FC) studies. Standardized reporting of LN-FNAC results could further enhance diagnostic reproducibility, improve clinician interpretation and utilization, guide optimal patient management, and reduce the need for more invasive surgical procedures.

Lymph node fine-needle aspiration (LN-FNA) has been utilized as a diagnostic modality since the early 1950s. However, until recently, there was no well-established system for standardized reporting. The Sydney System has been proposed to address this gap by promoting uniformity in reporting and guiding clinical management [9, 11]. As with any newly proposed classification system, its validity, reproducibility, and clinical utility must be thoroughly evaluated before it can be adopted for routine clinical use.

The present study validates the utility of the proposed Sydney system for reporting lymph node FNAB in our population. The distribution of the diagnostic categories in cytopathology was comparable to

other studies [20-24]. The distribution of the diagnostic categories in cytopathology was comparable to other studies [20-24].

The L1 category constituted 8.1 %. This rate could be due to improper training of junior residents which can be lowered by rapid onsite evaluation (ROSE) and guided aspirations. A significant proportion of these cases were EBUS-guided FNAB, which was inadequate despite rapid onsite evaluation. In such a scenario, where repeat FNAB is neither beneficial nor feasible, either core needle or excision biopsy is to be considered as proposed by the Sydney system in the management recommendation of L1 category lesions. In the other cases of superficial lymphadenopathies, the quality of the aspirate is largely dependent on the skill of the aspirator. The limitation of having different expertise is unavoidable in a teaching institution. Therefore, the repeat FNAB if mandated should be performed by an experienced aspirator to maximize the diagnostic yield.

The most frequent interpretation in category L2 was granulomatous lymphadenitis (GLN), followed by reactive lymphadenitis which contrasts to that reported by other studies [8,20-24]. This difference may be due to higher burden of tuberculosis in northern India

The frequency of category L3 ranges from 0.8 to 8.3% [8, 22]. The current study reports a rate of 8.4%. In category L5, metastatic malignancies were more frequent, which is similar to that observed by Gupta et al. [8].

CONCLUSION

The adoption of the Sydney System for reporting and classifying lymph node cytology at our tertiary care center has enhanced the uniformity and reproducibility of cytopathological diagnoses. This standardized approach facilitates more accurate risk assessments of malignancy, thereby improving clinical management strategies. Our institution has a longstanding practice of utilizing standardized reporting systems for various organ systems through cytology specimens. The recent implementation of the Sydney System for lymph node cytology, introduced as a pilot project in our region, has notably improved clinicians' understanding of malignancy risks and informed subsequent patient care decisions.

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