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Study of Spectrum of Lymph Node Lesions on Cytopathology with Emphasis on the Sydney System of Reporting and Classification of Lymph Node Cytology

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Abstract
Lymph node enlargement is commonly seen in clinical settings. But the diagnosis of lymphadenopathy merely by clinical judgement is difficult [1]. Fine Needle Aspiration Cytology (FNAC) becomes a vital investigation tool for diagnosis of lymph node enlargement [3]. It is safe, reliable, rapid, economic can be performed in outpatient department with minimal discomfort to the patient [4]. The cytological diagnosis of lymph node lesions is extremely challenging for cytopathologist due to diversity of the diseases and coinciding cytomorphological features [2]. Previously, there was no uniformity in reporting of FNAC of lymph node and there were no criteria's given for reporting, due to lack of reproducibility which was creating confusion among clinicians [6]. To overcome this pitfall, the Sydney system was recently introduced with 5 categories for reproducibility and standardization of reports [7]. It provides better communication between pathologist and clinician. It provides recommendation for each category and the calculation of Risk of Malignancy (ROM) related to each category of cytological diagnosis [7].

Keywords: Lymph node, FNA, Sydney system, Risk of Malignancy

1. Introduction

Lymph node enlargement is common finding in clinical settings. Diagnosis of lymphadenopathy merely by clinical judgement is difficult [1]. It occurs due to variety of causes including infective, benign, malignant, or metastatic [2]. Fine Needle Aspiration Cytology (FNAC) has become a vital investigation tool for diagnosis of lymph node enlargement [3]. It is safe, reliable, rapid, economic, and less painful procedures can be performed in outpatient department with minimal discomfort to the patient [4]. However, FNA is associated with few complications including hemorrhage, vasovagal reaction, and nerve damage[5]. The cytological diagnosis of lymph node lesions is extremely challenging for cytopathologist due to diversity of the diseases and coinciding cytomorphological features [2].

Previously, there was no uniformity in reporting of FNAC of lymph node and there were no criteria given

for reporting, due to lack of reproducibility which was creating confusion amongst clinicians [6]. To overcome this pitfall, the Sydney system was recently introduced for reproducibility and standardization of reports [7]. It provides better communication between pathologists and clinicians. It provides recommendations for each category and the calculation of Risk of Malignancy (ROM) related to each category of cytological diagnosis [7]. In May 2019, a system for performance, classification, and reporting of lymph node cytopathology was proposed at the 20th International Congress of Cytology held in Sydney [8]. According to this system, the cytologic aspirations from lymph nodes should be categorized into 5 categories based on specific cytological features [9]. The cytology report should provide one of the five level diagnostic categories followed by a description of cytomorphology. Further recommendations can be made regarding management options. The essential features of the five categories are as follows [8]:

I/L1-Inadequate/Insufficient: Non diagnostic due to scant cellularity, necrosis, or technical limitations; repeat FNAC/ biopsy should be requested based on the specific clinical context [8].

II/L2-Benign: Includes suppurative, granulomatous or specific infections in cases with a heterogeneous lymphoid population with small lymphocytes predominating [8].

III/L3-Atypical Lymphoid (Cells) of Undetermined Significance/ Atypical (Cells) of Uncertain Significance (ALUS/AUS): Cases with a heterogeneous lymphoid population suggest a reactive process, but a follicular lymphoma cannot be excluded/or excess of large cells/or immature small lymphoid cells/or atypical non lymphoid cells present [8].

IV/L4-Suspicious category: Small or medium-sized, monomorphic atypical lymphoid cells suspicious of lymphoma, but the cytomorphology alone is not sufficient [8].

V/L5-Malignant: Includes small to medium-sized cells of NHL supported by flow cytometry or molecular studies, Hodgkin's Lymphoma if diagnostic Reed-Sternberg cells seen as well as metastatic neoplasms [8].

Aims and Objectives

1. To study the cytomorphological features of various lymph node lesions by applying the Sydney System of Reporting and Classification of Lymph Node Cytology.
2. To correlate the cytomorphological spectrum of the various lymph node lesions with histopathology.

Materials and Methods

Patients presented with lymph node enlargement to the cytology section of our department from Dec 1, 2023, to Nov 30, 2024, in the period of 1 year were included in study. Written informed consent was taken from all the patients included in study.

Type of Study- It was a prospective cross- sectional study.

Inclusion and exclusion criteria – All the patients presented with complain of lymph node enlargement were included in study. Patients with bleeding diathesis and not willing to give written informed consent were excluded from the study.

Necessary and relevant clinical information and ultrasound (USG) report were taken into consideration whenever available. Under all the aseptic precautions aspiration was performed using 22-gauge needle. Cytology slides were stained using hematoxylin and eosin (H &E), Papanicolaou (PAP), May Grunwald-Giemsa Stain (MGG). Special stains such as Ziehl and Neelsen (ZN) stains are used whenever required. All the cytology slides were reported according to a Sydney system of reporting and classification of lymph node cytology. Histopathological slides were stained by H&E whenever available.

Figure 01: Material required for FNA

Figure 02: Photograph showing enlarged cervical lymph node

Result

A total of 374 cases of lymph node enlargement were analyzed in present study. The corresponding histopathology diagnosis was available in case of 210 cases. There was a wide age group from 7 years to 65 years. The most common age group was 3rd decade (98) cases followed by 5th decade and 4th decade respectively. The swelling was predominantly noted in cervical region more on left side. The most common category according to Sydney System of Reporting and Classification of Lymph Node Cytology was L2- Benign seen in 58.6% (219 cases) followed by L5- Malignant 28.3% (106 cases), L1-Insuufficient 5.2% (19 cases), L3- Atypical 4.2% (16 cases), L4- Suspicious 3.7% (14 cases).

The histopathology correspondence was noted in 210 cases out of 374 cases. There were 19 cases reported in insufficient L1 category. However, histopathology was not available for any of the cases due to loss to follow up. A total of 219 cases were of benign L2 category out of which histopathology correspondence

was seen in 112 cases. Majority of diagnosis in benign category included granulomatous lymphadenitis followed by Reactive Lymphadenitis.

Atypical L3 category included 16 cases out of which only one case was reported in histopathology. Most common diagnosis included in this category was Atypical lymphoid hyperplasia. Suspicious L4 category included 14 cases out of which histopathological association was seen in 14 cases. Majority of cases were diagnosed as lymphoma followed by metastatic epithelial malignancy on histopathology. Malignant L5 category included 106 cases of 83 cases noted histopathological correlation. Most of the cases were reported as non-Hodgkin's lymphoma, Metastatic epithelial malignancy and Hodgkin's Lymphoma respectively.

Categories	Frequency	Percentage (%)
Insufficient -L1	19	5.2
Benign – L2	219	58.6
Atypical – L3	16	4.2
Suspicious – L4	14	3.7
Malignant -L5	106	28.3
Total	374	100

Table 1: Distribution of cases according to Sydney system of reporting and classification of lymph node cytology.

There were 4 cases where cytological diagnosis was not correlated with histopathological diagnosis.

In discordant case no 1. FNA was moderately cellular showing well form granulomas composed of epithelioid cells against small lymphocytes in background. On histopathology it was reported as Hodgkin's Lymphoma. The likely reason for this discrepancy can be that the clusters of epithelioid cells hide the scanty number of lymphoid neoplastic cells in background. It may occur due to sampling errors causing absence of Reed-Sternberg cells.

In discordant case no 2. FNA was moderately cellular showing polymorphous population of cells composed of centroblast, centrocytes, plasma cells, small lymphocytes. On histopathology it was diagnosed as Non-Hodgkin's Lymphoma. We fail to diagnose the case correctly due to presence of few atypical cells in a sea of reactive small lymphoid cells. It can occur due to partial replacement of lymph node, and the architecture cannot be assessed on FNAC.

In discordant case no 3. FNAC was highly cellular showing polymorphous population of cells composed of centroblast, centrocytes, plasma cells, and small lymphocytes. Few of the cells show atypia. On histopathology it was reported as a Low-grade Lymphoma. It is difficult to diagnose low grade lymphoma on cytology. If careful clinical examination were done, we probably might not miss the diagnosis.

In discordant case no 4. FNAC was moderately cellular showing large areas of necrosis, which were admitted with inflammatory infiltrate. On histopathology diagnosis given was metastatic epithelial malignancy s/o Squamous cell carcinoma (SCC). Since some epithelial malignancy like SCC shows necrotic changes, this may occur due to sampling errors. If careful clinical examination and FNA by experienced Pathologists were carried out, we probably might not miss the diagnosis on cytology.

This discordant case highlights the importance of a careful evaluation of lymph node cytomorphology along with detailed clinical history and examination of patient along with good communication among the clinicians for accurate diagnosis.

In our study risk of malignancy was 100% for categoryL3, L4 and L5 was 00% for L1 (Table 2).

Fre-quency	Cytology Diagnosis	Histopathology Diagnosis
1.	Granulomatous Lymphadenitis (Figure 03)	Hodgkin's Lymphoma
2.	Reactive Lymphadenitis (Figure 03)	Non- Hodgkin's Lymphoma
3.	Atypical Lymphoid Hyperplasia	Low-grade Lymphoma
4.	Necrotizing Lymphadenitis	Metastatic Epithelial Malignancy s/o Squamous cell carcinoma

Table 2: Distribution of cases with discordant cyto-histological correspondence.

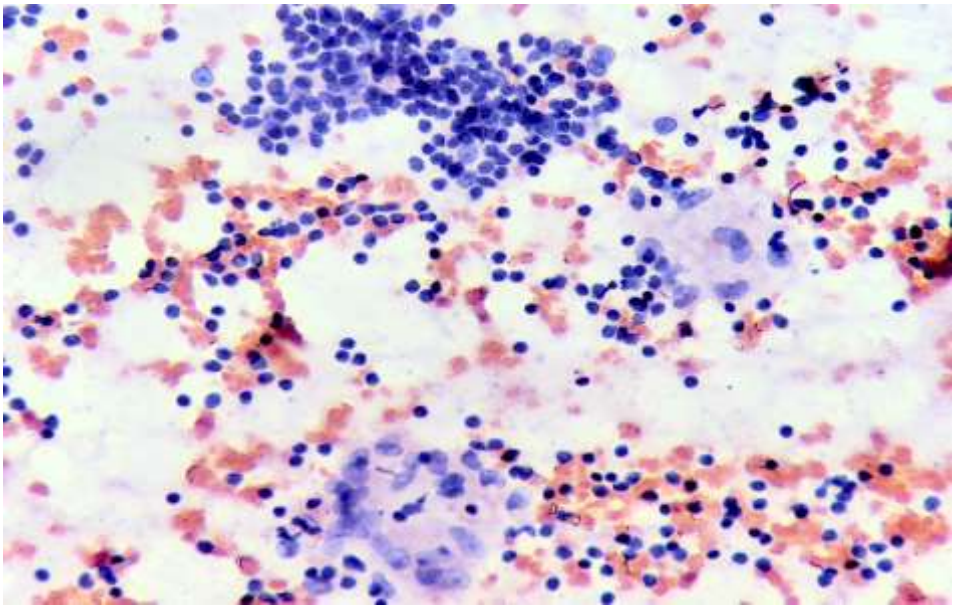

Figure 03: Photomicrograph demonstrating Granulomatous lymphadenitis with epithelioid cells, small lymphocytes in periphery without caseation granuloma (Papanicolaou stain, x40)

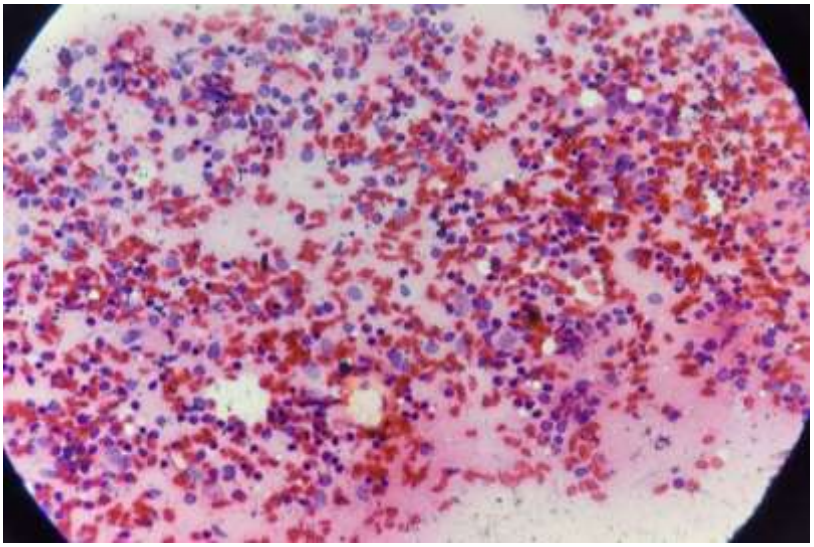

Figure 03: Photomicrograph demonstrating reactive lymphadenitis with polymorphous lymphoid population (Papanicolaou stain, x40)

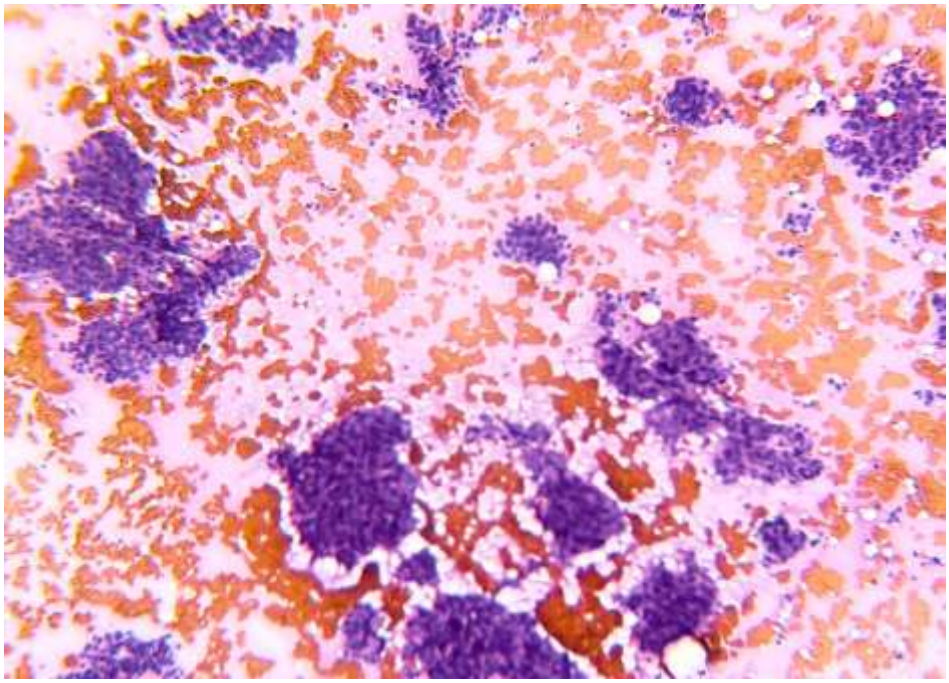

Figure 04: Photomicrograph demonstrating metastatic deposits from adenocarcinoma showing focal gland formation and clusters of atypical cells (Papanicolaou stain, x40)

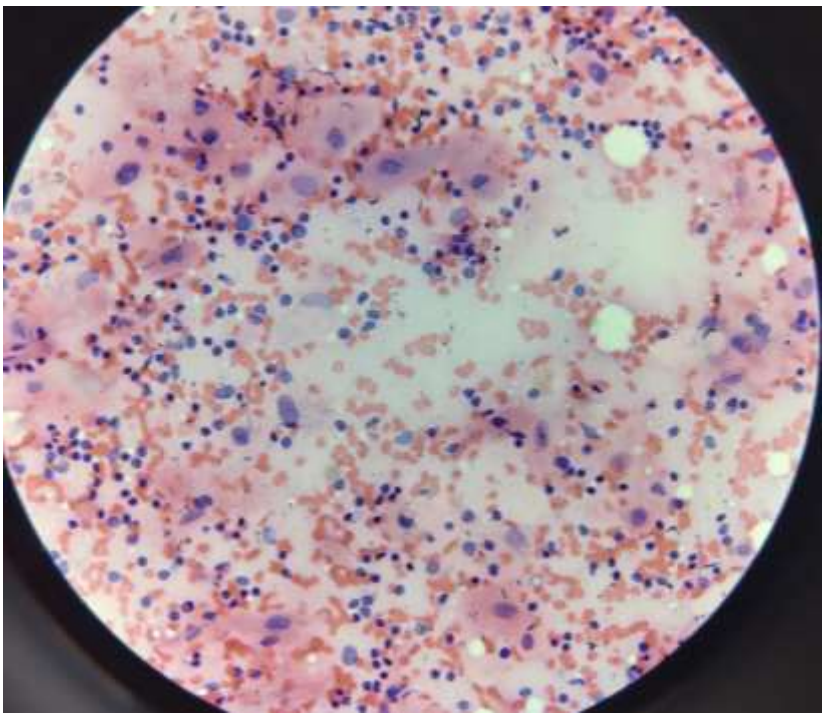

Figure 05: Photomicrograph demonstrating metastatic deposits from Squamous cell carcinoma (Papanicolaou stain, x40)

Categories	Frequency of biopsied in each category	Confirmed malignancy on histopathology	ROM
L1	00	00	0%
L2	112 (51.14%)	03	2.67%
L3	01 (6.25%)	01	100%
L4	14 (100%)	14	100%
L5	83 (100%)	83	100%

Table 3: Risk of Malignancy according to category.

Discussion

Lymphadenopathy is commonly seen in children as well as in adults. In children it is commonly a sign self-limited infection while in adult it represents commonly a metastatic malignancy [10]. The cause of lymphadenopathy varies according to geographical areas. In developing countries, it occurs most commonly due to tuberculosis [11]. Since lymphadenopathy is seen commonly in patients of outpatient department [12]. For the diagnosis of this lesion FNAC can be used as easy, quick, and appropriate test for diagnosis of variable spectrum of lesions from inflammatory to benign to neoplastic [13,14]. Nevertheless, FNAC of lymph node represents challenging scenario for pathologist to diagnose due to wide spectrum of lesions and nonavailability of standardize reporting system for categorization [15, 16]. To fulfil the above requirement, in 2020 an expert panel introduced the Sydney system for performing classification and reporting of lymph node cytopathology with 5 categories which will help in standardized and uniform reporting [17].

Site	**Present Study**	Pandya D. et al	Gupta P. et al
Cervical group	69.2	67.5	66.8
Axillary group	13	12.3	14
Inguinal group	5.9	5.15	8.1
Submandibular	7.8	5.15	02
Others	10.6	9.7	9.1

Table 4: Comparisons of sites of lymphadenopathy

Categories	**Present Study**	Pandya D. et al	Gupta P. et al	Sreelekshmi. et al[7]
L1	5.2	4.12	4.1	5.6
L2	58.6	61.34	48.6	63.6
L3	4.2	3.09	0.5	1.60
L4	3.7	13.4	1.4	02
L5	28.3	18.0	45.4	27.2
TOTAL	374	194	23,335	250

Table 5: Comparison of distribution according to the Sydney System of Reporting and Classification of Lymph Node Cytology

Limitations of the study

The sample size is small, and the cyto-histopathological correspondence is available only for 56.14% cases.

Conclusion

FNAC is a well-established method for diagnosis since its results are compared favorably with surgical biopsy. But due to lack of uniform reporting system and poor reproducibility and overlapping morphology of lesions and no defined criteria for grey zone creating confusion amongst the clinicians. Introduction of Sydney System of Reporting and Classification of Lymph Node Cytology provides uniform standardized reporting system along with recommendation. This boosts the confidence of reporting pathologist along with improving communication between clinicians and pathologists this will in turn help in better management of patients.

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