Journal of Chemical Health Risks

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JCHR (2024) 14(3), 1425-1430 | ISSN:2251-6727

Diagnostic Efficacy of Sydney System of Classification of Lymph Node Cytology with its Histopathological Correlation in the Diagnosis of Lymph Node Malignancy and Assessement of Risk of Malignancy.

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(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS
Lymph node cytology, Sydney system, HP correlation

ABSTRACT:
Background:Fine needle aspiration cytology(FNAC) has proved to be one of the minimally invasive, rapidand cost-effective method in the diagnosis of all kind of lymph node(LN)lesions. The Sydney system of cytological classification of LN- FNACs was proposed to bring uniformity in reporting LN cytology.The present study aims at reclassifying LN-FNACs according to the Sydney system, assessing its diagnostic accuracy and calculating the risk of malignancy (ROM) associated with each of the diagnostic categories with histopathological correlation.Results: This is 3year retrospective study carried out between July 2020 to June 2023 at a tertiary care hospital. A total of 660 patients between 5 to 75 years of age were included.Male to female ratio was 2:1. Commonest group of LN involved was cervical group. According to Sydney system LN cytology cases were categorized into L1: inadequate/nondiagnostic (46), L2: benign (296), L3: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance (50), L4: suspicious (104) and L5: malignant (164). HP correlation was obtained in 484 cases.Risk of malignancy for various categories were50%,12.5%,71.42%,95.83% and 100% respectively. The overall sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of LN-FNA were98.73%,90.5%, 90.12%,97.14% and 99.17% respectively. Conclusion:The application of the newly proposed Sydney system for reporting LN cytopathology produces uniformity in cytological diagnosis, improves the diagnostic accuracy and helps in risk stratification.

Introduction

Fine-needle aspiration cytology (FNAC) has always been a routine diagnostic tool for the preliminary evaluation of lymphadenopathy of unknown aetiology. Even though the histopathology (HP) still remains as the gold standard in the diagnosis of malignant lymphadenopathies, but with the advent of new ancillary techniques, accuracy of FNAC has improved. FNAC has proved to be one of the minimally invasive, rapidand cost-effective method in the diagnosis of all kind of lymph node (LN) lesions.[1]

In May 2019, Sydney system of cytological classification of LN-FNACswas proposed at the 20th International Congress Society. It was endorsed by International Academy of Cytology(IAC) and the European Federation of Cytology Society(EFCS). This has aided towards the uniformity in categorizing, classification and reporting of LN cytopathology.According to this system, the aspirates

Journal of Chemical Health Risks

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JCHR (2024) 14(3), 1425-1430 | ISSN:2251-6727

from theLNs are categorized into 5 categories:Category I/L1: inadequate/nondiagnostic, category II/L2: benign, categoryIII/L3: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance, category IV/L4: suspicious and category V/L5: malignant.[2,3]

The present study aims at reclassifying LN-FNACs according to the Sydney system, assessing its diagnostic accuracy and calculatingthe risk of malignancy (ROM) associated with each of the diagnostic categories when correlated with HP.

Materials and methods:

This is 3year retrospective study carried out between July 2020 to June 2023at a tertiary care hospital. A total of 660 patients between 5 to 75 years of age, who had undergone LN-FNACs were enrolled for the study with one year follow-up. Post chemo-radiotherapy treatment cases were excluded. Their clinical details, examination findings and relevant investigation results were retrieved from medical records. These LN-FNAC smears were reviewed and were recategorized according to newly proposed Sydney system. HP correlation was obtained in 484 cases. Only the malignant cases were considered as positive for calculation of ROM. All statistical analysis was done using SPSS version 29.Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated with the histologic diagnosis being the gold standard and considering malignant cases as positive.

Results:

Total of previously analysed 660 LN FNAC cases between July 2020 to June 2023 were considered for the study.The most common age group being 55-64years for both benign and malignant lesions(Figure 1).Male to female ratio was 2:1. Commonest group of LN involved was cervical group, followed by axillary, inguinal, mediastinal,submandibular and submental nodes. Out 660 cases,592(89.7%)cases had localized lymphadenopathy and 68(10.3%)cases had generalised lymphadenopathy.

In the present series, 46/660 were recategorized into L1: inadequate/nondiagnostic, 296/660 into L2: benign, 50/660 into L3: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance, 104/660 into L4: suspicious and 164/660 intoL5: malignant(Figure2)

The benign category (L1) was the most frequent constituting 296(45%)cases.The commonest lesion in this category was reactive lymphadenitis, followed by granulomatous lymphadenitis and sinus histiocytosis. Second most common category was L5: Malignant which mainly constituted mainly metastatic tumors (120 cases) and lymphomas(44cases).(Table 1)

HP correlation was obtained in 484/660cases and most of the cases correlated with cytological diagnosis(Figure 3). HP correlation with L5 category included maximum number of cases(45.04%). Thus89.9%(196/218)cases of Category 5 proved to have similar histology as the malignant cytological diagnosis. Remaining ones which were reported as poorly differentiated carcinoma turned out to lymphomas, mucoepidermoid carcinoma,sinus histiocytosis.

The ROM was calculated for each diagnostic category considering HP as gold standard where category L5 had the highest ROM (100%) and L2 had least ROM (12.5%)(Table 2).The present study statisticallyproves to have thesensitivity of 98.73%, specificity of 90.5%, PPV of90.12%, NPV of 97.14%, and accuracy of99.17%in LN FNAC diagnosis.

There were no discordant cases in category L5 as all thecases that had HP follow-up were reportedas malignant in cytology.Chi-square test revealed that this difference between Category II and V was statistically significant ($P < 0.05$).

Discussion:

The cytological evaluation of lymphadenopathies can be enormously thought-provoking. But with advent new auxiliary techniques and proper handling of the samples, when united with clinical data it ensures pleasing diagnostic accuracy. In order to fetch homogeneity in reporting of lymph node FNAC and to guide management the Sydney system has been proposed.In the present study the commonest age group of LN cytology was 55-64years when compared to <20years of age in Baruah AK et al study. [4] Male preponderance was noted.[5] Cervical LN was the commonest site of lymph node FNAC followed by

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JCHR (2024) 14(3), 1425-1430 | ISSN:2251-6727

axillary in present as well as in many studies.[4,5] Among various categories in the present study, L2 category showed more prevalence (45%) which could be due to increased cases of reactive and granulomatousinflammation. On the contrary, Vigliar E et al.and Gupta P et al.showed equal distribution between benign and malignant lesion categories.[7,8](Table 3) The present study showed the capability of the Sydney system to stratify lymph node FNACs into categories and calculate ROMs.Interestingly, ROM of L1 category showed remarkably high (50%) value, perhaps due to the small number of histological controls available.This was in par with Vigliar E et al observation.[7] L2 category showed the lowest ROM (12.5%) similar to Gupta P et al(11.5%),but higher than Vigliar E et al (1.92%)and Baruah et al (7.80%). [4,7,8]But cases of histiocytosis turned out to be metastasis which may be because of partial replacement of lymph node by the metastasictumor.On the other hand morphology of neoplastic lymphoid cells might have been mistaken as normal cells in case of lymphoma. Hence the utility of FNAC as a noninvasive procedure in such settings cannot be exaggerated universally.[7] In our experience,L3 category represents an heterogenous group of entities that showed higher ROM of 71.42%, parallel to that of Shanmugasundaram S et al (76.9%) but comparatively higher than that of Vigliar et al(58.3%) and Gupta et al(66.%). [6,7,8]

L4 and L5 showed the highest ROM of 95.83% and 100% respectively which is comparable with many studies. [4,5,6,8] Hence we can safely assume that a "second-line" approach of management for L4, including FNC repetition with acquisition of additional material for ancillary studies or core needle biopsy may be considered as ROM is higher.[7]

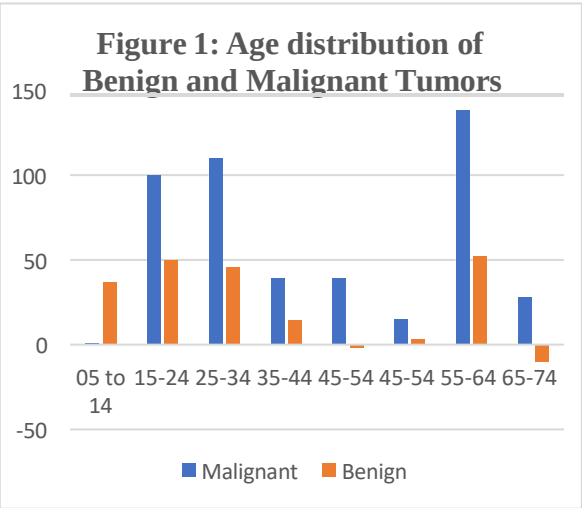
The present study showed higher sensitivity (98.73%) in diagnosing FNA LN lesion by using Sydney system of reporting to be similar to the other studies by Vigliar E et al.[7], and Cupato A et al.[10] But specificity(90.8%) is comparatively lower than other studies(Table 4). But the present study had higher diagnostic accuracy when compared to Baruah A.K et al and Gupta P et al.[4,8]

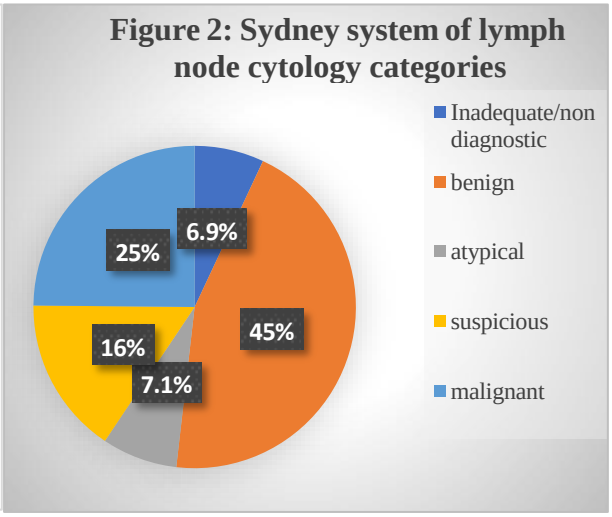
The main limitation of the study is lack of HP correlation in all cases as it was a retrospective study and lacked followup. However, the present study included a variety of LN pathologies.

Conclusion:

The application of the newly proposed Sydney system for reporting lymph node cytopathology improves diagnostic accuracy and achieves uniformity and reproducibility in cytological diagnosis.It also will bridge the communication gap between the clinicians and pathologist for better patient management. The specificity and positive predictive value of FNAC are high when category L3 (atypical) is considered negative for malignancy.

Figures:





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JCHR (2024) 14(3), 1425-1430 | ISSN:2251-6727

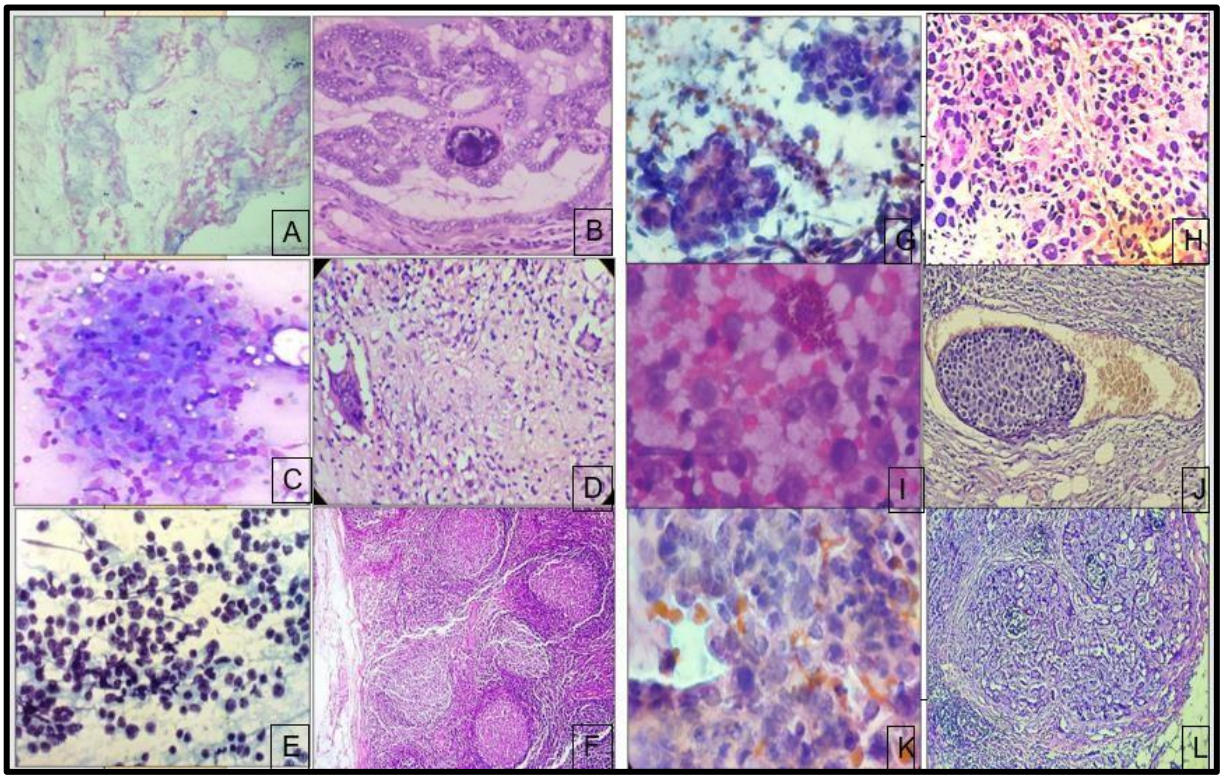

Figure 3: Microphotographs showing Lymph node cytology(A,C,E,G,I,K) and its corresponding Histopathology(B,D,F,H,J,L) .

A: L1-Cyst fluid aspirated(inadequate)-cervical lymph node, B:Metastatic Papillary Carcinoma , C: L2-Granulomatous Lymphadenitis- cervical LN , D: Tuberculous Lymphadenitis, E: L3-Atypical lymphoid proliferation- axillary LN, F:Follicular Lymphoma, G: L4-Suspicious for adenocarcinoma- Hilar LN, H: Metastatic Adenocarcinoma of Lung, I:L4- Suspicious for Malignancy-inguinal LN, J:Metastatic Melanoma of Foot, K: L5:Malignant- Carcinoma breast -axillary LN, L: Metastatic Invasive (Ductal)Carcinoma Breast.

Table 1: Details of FNAC cases with cytological diagnosis

Sydney system of LN cytology categories	**No of cases**	**Subcases (LN FNACs)**
L1: Inadequate/ nondiagnostic	46	Non representative (13),cystic fluid (7),scant lymphoid tissue(15),blood only(9),necrosis(2)
L2: Benign	296	Lymphadenitis- Reactive (138), Granulomatous(105), suppurative(26), histiocytosis (27)
L3: Atypical	50	atypical lymphoid cells(18), atypical nonlymphoid cells(30), atypical cell(2)
L4: Suspicious	104	Lymphoid: NHL (20) HL (30); Metastatic(54)
L5: Malignant	164	Lymphomas=54(NHL=15, HL=39), Metastatic:110 (SCC (47), Adenocarcinoma (42), Small Cell Carcinoma(07), Melanoma(5), Papillary

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JCHR (2024) 14(3), 1425-1430 | ISSN:2251-6727

		carcinoma thyroid(5),Anaplastic carcinoma(4))
Total	660	

Table 2:FNAC with histopathological(HP) correlation and calculated rate of malignancy (ROM) in each category

Sydney system of LN cytology categories	**Total no of FNAC cases(%)**	**FNAC with HP correlation**	**HP Benign**	**Confirmed malignant cases**	**ROM%**
L1: Inadequate/ nondiagnostic	46(6.9%)	12(2.48%)	6	6	50
L2: Benign	296(45%)	144(29.75%)	126	18	12.5
L3: Atypical	50(7.1%)	14(2.89%)	4	10	71.42
L4: Suspicious	104(16%)	96(19.84%)	4	92	95.83
L5: Malignant	164(25%)	218(45.04%)	0	218	100
Total	660(100%)	484(100%)	140	344	

Figure 3. Comparison of distribution of cases according to various categories in the present study with other studies [4-9]

Sydney system of LN cytology categories	**Baruah A.K et al[4]**	**Pandya D et al[5]**	**Shanmuga-sundaram S et al[6]**	**Vigliar E. et al[7]**	**Gupta P et al [8]**	**Ahuja S et al [9]**	**Present study**
L1: Inadequate/ nondiagnostic	3.18%	4.12%	10.57%	6.7%	4.1%	4.4%	6.9%
L2: Benign	64.09%	64.34%	54.6%	34.7%	48.6%	40.5%	45%
L3: Atypical	20%	3.09%	4%	8.3%	0.5%	0.8%	7.1%
L4: Suspicious	3.63%	13.4%	3.7%	4.3%	1.4%	22.8%	16%
L5: Malignant	9.09%	18.04%	27.04%	46%	45.4%	31.5%	25%

Table 4: Comparison of various statistical parameters of present study with other similar studies[4,5,7,8,9]

Table 4: Statistics Parameters	Baruah A.K et al [4]	Pandya D et al [5]	Vigliar E. et al [7]	Gupta P et al [8]	Cupato A et al[10]	Present study
Sensitivity	80.36%	95.23%	98.4%	79.9%	97.9%	98.73%,
Specificity	85.71%	94.11%	95.3%	98.1%	96.2%	90.5%,
PPV	70.31%	98.36%	96.3%	98.4%	99.5%	90.12%,

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NPV	91.20%	84.21%	98.1%	83.1%	86.3%	97.14%,
Diagnostic accuracy	84.13%			89.3%		99.17%

Acknowledgements: The authors declare that there is no conflicts of interest. There was no financial support provided for the study.

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