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Application of the proposed Sydney system of reporting lymph-node cytopathology: A retrospective study in a tertiary institute

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ABSTRACT

Pituitary apoplexy is a significant complication of pituitary adenomas, posing diagnostic challenges, particularly when patients exhibit indications of meningeal irritation or electrolyte imbalances. When left undiagnosed and untreated, the outcomes can be dire. This condition frequently marks the initial clinical manifestation of most pituitary adenoma cases. Its pathophysiology is linked to pituitary enlargement, characterized by hemorrhage or ischemia. In the present case report, we describe a case of pituitary apoplexy that manifested subsequent to major abdominal surgery. The patient presented with symptoms, including headaches, hypertension, and visual impairment. Following a confirmed diagnosis through a CT scan, the patient underwent surgical decompression via a transsphenoidal approach. In conclusion, this case underscores the importance of a holistic approach that encompasses clinical vigilance, precise diagnostic evaluations, and timely interventions to address pituitary apoplexy. Through continued research and collaborative efforts, we endeavored to enhance our ability to recognize, diagnose, and manage pituitary apoplexy, ultimately contributing to improved patient care and outcomes.

Keywords: pituitary apoplexy, hepatic hydatid cyst resection, major abdominal surgery, pituitary adenoma, surgical intervention, Saudi Arabia

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INTRODUCTION

Fine Needle Aspiration Cytology (FNAC) is one of the most routinely used techniques for evaluating Lymphadenopathy and is well accepted by patients as well as consultants due to its minimally invasive, safe, fast and inexpensive form of evaluating lymphadenopathy [1]. It also provides cytomorphological information and material for ancillary testing [2]. FNA is particularly useful for evaluating deep-seated lymphadenopathy (e.g., abdominal, mediastinal, retroperitoneal) where surgical intervention carries risk. It helps differentiating benign reactive processes from malignant neoplasms and provides information for staging [3]. Although there is no formal classification, Usually, they are classified in several broad categories: nondiagnostic (unsatisfactory), benign, suspicious and malignant [4].

On the other hand, FNAC has some limitations, mainly its ability to diagnose false-negative or false-positive [5]. This may be due to inadequate or suboptimal sampling. This includes lesion type and size, site, number of passes, FNA needle size, and expertise of the cytopathologist [6].

Interpretation of LN FNAC smears is not easy because of considerable similarities and overlapping features among the plethora of pathologies that are encountered. This difficulty is compounded by the lack of a uniform reporting system for lymph node cytology, which could guide further management.

However, there are no guidelines and no classification of cytopathological diagnosis for the accurate evaluation or diagnosis of lymphadenopathy. Therefore, maintaining consistent reporting and increasing interdisciplinary understanding of procedural outcomes is very important.

A group of experts have proposed, The Sydney system for reporting lymph node fine needle aspiration cytology. This proposed Sydney system is based on a review of the international literature and on the expertise of the committee members, that integrates clinical and imaging information with key diagnostic cytopathological features and ancillary techniques. According to this system, the cytologic aspirates from lymph nodal masses should be categorized into 5 different diagnostic categories based on the specific cytologic features observed on the smears. These categories include Category I/L1: inadequate/nondiagnostic, category II/L2: benign, category III/L3: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance, category IV/ L4: suspicious, and Category V/L5:

malignant [7].

The purpose of this study was to categorize LN aspirates according to the Sydney system for reporting lymph node cytology and to document sensitivity, specificity, the Risk Of Malignancy (ROM), diagnostic accuracy, and utility of the Sydney system of reporting.

MATERIALS AND METHODS

Study Design

This was a retrospective study conducted over one year, from 1st Jan 2019 to 31st Dec 2019. The study was undertaken at the Department of Pathology, Jagadguru Jaya deva Murugarajendra Medical College, Davangere, Karnataka, India. The study was approved by the institutional ethics committee. Detailed demographic, clinical history, clinical diagnosis and FNAC reports were retrieved from the cytopathology electronic data base.

Inclusion criteria

All palpable LN aspirates from all age group and both sexes were included

Exclusion criteria

Non lymph node aspirates were excluded.

Sampling, Smear preparation and staining

In all cases, FNA was performed with all aseptic measures after obtaining informed consent from the patient. For superficial lymph nodes, FNAC was performed percutaneously using a 10ml 24G needle. For deep lymph nodes, ultrasound guided FNAC was performed using a 20/ 22guage spinal needle. After obtaining material from aspiration, smears were made on 3 slides in which one air-dried smear was stained with May-Grunwald-Giemsa (MGG) stain and two wet-set smears, one with Papanicolaou staining and the other with hematoxylin and eosin (H & E). Additional smears were prepared according to clinical suspicion and the nature of the aspiration. For example, in the case of pus aspiration, an air-dried smear for Ziehl-Neelson staining was done.

All the smears were retrieved and independently reported and classified by 2 pathologists as per The Sydney system of reporting lymph node cytopathology and they were blinded to the final histopathological diagnosis. Any discrepancies in the classification were resolved by consensus.

Histopathologic correlation

The histopathology database was searched for the histopathology specimens of the included cases. Cytopathological diagnoses were correlated with available histopathological diagnoses. Wherever available discordant cases were reviewed and the probable reason for discordance was ascertained.

Statistical analysis

SPSS 24th version was used to calculate the statistical significance

To document the sensitivity, specificity, diagnostic accuracy, Positive Predictive Value, Negative Predictive Value. ROM between 5 Categories was calculated as well.

RESULTS

A total of 300 LN FNAC samples were included in the study. 145(48%) were males and 155 (51.7%) were females. The mean age of the patients was 34.34 years. Most commonly aspirated lymph nodes were cervical groups of lymph nodes 173 (57.7%) followed by involvement of the supraclavicular 22 (9.3%), axillary 25(8.3%), mandibular 22 (7.3%) and inguinal 15(5%), respectively (Table 1).

Tab. 1. Shows various sites of FNA done for lymph node

SITE	No. of case	Percentage (%)
Cervical	173	57.70%
Supraclavicular	28	9.30%
Axillary	25	8.30%
Submandibular	22	7.30%
Inguinal	15	5.00%
Auricular	10	3.30%
Triangle neck	10	3.30%
Clavicular	4	1.30%
Nape of neck	4	1.30%

Submental	3	1.00%
Jugulodigastric	2	0.70%
Ileac	1	0.30%
Parotid	1	0.30%
hypochondrial	1	0.30%
Lumbar	1	0.30%
Total	300	100%

Diagnostic categories

In the present series, a total of 35 cases (11.6 %) were deemed to be category (L1) i.e., non -diagnostic /inadequate for interpretation. Category benign (L2) included 188 cases (62.8%) and included reactive lymphadenitis 87 (46.2 %), granulomatous lymphadenitis 51 (27.1%), caseating granulomatous lymphadenitis 35 (18.6%), suppurative lymphadenitis 12 (6.3%), non-specific lymphadenitis 1(0.5%), sialadenitis 1 (0.5%), BCG lymphadenitis 1(0.5%).
No cases were recategorized under category L3. Category L4 included 1 case which was reported as suspicious of malignancy. Category V (L5) includes 76 cases. These included 65 cases of metastatic carcinoma and 11 cases of lymphomas. Among 65 (85.52%) cases of metastatic carcinomas, 32 (42.1%) cases were metastatic squamous cell carcinoma, 24 (18.24) cases were metastatic epithelial carcinoma, 8 (10.5%) cases of metastatic adenocarcinoma and 1 (1.3%) cases of infiltrating ductal carcinoma which was a known case of breast carcinoma. 11 cases of lymphoma that included 8 cases of (10.5%) non-Hodgkin's lymphoma and 3(3.9%) cases Hodgkin's lymphoma (Table 2).

Tab. 2. Categorization according to Sydney system for reporting LN- FNAC

Category	No. of cases	Percentage (%)
I (L1) -Inadequate	35	11.60%
II (L2) – Benign	188	62%
III (L3) - ALUS/AUS	0	0
IV (L4) – Suspicious	1	0.33%
V (L5) – Malignant	76	25.30%

Corresponding histopathology samples were available for only 26 cases (8.6 %). From Category I – only one case was available for correlation and was found to be reactive lymphadenitis on biopsy. From Category II – 22, cases of histopathology were available for correlation. Of which 11 (42.3%) cases of reactive lymphadenitis on FNA were reported as caseating granulomatous lymphadenitis on histopathology and another 11 cases of caseating granulomatous lymphadenitis on FNA remained the same on biopsy as well. Category III and IV there are no cases available for correlation. Category V- Only 3 cases were available for correlation and included one case each of NHL, HL and metastatic adenocarcinoma, which remained the same in histopathology as well (Table 3).

Tab. 3. List of the cytology Diagnoses and the Corresponding Histopathology Diagnosis with the Concordant and discordant cases in each Diagnostic category

Cytologic diagnosis as per the proposed Sydney system for reporting lymph node cytopathology	Histopathology diagnosis
Category I-Inadequate	Reactive lymphadenitis
Category II- Caseating granulomatous lymphadenitis	Caseating granulomatous lymphadenitis
Category II- Reactive lymphadenitis	Caseating granulomatous lymphadenitis
Category V- Metastatic adenocarcinoma	Metastatic adenocarcinoma
Category V- Non- Hodgkin's lymphoma	Non- Hodgkin's lymphoma
Category V- Hodgkin's lymphoma	Hodgkin's lymphoma

In our study, FNAC was found to have a sensitivity of 85%, specificity of 100%, positive predictive value of 100 %, negative predictive value of 10 %, and diagnostic accuracy of 85 % in differentiating malignant from benign lesions based on the Sydney system of reporting lymph nodes from the conventional system (Table 4).

Tab. 4. The Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Accuracy of Sydney system of reporting from conventional system

Agreement between two methods of assessment	Malignant & benign	Non- Specific	Total
Malignant & benign	251	0	251
Non- Specific	44	5	49
Total	295	5	300

The risk of malignancy (ROM) in our study wherein a histopathological diagnosis was available was calculated. The ROM was highest in category V (100%) and for the rest of the categories, i.e. I, II, III & IV, it remained 0%. Since, larger number of cases the corresponding histopathology correlation under these categories was unavailable (Table 5, figure 1).

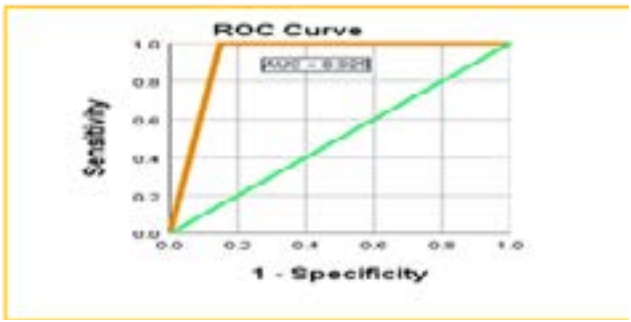

Fig. 1. Risk of Malignancy Associated with each Diagnostic of the proposed Sydney system for Reporting Lymph node cytopathology of available 26 cases

Tab. 5. Risk of Malignancy Associated with each Diagnostic of the proposed Sydney system for Reporting Lymph node cytopathology of available 26 cases

Cytological category as per the proposed Sydney for reporting lymph node cytopathology	Total no. of cases with histopathologic diagnosis in each diagnostic category N=26(%)	Total cases reported as malignant on histopathology N=26 (%)	Overall risk of malignancy (%)
Category I (L1): Non-diagnostic/ inadequate (n=35)	1(3.8%)	0(0%)	0(0%)
Category II (L2) – Benign(n=188)	22(84.6%)	0(0%)	0(0%)
Category III (L3) - ALUS/AUS(n=0)	0(0%)	0(0%)	0(0%)
Category IV (L4) – Suspicious(n=1)	0(0%)	0(0%)	0(0%)
Category V (L5) –Malignant(n=76)	3(11.53%)	3(11.53%)	3(100%)

DISCUSSION

In recent decades, LN-FNA has been used as a diagnostic modality. Cytological evaluation of lymph nodes can be extremely difficult. As of 2020, there is no well-established reporting system followed by cytopathologists around the world. Like standard reporting system methods for thyroid (Bethesda), salivary glands (Milan), etc., to maintain uniformity and better communication between clinician and pathologist, an international expert group of cytopathologists has proposed The Sydney system of reporting lymph nodes. [7,8] To our knowledge, only a few studies have validated the proposed Sydney system for LN-FNA

There was a total of 300 LNFNAC samples which were categorized according to the Sydney system in our study. For subsequent comparison and correlation, only 26 biopsy specimens were available from these aspirates.

In category I, only 1 case was available and was found to be reactive lymphadenitis on biopsy. On FNAC, this case showed RBCs and few scattered lymphocytes (Figure 2 & 3).

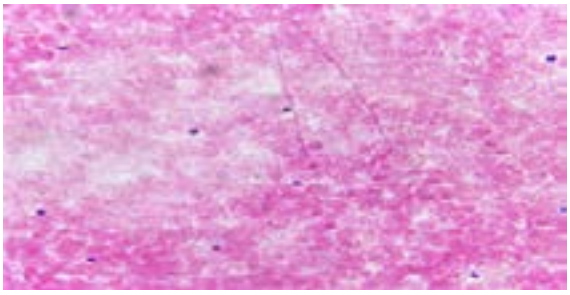

Fig. 2. Inadequate smear showing RBCs on cytology smear

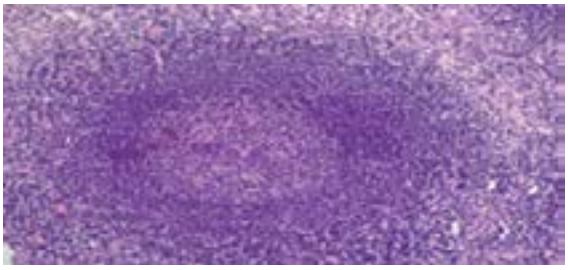

Fig. 3. showing Reactive lymphadenitis on biopsy

This perhaps reflects a sampling error which depends on the expertise of the cytopathologist. It can also be due to fibrotic nodes, necrosis, haemorrhage and cystic degeneration [9].

In such a situation, a repeat aspiration can be performed by a more experienced cytopathologist and ROSE (Rapid on-site evaluation) technique can be employed to check for adequacy of the sample, which also has been recommended by the Proposed Sydney system. Studies have shown that ROSE also reduces inadequacy as well as false negative rates [10,11].

We also recommend that clinically suspicious cases, but inadequate FNAC should be closely followed up either by repeat image guided FNA or excision biopsy to rule out or confirm malignancy.

Of the total 188 cases in Category II, only 22 cases had histopathology correlation, 11cases found to be concordant with all 11 cases being caseating granulomatous lymphadenitis, on cytology as well as histopathology

The remaining 11 cases reported as reactive lymphadenitis on cytology turned out to be discordant and showed caseating granulomatous lymphadenitis on biopsy (Figure 4 & 5). On reviewing these slides, the smear revealed ill formed granulomas in a reactive background which showed a polymorphous population of lymphocytes and a good number of plasma cells which were probably missed during the initial cytologic examination.

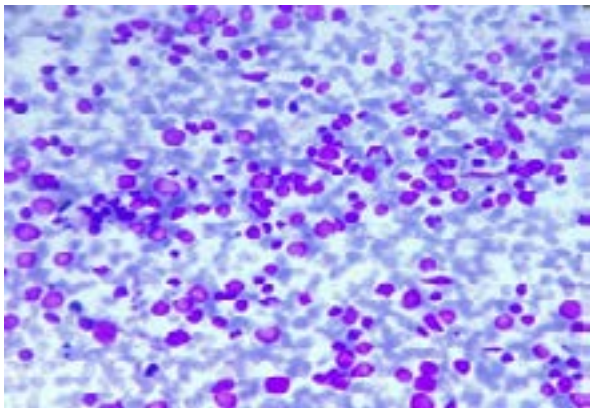

Fig. 4. Reactive lymhadenitis on cytology smear

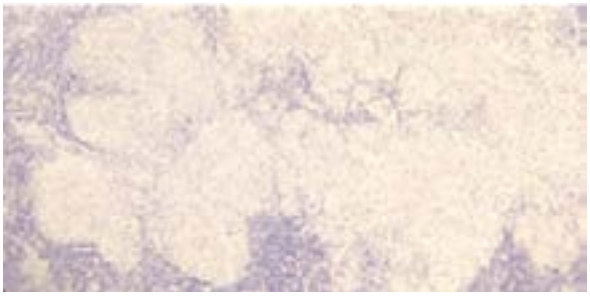

Fig. 5. Showing caseating granulomatous lympadenitis on biopsy

With the knowledge of histopathological diagnosis, we can acknowledge sampling as well as interpretation errors. It was mainly because of the presence of florid reactive lymphoid cells in the background, which is striking and leads to misinterpretation of reactive lymphadenitis and the missing on the ill-formed granulomas [12].

Paliwal et.al's study showed polymorphs with necrosis with or without epithelioid granulomas and another series of cases in Gupta et al study showed a much higher percentage of cases showing epithelioid cell clusters with or without langhans giant cells with necrosis [13, 14].

Thus, we recommend that cases with strong clinical suspicion of tuberculosis should also be advised for additional tests like CB-NAAT, culture and sensitivity for the benefit of the patients [15].

We had no cases classified under category III and IV. We attribute this to our pathologist who probably has more than 10 years' experience in the pathology field and also strictly followed the Sydney categorical system which helped in precise categorisation of the FNAC's.

Of a total of 76 cases in category V, a histopathological diagnosis was available for 3 cases. All these 3 cases were concordant on histopathology as well. We had one case of Hodgkin's lymphoma with FNAC smears showing a few mononuclear Hodgkin Reed-Sternberg (RS) cells, on a polymorphic reactive background (Figure 6 & 7). FNAC smears of a non- Hodgkin's lymphoma showed large cells with round to irregular nuclei, a thin rim of cytoplasm against the background of small lymphocytes, intermediate and larger cells with prominent 1-2 nuclei, and one case of metastatic adenocarcinoma showed tumor cells arranged in acinar pattern and occasionally singly scattered. The individual cells are usually cuboidal to columnar with indistinct cell border, an increase in nucleocytoplasmic ratio, a moderate amount of vacuolated eosinophilic cytoplasm and nuclei with prominent nucleoli.

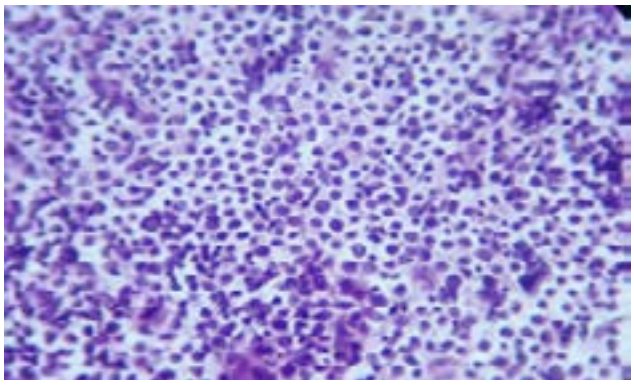

Fig. 6. PAP stained smear shows NHL

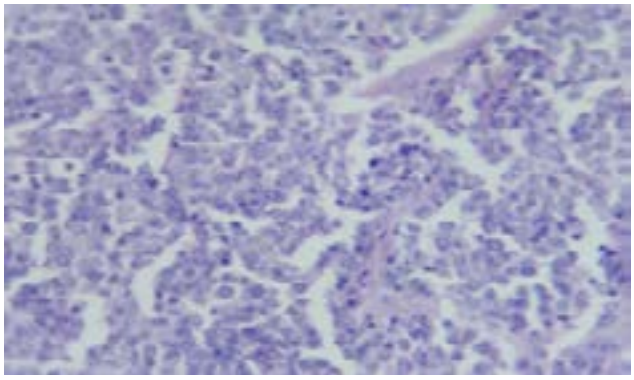

Fig. 6. Smear from a case reported NHL on cytology, showing large atypical lymphoid cells

The total number of corresponding histopathology cases was low in our study. This is because the bulk of our study cases included category II, V and I. Category I and II cases don't require biopsy for treatment of the patient and hence they were advised to follow up in OPD after a FNAC diagnosis was rendered. Whereas patients in Category V were referred to higher centres for further management. As facilities like ancillary tests, cell-block immunocytochemistry (ICC), flow cytometric immunophenotyping and treatment options for radiotherapy or chemotherapy are not available in our centre.

All aspirates for which subsequent histopathology was available. The percentages of cases in each category and risk of malignancy (ROM) for each cytological diagnosis was calculated. In the present series, the risk of malignancy (ROM) turned out to be 100% for category L5 whereas the rest turned out to be 0%. This is attributed to a smaller number of histopathology specimens available in categories I, II, III, & IV.

When we compare our result of risk stratification with another study conducted by vigliar et al they obtained an increased ROM in category L1, constituting up to 50 % and this, is may be because of lack of availability of histopathological control. [16] So, we believe that the ROM associated with each diagnostic category of proposed the Sydney system, if calculated separately using cytomorphological evaluation and after combining with histopathology and ancillary techniques might not differ significantly.

In our study, we had our limitations, mainly being a single institution, retrospective nature, lack of sufficient sample for histopathological correlation under different categories and follow-up de-

tails. Other techniques like lack of ancillary techniques and loss of follow up of the patients were also major limitations of the study. Therefore, further studies with larger sample sizes and better ancillary techniques for confirmation are required to assess the validity, reliability and reproducibility of this system.

Both cytopathologists involved in the categorisation of lymph node aspirates were of the opinion that the proposed system is convenient, easy to understand, adapt to and also implement in an under resourced setup like ours.

In conclusion, FNAC, coupled with ancillary techniques, is effective in the evaluation of lymphadenopathies; the implementation of the Sydney system, through introduction of standardized categorization, may improve lymph node FNAC diagnostic accuracy. And it can also help in achieving uniformity, reproducibility in cytology diagnosis and risk – stratification cytology.

The Sydney system of reporting LN FNAC is convenient, easy to follow and adapt to in under resourced institutions. The Sydney system integrates clinical and imaging information with key diagnostic cytopathological features and ancillary techniques, and is linked to a management algorithm, including options, which reflects the varying medical infrastructure available internationally and hence improves reporting quality by further reducing false negative and false positive results. It also guides clinicians to take the right decision about investigation and appropriate management for the patient.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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