



DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN CERVICAL LYMPHADENOPATHY

Pathology

Sarumathy Ganesan*

Sri Muthukumaran Medical College And Research Institute. *Corresponding author

Sridevi V

Sri Muthukumaran Medical College And Research Institute.

Lionel Rohit Mathew

Sri Muthukumaran Medical College And Research Institute.

Saraswathi Manickam

Sri Muthukumaran Medical College And Research Institute.

Vijayalakshmi CS

Sri Muthukumaran Medical College And Research Institute.

ABSTRACT

Background: Fine-needle aspiration cytology (FNAC) is the least invasive technique for the pathological diagnosis in cervical lymphadenopathy. Aim of this study was to characterize the cyto-morphological features of various cervical lymph node diseases on FNAC and to analyse the diagnostic accuracy of FNAC in comparison to the histopathological examination in cervical lymphadenopathy.

Materials and methods: This is a retrospective study carried out in the Department of Pathology, Sri Muthukumaran Medical College. Data concerning cervical lymph node FNAC was retrieved over a period of 2 years, from January 2018 to January 2020. A total of 110 patients with cervical lymphadenopathy were subjected for FNAC during this period. The cytological diagnosis was analysed in comparison to the histopathological diagnosis of those cervical lymph nodes which had undergone excision biopsy during the study period.

Results: The cytological diagnosis was found to be non-neoplastic in 94 cases (85.45%) and neoplastic in 16 cases (14.55%). When compared with the histopathological diagnosis, FNAC in cervical lymphadenopathy has the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of 85.7%, 94.1%, 85.7%, and 94.1%, respectively. The overall diagnostic accuracy was 81.1% while the overall discordance rate was 18.9%. The best diagnostic accuracy on cyto-histological correlation was in cases of metastatic carcinoma (100%) followed by reactive hyperplasia (81.25%), then Non Hodgkin's lymphoma (80%) and then tuberculous lymphadenitis (77.7%).

Conclusion: With keeping in mind of the possible causes for its diagnostic inaccuracies in certain specific scenarios, FNAC can be a rapid, reliable, least invasive method for the diagnosis of most of the cervical lymph nodal diseases.

KEYWORDS

Cervical lymphadenopathy, FNAC, Lymphadenitis, Lymphoma.

Background

Lymph nodes are an integral component of the immune system. The lymphoid system grows rapidly during childhood and it reaches stable adult size in 20-25 years. Lymph nodes are clustered along the lymphatic vessels and are not seen normally because they are embedded in the connective tissue¹. Cervical lymphadenopathy is a common clinical presentation and seen in a wide variety of diseases, like infection and malignancy².

Fine Needle Aspiration Cytology (FNAC) is a simple outpatient procedure. It is the safe, rapid and the least invasive method for pathological diagnosis of cervical lymphadenopathy³. In most of the cases, it offers an accurate diagnosis and avoids the need for the more invasive biopsy, thereby allowing rapid onset of therapy⁴. Most of the metastatic lymph nodal carcinoma can be diagnosed by their cyto-morphological characteristics alone, and FNAC can also give clues regarding the origin of their primary tumour. In some instances, features of different tumours overlap and the definitive diagnosis of the primary tumour remains obscure⁵. In these cases, ancillary techniques such as immunocytochemistry can be used to overcome these difficulties and support the cyto-diagnostic interpretation⁶. In cases of primary lymphoid malignancies, FNAC can also be used for staging the disease and also to recognise the residual and recurrent lymphoid malignancies⁷.

Aim of this study was to characterize the cyto-morphological features of various cervical lymph node diseases on FNAC and to analyse the diagnostic accuracy of FNAC in comparison to the histopathological examination in cervical lymphadenopathy.

MATERIALS AND METHODS

This is a retrospective study carried out in the cytopathology section of Department of Pathology, Sri Muthukumaran Medical College. Data concerning cervical lymph node FNAC was retrieved over a period of 2 years, from January 2018 to January 2020. A total of 110 patients with cervical lymphadenopathy were subjected for FNAC during this period. The cytological diagnosis were analysed and were compared in

relation to the histopathological diagnosis of those cervical lymph nodes which had undergone excision biopsy during the study period. Out of the 110 cervical lymph nodes aspirated during the study period, 48 lymph nodes had undergone excisional biopsy.

STATISTICS

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

RESULTS

Among 110 cases with cervical lymphadenopathy, 47 cases (42.73%) were females and 63 cases (57.27%) were males with male: female ratio of about 1.3:1. The age at presentation ranged from 3 years to 68 years. Maximum number of patients were in the 21-30 years age group (36 cases, 32.72%) followed by 31-40 years (26 cases, 23.63%), and the least in the 1-10 years age group (7 cases, 6.36%).

Of the 110 cases studied, non-neoplastic pathology was reported in 94 cases (85.45%) while neoplastic pathology was reported in 16 cases (14.55%). Reactive lymphoid hyperplasia was the most common pathology and it was noted in 44 (40%) patients. Next common pathology noted was the tuberculous lymphadenitis which accounted for 36 cases (32.72%). Acute suppurative lymphadenitis was observed in 14 cases (12.72%). Out of the neoplastic pathology reported in 16 cases (14.55%), lympho-proliferative disorders was found in 10 cases (7 cases of non-Hodgkin's lymphoma and 3 cases of Hodgkin's lymphoma) and lymph nodal metastasis was found in 6 cases (5 cases of squamous cell carcinoma and 1 case of adenocarcinoma). (Table 1).

Table 1: Cytological diagnosis of cervical lymph nodal diseases

Lesions	Number of cases	1-10	11-20	21-30	31-40	41-50	51-60	61-70	Percentage
Reactive	44	2	8	15	14	4	1	0	40
Tuberculous	36	2	8	14	7	4	1	0	32.72
Acute suppurative	14	3	2	6	2	1	0	0	12.72

Hodgkins	3	0	0	1	2	0	0	0	2.72
Non Hodgkins	7	0	0	0	1	2	3	1	6.36
Metastasis	6	0	0	0	0	0	4	2	5.45
Total (%)	110 (100)	7 (6.4)	18 (16.4)	36 (32.7)	26 (23.6)	11 (10)	9 (8.1)	3 (2.7)	

The cytological diagnosis were then compared with the histopathological diagnosis of the corresponding excised cervical lymph nodes. Among the 34 cytologically diagnosed non-neoplastic cases, 32 cases were proven histopathologically to be non-neoplastic (true negative cases) but 2 cases were diagnosed histopathologically as neoplastic (false negative cases). Out of the 14 cytologically diagnosed neoplastic cases, 12 cases were proven histopathologically to be neoplastic (true positive cases) but 2 cases were diagnosed histopathologically as non-neoplastic (false positive cases). Accordingly, the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value for FNAC of cervical lymphadenopathy in differentiating neoplastic and non-neoplastic pathologies were 85.7%, 94.1%, 85.7%, and 94.1%, respectively. The overall diagnostic accuracy was 81.1% while the overall discordance rate was 18.9%. (Table 2).

Table 2: Comparison of the cytological diagnosis with the corresponding histopathological diagnosis in cervical lymphadenopathy

Cytological diagnosis	Total number of cases	Final histopathological diagnosis					Accuracy (%)
		Reactive	Tuberculosis	Hodgkins	Non Hodgkins	Metastasis	
Reactive	16	13	2	1			81.25
Tuberculous	18	3	14	1			77.7
Hodgkins	3		1	2			66.6
Non Hodgkins	5	1			4		80
Metastasis	6					6	100

DISCUSSION

Inflammatory processes are the most common causes of cervical lymphadenopathy. Cervical lymph nodal diseases may range from treatable infections to malignant neoplasm. Accurate diagnosis is mandatory, so that appropriate treatment can be initiated as soon as possible. While surgical excision of a cervical lymph node requires hospitalization, anaesthesia, time consuming and scar in the neck for lifetime, FNAC is a simple, quick, safe, and reliable alternative diagnostic tool for the diagnosis of the various cervical lymph nodal diseases. However, FNAC also has its own limitations and pitfalls. Adequate experience of the pathologist in aspiration and cytomorphological analysis, can provide with more accurate cytological diagnosis, comparable to histopathology⁸.

In this study, peak incidence for the non-neoplastic lesions was in the 2nd decade while the peak incidence for neoplastic lesions was in the 5th decade. Also in the study done by Sarda et al⁹ and Ahmad et al¹⁰, the peak incidence for neoplastic lesions was in the 5th decade. Saluja and Ajnyka¹¹ attributed the cause of the presence of more malignancy in older age to the fact that adult or elderly patients often react to the infection with only slight to moderate lymph node enlargement. Therefore distinct lymphadenopathy in an elderly patient should arouse suspicion of malignancy and justify immediate investigation.

In this study, 96 out of 110 cases (80%) were of non-neoplastic pathology whereas 14 cases (20%) had a neoplastic pathology. Among the non-neoplastic diseases, the most common was reactive lymphoid hyperplasia accounting for 44 cases (40 %) followed by tuberculous lymphadenitis (32.72 %). In this study, non-neoplastic lymph nodes size was mostly equal or less than 2 cm in 89% cases, whereas neoplastic lymph nodes were over 2 cm in 80.2% of cases. These results were similar to the study done by Tilak et al¹².

In our study, reactive lymphoid hyperplasia was the most common diagnosis (40 %) found in the cervical lymph node aspiration. The reason may be due to the infections commonly affecting the oral cavity, nose and ears. This was found to be more common in younger age groups i.e. less than 30 years.

Tuberculous cervical lymphadenitis was the most common form of

extrapulmonary tuberculosis. In our study, the second common cause for cervical lymphadenopathy was tuberculosis. This was similar to the study done by KhubaRet al¹³. Bezabih et al¹⁴ found that FNAC decreases the need for more invasive procedure for the diagnosis of tuberculous adenitis. They suggested that Ziehl-Neelsen staining for identification of acid-fast bacilli will increase the diagnostic accuracy of tuberculosis. In the study done by Tariq et al¹⁵, tuberculous lymphadenitis was found to be the most common pathology of cervical lymph node lesions. AFB positivity is seen maximally in cases showing caseous necrosis with occasional epithelioid cells.

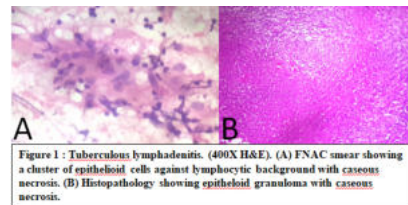
In our study, lymphoma (9.1 %) were found to be the most common neoplastic disease.

Among lymphoma, non Hodgkins lymphoma (66.7%) was more common than Hodgkin lymphoma (33.3%). Egea et al¹⁶ also reported a lower incidence of lymphoma, 9.5% of their cases. But Rakhshan M and Rakhshan A¹⁷ reported higher incidence (22.4%) of lymphoma in their series.

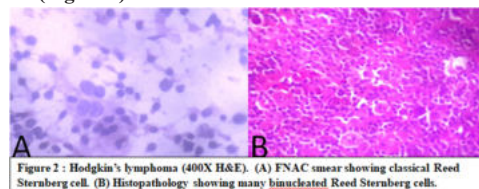
In our study, metastatic nodes were seen in the age group of 51-70 years and squamous cell carcinoma was the commonest metastatic nodal lesion (5 out of 6 cases). Hirachand et al also observed squamous cell carcinoma as the commonest metastatic cervical lymph nodal disease¹⁸.

In our study, based on the cyto-morphological features alone, the overall diagnostic accuracy of FNAC (as compared to the biopsy) was 81.1%. This was similar to the study done by Nesreen H. Hafez et al¹⁹ with a diagnostic accuracy of 82.2%.

In our study, FNAC provided a correct diagnosis in 81.25% of cases of reactive lymphoid hyperplasia on histological correlation, in comparison to 75% in the study done by Umeshkumaret al²⁰ and 100 % in the study done by Chu et al²¹. Among 18 cases diagnosed as tuberculous lymphadenitis by FNAC, 14 cases were confirmed by histopathology but 3 cases were found to be reactive lymphoid hyperplasia and 1 case was found to be Hodgkin's lymphoma. To increase the diagnostic accuracy of FNAC in tuberculous lymphadenitis, Ziehl-Neelsen staining should be performed in all cases showing cyto-morphological features of tuberculous lymphadenitis. (Figure 1).



Out of the three cases of Hodgkin's lymphoma (HL) diagnosed by FNAC in our study, 2 cases were confirmed by histopathology but one false positive case was found to be tuberculous lymphadenitis on histopathology. This would have happened because tuberculous and reactive lymphoid hyperplasia exhibit a polymorphous picture similar to HL. Henceforth Malakaret al²² proposed that for the cytological diagnosis of HL, classic R-S cells in an appropriate polymorphous cellular background is mandatory. The presence of only mononuclear cells (Hodgkin cells) or apoptotic cells was considered as only suspicious but not diagnostic of HL. However, if the diagnosis of HL had already been established in a case, these findings were sufficient enough to make the diagnosis of recurrent or residual disease. Among the 2 false negative cases diagnosed by FNAC in our study, tuberculous lymphadenitis (1 case) and reactive hyperplasia (1 case) were found to be HL on histopathology. Zhang et al²³ concluded that classic R-S cells were infrequent in many cases and in such cases, the diagnosis of HL should be suspected when atypical mononuclear R-S cell variant with prominent macronucleoli seen together with granuloma. (Figure 2).



Among 5 cases diagnosed as Non-Hodgkin's lymphoma (NHL) by FNAC in our study, 4 cases were confirmed as the same by histopathology but 1 case was found to be reactive hyperplasia (False positive). Unlike in our study, false negativity of Non-Hodgkin's lymphoma on FNAC is the common diagnostic inaccuracy (mistaken for reactive lymphoid hyperplasia), because in the early stages, NHL may involve only some part of the lymph node, and the needle aspiration may miss that particular area of involvement; so FNAC should be done with caution in early stages of disease, if there is strong clinical suspicion of lymphoma²⁴. Hehn et al²⁵ found out that the presence of macrophages with tingible bodies favours the reactive process but do not rule out high grade lymphoma, especially with high turnover of cells. They concluded that if there were numerous mature lymphocytes and plasma cells, one should not diagnose lymphoma. (Figure 3).

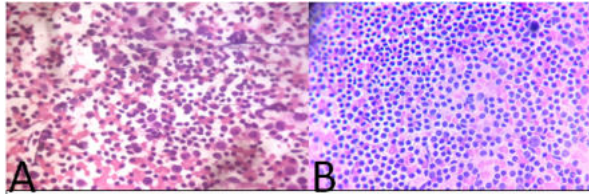


Figure 3 (400X H&E). (A) FNAC smear showing polymorphous population of lymphocytes in reactive lymphadenitis. (B) FNAC smear showing monotonous population of round lymphoid cells with scanty cytoplasm and nuclei with coarse chromatin in Non-Hodgkin's lymphoma.

In our study, Cyto-histological correlation was 100% for metastatic lymph nodes. This was similar to 100% in the study done by Umeshkumaret al²⁰ and the same was 97% in the study done by Shour et al²⁶. FNAC has higher sensitivity and specificity in diagnosing the nodal metastatic diseases, because malignant cells are usually abundant in the metastatic lymph nodes and their diagnostic cytomorphologic features are not similar to that of the normal or hyperplastic lymph nodes^{24,27}. So cervical lymph node metastasis constitute one of the strong indication for FNAC. FNAC also can provide clues to the nature and primary site of the disease in most of the cases. (Figure 4).

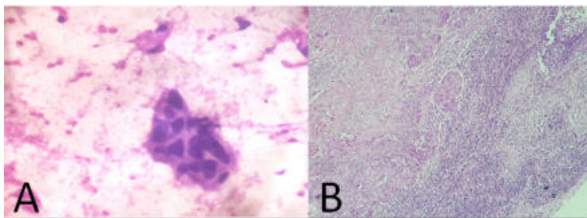


Figure 4: Metastatic nodal squamous cell carcinoma deposit (400X H&E). (A) FNAC smear showing a sheet of round to polygonal cells with scanty to moderate eosinophilic cytoplasm, high N/C ratio and pleomorphic hyperchromatic nuclei. (B) Histopathology showing clusters and sheets of malignant squamous epithelial cells admixed with lymphocytes

CONCLUSION

With keeping in mind of the possible causes for its diagnostic inaccuracies in certain specific scenarios, FNAC can be a rapid, reliable, least invasive method for the diagnosis of most of the cervical lymph nodal diseases, especially in a metastatic nodal disease.

REFERENCES

- Kumar V, Abbas AK, Fausto N, Aster JC. Robbins Pathologic basis of disease. 8th ed. India: Elsevier; 2010. p.595.
- Pandav AB, Patil PP, Lanjuvua DN. Cervical lymphadenopathy - diagnosis by FNAC, a study of 219 cases. *Asian J Med Res* 2012; 1(3): 79-83.
- Smita. Bhide et al. Cytological Evaluation of Fine Needle Aspiration Cytology in Lymph node lesion. *JMSCR Volume 05 issue 08 August 2017*: 26869-26876
- Howlett DC, Harper B, Quante M, Berresford A, Morley M, Grant J. Diagnostic adequacy and accuracy of fine needle aspiration cytology in neck lump assessment: results from a regional cancer network over a one year period. *J Laryngol Otol* 2007; 121(6):571-9.
- Al-Mulhim AS, Al-Ghamdi AM, Al-Marzooq HM, Mohammad HA, Gharib IA. The role of fine needle aspiration cytology and imprint cytology in cervical lymphadenopathy. *Saudi Med J* 2004;25:862-5.
- Haque MA, Talukder SI. Evaluation of fine needle aspiration cytology of lymph node in Mymensingh. *Mymensingh Med J* 2003;12(1):33-5.
- Raghuvveer CV, Leekha IL, Pai MR, Adhikari P. Fine needle aspiration cytology versus fine needle sampling without aspiration. A prospective study of 200 cases. *Indian J Med Sci* 2002;56:431-9.
- Kose LG. Diagnostic Cytology and the Histopathological Basis. 4th ed. Philadelphia: Lippincott Company; 1994:pp.194-98
- Sarda AK, Bal S, Singh MK, Kapur MM. Fine needle aspiration cytology as a preliminary diagnostic procedure for asymptomatic cervical lymphadenopathy. *JAPI* 1990;38(3):46-9.
- Ahmad SS, Akhtar S, Akhtar K, Naseen S, Mansoor T. Study of fine needle aspiration cytology in lymphadenopathy with special reference to acid fast staining in cases of tuberculosis. *J K Sci* 2005;7(1):1-4.
- Saluja JG, Ajnyka MS. Comparative study of fine needle aspiration cytology, histology, and bacteriology of enlarged lymph node. *Bombay Hosp J* 2000;42(2):1-7.
- Tilak V, Dhadel AV, Jain R. Fine needle aspiration cytology of the head and neck masses. *Ind J Pathol Microbiol* 2002;45(1):23-30.
- Janagam C et al. *Int J Res Med Sci*. 2017 Dec;5(12):5237-5241
- Bezabih M, Mariam DW, Selassie SG. Fine needle aspiration cytology of suspected tuberculous lymphadenitis. *Cytopathology*. 2002;13(5):284-290
- Tariq Ahmed, Mohammed Nazeem, Siddique A H MED, Ambreen Samad, Amir Nasir. FNAC and swellings in the surgical output. *J Ayub Med Coll Abbottabad*. 2008; 20(3):30-33.
- Egea AS, Gronzalez MAM, Cohen JM. Usefulness of light microscopy in lymph node fine needle aspiration biopsy. *Acta Cytol* 2002;46:368-9.
- Rakhshan M, Rakhshan A. The diagnostic accuracy of fine needle aspiration cytology in Neck lymphoid masses. *Iranian J Pathol* 2009;4(4):147-50.
- Hirachand S, Lakhey M, Akhter J, Thapa B. Evaluation of fine needle aspiration cytology of lymph nodes in Kathmandu Medical College, Teaching hospital. *Kathmandu Univ Med J*. 2009;7(26):139-142.
- Nesreen H. Hafez, Neveen S. Tahoun. Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy. *Journal of the Egyptian National Cancer Institute* (2011) 23, 105-114
- Umesh Kumar Paliwal, Sanjay Kumar Nigam. "Diagnostic accuracy of fine needle aspiration cytology in cervical lymph nodes with histopathological correlation". *Journal of Evolution of Medical and Dental Sciences* 2013; Vol2, Issue 32, August 12; Page: 5936-5942.
- Chu EW, Hoyer RC. The clinician and the cytopathologist evaluate fine needle aspiration cytology. *Acta Cytol*. 1973 Sep-Oct; 17(5):413-7.
- Malakar D, Jajoo N, Gupta OP, Jain AP. A clinical evaluation of fine needle aspiration cytology in the diagnosis of lymphadenopathy. *Ind J Tuberc* 1991;38(17):17-8.
- Zhang JR, Raza AS, Greares TS, Cobb CJ. Fine needle aspiration diagnosis of HL using current WHO classification, review of cases from 1999-2004. *Diagn Cytopathol* 2006; 34(6):397-402
- Frable WJ. Fine-needle aspiration biopsy: a review. *Hum Pathol*. 1983;14(1):9-28.
- Hehn ST, Grongan TM, Miller TP. Utility of fine needle aspiration as a diagnostic technique in lymphoma. *J Clin Oncol* 2004;22(15):3046-52.
- Schour L, Chu EW. Fine needle aspiration in the management of patients with neoplastic disease. *Acta Cytol*. 1974 Nov-Dec; 18(6):472-6.
- Volmar KE, Singh HK, Gong JZ. The advantages and limitations of the role of core needle and fine needle aspiration biopsy of lymph nodes in the modern era. *Hodgkin and non-Hodgkin lymphomas and metastatic disease. Pathol Case Rev*. 2007;12(1):10-26.