Research article

An approach to classification and reporting lymph node cytopathology using Sydney system and evaluating the likelihood of malignancy

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ABSTRACT

Introduction and Aim: Fine needle aspiration cytology (FNAC), is a frequently employed diagnostic procedure in identifying lymph node pathology. This study aims to categorise cytological aspirates from lymph nodes according to the Sydney system and in addition determine the likelihood of cancer occurrence in the classified categories.

Materials and Methods: A cross-sectional study analysing lymph node cytology was performed retrospectively between January 2021 to December 2022, and the findings were classified into five groups from L1 to L5 as proposed by the Sydney System. By comparing the diagnoses with the corresponding histological diagnosis, statistical analysis was used to evaluate the probability of malignancy linked with each group.

Results: Out of 279 fine needle aspiration cytology (FNAC) tests performed for lymphadenopathy, 39 cases were compared with histopathological results. The cases classified to the categories L1, L2, L3, L4, and L5 were 11/279 (3.9%), 170/279 (60%), 2/279 (0.7%), and 93/279 (33%) accordingly. The likelihood of developing cancer was found to be 33.33%, 8.8%, 56.4%, 83.33%, and 94.74% for each group.

Conclusion: To achieve uniformity and repeatability in cytopathological diagnosis, the recommended Sydney method of lymph node cytology reporting and classification can be effective.

Keywords: Cytology; lymph node; likelihood of cancer.

INTRODUCTION

Lymphadenopathy evaluation often involves the use of fine needle aspiration cytology (FNAC) as a frequently employed method in diagnosis. It also yields material for evaluating cytomorphology and allows for the use of various additional tests such as microbiological cultures, immunocytochemistry on cell blocks, flow cytometry, polymerase chain reaction, and more (1).

Reporting cytopathology of lymph nodes can be especially challenging due to overlapping morphologies in various conditions. The difficulty is made worse due to paucity of a standardised method for documenting lymph node cytopathology that would help in making the right patient management decisions.

A categorical approach for performing, categorising, and reporting cytological findings in lymph nodes was suggested at Sydney-hosted International Congress of Cytology, May 2019 (2). The approach necessitates the cytomorphological study from lymph nodes aspirates be divided under five groups (3). Categories include: 1- Inadequate/non-diagnostic; 2- Benign; 3- Atypical Cells of Uncertain Significance/Atypical Lymphoid Cells of Uncertain Significance; 4- Suspicious; 5- Malignant.

The study aimed to categorize cytological aspirates from lymph nodes according to the Sydney System and determine the probability of cancer in each diagnostic category. This research is expected to establish a shared understanding and communication framework among medical interprofessionals. Furthermore, the study is intended to offer guidance on management recommendations based on the reporting categories, which may consist of clinical and imaging follow-up or lymph node removal.

MATERIALS AND METHODS

This research comprises the retrospective study of cytology samples taken from lymph nodes using fine needle aspiration (FNA) collected between 1st January 2021 and 31st December 2022. The Sydney System was employed in the classification of the lymph node aspirates (4).

Inadequate/insufficiency: Samples in which a diagnosis could not be made because of technical difficulties, severe tissue necrosis, or a deficiency of cellular material.

Benign: Cytology samples showing granulomatous or suppurative inflammation or infections are regarded as benign. Additional cases include a diverse population that is dominated by small lymphocytes, and germinal centres that contain dendritic and tingible body macrophages.

Atypical cells of indeterminate significance and atypical lymphoid cells of uncertain significance

(AUS/ALUS): Cytology samples showing a mixed population of lymphocytes favouring reactive lymphadenitis nonetheless a follicular lymphoid neoplasm cannot be ruled out due to the presence of

atypical cells, an increase in number of immunoblasts, centroblasts and lymphocytes that are immature.

Suspicious: Cytology samples showing abnormal lymphoid population with atypical features but insufficient for a definitive diagnosis.

Malignant: The malignant category of lymph node aspirates comprises presence of suitable cellular background and the identification of diagnostic cells such as Hodgkin and Reed-Sternberg cells in Hodgkin's lymphoma. This group also includes non-Hodgkin's lymphoma as well as metastatic neoplasms.

Inclusion criteria

Lymph node FNACs

Statistical analysis

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were evaluated after categorising lymph nodes proposed by the Sydney System. Histopathologically confirmed malignancy with malignant (L5), suspicious (L4), or cytological atypia (L3) is referred to as true positive. Any benign entity with a benign (L2) cytological finding that has been histologically or clinically confirmed is considered as true negative. Histopathologically confirmed benign entities with L3, L4, or L5 cytomorphological findings are considered a false positive. Histopathologically confirmed malignant entities categorized under L2 are referred to as a false negative. FNAC samples that produced insufficient or non-diagnostic material (L1) were not included in this analysis. ROM was computed by dividing the sum of cases in each category confirmed histopathologically, by the sum of cases with confirmed malignant lesions.

RESULTS

Cytology samples

Among the 279 patients who underwent lymph node fine needle aspirations, the age ranged from one to 85 years and comprised 128 women (45.8%) and 150 men (53.7%). There were 23 lymph nodes in the axilla (8%), 171 in the cervical region (61%), one in the infraclavicular region (0.3%), two in the iliac crest (0.7%), 21 in the inguinal region (7.5%), one in the occipital region (0.3%), one in the peripancreatic region (0.3%), 47 in the supraclavicular region (16%), and 11 in the submandibular region (3.9%).

Diagnostic categories

The category L1, indicating inadequate or non-diagnostic samples, was assigned to 11 out of the 279-lymph node fine needle aspirations, comprising 3.9% of the total cases. Majority of these cases showed predominantly haemorrhage or necrosis or minimal lymphoid cells. L2 (benign) cytological diagnosis was rendered in 170/279 (60%) cases and included reactive lymph node hyperplasia (n=93 (33%), caseating granulomatous lymphadenitis (n=2 (0.7%), granulomatous lymph node (n=36 (12%) and tuberculous lymphadenitis (n=39 (13%). L3 included two cases (0.7%) and L4 included two cases (0.7%). L5 category had 93 aspirates (33%). Among these 17 (6%) were reported as lymphomas, 75 (26%) as metastases and one as extraosseous plasmacytoma. Among the lymphomas, three (1%) were Hodgkin lymphoma and 12 (4%) were non Hodgkin lymphoma.

Histopathological correlation

Histopathological (HP) correlation was available for 39 cases (Table 1). In L5, 15 cases (5%) had HP correlation. HP confirmed malignancy in all the 15 cases. There were 7 cases of non-Hodgkin lymphoma, four Hodgkin lymphoma cases and four cases of metastasis. Among the four metastases cases, two were metastatic squamous cell carcinomas, one each of metastatic adenocarcinoma and metastatic poorly differentiated carcinoma. In the L1 category, 10 HP were available. Of these, one proved to be NHL and the other turned out to be Hodgkin lymphoma. Ten HP were offered in the L2 category. One of them turned out to be a false negative after HP revealed follicular lymphoma, while the other (Fig. 1 and 2) was NHL. In the L3 category, HP was available in two cases; one (Fig. 3 and 4) proved to be a reactive lymph node, and the other proved to be NHL. In L4, HP confirmed the cytological diagnosis. These were one case each of non-Hodgkin lymphoma and Hodgkin lymphoma (Fig. 5 and 6).

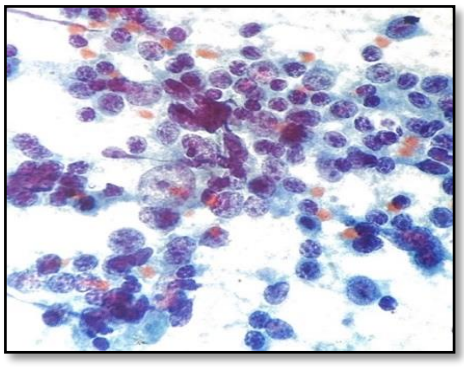

Fig. 1: Smear exhibiting a diverse population of lymphoid cells, including centrocytes, centroblasts, and small lymphocytes. Categorized as L 2, benign. (Papanicolaou stain, 40x)

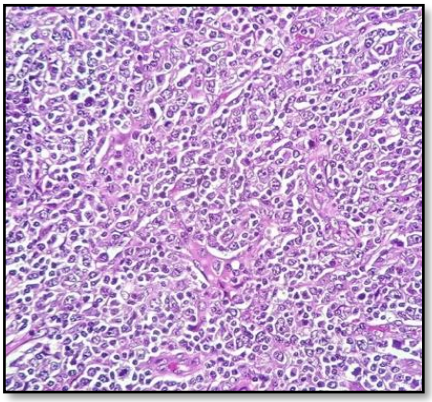

Fig. 2: Large atypical lymphoid cells with vesicular nuclei, conspicuous nucleoli, and minimal cytoplasm observed in a lymph node section. (H&E, 40x)

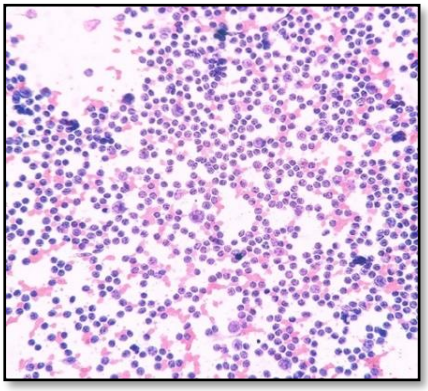

Fig. 3: Smear displaying polymorphic lymphoid cell population with a few large cells having prominent nucleoli, categorized under L3, atypia of undetermined significance. (Papanicolaou stain, 10x)

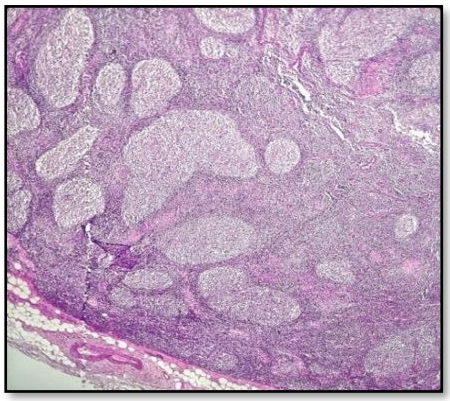

Fig. 4: Section from lymph node showing interfollicular expansion, which was reported as benign reactive lymphadenopathy. (H&E, 10x)

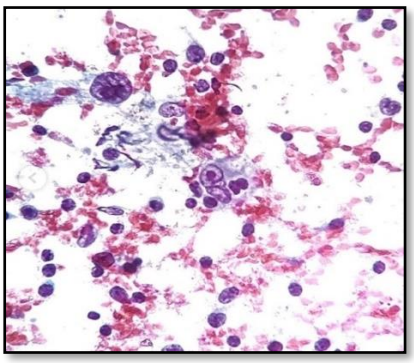

Fig. 5: Smear shows RS cells in a background of mixed inflammatory cells reported as Hodgkin lymphoma. Categorized into L5, malignant. (Papanicolaou stain, 40x)

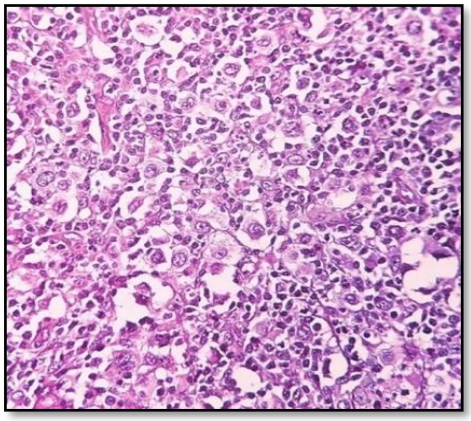

Fig. 6: Section from lymph node showing RS cells in a background of mixed inflammatory cells. (H&E, 40x)

Immunohistochemistry

To confirm suspected cases of lymphoma, immunohistochemistry (IHC) was carried out according to procedure. To differentiate between reactive lymphadenopathy and lymphoma, a panel of kappa and lambda antibodies was used. The panel further divided the patients into subcategories using CD5, CD79a, CD 20, CD3, LCA, CD10, Bcl-6 and Bcl-2, among other markers.

Our study revealed the statistical analysis as follows- sensitivity 94%, specificity 90%, Positive predictive value 94.7% and Negative predictive value 90%. The probability of malignancy was assessed for each category in cases where there was a histological correlation. Lowest ROM was seen in L2 (10%). L3 showed ROM of 50%. Highest ROM was seen in L4 and L5 (100%) (Table 2)

Table 1: Comparison between the cases in each category and the final diagnosis determined by histopathological correlation

Categorization based on Sydney system	**Non neoplastic lesions**	**Malignant**
L1 (11 cases)	Granulomatous lymphadenitis (3cases) Reactive lymphadenopathy (3 cases) Caseating granulomatous lymphadenitis (one case) Dermatopathic lymphadenitis (one case)	NHL (one case) HL with granuloma (one case)
L2 (10 cases)	Reactive lymphadenopathy (2 cases) Granulomatous lymphadenitis (4 cases) Castleman disease (one case) Tuberculous lymphadenitis (one case)	Non Hodgkin lymphoma (2 cases)

L3 (2 cases)	Reactive lymphadenopathy (one case)	Follicular lymphoma (one case)
L4 (2 cases)	Nil	Hodgkin lymphoma (one case) Non Hodgkin lymphoma (one case)
L5 (15 cases)	Nil	Non Hodgkin lymphoma (7 cases) Hodgkin lymphoma (4 cases) Metastasis (4 cases)

Table 2: Categorizing the likelihood of cancer into different diagnostic categories using the Sydney system

Cytological classification according to the Sydney System	**Malignant lesions with histopathological confirmation**	**Overall likelihood of cancer %**
L1	2	20%
L2	1	10%
L3	1	50%
L4	2	100%
L5	15	100%

DISCUSSION

Aspiration cytology is frequently employed as the first step when assessing lymphadenopathy with an unknown aetiology. Rapidity, cost-effectiveness, minimal invasiveness and its broad usefulness in the assessment of lymphadenopathy is facilitated by its capacity to offer material for a number of supplementary procedures (5,6). The evaluation of lymph nodes in cytology can be challenging. Use of lymph node FNAC reporting is still not accepted uniformly by clinicians. This is brought about by absence of guidelines and standard reporting procedures. It is necessary to examine the risks and estimate the likelihood of developing cancer.

In this study, lymph node FNACs were stratified into categories based on the Sydney system. ROM in category L1 was observed to be 20%. This was comparable to the study by Baruah *et al.,* (7) wherein ROM was calculated to be 28.5%. L2 category showed ROM of 10%. One case of follicular lymphoma that was observed in this category showed a polymorphous population of lymphoid cells that could have been mistaken as reactive lymphadenopathy. This result matched the findings of the study by Baruah *et al.,*(7), wherein they observed 7.8% cases in this category. Gupta *et al.,* (2) conducted research that revealed a risk of malignancy (ROM) of 11.5%, while Vigliar *et al.,* (3) observed a ROM of 1.92% in their study.

Most reporting systems now use the L3 category in an effort to preserve high malignant and benign categories' positive and negative predictive values, respectively. Their investigation revealed ROM to be 50%. ROM was 54.5% in L3 category, according to the study conducted by Baruah *et al.,*(7). Histopathology revealed one case each of NHL and reactive lymphadenopathy. The case that was classified as reactive lymphadenopathy in histology showed interfollicular expansion; therefore, the cytological smears revealed cells with large irregular nuclei, conspicuous nucleoli, sparse cytoplasm, which led to an erroneous diagnosis L3. L4 and L5 showed a 100% risk of malignancy. Due to the use of ancillary methods in their research, Vigliar *et al.,* (3) calculated ROM to be 100% for both L4 and L5 categories. In the study by Ahuja and Malviya (8), 1205 aspirates from the lymph node were classified as 53 (4.4%) non-diagnostic, 488 (40.5%) benign, 10 (0.8%) AUS/ALUS, 275 (22.8%) suspected for malignancy, and 379 (31.5%) malignant. The risk of malignancy was 9%, 2%, 37%, 97%, and 98% for each category, respectively. According to Caputo *et al.,* (9) study, ROM ranged from 66% for L1, 9.38% for L2, 28.6% for L3, 100% for L4, and 99.8% for L5 categories. The sensitivity, specificity, PPV and NPV observed in FNAC from lymph node aspirates were all 97.94%, 96.92%, 99.58% and 86% respectively. The NPV, PPV, sensitivity, and specificity were found to be comparable to those of prior research done by Baruah *et al.,* (7), with sensitivity of 98.4%, specificity of 95.3%, PPV of 96.2% and NPV of 98%.

CONCLUSION

The proposed Sydney approach for reporting and classifying lymph node cytology can assist in attaining consistency and repeatability of cytopathological diagnosis. It will result in a reasonably accurate estimate of the risk of malignancy for subsequent clinical therapy.

CONFLICT OF INTEREST

None.

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