

Fine Needle Aspiration Cytology in Evaluation of Lymphadenopathy in Pediatric Age Group: Our Experience at Tertiary Care Centre

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ABSTRACT

Introduction: Lymphadenopathy is a common problem in children. The aim of the present study is to evaluate the role of FNAC in the diagnosis of pediatric lymphadenopathy and to study varied cytomorphological patterns and their frequency in lymph node aspirates.

Material and Methods: Total number of cases of lymphadenopathy in the pediatric age group (<16years) during the study period were 498, out of which 325 were retrospective and 173 were prospective cases respectively. Aspirated material was stained with Leishman and Giemsa stain, Papanicolaou, Hematoxylin and Eosin and Ziehl Neelsen stain (wherever required). For histological analysis, H and E stained sections were studied.

Results: Most of the patients were in the age group of 5-10 years i.e. 242/498 cases (48.59%). Cervical lymph nodes were the most commonly involved in 482/498 cases (96.79%). The largest group of lesions comprised of non-neoplastic lesions 456/498 (91.57%) cases. Only 8/498 (1.61%) cases were in the neoplastic category, whereas in 34/498 (6.82%) cases, material was inadequate for diagnosis. Among the non-neoplastic lesions, diagnoses in order of frequency were:- Non-specific reactive lymphadenitis (324 cases)- 71.05%, Tuberculous lymphadenitis (78 cases) – 17.11%, Granulomatous lymphadenitis (38 cases) – 8.33% and Acute suppurative lymphadenitis (16 cases)- 3.51%. Among the neoplastic lesions (8/498), five cases showed features of Hodgkin's lymphoma, whereas two cases were classified as Non-Hodgkin's lymphoma and one case as metastatic deposit from rhabdomyosarcoma to lymph node.

Conclusion: FNAC is an important diagnostic tool in the pediatric population. As a safe, minimally invasive and rapid procedure, clinicians can reliably utilize FNAC in the management of lymphadenopathy in children. Results of FNAC are comparable with those of tissue biopsies. So, it can be easily done in a cost-effective manner.

Keywords: Fine needle aspiration, pediatric lymphadenopathy

INTRODUCTION

Lymphadenopathy is a common problem in children.¹⁻³ Evaluation of a child with lymphadenopathy is a common clinical scenario for the pediatricians.² Lymph nodes are a part of reticuloendothelial system. They serve as the termination point for lymphatic vessels draining lymph from most tissues of the body. Presence of abundant phagocytic cells, antigen presenting cells and lymphocytes provides ideal first line of defense against pathogens. As a result, most of the normal children have small palpable cervical, axillary and inguinal lymph nodes.^{2,4,5} They are not considered enlarged until their diameter exceeds 1cm for cervical and axillary nodes and when it is more than 1.5 cm for inguinal nodes. Other lymph

nodes usually are not palpable or visualized with plain radiographs.⁶ Palpable supraclavicular nodes are always considered abnormal.^{4,7}

A wide variety of diseases and conditions may present as lymphadenopathy. An understanding of these conditions is essential to determine the most appropriate diagnostic work-up.³

Aspiration of lymph nodes for diagnostic purpose was first reported in 1904 by Grieg and Gray in the diagnosis of Trypanosomiasis.⁸⁻¹⁰ In 1921, Guthrie attempted to correlate lymph node aspiration cytology with various disease processes.^{8,10} Fine needle aspiration cytology (FNAC) is particularly helpful in the workup of cervical masses because biopsy of cervical adenopathy should be avoided unless all other diagnostic modalities have failed.¹¹

FNAC is now recognized as a rapid diagnostic technique because it is relatively painless, gives a speedy result and is inexpensive.¹² Nowadays, FNAC is increasingly being applied to pediatric lesions as it permits rapid diagnosis with minimal intervention.

The dilemma to approach a child with lymphadenopathy, its evaluation and management, considering various differential diagnoses, prompted us to take up this study. We conducted this study to evaluate the role of FNAC in the diagnosis of pediatric lymphadenopathy and to study varied cytomorphological patterns and their frequency in lymph node aspirates.

MATERIAL AND METHODS

We conducted this study in the Department of Pathology, LLRM Medical College, Meerut. This included a retrospective as well as prospective analysis during the period January 2012 to June 2015. Total number of cases of lymphadenopathy in the pediatric age group (<16years)¹³ during the study period were 498. Number of retrospective and prospective cases were 325 and 173 respectively.

All the cases fulfilling the following criteria were included in the study:-

- Age \leq 16 years.¹³
- Lymph node enlargement with diameter exceeding 1cm for cervical and axillary nodes and 1.5cm for inguinal

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nodes.⁶

Following exclusion criteria were applied:-

- Un-cooperative child.
- Overlying skin showing acute inflammatory changes.

Five cases for which preoperative cytological findings and subsequent histological diagnosis were available during this period were included in the study and cyto-histological correlation was done.

Retrospective cases

Cytology smears of 325 cases of lymphadenopathy in the pediatric age group were retrieved from records of Pathology Department. In each case, cytomorphologic features were analysed and correlated with histology findings, wherever available.

Prospective cases

Detailed history, clinical and laboratory data of these patients were recorded on a structured proforma. Thorough general physical examination was carried out. Palpable peripheral lymph nodes were examined noting their size, location, consistency, number, mobility, presence of matting and any local changes like redness, discharge or sinus formation.

FNAC was performed in 173 cases by non-aspiration/aspiration technique using the syringe with 22-24 gauge needle fitted in Franzen's handle. Depending on the aspirate obtained, minimum of two smears were air dried and stained with Leishman and Giemsa stain and two smears were wet fixed (ethyl alcohol) and stained with Papanicolaou and Hematoxylin and Eosin stain. Wherever required, Ziehl Neelsen staining for demonstration of AFB was done.

Stained smears were examined under the microscope. Smears stained with Ziehl Neelsen stain were observed for AFB and results were reported as positive and negative accordingly.

Histological analysis

For histological analysis, we used formalin fixed paraffin embedded H and E stained sections. The cytomorphologic features were correlated with the concomitant histology sections, wherever available.

STATISTICAL ANALYSIS

For data analysis, we used Statistical Package for the Social Sciences (SPSS) version 10. Age, gender, site of FNAC and cytomorphological patterns were expressed as frequency and percentage. Correlation of cytodiagnosis with age and gender was done on the basis of Chi-Square test (χ^2), taking into consideration the degrees of freedom (df). Significance was estimated by p-value.

RESULTS

Age and gender distribution

The study group was divided into three age groups – 0-5 years, 5-10 years and 10-16 years.

Most of the patients with lymphadenopathy were in the age group of 5-10 years 242/498 cases (48.59%), followed closely by 10-16 years age group 176/498 cases (35.34%) and least in 0-5 years age group 80/498 cases (16.06%). Lymphadenopathy was much more commonly observed in male children 349/498 cases (70.08%) than in female children 149/498 cases (29.92%). The male to female ratio was found

to be 2.34:1.

Among the patients in age group 0-5 years, 61/80 were males and 19/80 were females with M: F ratio 3.21:1. In 5-10 years age group, 187/242 were males and 55/242 were females with M: F ratio 3.4:1. In 10-16 years age group, 101/176 were males and 75/176 were females with M: F ratio 1.35:1.

Distribution according to the site of FNAC

Out of 498 cases, cervical group of lymph nodes were most commonly involved in 482/498 cases (96.79%), followed by axillary lymph nodes in 9/498 cases (1.61%), whereas inguinal and supraclavicular lymph node enlargement was found in four (0.80%) and three cases (0.60%) respectively.

During the study, 287/498 (57.63%) patients presented with multiple lymph node involvement as compared to solitary lymphadenopathy seen in 211/498 (42.37%) cases.

In 37 cases, more than one group of lymph node was involved. Among the cases with single lymph node involvement, anterior cervical group was involved in 233 cases, posterior cervical in 140 cases, submandibular in 42 cases, submental group in 14 cases, postauricular in 13 cases, axillary in 8 cases, occipital group in 5 cases, inguinal in 4 cases and supraclavicular in 2 cases 9 (Table-1).

Cytomorphological patterns

On the basis of cytomorphology, lymphadenopathy was classified into one of the following categories - Non-neoplastic, Neoplastic and Inconclusive.

Criteria for adequacy of smears¹⁴

All those smears were considered inconclusive where lymphoglandular bodies could not be identified in the FNAC sample or cytologic material obtained was insufficient to give definitive diagnosis or smears contained only blood.

Varied cytomorphologic patterns obtained during the study period showed the following distribution (Table-2):-

- Non-specific reactive lymphadenitis (324 cases)- 71.05%
- Tuberculous lymphadenitis (78 cases) – 17.11%
- Granulomatous lymphadenitis (38 cases) – 8.33%
- Acute suppurative lesions (16 cases)- 3.51%
- Neoplastic lesions (8 cases)- 1.61%
- Inconclusive (34 cases)- 6.83%

Among the neoplastic lesions (8/498), five cases showed features of Hodgkin's lymphoma, whereas two cases were classified as Non-Hodgkin's lymphoma and one case as me-

Lymph node groups	No. of cases	Percentage
Axillary	8	1.6
Supraclavicular	2	0.4
Inguinal	4	0.8
Anterior cervical	233	46.8
Posterior cervical	140	28.1
Submandibular	42	8.4
Submental	14	2.8
Postauricular	13	2.6
Occipital	5	1.0
More than one group	37	7.4
Total	498	100

Table-1: Distribution according to groups of lymph nodes involved

tastasis to lymph node (Table-2).

Correlation of age group with cytodiagnosis

Agewise distribution of cytomorphologic patterns of diagnosed cases (n=464) showed that non-specific reactive and acute suppurative lymphadenitis were more commonly seen in 5-10 years age group (169/324 and 10/16 cases), granulomatous and tubercular lymphadenitis were more common in 10-16 years age group (18/38 and 41/78 cases). Among the neoplastic cases, Hodgkin's lymphoma was more common in 10-16 years age group 3/5 cases, whereas one case each of Non-Hodgkin's lymphoma was seen in 5-10 years and 10-16 years age group. Only one case of metastatic lymph node was seen in 5-10 years age group (Table-3).

Association of male: female ratio with cytodiagnosis

Males more commonly had acute suppurative, non-specific reactive and granulomatous lymphadenitis. Among the neoplastic lesions, both the cases of Non-Hodgkin's lymphoma were seen in males, whereas four out of five cases of Hodgkin's lymphoma were found in males.

AFB positivity among granulomatous lesions

Out of 78 cases of tuberculous lymphadenitis, 76 cases showed granulomas on cytologic examination, whereas 2 cases showed features of suppuration. In all these cases, ZN stain was used. Among the granulomatous lesions, ZN stain showed presence of acid fast bacilli in 76/114 (66.67%) cases whereas 38/114 (33.33%) cases did not reveal acid fast bacilli.

Histopathologic examination

Four cases of Non-specific reactive lymphadenitis on FNAC were sent for histopathologic examination and the final diagnosis remained same. In one case, metastasis of small round cell tumour to lymph nodes was seen on FNAC and on histopathologic examination, diagnosis of Embryonal Rhabdomyosarcoma was made which was confirmed by immunohistochemistry.

DISCUSSION

Age and gender correlation

In this study, maximum number of patients were in the age group of 5-10 years (48.59%) followed by 10-16 years age group (35.34%). Wakely PE Jr, Kardos TF and Frable WJ. also reviewed FNACs in <16 years age group and found that majority cases were seen in age group of 6-11 years (34.82%).¹⁵ Similar results were seen in a study done by Ponder TB, Smith D and Ramzy I.¹⁶ Normal peak lymphoid growth occurs in the age group of 4-8 yrs, nearly reaching pathological size. So with on-going antigenic stimulus, the lymphoid growth may exceed the normal limits. This could be the reason for maximum number of cases in this age group.

In our study, incidence in males (70.08%) was more than that in females (29.92%) with male to female ratio 2.34:1. Male predominance was more evident in age group of 5-10 years (M:F= 3.4:1). Similar results were obtained in studies of Bezabih M, Mariam DW and Selassie SG (1.3:1)¹⁷ and Mitra S, Ray S and Mitra PK (1.3:1).¹⁸ This could be due to the prevailing custom of paying more attention to male children in Indian society rather than the actual increased bi-

Cytodiagnosis	No. of cases	Percentage
Non-neoplastic lesions		
Non-specific reactive	324	71.05
Tuberculous	78	17.11
Granulomatous	38	8.33
Acute suppurative	16	3.51
Total	456	100
Neoplastic lesions		
Hodgkin's lymphoma	05	62.5
Non-Hodgkin's lymphoma	02	25.0
Metastatic tumor	01	12.5
Total	08	100

Table-2: Spectrum of non-neoplastic and neoplastic lesions

Cytologic diagnosis	0-5 Year	5-10 Year	10-16 Year	Total
Non-specific reactive	60	169	95	324
Granulomatous	3	17	18	38
Tuberculous	12	25	41	78
Acute suppurative	2	10	4	16
Hodgkin's lymphoma	0	2	3	5
Non-Hodgkin's lymphoma	0	1	1	2
Metastatic	0	1	0	1
Total	77	225	162	464

Table-3: Correlation of age group with cytodiagnosis (n=464)

ological susceptibility in boys. Other studies showed almost equal incidence in males and females in the groups studied by - Haque MA and Talukder SI¹⁹ and Pandit AA, Candes FP and Khubchandani SR.²⁰ A study done by Ahmad T et al. showed reverse ratio (0.47:1) with predominance of females in the study group.²¹

Sites of lymphadenopathy

In the present study, cervical group of lymph nodes was most commonly involved (96.79%), followed by axillary group (1.81%). Among the cervical group, anterior cervical group (51.64%) was most frequently involved followed by posterior cervical group (31.60%). Multiple lymph node involvement (57.63%) was more commonly seen as compared to solitary lymphadenopathy (42.37%) in this study. Other studies done by Haque MA and Talukder SI,¹⁹ Pandit AA, Candes FP and Khubchandani SR,²⁰ Steel BLS, Schwartz MR and Ramzy I²² and Hussain M et al.²³ also showed predominantly cervical lymph node involvement. In a study by K Alam et al., maximum number of aspirations were done from cervical lymph nodes (74.2%).²⁴ The reason behind this may be the easy accessibility of cervical lymph nodes for examination and evaluation.

In present study, only three cases were found to involve supraclavicular lymph node (two of right side and one on left side), out of which only one was diagnosed as Hodgkin's lymphoma on FNAC. In a study by K Alam et al., frequency of malignancy was found to be higher in males (M:F=2.4:1).²⁴

Cytomorphologic patterns

Spectrum of pediatric lymphadenopathy on FNAC in various studies

Cytomorphologic patterns obtained in this study were predominantly non-neoplastic 456/498 cases (91.57%) as com-

pared to neoplastic lesions 8/498 cases (1.61%). Similar results were seen in studies done by Kumral A et al.²⁵ and Wakely PE Jr, Kardos TF and Frable WJ.¹⁵

Among the non-neoplastic lesions in this study, non-specific reactive lymphadenitis was the most common pattern 324/456 (71.05%), followed by tuberculous lymphadenitis 78/456 (17.11%), granulomatous lymphadenitis 38/456 (8.33%) and acute suppurative lymphadenitis 16/456 (3.51%). Other studies showing similar results with non-specific reactive hyperplasia as the predominant pattern, were done by Lake MA and Oski FA,²⁶ Annam V, Kulkarni MH and Puranik RB²⁷ and Hag IA et al.²⁸

In our study, both granulomatous lesions and tubercular lymphadenitis were frequently seen in 10-16 years age group. Male preponderance was seen in granulomatous lesions (24/38 males: 14/38 females), whereas almost equal male: female ratio was seen in cases of tuberculous lymphadenitis (38/78 males: 40/78 females). Thomas JO, Adeyi D and Amanguno H in their study concluded that tuberculosis was more common in <20 years age group and involved cervical group of lymph nodes most frequently.²⁹

In this study, only 8/498 cases (1.61%) were neoplastic, out of which five cases were of Hodgkin's lymphoma whereas two were Non-Hodgkin's lymphoma. Only one case of metastasis was detected in this study group. Other studies involving children with lymphadenopathy where similar incidence of neoplastic lesions was seen along with predominance of lymphomas were done by Bhandari B and Jain AM,³⁰ Lake MA and Oski F,²⁶ Annam V, Kulkarni MH and Puranik RB,²⁷ Wakely PE Jr, Kardos TF and Frable WJ,¹⁵ Hussain M et al.²³ and Ponder TB, Smith D and Ramzy I.¹⁶

In this study, 34/498 (6.83%) were included in inconclusive category as the cytological material was inadequate for reporting. Other studies done by Ahmad T et al. (8%),²¹ Annam V, Kulkarni MH and Puranik RB (3.57%),²⁷ Pandit AA, Candes FP and Khubchandani SR (8.04%),²⁰ Steel BL, Schwartz MR and Ramzy I (10.88%),²² Ponder TB, Smith D and Ramzy I (4.72%)¹⁶ and Hussain M et al. (3.71%)²³ showed similar incidence of unsatisfactory samples for diagnosis.

CONCLUSION

FNAC is an important diagnostic tool in the pediatric population. As a safe, minimally invasive and rapid procedure, clinicians can reliably utilize FNAC in the management of lymphadenopathy in children. Moreover, FNAC permits a rapid diagnosis with additional availability of ancillary techniques such as flow cytometry, cytogenetics, electron microscopy and cell block preparation with immunocytochemistry for definitive diagnosis. Results of FNAC compare favourably with those of tissue biopsies. So, it can be easily done in a cost-effective manner at places where facilities of histopathology are not available, as well as a preliminary diagnostic procedure to plan the management of lymphadenopathies in pediatric age group.

REFERENCES

- Kelly CS, Kelly RE Jr. Lymphadenopathy in children. *Pediatr Clin N Am*. 1998;45:875-888.
- Lymphadenitis and Lymphangitis. In: Case Based Pediatrics For Medical Students and Residents. New York: Churchill Livingstone. 2003:34.
- Nack-Gyun Chung. Lymphadenopathy. *Korean J Pediatr*. 2008;51:797-803.
- EU Regulations for Clinical Studies in Pediatric Patients. EU Pediatric Patient Guidelines. (EC) No. 1901/2006 (amended by 1902/2006).
- Andrew W. Bazemore. Lymphadenopathy and Malignancy. *Am Fam Physician*. 2002;66:2103-2111.
- Chesney P. Cervical Adenopathy. *Pediatrics in Review*. 1994;15:276-284.
- Kliegman M. Robert, Behrman E. Richard. The Lymphatic System. In: Nelson Textbook of Pediatrics 18 Ed. Elsevier. 2007;2:2093.
- Berliner Nancy. Approach to the patient with lymphadenopathy. In: Best Practice of Medicine. 2000:284.
- R.K. Narang, S. Pradhan, R.P. Singh And S. Chaturvedi. Place of fine needle aspiration cytology in the diagnosis of lymphadenopathy. *Ind. J. Tub*. 1990;37:29.
- Grieg, E.D. and A.C. Lymphatic gland in sleeping sickness. *Br. Med. J*. 1904;1:1252.
- Godwin J.T. Aspiration Biopsy: Technique and Application. *Annals of the New York Academy of Sciences*; 1956;63:1348-1373.
- Layfield LJ. Fine-needle aspiration of the head and neck. *Pathology (Phila)* 1996;4:409-38.
- Orell SR, Sterett GF, Whitaker D. Introduction. *Fine Needle Aspiration Cytology*, 4th Ed. Elsevier: New Delhi. 2005;1-3.
- Kardos TF, Maygarden SJ, Blumberg AK, Wakely PE Jr, Frable WJ. Fine needle aspiration biopsy in the management of children and young adults with peripheral lymphadenopathy. *Cancer*. 1989;63:703-7.
- Wakely PE Jr, Kardos TF, Frable WJ. Application of fine needle aspiration biopsy to pediatrics. *Hum Pathol*. 1988;19:1383-6.
- Ponder TB, Smith D, Ramzy I. Lymphadenopathy in children and adolescents: role of fine-needle aspiration in management. *Cancer Detect Prev*. 2000;24:228-33.
- Bezabih M, Mariam DW, Selassie SG. Fine needle aspiration cytology of suspected tuberculous lymphadenitis. *Cytopathology*. 2002;13:284-90.
- Mitra S, Ray S, Mitra PK. Fine needle aspiration cytology of supraclavicular lymph nodes: Our experience over a three-year period. *J Cytol*. 2011;28:108-10.
- Haque MA, Talukder SI. Evaluation of fine needle aspiration cytology (FNAC) of lymph node in Mymensingh. *Mymensingh Med J*. 2003;12:33-5.
- Pandit AA, Candes FP, Khubchandani SR. Fine needle aspiration cytology of lymph nodes. *J Postgrad Med*. 1987;33:134.
- Tariq Ahmad, Mohammad Naeem, Siddique Ahmad, Ambreen Samad, Amir Nasir. *J Ayub Med Coll Abbottabad*. 2008;20:34-37.
- Steel BL S, Schwartz MR, Ramzy I. Fine needle aspiration biopsy in the diagnosis of lymphadenopathy in 1,103 patients. Role, limitations and analysis of diagnostic pitfalls. *Acta Cytol*. 1995;39:76-81.
- Mukhtar Hussain, Akram Shad Chisti, Rubina Mukhtar, Hanif Khan, Hussain Siddiqui, Haroon Kd Pasha. Peripheral Lymphadenopathy in Children, Comparison of Fine Needle Aspiration Cytology with Open Biopsy. *Ann King Edward Med Coll*. 2005;11:398-9.
- K. Alam, V. Maheshwari, N. Haider, F.A. Siddiqui, A. Jain, A.H. Khan: Fine needle aspiration cytology

- (FNAC), a handy tool for metastatic lymphadenopathy. *The Internet Journal of Pathology*. 2010;10:21-28.
25. Kumral A, Olgun N, Uysal KM, Corapcioglu F, Oren H, Sarialioglu F. Assessment of peripheral lymphadenopathies: experience at a pediatric hematology-oncology department in Turkey. *Pediatr Hematol Oncol*. 2002;19:211-8.
 26. Lake MA, Oski FA. Peripheral lymphadenopathy in childhood. *Am J Dis child*. 1978;132:357-359.
 27. Annam V, Kulkarni MH, Puranik RB. Clinicopathologic profile of significant cervical lymphadenopathy in children aged 1-12 years. *Acta Cytol*. 2009;53:174-8.
 28. Hag IA, Chiedozi LC, al Reyees FA, Kollur SM. Fine needle aspiration cytology of head and neck masses. Seven years' experience in a secondary care hospital. *Acta Cytol*. 2003;47:387-92.
 29. Thomas JO, Adeyi D, Amanguno H. Fine-needle aspiration in the management of peripheral lymphadenopathy in a developing country. *Diagn Cytopathol*. 1999;21:159-62.
 30. Bhandari B, Jain AM. Lymph node biopsy in infants and children A new bedside method. *Arch of Dis child*. 1970; 45:510-512.

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