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Reliability and diagnostic accuracy of FNAC in cases of lymphadenopathy- A retrospective study from a tertiary care centre, Katihar, Bihar

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Abstract

Context: Lymphadenopathy is the major cause of morbidity and one of the most common clinical presentations with variable aetiologies. Fine needle aspiration cytology (FNAC) is the simple, quick, inexpensive, minimally invasive OPD technique and first line of investigation for any individual with significant lymphadenopathy.

Aim: The aim is to evaluate the reliability and diagnostic accuracy of fine needle aspiration cytology (FNAC) of peripheral lymph nodes with an emphasis on discordant cases between the cytology and the histopathology.

Material and Method: The study was conducted in the department of pathology, Katihar Medical College, Katihar. A retrospective study including 300 cases of peripheral lymphadenopathies over a period of 1 year from April 2020 - April 2021.

Results: 39.6% cases of lymphadenopathies were seen in age group between 21-40 years with cervical lymph node swelling commonly involved. On cytological examination, most frequent findings are reactive lymphoid hyperplasia in benign and lymphoma in malignant cases and after histopathological examination of the same excised lymph node biopsy, diagnostic accuracy is 87.5%

Conclusion: In developing countries like India, FNAC alone used as specific tool for early detecting primary malignancy and metastatic lesions due to its high sensitivity.

Keywords: Cervical lymph node, Fine needle aspiration cytology, Lymphoma.

Introduction

Lymphadenopathy is one of the commonest clinical presentations of patients especially in paediatric age groups attending the outdoor clinics in hospitals.[1] The aetiology varies from an inflammatory condition to a malignant condition.[2] Infective lymphadenopathy is quite common in developing countries, mostly due to high prevalence of tuberculosis. However, still a significant percentage of lymphadenopathies turn out to be malignant.[3]

Fine needle aspiration cytology (FNAC) of lymph node is considered as superior and more cost effective tool in comparison to expensive surgical excision biopsies in developing countries with limited financial and health care resources in diagnosis and management of patients with lymphadenopathy due to early availability of results, simplicity, and minimal trauma with less complication.[4] It is widely used to obtain cells, tissues or fluid through a needle attached with disposable syringe for the diagnosis of masses. The number of cells obtained from the lymph node during FNAC is often sufficient for making the diagnosis.[5] The FNAC result are comparable with those of histopathology and the aspirate has characteristics of a micro-biopsy.[6] It can easily differentiate between neoplastic and non-neoplastic lesions. [7,8]

On cytological smear, the diagnosis of metastatic tumour to the lymph node is highly reliable and crucial. It would be the sole indication for searching the primary tumour, mainly in cases of occult carcinoma.[9] However, the primary tumour is clinically known in most of these cases and FNAC is used widely for the follow up of these patients. Metastatic carcinoma can mostly be identified by their cytomorphological characteristics alone. However, in some instances, features of different tumours overlap and the precise diagnosis of the primary tumour remains obscure.[10] Enlarged cervical lymph nodes are very common and worrying presentation in paediatrics as well as in adults. It is often involved in all types of lymphadenopathy mainly reactive hyperplasia and lymphoma. Although the reliability of FNAC of cervical lymph node has been shown in some studies but there are also some reports in contrary.[11]

Therefore, the aim of our study is to report the results of FNAC of cervical lymphadenopathy, that depend on the cytomorphological features and comparison to the results of histopathology in an attempt to highlight the reliability and diagnostic accuracy of FNAC of lymph nodes with an emphasis on discordant cases between the cytology and the histopathology.

Material And Method

The study was retrospective which was conducted in the Department of Pathology, Katihar Medical College, Katihar on 300 patients with enlarged peripheral lymph nodes swelling during the year 2020-2021. The study was approved by the ethics committee of the institution. Relevant clinical details of all patients were noted. FNAC of lymph nodes swelling was done and smears were stained with Giemsa stain/Papanicolaou stain and Ziehl Neelsen (ZN) stain for Acid fast bacilli. Histopathology slides were stained with Haematoxylin and Eosin (H & E) stain. The smears were examined to determine the cytomorphological features. These features included adequacy, cellularity, arrangement of cells, and nuclear as well as cytoplasmic features. The background was noted in all slides for the presence of necrosis and granuloma formation as well as for the type of inflammatory cells and the results were classified as non-neoplastic and neoplastic lesion.

Hypocellular slides were excluded from the present study.

Four main diagnosis were included by cytologic results; (a) Smears having no malignant tumour cells considered as ‘‘benign diagnosis with recommendation of follow up’’. (b) ‘‘Malignant metastatic diagnosis with recommendation of searching for the primary tumours’’ that comprised of cytological presentation of malignant metastatic tumour cells. (c) ‘‘Malignant primary lymphoma with recommendation of excision for confirmation and immunophenotyping’’ that showed large malignant-looking lymphoid cells. (d)

‘‘Suggestive of or suspicious for lymphoid malignancy with a recommendation of biopsy and immunophenotyping’’ that showed atypical small or large lymphoid cells or revealed R–S and Hodgkin-like cells.

In our study, we considered suggestive or suspicious cases as positive for malignancy and these cases were investigated further. The histopathological assessment was done in few cytologically benign cases either due to clinical persistent, multiple, or enlarged lymphadenopathy or due to suspicious radiological or laboratory result.

Lymph node biopsy was done in 40 patients. The histopathological examination was done in few included cytologically diagnosed malignant metastatic cases as the metastatic work up of such cases failed to identify the primary tumours & malignant lymphoma. The histopathological slides were then reviewed and the results were classified as non-neoplastic lesion and neoplastic lesion. The histopathological results of the same excised nodes then were compared with the cytopathological results. In cases of any discrepancy, special attention was focused on the cytomorphological features for all discordant cases & histopathologic diagnosis were considered as the gold standard.

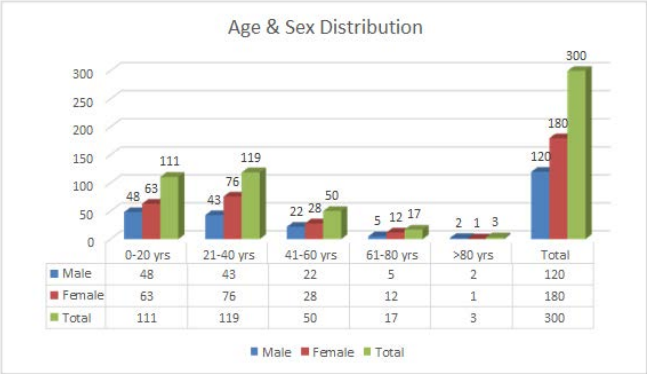
Diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and discordance rate were calculated and compared with other studies.

Results

In our study out of total 300 lymphadenopathy cases, 120 (40%) were male and 180 (60%) were female with male to female ratio1:1.5. The age of the patients ranged from 2 years to 82 years. The disease was more frequently seen in the age group of 21-40 years.

Table1: Age and Sex Distribution

Age (years)	Male	Female	Total	%
0-20 yrs	48	63	111	37
21-40 yrs	43	76	119	39.6
41-60 yrs	22	28	50	16.6
61-80 yrs	5	12	17	5.6
>80 yrs	2	1	3	1
Total	120	180	300	100

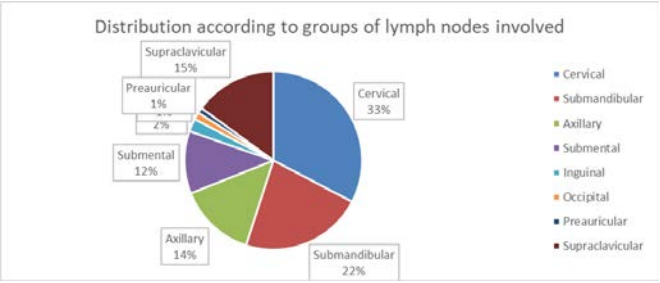


Graph 1

In the present study, the most common site was observed is cervical lymph node 98 (32.6%) followed by submandibular lymph nodes 67 (22.3%), supraclavicular lymph nodes 45 (15%), axillary in 42 cases (14%), submental in 34 cases (11.3%), inguinal in 7 cases (2.3%), occipital in 4 cases (1.3%) and preauricular in 3 case (1%).

Table 2: Distribution according to groups of lymph nodes involved

Lymph Node Group Affected	No. of Patients	%
Cervical	98	32.6
Submandibular	67	22.3
Axillary	42	14
Submental	34	11.3
Supraclavicular	45	15
Inguinal	7	2.3
Occipital	4	1.3
Preauricular	3	1
Total	300	100



Graph 2

The cytological diagnoses by FNAC were found to be benign in 210 cases (70%) and malignant in 90 cases (30%). Among the malignant cases, 30 cases (10%) were diagnosed as malignant metastatic tumors. The largest group in the present study were benign. Among benign cases, reactive hyperplasia was most common 145 (48.3%) followed by granulomatous lesion 45 (15%), necrotizing lesion 20 (6.6%). Metastatic cases were seen most often over the age of 40 years, 30 cases (10%). Out of the 30 metastatic cases to the lymph nodes, the most common were metastatic squamous cell carcinoma, 17 cases (56.6%). 7 cases (23.3%) were metastatic adenocarcinoma, 5 cases (16.6%) were metastatic undifferentiated carcinoma, and 1 case (3.3%) were metastatic small cell carcinoma. Lymphoma cases were distributed over wide age range. In our study, cases with cytologic features diagnostic of or suspicious for malignant lymphoma were the largest group, 60 smears (20%). Of them, 48 cases were NHL and 12 cases were HL.

Table 3: Cytological diagnoses of the 300 studied cases

Cytological diagnoses	No. of cases	%
Benign Cases	210	70
Reactive lymphoid hyperplasia	145	48.3
Chronic granulomatous lymphadenitis	45	15
Chronic necrotizing lymphadenitis	20	6.6
Malignant and suspicious cases	90	30
Metastatic malignant tumours	30	10
Diagnostic of Non-Hodgkin lymphoma	6	2
Suspicious for Non-Hodgkin lymphoma	42	14
Diagnostic of Hodgkin lymphoma	2	0.66
Suspicious for Hodgkin lymphoma	10	3.33
Total	300	100

The results from cytopathological diagnosis in this study were then compared with the histopathological diagnoses of the corresponding excised lymph nodes. Among the 40 cytologically benign cases, 38 cases (95%) were proved histopathologically as benign, true negative and 2 cases (5%) were diagnosed histopathologically as malignant, false negative. 32 cases (80%) cytologically diagnosed malignant cases were proved histopathologically to be malignant, true positive and 8 cases (20%) were diagnosed benign by histopathology, false positive.

Table 4: Comparative analysis of cyto-histopathological diagnoses in patients with lymphadenopathy

Cytopathological diagnoses	Histopathological diagnoses		Total
	Benign	Malignant	
Benign	38 (True negative)	2 (False negative)	40
Malignant	8 (False positive)	32 (True positive)	40

The overall diagnostic accuracy of FNAC was found to be 94.11% sensitivity, 82.60% specificity, 80% positive predictive value, 95% negative predictive value and 87.5% accuracy.

Table 5: Detailed comparison of cytopathological diagnoses with the corresponding histopathological diagnoses.

Cytopathological diagnoses	No. of case	Histopathological diagnoses					Accuracy (%)
		Reactive lymphoid hyperplasia	Granulomatous lymphadenitis	Metastatic malignant tumours	NHL	HL	
Reactive lymphoid hyperplasia	30	29	-	-	1	-	96.6
Chronic granulomatous lymphadenitis	6	-	5	-	-	1	83.3
Chronic necrotizing lymphadenitis	4	-	4	-	-	-	100
Metastatic malignant tumours	12	-	-	12	-	-	100
NHL	25	6	1	-	18	-	72
HL	3	1	-	-	-	2	66.6

Out of 30 cases of reactive lymphoid hyperplasia, 29 cases were also confirmed as reactive lymphoid hyperplasia with diagnostic accuracy of 96.6% while 1 case was re diagnosed as non-Hodgkin lymphoma. Diagnostic accuracy of chronic granulomatous lymphadenitis on histopathological examination was 83.3%, 1 case was re diagnosed as Hodgkin lymphoma. Chronic necrotizing lymphadenitis & Metastatic malignant tumours reported exact same on lymph node biopsy with 100% accuracy rate. Out of 25 cases of NHL, 18 cases also confirmed as NHL histopathologically with accuracy of 72% while 6 cases were re diagnosed as reactive lymphoid hyperplasia and 1 case was re diagnosed as granulomatous lymphadenitis on histopathological examination. 2 out of 3 cases were correctly diagnosed as NHL on histopathology while 1 case was reported as reactive lymphoid hyperplasia.

Figure 1: Giemsa stained smear shows hyperplasia of lymphoid cells(100X)

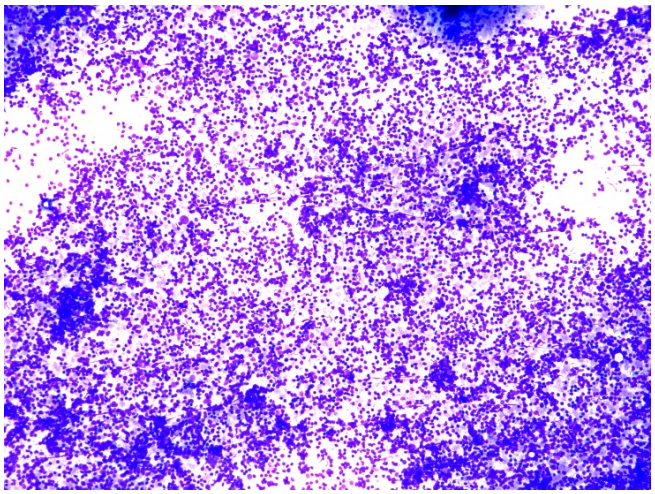


Figure 2: Giemsa stained smear shows granuloma(400X)

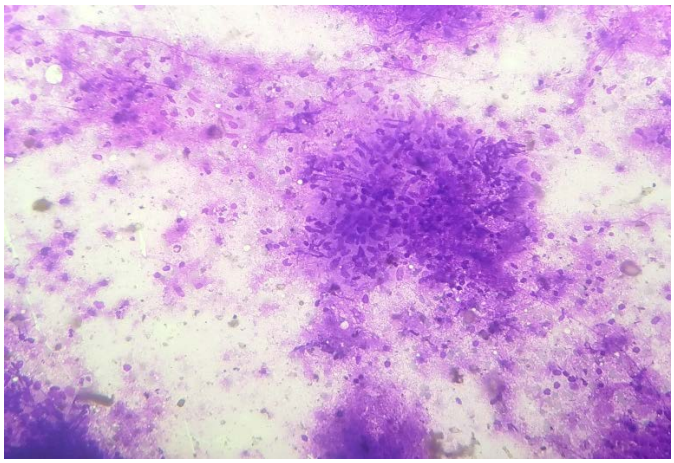


Figure 3: Giemsa stained smear shows atypical squamous cells in cervical lymph node (400X)

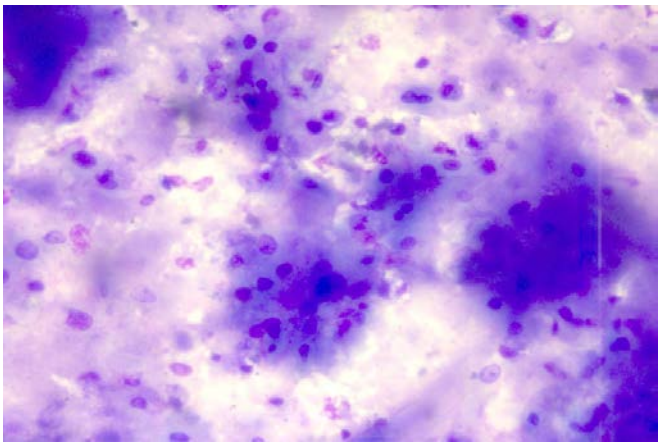


Figure 4: Giemsa stained smear shows RS cells (400X)

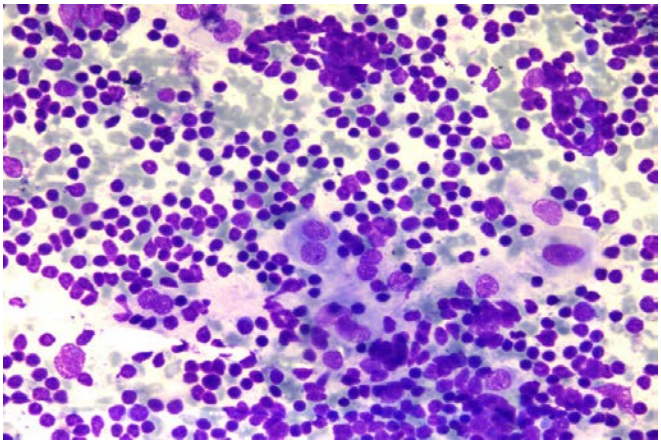


Figure 5: Giemsa stained smear shows monomorphic cells in NHL (400X)

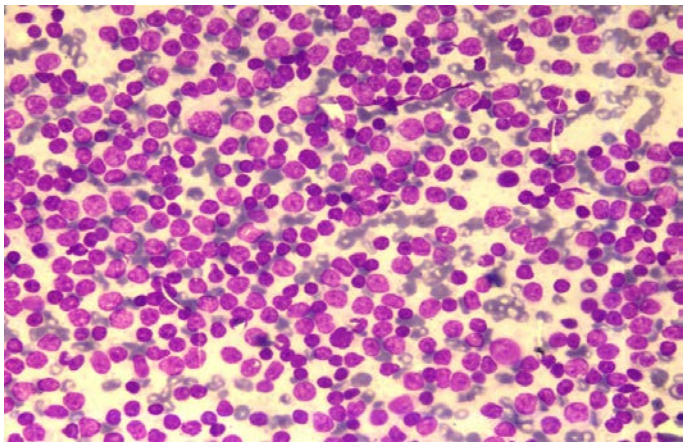


Figure 6: H&E stained smear shows capsules with total effacement of lymphoid follicles in NHL (100X)

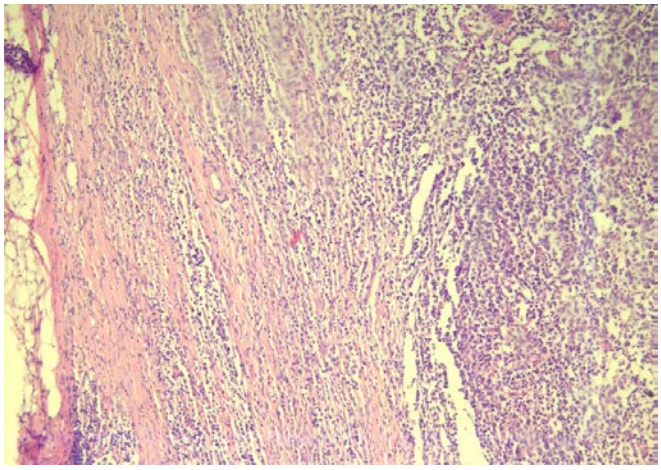
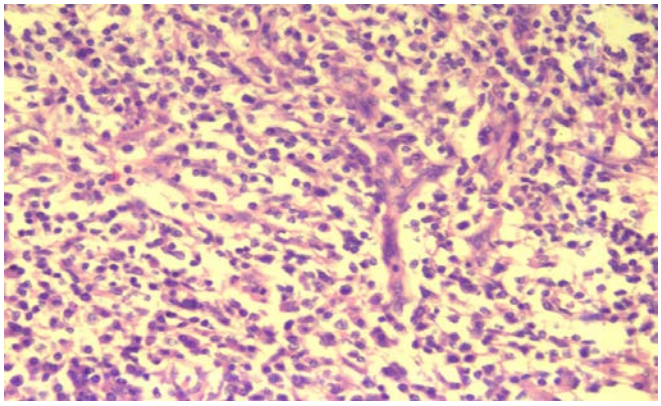


Figure 7: H&E stained smear shows small, monomorphic atypical cells in NHL (400X)



Discussion

Lymphadenopathy as a clinical manifestation of the regional or systemic disease serves as an excellent clue

to the underlying disease. The aetiology of which may be benign or malignant lesions. The term Lymphadenopathy is used to describe the conditions in which lymph nodes become abnormal in size, consistency, and number.[12] The lesion arising in lymph nodes can be found in patients ranging from an early age group to advanced age group.[13]

In the present study, the youngest age was 3 years old and the oldest one was 81 years old. These figures came in close comparison to the study done by C. Pramod et al[14], J. Chandralekha et. al [15] , S. Bhatta et al[16] & H. Nesreen et al.[17]

The male to female ratio is 1:1.5. Thus, there is slight female predominance. These finding were in agreement with the study done by J. Chandralekha et. al[15] whereas study done by S. Bhatta et al[16], H. Nesreen et al[17] have reported male predominance.

In our study, cervical lymph nodes were most commonly involved (33%). Similar result was seen by S. Neha et al[18], Haque MA et al[19] and Khubchandani SR et al[20] where predominance of cervical lymph nodes also noted.

Cytological features of all cases were studied in detail. In the present study, out of 300 cases, 210 cases were diagnosed as non-neoplastic. In a study conducted by S. Neha et al[18], showed 456 cases out of 498 cases (91.57%) as non-neoplastic. A similar study was done by J. Chandralekha et al[15] in which 170 cases (85%) out of 200 cases were reported as benign. Tariq et al evaluated 100 cases in which 54 cases were diagnosed as non-neoplastic whereas a study done by H. Nesreen[17] reported 109 cases (69.4%) out of 157 cases as malignant and only 8 cases (30.6%) were benign. Similar result was seen by a study done by C. Pramod et al[14] in which 584 (51.27%) were malignant and 545 (48.27%) were benign. These findings were consistent with the study done by Steel et al[21], in which the majority of their cases (59%) were malignant and (34%) were benign. Benign reactive hyperplasia is the most common findings in our study and this finding correlate well with most of other similar studies.

In the neoplastic cases, the majority of our cases were malignant lymphoma, 60 cases (66.6%) out of 90 cases. This observation was much higher than the study done by H. Nesreen et al[17] who reported 49.7% as malignant lymphoma. Ahmad et al[22] reported only 4.5% cases as malignant lymphoma in their study. They concluded the fact that due to study done mainly on children with large percentage of non- specific infection, there is lower lymphoma incidence. Their finding was consistent with the study done by Egea et al[23] who also reported a lower incidence of lymphoma, 9.5% of their cases. In our study, the cause of the large percentage of lymphoma by cytological examination may be due to two factors: (1) We considered suggestive or suspicious cases as positive for malignancy. (2) Our study was carried out in the tertiary centre due to most referral cases.

In the present study, out of 90 malignant cases 30 cases (33.3%) were reported as metastatic carcinoma. Our result is similar to the the study done by Koo V et al[24] who also reported the exact same figure (33.3%) as we reported for metastatic carcinoma while Kuba R et al[25] reported only 6%, Tariq et al[26] reported 14% and H. Nesreen et al[17] reported 19.7% metastatic carcinoma.

After examine lymph node biopsy histopathologically from included few cytological benign and malignant cases, out of 40 cytological benign cases, 38 cases (True negative) also reported benign with accuracy of 95% while 2 cases (False negative) reported as malignant histopathologically whereas 32 cases (True positive) out of 40 from cytological malignant cases

diagnosed malignant with accuracy of 80% and 8 cases (False positive) reported as benign after histopatological examination. Similar finding was reported by H. Nesreen et al[17] in which out of 48 cytological benign cases, 39 cases (81.3%) was true negative and out of 109 cytological malignant cases, 90 cases (82.6%) was true positive histopatologically.

On cytological benign cases, all cases of chronic necrotizing lymphadenitis to the lymph nodes showed exact corroboration with the histopathology. The diagnostic accuracy of these cases was 100% whereas a study done by H. Nesreen et al[17] reported 70% diagnostic accuracy. In our study, diagnostic accuracy of reactive lymphoid hyperplasia on histopathological base was found to be 96.6% whereas diagnostic accuracy of chronic granulomatous lymphadenitis was 83.3%.

In the present study, on cytological malignant cases, all cases of metastatic malignant tumours to the lymph nodes showed exact corroboration with the histopathology. The diagnostic accuracy of these cases was 100%. This finding showed exact correlation with the study done by H. Nesreen et al[17] who also reported 100% accuracy rate while Khajuria et al[27] reported 87% diagnostic accuracy. Diagnostic accuracy of non-Hodgkin lymphoma on histopathological base in our study was found to be 72% whereas diagnostic accuracy of Hodgkin lymphoma was 66.6%.

Out of 2 false negative cases from 40 cases, it was found that 1 case was underdiagnosed as reactive lymphoid hyperplasia on FNAC and re-diagnosed as non-Hodgkin lymphoma on histopathology and 1 case was underdiagnosed as Chronic granulomatous lymphadenitis cytologically and re-diagnosed as Hodgkin lymphoma on histopathology. Our result was less than the study done by H. Nesreen et al[17] who reported 9 cases as false negative out of 48 cases.

Regarding to the 8 false positive cases, 7 cases were over diagnosed by cytologic examination as positive for non-Hodgkin lymphoma and turned to be benign after histopathological diagnosis. These cases showed cytologically highly cellular with presence of numerous individually scattered large atypical lymphoid cells demonstrating conspicuous nucleoli in reactive lymphoid background having plasma cells. On histopathology, 6 cases were diagnosed as reactive lymphoid hyperplasia and 1 case was diagnosed as granulomatous lymphadenitis. Examination of these smears who were proved to be reactive lymphoid hyperplasia on histopathology showed multiple areas of monotonous population of small lymphoid cells with rounded slightly enlarged nuclei having coarse chromatin pattern. Landgren et al. reported that in reactive lymphoid hyperplasia, immature lymphoid cells might increase due to the presence of hyperplasia of lymphoid cells and therefore cell division and concluded that lymphoma should be diagnosed when these immature cells account greater than 50% of the cell population. Mendon et al in their study concluded that if the aspiration of the reactive node is derived from the large germinal centre, the proportion of the large cells as well as the number of mitoses was enough to suggest it as malignant lymphoma.

In the present study, 1 case had an initial cytologic diagnosis of Hodgkin lymphoma, while after histopathology examination it was re-diagnosed as reactive lymphoid hyperplasia. Heterogenous population of small and large lymphoid cells in various stage of maturation was revealed after reviewing the smear. No classic R-S cells with large prominent nucleoli were detected. Malakar et al[28] concluded that

the diagnosis of Hodgkin lymphoma on cytology was the finding of the classic R-S cells in an appropriate polymorphous cellular background and the sole presence of mononuclear cells Hodgkin cells was only suspicious but not diagnostic for Hodgkin lymphoma. However, Zhang et al[29] concluded that the clue to the diagnosis of Hodgkin lymphoma in situation where the classic binucleated or multinucleated R-S cells were infrequent was made by finding atypical mononuclear R–S cell variant with prominent macro nucleoli and granuloma together in the smear.

Conclusion

Preoperative cytology is a useful quick reliable diagnostic modality specific tool for early detecting primary malignancy and metastatic lesions due to high accuracy, sensitivity and specificity of FNAC. It appears as a good first line method for investigating the cases of lymphadenopathy. Many inflammatory lesions can be treated based on FNAC alone. Due to limited financial and health care resources, it is suitable for developing countries by which in the hands of an experienced pathologist can minimize the economic burden and avoid the need for lymph node excision biopsy.

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