CLINICO-CYTOLOGICAL AND HISTOPATHOLOGICAL CORRELATION OF LYMPHADENOPATHY IN PEDIATRIC PATIENTS

RIYA MAHAJAN¹, POONAM SINGAL¹*, SHIVANSHU KUNDAL², HARJINDER SINGH³, RAMESH KUMAR KUNDAL¹, PRIYASI MONGA⁴

¹Department of Pathology, Government Medical College, Patiala, Punjab, India. ²Department of Surgery, Government Medical College, Patiala, Punjab, India. ³Department of Pediatrics, Government Medical College, Patiala, Punjab, India. ⁴Department of Medicine, Government Medical College, Amritsar, Punjab, India. Email: nikkirajesh99@gmail.com

ABSTRACT

Objective: The aim of the present study was to evaluate the cytological and histopathological (wherever possible) patterns of lymph node (LN) lesions along with clinical correlation in the pediatric population.

Methods: This was a prospective study conducted on 100 pediatric patients (aged <12 years) who presented with lymphadenopathy (LAP). Fine-needle aspiration cytology (FNAC) was performed on all cases out of which only 22 underwent surgical excision and histopathological examination. Aspirated material was stained with May-Grunwald Giemsa, Papanicolaou, Z-N stain (wherever required) and for histopathology, Hematoxylin and eosin stain was used.

Results: Majority number of patients was in the age group of 5–8 years (44%). Cervical LN s were most commonly involved (71%). Out of the total 100 cases, 91% were benign, 3% were malignant and 6% were inadequate. Most common cytologically diagnosed entity was non-specific reactive lymphadenitis (68%). There was one case of reactive lymphadenitis on cytology that proved to be Hodgkin lymphoma on histopathology. Two cases of generalized LAP given as atypical lymphoproliferative lesion on cytopathology proved to be acute lymphoblastic leukemia/lymphoma on further investigation. The cytomorphological findings were found to be concordant with histopathology in 21 cases out of 22 with a diagnostic accuracy rate of 95.45%.

Conclusion: FNAC is especially helpful as LN biopsy is a difficult and invasive procedure in children. Although excision biopsy is the gold standard, FNAC is preferred as first-line investigation. Along with cell block analysis and ancillary techniques, it provides an excellent diagnostic accuracy.

Keywords: Fine needle aspiration cytology, Paediatric lymphadenopathy, Lymphadenitis.

INTRODUCTION

Lymphadenopathy (LAP) is defined as an abnormality in the size or character of lymph node (LN) caused by the invasion or propagation of either inflammatory or neoplastic cells into the nodes [1]. LNs are not considered significantly enlarged until their diameter exceeds 1 cm for cervical and axillary nodes and 1.5 cm for inguinal nodes. However, palpable supravacular nodes are always considered abnormal [2]. In the majority of the pediatric cases, the enlarged LNs are due to reactive causes and are self-limiting. Hence, it is neither possible nor desirable to perform an excision biopsy in all these cases. Also, excision biopsy is an invasive procedure requiring anesthesia and is associated with potential complications [3]. Fine needle aspiration cytology (FNAC) is being increasingly used in pediatric patients as it promotes rapid diagnosis with minimum intervention. The cytomorphological features collaborate with histopathology and have the qualities of a micro-biopsy [4,5].

We conducted this study to evaluate the cytological and histopathological (wherever possible) patterns of LN lesions with clinical correlation in the pediatric age group.

METHODS

The study was conducted in Department of Pathology, GMC Patiala after approval from the ethics committee of the institute. This was a prospective study conducted on 100 cases in pediatric age group below 12 years presenting with LN swelling.
Maximum patients were males (67%) with male to female ratio of 2.03:1 (Table 3).

Cervical group of LNs were most commonly involved (71%) followed by Submandibular group (12%) (Table 4).

Most of the patients (61%) presented with significant enlargement of LNs between 1 and 2 cm. Only 27% of cases presented with size >2 cm (Table 5).

97 cases (97%) had localized LAP predominantly in cervical nodes and 3 cases had generalized LAP (Table 6). In generalized LAP, two out of three cases were of atypical lymphoid proliferation on FNAC. On further evaluation, they were diagnosed as Acute Lymphoblastic leukemia/lymphoma (ALL/L).

On palpation of LNs, 66% of the nodes were firm in consistency while matted was noted in 11% of the cases (Table 7).

Maximum patients were males (67%) with male to female ratio of 2.03:1 (Table 9).
Majority of patients had non tender LNs (64%) and three cases (3%) also had raised local temperature (Table 8).

Analysis of symptoms showed that most of the patients (65%) presented with fever followed by cough (28%) (Table 9). However, 35% of the patients presented with more than one symptom. Among the 65% of patients with fever, 4% cases also had history of rash suggesting viral etiology.

In the present study, the most common cause of LAP turned out to be idiopathic (28%) while specific diseases such as tuberculosis, viral lymphadenitis (LAD), ALL/L, and Hodgkin lymphoma (HL) were seen in 16%, 4%, 2%, and 1%, respectively (Table 10).

All the patients were subjected to routine investigations like TLC, DLC, ESR, Hb, Mantoux test, chest X-ray, and peripheral smear examination for the establishment of diagnosis. Analysis revealed that 40% of the patients had leucocytosis and 44% of the patients had anemia. ESR was raised in 37% of patients. Among 100 patients Mantoux test was done in 20 patients among which 16 were positive. Abnormal chest x-ray was seen in 15% of patients (Table 11).

The most common cytologically diagnosed entity was non-specific reactive LAD (68%) followed by granulomatous LAD (20%) (Table 12). Two cases (2%) were diagnosed as atypical lymphoid proliferation (Fig. 1) in which complete hematological workup was done in higher centers including bone marrow aspiration and immunophenotyping. It came out to be ALL.

On further evaluation of cases of granulomatous LAD, specific diagnosis of tuberculosis was made in 16 cases. Epithelioid granulomas can be seen in non tuberculous lesions such as sarcoidosis, brucellosis, cat scratch disease, leprosy and occasional malignancies. So to rule out these diseases, Z-N stain was done on all cases of granulomatous LAD. Cytodiagnosis of tuberculosis was made by demonstration of epithelioid cells and langhans giant cells with or without necrosis (Fig. 2) along with positive acid-fast bacteria (AFB) stain (Fig. 3).

Table 13 shows 16 out of 20 cases of granulomatous LAD were AFB positive. Therefore, in the present study, tubercular LAD was the most common entity among granulomatous LAD. AFB positivity in the study was 73.33%.

In the present study, cytological and histopathological correlation was available in only 22 cases out of 100 (22%) (Table 14). Maximum number of cases diagnosed in cytology was of reactive LAD which usually disappear after short antibiotic therapy. Hence, they were probably not subjected to any surgical excision or biopsy. Most of these patients were followed up in the out-patient department to check for any recurrence. The cytological findings were found to be concordant in 21 cases out of 22 with diagnostic accuracy rate of 95.45%. However, one case of reactive LAD (Fig. 4) on follow-up did not resolve after antibiotic treatment, so was subjected to excision biopsy which proved to be a case of Hodgkin lymphoma on HPE (Fig. 5).

On statistical analysis, FNAC in the present study shows sensitivity, specificity, positive predictive value, negative predictive value, and
diagnostic accuracy of 100%, 66.7%, 98.3%, 100%, and 95.45% respectively, as shown in Table 15.

As seen in Table 16, a clinical diagnosis of reactive LAP was made for 61 cases which on histopathology were confirmed as reactive LAP in 60 cases and Hodgkin’s lymphoma in one case. A clinical diagnosis of granulomatous LAP was made in 28 cases and on histopathological examination, 20 were confirmed as granulomatous LAD and eight were reactive LAD. A clinical diagnosis of inflammatory LAP was made in nine cases out of which four cases were confirmed as inflammatory LAD on histopathological examination while five cases were diagnosed as reactive LAD. Clinically, two suspected cases of malignancy were confirmed histopathologically.

Clinicopathological concordance was observed in 86% of cases. Statistical analysis was performed upon this correlation and p value came to be ≤0.05 (0.04) suggesting that it was significant (Table 16).

DISCUSSION

The present study consists of 100 cases of FNAC of LAP in pediatric age group with clinicopathological and cytohistopathological co-relation done. Histopathology was available in 22 cases. This is because majority of the cases were of reactive hyperplasia which regresses after antibiotic therapy and does not require excisional biopsy and histopathological evaluation. FNAC is particularly useful in such cases as it obviates the need for surgical intervention and also helps to rule out underlying serious systemic diseases.

Majority of the patients were in the 5-8 age group i.e. 44%. This is because normal peak lymphoid growth occurs in this age group. So with any ongoing antigenic stimulus, the lymphoid growth may exceed the normal limits. The results of the present study closely resemble the results of Ponder et al. [6], Reddy et al. [7], and Kondapalli et al. [8]. The cervical group of LN’s was the most commonly involved (71%). This could be attributed to the predominant reporting population to our center being from low socio-economic group. They have high incidence of oropharyngeal, dental and scalp infections which results in enlargement of draining LN which is the cervical group. This could also be due to the rich lymphatic supply of the neck region and easy accessibility of cervical nodes for examination and evaluation [9]. These findings were in concordance with studies conducted by Ahmed et al. [10] and Vasuki et al. [11].

Frequency of distribution of benign lesions and malignant tumors was 91% and 3% respectively. The remaining 6% of the cases were inadequate to report. Hence, according to the present study benign
lesions were more common in pediatric age group. This observation was in concordance with the study done by Ahmed et al. [10] and Sawaimul et al. [12] in which the frequency of distribution of benign and malignant tumors was 90% and 10%, 96.80%, and 3.20%, respectively.

In the present study, inadequate/unsatisfactory material was found in 6% (6 cases) comparing well with findings in other studies conducted by Handa et al. [13] and Sawaimul et al. [12]. In most of the cases, cytological material was insufficient to give any definite diagnosis or smears contained only blood. Among the benign lesions, majority of the cases were of non-specific reactive hyperplasia (67%) followed by granulomatous LAD (20%) and acute supplicative LAD (4%). The results of the present study were in concordance with Singh et al. [13] who observed 71% cases of reactive LAD, 25.8% of granulomatous LAD, and 3.5% of acute supplicative LAD. Similar results with non-specific reactive LAD as predominant pattern were seen in studies by Handa et al. [13] and Aggarwal et al. [15].

On cythohistological correlation, there was one false-negative case where a case of Hodgkin’s lymphoma was missed and reported as reactive LAD on cytology. Since a focal area of LN is sampled on FNA, representative area may be missed. Detailed clinical history and physical examination should always be carried out to avoid false-negative diagnosis in such cases. FNA is more accepted for the diagnosis of Hodgkin lymphoma than for Non-Hodgkin lymphoma and it may be diagnostic in high-risk surgical candidates and in patients where masses are inaccessible. Amongst granulomatous LAD, tubercular LAD constituted the largest group (16%). Similar findings were reported by Singh et al. [14]. In a country like India where tuberculosis is highly prevalent, FNA offers an easy, quick, and effective means for making early diagnosis and preventing further transmission and spread of disease [9]. As the confidence of clinician increases, as indicated on cytology reports the excison biopsy can be avoided [16]. AFB positivity in the study was 73.3%. The detection of AFB was more in smears containing necrotic material with or without granulomas. Many cases show caseous necrosis along with polymorphs and histiocytes.ZN stain should be performed in all such cases of acute necrotizing lymphadenitis.

About 4% of the cases in the study showed features of acute supplicative lymphadenitis. In such cases, FNA is diagnostic and is also helpful in obtaining material for culture and sensitivity. ZN staining should be done in all cases of suppurative lymphadenitis to rule out tuberculosis [9]. About 2% of the cases were diagnosed as atypical lymphoid proliferation on FNAC and they were investigated on hematological lines. Bone marrow aspiration and immunophenotyping were done and it proved to be a case of ALL/L.L. FNA cytology can be particularly useful in cases of lymphomas to obtain samples for cytogenetic analysis.

The sensitivity of FNAC in the present study was 100%. When it is compared with the studies of other authors the sensitivity was comparable with studies by Singh et al. [14], Malhotra et al. [17] and Kondapalli et al. [8] where the reported sensitivity was 97.5%, 94.49%, and 100%, respectively.

In the present study comparison between cytological and histopathological diagnosis was available in 22% of cases; with concordance in 95.45% of cases and discrepancy in 4.55% of cases. The results of the present study were in accordance with the studies conducted by Mohan et al. [18] and Prathima et al. [19].

CONCLUSION

FNACs is a simple bedside investigation which is a safe, affordable, effective and non-invasive technique with high patient acceptance, especially in pediatric age group as excision biopsy is difficult in children. FNAC acts both as a screening as well as a diagnostic procedure in various clinical conditions. Even though excision biopsy is the gold standard, FNAC is preferred as a first-line investigation and along with cell block analysis and application of ancillary tests (including immunocytochemistry), it helps to achieve an excellent diagnostic accuracy.

AUTHORS CONTRIBUTION

Dr. RIVA MAHAJAN: Collection of data and writing of manuscript; Dr. POONAM SINGAL: Writing of manuscript; Dr. HARINDER AND DR. RAMESH KUMAR KUNDAL: Analysis of data and proof reading of manuscript; Dr. SHIVANSHU KUNDAL: Collection of data and statistical analysis; Dr. PRIYASI MONGA: Collection of data.

CONFLICT OF INTEREST

None.

AUTHORS FUNDING

None.

REFERENCES

1. Sambandan T, Mahel RC. Cervical lymphadenopathy a review. J Indian Acad Dent Spec 2011;2:31-3.
2. Robert K, Richard B, Jenson H. The lymphatic system. In: Nelson Textbook of Pediatrics. Vol. 18. Philadelphia, PA: Saunders; 2007. p. 2093.
3. Bilal JA, Elshibly EM. Ectoило and clinical pattern of cervical lymphadenopathy in Sudanese children. Sudanese J Paediatr 2012;12:97-103.
4. Steel BL, 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.
5. Ahmad SS, Akhtar S, Akhtar K, Naseem S, Mansoor S. Study of fine needle aspiration cytology in lymphadenopathy with special reference to Acid-fast staining in cases of tuberculosis. JK Sci 2005;7:1-4.
6. Ponder TB, Smith D, Ramzy I. Lymphadenopathy in children and adolescent: Role of FNAC in management of cancer detection and prevention. Cancer Detect Prev 2000;24:228-33.
7. Reddy MP, Moorchunga MA. Clinico-pathological profile of pediatric lymphadenopathy. Indian J Pediatr 2002;69:1047-51.
8. Kondapalli CS, Mandal G. Usefulness of fine needle aspiration cytology in diagnosis of causes of lymphadenopathy in children. Int J Contemp Pediatr 2019;6:253-9.
9. Vimal S, Kulkarni S, Dharwadker A, Mukesh KK, Bamunukula S, Kumar H. Fine needle aspiration cytology as a diagnostic tool in lymphadenopathy for paediatric age group-tertiary care centre, Eur J Pharm Med Res 2017;4:552-9.
10. Ahmed HG, Elmubasher MB, Salih RA, Ellhuseein GE, Ashankty JM. Fine needle aspiration cytophotology of pediatric lymphadenopathy among Sudanese children. Asian Pac J Cancer Prev 2013;14:4359-63.
11. Vasuki S, Swaminathan K, Lavanya VS. FNAC profile of lymphadenopathy in children. J Dent Med Sci 2016;15:12-5.
12. Sawaimul K, Iqbal MB, Sawaimul K, Kamble T. Fine needle aspiration cytology: A diagnostic tool in evaluation of lymphadenopathy in paediatric age. Indian J Pathol Oncol 2018;5:184-8.
13. Handa U, Mohan H, Bal A. Role of fine needle aspiration cytology in evaluation of pediatric lymphadenopathy. Cytopathology 2003;14:66-9.
14. Singh N, Singh A, Chauhan R, Singh P, Verma N. Fine needle aspiration cytology in evaluation of lymphadenopathy in pediatric age group: Our experience at tertiary care centre. Int J Contemp Med Res 2016;3:1347-51.
15. Agarwal D, Dutta S, Awasthi S, Agarwal D, Bansal R, Bansal P. Evaluation of fine needle aspiration biopsy as a diagnostic tool in pediatric head and neck lesions. Pathol Lab Med Int 2010;2:131-6.
16. Gupta S, Khajuria R. Fine needle aspiration cytology of peripheral lymphadenopathy in children-A 3 year experience. J Evid Based Med Healthe 2018;5:3001-7.
17. Malhotra AS, Lahori M, Nigam A, Khajuria A. Profile of lymphadenopathy: An institutional based cytomorphological study. Int J Appl Basic Med Res 2017;7:100-3.
18. Mohan MS, Siddique AM, Sonnaih G, Prasad AS, Prasad SG. Cervical lymphadenopathy and its clinicopathological profile in children. Sch J Appl Med Sci 2014;2:216-20.
19. Prathima S, Suresh TN, Kumar MH, Krishnappa J. Fine needle aspiration cytology in pediatric age group with special reference to pediatric tumors: A retrospective study evaluating its diagnostic role and efficacy. Ann Med Health Sci Res 2014;4:44-7.