Intelligent Technology to Screen for Pediatric Lymphadenopathy in Medical Laboratories

Wael Alturaiki, Ph.D* Hrbi F, BSc** Awed, BSc** Enezy S, BSc** Nahed Alharthi, Ph.D** Abdulkarim S. BinShaya, Ph.D** Abdulaziz Alfahed, Ph.D** Talat Bukhari, Ph.D*** Amna Alotiby, Ph.D*** Aisha Alanazi, MD**** Noufa Alonazi, MD**** Rawiah Alsiary, Ph.D**** Abeer Alsofyani, Ph.D***** Hajir Alsaihati, Ph.D***** Mashael Altoub, Ph.D***** Awal Zaki, MD****** Arwa F. Alanazi, BDS****** Amani F. Alanazi, BRT******* Asma Alanazi, Ph.D****** Faris Q.B. Alenzi, Ph.D**

ABSTRACT

Objective: Fine Needle Aspiration Cytology (FNAC) is considered as a well-established method in adult oncology, and it is also highly recommended for the diagnosis of childhood tumors. This study aims to investigate the common causes of lymphadenopathy in pediatric population particularly in Saudi children by using FNAC technique.

Methodology: The study samples were collected randomly from 100 pediatric patients of 1 to 15 years of age who visit different pediatric clinic centers of Riyadh, KSA. The samples were obtained by professional pathologists and pediatric surgeons in accordance with the standard procedure.

Results: Cytological diagnosis revealed 11 cases of reactive lymphadenopathy, 3 cases of granulomatous lymphadenitis, and 16 cases of malignancy out of which 10 patients had non-Hodgkin's (NHD) and 6 patients had Hodgkin's lymphomas (HD)

Conclusion: This study confirmed that the FNAC is a useful diagnostic tool and can be used during the investigation of peripheral lymphadenopathy in pediatric patients.

Keywords: Lymphadenopathy, Tumors, Infection, Malignancy, Surgery, Saudi Arabia

INTRODUCTION

Pediatric lymphadenopathy is a strenuous medical condition characterized with abnormal changes in the lymph nodes with respect to their number or size or consistency. This condition frequently occurs in children; however, most of these lymphadenopathy masses are benign^{1,2}. Lymphadenopathy might also be considered as an early sign of some life-threatening diseases. The greatest challenge for the pediatric clinicians is to examine the children with enlarged lymph nodes not only because of a wide-ranging differential diagnosis but also on account of uncertainty when to do a surgery for biopsy or a fine needle aspiration (FNA) and culture³⁻⁵.

Generalized lymphadenopathy is a medical condition characterized with the enlargement of several lymph glands in multiple areas of the body. This type of lymphadenopathy is frequently associated with viral infection, but it is also occasionally observed in other medical condition such as collagen vascular diseases, malignancies and medications^{1,6,7}.

Enlargement of cervical lymph node is one of the most common temporary lymphadenopathies that can be seen in children and adults in the form of an immune response as a result of local or systemic infections^{8,9}. Generally, acute lymphadenitis of bilateral cervical lymph node is frequently seen in viral upper respiratory tract infection and in pharyngitis caused by bacterial infection. Acute unilateral cervical lymphadenitis is observed in approximately 40% to 80% cases of streptococci or staphylococci bacterial infection. Chronic or subacute lymphadenitis is usually caused by mycobacterial infection, toxoplasmosis and cat scratch disease⁸⁻¹¹.

| * | Department of Medical Laboratory Sciences |
|--------|--|
| | College of Applied Medical Sciences |
| ** | Department of Medical Laboratory Sciences |
| | College of Applied Medical Sciences |
| | Prince Sattam University, Saudi Arabia |
| | E-mail: f.alenzi@psau.edu.sa |
| *** | Department of Immunology |
| | Um Qura University |
| **** | Military Hospital |
| **** | KAIMRC center |
| ***** | Department of Medical Laboratory Sciences |
| | College of Applied Medical Sciences |
| | Hafr Albatan University |
| ***** | Department of Medical Laboratory Sciences |
| | College of Applied Medical Sciences, KSU |
| ***** | Dammam Regional Lab |
| ***** | Department of Dentistry |
| | Riyadh Alm University |
| ****** | Department of RT, Al-Marafa University |
| ****** | * College of Medicine, KSAUHS, Riyadh, Saudi Arabia. |
| | |

However, it's important to take into consideration the fact that not all the cervical lymphadenopathies result from bacterial or viral infection and could be a sign of severe life-threatening disorders such as cancer^{8,9}. According to Alexander et al., the posterior or supraclavicular cervical lymphadenopathy is considered to be a medical condition with a high risk of malignancy in comparison with the anterior cervical lymphadenopathy¹⁰. Therefore, it is crucial to examine the lymph nodes of both healthy and ill children during general body examination. The abnormal appearance of lymph nodes could be a sign of lymphadenopathy; consequently, lymphadenopathy differential diagnosis is recommended^{1,12}.

Fine needle aspiration cytology (FNAC) is considered as a well-established method in adult oncology and it is also highly recommended for the diagnosis of childhood tumors. This is because of the versatility of this technique its rapid diagnosis with low injury and minimal complication rate. FNAC is thus considered as a worthy tool to screen both palpable and non-palpable masses^{4,13,14}.

Moreover, FNA is a non-invasive, less painful and faster method in comparison with other methods related to tissue sampling such as surgical biopsy. Generally local anesthesia administration is not required for using FNA test because this procedure is not painful^{4,14}. The current study, therefore, aims to investigate the common causes of lymphadenopathy in pediatrics particularly in Saudi children by using FNAC technique.

METHODOLOGY

The samples of this study were collected from 100 pediatric patients whose ages ranged from 1 to 15 years (65male: 35female) and who had enlarged peripheral lymph nodes and had been referred for FNAC test. The participants were included if they were required the FNAC investigation as an initial diagnostic tool. The patients were selected from different clinics based in Riyadh, KSA. The FNAC test was carried out by the professional pathologist and pediatric surgeon in accordance with the standard procedure.

The material from the mass was aspirated and thrown instantly onto several slides to prepare the smears. The quality of aspirate was determined by staining one air dried smear slide immediately with Giemsa stain. The second smear was stained by using the Papanicolaou method and was fixed with 95% ethanol. All other smears were stained by the May-Gru"nwald-Giemsa method.

The cytological diagnosis is divided into four categories: benign, malignant, inflammatory and inadequate material for diagnosis. The finding of the cytological diagnosis was confirmed by sixmonths clinical follow-up and the malignant cases were verified by histopathology and further referred to oncologist. Written informed consent from all patients were obtained and signed by their fathers/mothers.

RESULTS

In the current study, the investigation of lymphadenopathy was carried out by using FNAC test in 100 children of 1 to 15 years of age. The average age of the children was 8 years. The results in table 1 and 2 show the distribution of the aspiration sites:70cervical, 5auxiliary, 21sub-mandibular, 2 generalized, and 2inguinal (Table 1). Cytological diagnosis revealed 11 cases of reactive lymphadenopathy, 3 cases of granulomatous lymphadenitis, and 16 cases of malignancy out of which 10patients had non-Hodgkin's (NHD) and 6 patients had Hodgkin's lymphomas (HD) (Table 2).

Table 1: Aspirated lymph node sites

| Site | Number |
|----------------|--------|
| Cervical | 70 |
| Auxiliary | 5 |
| Sub-mandibular | 21 |
| Inguinal | 2 |
| Generalized | 2 |
| Total | 100 |

Table 2: Age Distribution of Study Population

| Age | Lymphoma | Reactive lymphadenopathy | Granulomatous lymphadenitis | Total |
|-------------------|----------|--------------------------|-----------------------------|-------|
| Less than 5 years | 0 | 4 | 0 | 4 |
| 6-10 years | 1 | 4 | 0 | 5 |
| 11-15 years | 15 | 3 | 3 | 21 |

DISCUSSION

FNAC is a broadly accepted diagnostic procedure for the diagnosis of lymphadenopathy in adults, hence, it is rapidly gaining acceptance of pediatricians^{4,13}. Therefore, the current study chose this technique to find out the common causes of pediatric lymphadenopathy.

The current study revealed that all the 100 pediatric patients had enlarged lymph nodes in the different parts of their bodies. The peripheral lymphadenopathy in children is a regular clinical problem since there are multiple causes of peripheral lymphadenopathy; however, majority of these conditions (about 84%) are considered as benign self-limiting conditions^{1,12}.

Several studies reported that enlargement of lymph node is mostly associated with reactive lymph node and it is a benign revisable process. The reactive lymph node results from different etiologies with most commonly infectious agents^{6,8,9}. Crucially, the reactive lymph nodes which are caused by infectious agents are diagnosed by additional clinical assessment such as imaging techniques and microbiological, serological and molecular tests. A common condition which is associated with lymphadenopathy is granulomatous lymphadenitis and this condition mainly results from the infection of *Mycobacterium tuberculosis*^{9,11,12,15}.

The result of this study showed that 3% of the cases are diagnosed with granulomatous lymphadenitis. This finding is agreement with Annam's study who examined 336 children of 1 month to 12 years of age¹⁶. In his study he noticed that the following cytomorphological characteristics of the lymph node:58% of the cases were classified as reactive lymphadenitis and 30% were classified as granulomatous lymphadenitis¹⁶. This study found lymphoma in 90% of males and 10% of females. These findings are in line with other studies^{2,4,9}.

The results of this study revealed that lymphoma was recognized in the pediatric patients who were 10 or more years old. These results are in line with other several studies¹⁷⁻²². There might be some variations, which could be attributed to the sample size and many obstacles including time duration and ethical approvals.

CONCLUSION

The current study found that the both types of lymphomas Hodgkin and non-Hodgkin might be highly suspected in Saudi children with peripheral lymphodenopathy. Moreover, this study realized that

the FNA is a worthy diagnostic tool and can be used during the investigation of peripheral lymphadenopathy in pediatric patients.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflict of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 11 August 2021

Acknowledgement: This work was supported by the PSAU (grant no:2019/03/10211).

REFERENCES

- 1. Freeman AM, Soman-Faulkner K, Matto P. Book; Treasure Island (FL): StatPearls Publishing; Adenopathy. 2018.
- Bilal JA, Elshibly EM. Etiology and clinical pattern of cervical lymphadenopathy in Sudanese children. Sudan J Paediatr 2012;12(1):97-103.
- 3. Sharma M, Gupta A, Kaul R. Pediatric Lymphadenopathy: Cytological Diagnosis Over a Period of Two Years in a Rural Teaching Hospital. Ped Health Res 2017;2(3):16.
- 4. Wilkinson AR, Mahore SD, Maimoon SA. FNAC in the diagnosis of lymph node malignancies: A simple and sensitive tool. Indian J Med Paediatr Oncol 2012; 33(1): 21-4.
- 5. Zeharia A, Eidlitz-Markus T, Haimi-Cohen Y, et al. Management of nontuberculous mycobacteria-induced cervical lymphadenitis with observation alone. Pediatr Infect Dis J 2008; 27(10):920-2.
- 6. Olu-Eddo N, Egbagbe E. Peripheral lymphadenopathy in Nigerian children. Niger J Clin Pract 2006; 9(2):134-8.
- Jackson MA, Chesney PJ. Lymphatic system and generalized lymphadenopathy. In: editors. Principles and Practice of Pediatric Infectious Disease. Elsevie 2008; 135-43.

- 8. Al-Tawfiq JA and Raslan W. The analysis of pathological findings for cervical lymph node biopsies in eastern Saudi Arabia. J Infect Public Health 2012; 5(2):140-4.
- 9. Weinstock MS, Patel NA, Smith LP. Pediatric cervical lymphadenopathy. Pediatr Rev 2018;39(9):433.
- 10. Leung AK, Robson WLM. Childhood cervical lymphadenopathy. J Pediatr Health Care 2004;18(1):3-7.
- 11. Shah I, Dani S. Profile of tuberculous cervical lymphadenopathy in children. J Trop pediatr 2017;63:395-8.
- 12. Cipullo C, Amato B, Vigliar E, et al. Lymph node fine needle cytology in the diagnosis of infectious diseases and reactive unspecific processes. Infez Med 2012;20(3):30-3.
- 13. Howell LP. Changing role of fine-needle aspiration in the evaluation of pediatric masses. Diagn Cytopathol 2001;24(1):65-70.
- Mittal P, Handa U, Mohan H et al. Comparative evaluation of fine needle aspiration cytology, culture, and PCR in diagnosis of tuberculous lymphadenitis. Diagn Cytopathol 2011;39(11):822-6.
- Harris RL, Modayil P, Adam J, et al. Cervicofacial nontuberculous mycobacterium lymphadenitis in children: is surgery always necessary? Int J Pediatr Otorhinolaryngol 2009;73(9):1297-1301.
- 16. Annam V, Kulkarni MH, Puranik RB. Clinicopathologic profile of significant cervical lymphadenopathy in children aged 1–12 years. Acta cytologica 2009;53(2):174-8.
- 17. Birch J, Alston R, Quinn M, et al. Incidence of malignant disease by morphological type, in young persons aged 12–24 years in England, 1979–1997. Eur J Cancer 2003;39(18): 2622-31.
- Burkhardt B, Zimmermann M, Oschlies I, et al. The impact of age and gender on biology, clinical features and treatment outcome of non-Hodgkin lymphoma in childhood and adolescence. Br J Haematol 2005;131(1):39-49.
- Chiu BC-H, Weisenburger DD. An update of the epidemiology of non-Hodgkin's lymphoma. Clin Lymphoma 2003;4(3):161-8.
- Heerema NA, Bernheim A, Lim MS, et al. State of the Art and Future Needs in Cytogenetic/Molecular Genetics/Arrays in childhood lymphoma: Summary report of workshop at the First International Symposium on childhood and adolescent non-Hodgkin lymphoma, April 9, 2003, New York City, NY. Pediatr Blood Cancer 2005;45(5):616-22.
- 21. Clarke CA, Glaser SL. Changing incidence of non-Hodgkin lymphomas in the United States. Cancer 2002; 94(7):2015-23.
- 22. Ronchi A, Di Martino M, Caputo A, et al. Fine-Needle Aspiration Cytology Is an Effective Diagnostic Tool in Paediatric Patients with Mucoepidermoid Carcinoma as Secondary Neoplasm. Acta Cytol 2020;64(6):520-31.