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PERIPHERAL LYMPH NODE EXCISIONAL BIOPSY IN CHILDREN: YIELD IN A TERTIARY CARE CENTRE

Surgery

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ABSTRACT

AIM: To study the pediatric patients in a developing country undergoing peripheral lymph node excision biopsy in terms of demographics and histopathological findings and evaluate the diagnostic yield of peripheral Lymph node excision biopsy in children.

MATERIALS AND METHODS: A retrospective study of 402 patients was done of the children undergoing peripheral lymph node excision biopsy in a tertiary care center from 1st January 2013 to 31st December 2018 (6 years). Demographics, histopathological findings and yields were studied.

RESULTS: Out of the 402 patients, 218 (54.2%) were males and 184(45.8%) were females. Male to female ratio 1.18: 1. Maximum patients belonged to the age group of 4-6years (26.87%) followed by the age group of 2-4years of age (22.89%). Most common group of nodes excised were cervical (77.9%) followed by axillary and inguinal lymph nodes (9.2%) each. The most common etiology was reactive lymphoid hyperplasia (63.18%) in our study followed by tuberculous lymphadenitis(31.84%). Specific findings were seen in 35.58% and non-specific findings were seen in 64.42% patients. Malignancy was seen in 8 patients (2%).

CONCLUSION: Peripheral Lymphadenopathy in pediatric population is always a diagnostic challenge. While FNAC tends to be investigation of choice for adults, in a developing country with limited resources and high prevalence of tuberculosis, peripheral lymph node biopsy is the gold standard with a good diagnostic yield and should always be considered for patients with persistent lymphadenopathy.

Clinical significance: The study highlights the importance of excision biopsy in peripheral lymphadenopathy in children in a developing nation with limited resources and high prevalence of infectious diseases.

KEYWORDS

Lymph node, biopsy, yield, FNAC, tuberculous lymphadenitis

INTRODUCTION:

Peripheral Lymphadenopathy is a common finding in the pediatric population creating anxiety amongst both the parents and the health care professionals. It is defined as any lymph node enlargement that is detectable on palpation and is >1cm or smaller but multiple except at intrathoracic, mediastinal, intra-abdominal or retroperitoneal locations.[1,2]

The size, the number, the location and the rate of growth and the response to antibiotics are important in determining the need for biopsy.[3]

Excisional Lymph node biopsy in the children is the most traditional method and the gold standard for diagnosis in children.[4] Recent recommendations suggest the use of high frequency ultrasound guidance or FNAC (fine needle aspiration cytology) to reduce the number of such biopsies.[5,6] But both these methods add to the cost and need expertise.

These findings need to be interpreted in the light of situation like in India where there is high prevalence of tuberculosis and modern diagnostic facilities are not freely available. FNAC sometimes need confirmation with biopsy results.[5]

We give the results of our study to determine the diagnostic yield of the patients younger than 12 years undergoing a peripheral lymph node excisional biopsy.

AIM:

To study the pediatric patients in a developing country undergoing peripheral lymph node excision biopsy in terms of demographics and histopathological findings and evaluate the diagnostic yield of peripheral Lymph node excision biopsy in children.

MATERIALS AND METHODS:

- A retrospective study was done of children undergoing peripheral lymph node excision biopsy in LTMMC and LTMGH, India from 1st January 2013 to 31st December 2018. A total of 402 were included in the study.
- Pre-operatively all patients went through an array of investigations which included hemogram, ESR, Chest Xray, Mantoux test. Patients satisfying the inclusion criteria were included in the study. Most of them underwent biopsy under local anesthesia except 40 (10%). Biopsy proceeded with local infiltration of anesthesia. Incision was taken, lymph node dissected from surrounding structures and excised without rupturing the capsule. The specimen was sent for histopathological review. Wound was closed in layers. Patient was observed for 3 hours for any complications and discharged on day care basis with analgesics. No perioperative complication was found. Patients were asked to follow-up after a week for suture removal and report tracing. Only 5 patients developed post-operative wound infection.
- The following were the inclusion and exclusion criteria for the patients in our study.

INCLUSION CRITERIA:

1. Age < 12 years
2. Significant localized or generalized peripheral lymphadenopathy > 2 weeks.
3. Lack of response to conservative treatment

4. Suspicion of Tuberculosis
5. Suspicion of malignancy- primary or occult primary.

EXCLUSION CRITERIA:

1. Age > 12 years
2. Lymph node dissection as a part of more elaborate process like
- Neck dissection associated with head and neck Carcinoma with cervical lymphadenopathy.
- Inguinal block dissection associated with Lower extremity Carcinoma with inguinal lymphadenopathy.
- Axillary dissection associated with breast carcinoma with axillary lymphadenopathy.

The results were calculated and tabulated using Microsoft Excel and SPSS Version 25.

RESULTS:

A. Sex-wise distribution:

Out of the 402 patients, 218 (54.2%) were males and 184(45.8%) were females. Male to female 1.18: 1.

B. Age wise distribution of the results:

Maximum patients belonged to the age group of 4-6years (26.87%) followed by the age group of 2-4years (22.89%) of age. Most common age group involved was 4-6years. (Figure 1)

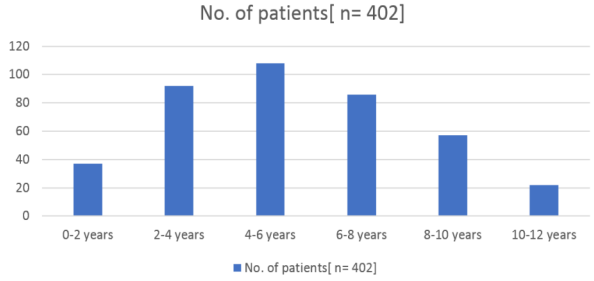

Figure 1: Age-wise distribution of the results

C. Distribution of Lymph node biopsy site

Most common group of nodes excised were cervical (77.9%) followed by axillary and inguinal lymph nodes (9.2%) each.

The other uncommon nodes to be excised where from forearm, hand, supratrochlear etc. all accounting for 3.7%. (Table 1)

Table 1: Distribution of lymph node biopsy site

Sr.no	Site	Number	Percentage
1.	Cervical region	313	77.9%
2.	Axillary region	37	9.2%
3.	Inguinal region	37	9.2%
5.	Others	15	3.7%
	Total	402	

D. Laterality of Lymphadenopathy

Most commonly the left nodes were involved (54.7%), 33.6% cases had nodes on the right side and 11.70% had bilateral presentation.

E. Node excised

Most commonly the left cervical group of nodes were excised (49.3%) followed by right cervical (28.6%).

F. Histopathological correlation

- **Overview:** Histopathological findings were as shown in the Table 2.

The most common etiology was reactive lymphoid hyperplasia (63.18%) in our study followed by tuberculous lymphadenitis(31.84%). Malignancy was seen in 8 patients (2%).

Table 2: Histopathological results:

Sr.no	Histopathological results	No. of patients	Percentage
1.	Reactive lymphoid hyperplasia	254	63.18%
2.	Sinus histiocytosis	4	1%
3.	Granulomatous lymphadenitis-TB	128	31.84%
4.	Hodgkins lymphoma	7	1.74%
5.	Non-Hodgkins lymphoma	1	0.25%
6.	Suppurative lymphadenitis	1	0.25%
7.	Chronic non-specific Lymphadenitis	5	1.24%
8.	TB abscess	2	0.5%
Total		402	

- Specific findings were seen in 35.58% and non-specific findings were seen in 64.42% patients. These results were found to be statistically significant at $p< 0.05$ and a p value of < 0.0001 was obtained using the Z-test. (Table 3)

Table 3: Specific findings and diagnostic yield of the study:

Specific findings	Number	Percentage
Granulomatous lymphadenitis-TB	130	32.34%
Malignancy	8	2%
Infections	5	1.24%
Total	141	35.58%

- Age wise distribution of the histopathological report: The yield was maximum in 10-12 years (45.5%) of age group followed by 6-8 years (38.4%) of age. Malignancy was seen maximally in the age group 8-10 years (37.5%) followed by 4-6 years (25%) of age. Tuberculosis was seen in the age group 4-6 years (25%) followed by 6-8 years (24.12%).
- The sex wise distribution of the Histopathological reports: Tuberculous lymphadenopathy (1.09:1) had the same M:F ratio and malignancy-Hodgkin's lymphoma was more in females (Ratio= 1:2.5)
- Location-wise distribution of HPE results The highest yield was seen in the inguinal lymph nodal biopsy (59.46%). Least yield was seen with the cervical group of lymph nodal biopsy. (30.55%)

Malignancy was most commonly seen in the cervical group of lymph nodes (87.5%). Tuberculosis was seen maximally in the cervical group (66.15%) of lymph nodes followed by the inguinal (16.92%) of lymph nodes.

DISCUSSION:

There are approximately 600 lymph nodes in the human body, which act as filters between the lymphatic and hematological circulations. They consist of structural cells, fibroblasts and immunological cells. The immunological components include cells from the innate immune system (macrophages, dendritic cells and Langerhans cells) and the adaptive immune system (T and B lymphocytes). The cells are contained within connective stroma and encased in a capsular shell. Lymph nodes filter lymph from set anatomical areas and the location of an enlarged node may give a clue as to the site of the underlying pathology.[1,6]

Summary of sites of lymph node and area drained is as below:

Lymph node – Area drained
1. Cervical- Head and neck
2. Submandibular and submental- Buccal mucosa, cheek and nose
3. Supraclavicular- Right-sided—thorax, Left-sided—abdominal
4. Axillary- Ipsilateral arm, breast, neck and thorax
5. Inguinal- Ipsilateral leg, buttock and lower half of abdominal wall.[2,7]

Etiology:

Lymphadenopathy may occur as a result of infection, inflammation, malignancy, drugs or other disease processes.[3] Lymphadenopathy is a common finding in the pediatric population creating anxiety amongst the parents. Peripheral Lymphadenopathy can be classified may be broadly classified into generalized (when two or more non-contiguous sites are involved) or localized (when only one site is involved). Generalized lymphadenopathy being almost always systemic, it is the localized lymphadenopathy that poses a diagnostic challenge.[3,4,8]

The summary of etiology of lymphadenopathy is as follows. (Table 4)

Table 4: Summary of causes and mechanisms of lymphadenopathy

Cause	Mechanism	Examples
Infection	Cellular proliferation as a result of antigenic stimulus as a result of a local nodal infection or regional infection	Viral—URTI, EBV, CMV, Rubella, HIV Rubeola, VZV, HSV, CoxsackievirusBacterial—Staphylococcus aureus, Group A β-haemolytic streptococcus, anaerobes, diphtheria, cat-scratch disease, tuberculosis, non-tuberculous mycobacterium Protozoa—toxoplasmosis

Malignancy	Neoplastic proliferation of inflammatory cells or infiltration of neoplastic cells carried in the lymphatic or haematological circulations	Neuroblastoma, leukaemia, lymphoma, rhabdomyosarcoma
Inflammatory	Immune response to antigen or antibodies	Kawasaki disease, juvenile rheumatoid arthritis, systemic lupus erythematosus, serum sickness, dermatopathic adenopathy
Drugs		Phenytoin, isoniazid, post DTP immunization
Other		Rosai-Dorfman disease (benign histocytosis), Kikuchi-Fujimoto disease (necrotising lymphadenitis), storage diseases (infiltration of macrophages filled with metabolite deposits), autoimmune lymphoproliferative syndrome (failure of apoptosis), Castleman's Disease (lymphoproliferative disorder), progressive transformation of germinal centers

Methods of sampling

There are three main options for sampling lymph nodes in children: excision biopsy, fine needle aspiration cytology (FNAC) and core needle biopsy[5]. The gold standard technique for lymph node biopsy in children is excision biopsy as it removes the entire lymph nodes and, thus, usually provides sufficient tissue and allows microscopic examination of all regions of the lymph nodes.[5,6] Tissue obtained by excision biopsy is sent for histological analyses, which comprise morphological assessment, immunohistochemical stains and, in some cases, tests for specific mutations such as translocations or point mutations. In addition, lymph nodes can be disaggregated and analyzed by flow cytometry, similar to blood and bone marrow. The tissue can also be sent for microbiological analysis as dictated by clinical assessment. The main disadvantage of excision biopsy is that it is an invasive procedure and is associated with risk of nerve damage, bleeding, infection, scaring and sometimes anesthetic complications.[4,5,6] FNA involves the insertion of a fine needle into a mass to aspirate cells. The aspirated cells are expelled onto slides. The needle is then rinsed in saline and specimen sent for cytological investigations, such as morphological assessment, immunophenotyping or microbiological studies[6]. The procedure has successfully been performed in children under local anesthesia only without the need for sedation, although many children, in particular young ones, will require sedation or a general anesthetic.[5,6] There are few reported complications. FNAC is widely used in adults but has not been adopted in pediatric practice. This is due to a lack of experience in interpreting the cytomorphological features of malignant cells in children, due to concerns regarding the validity of cytology in evaluating lymph nodes in children and it adds to the cost of the overall diagnosis in a developing nation. Hence, we in our institute prefer excision biopsy over FNAC. [9,10]

- In our study, we have analyzed 402 cases of pediatric lymphadenopathy over 5 years. Most of the cases are benign (98.11%) and only 1.99% account for malignant cases. This pattern is similar to the incidence reported in the study done by Shilpa G et al and Maria B et al and other studies. [4,11,13,15] This is because in pediatric population most of the lymph node enlargement occurs due to recurrent upper respiratory tract infection.[7] The most common nodes excised were the cervical lymph nodes (77.9%) which is similar to the study by Tariq et al, Mona-Al-Nazer et al and Steel BL et al. [14,15] This could be due to the ease of accessibility. Also, lymph nodes in the cervical region drain areas that are common portals of entry for a large variety of infectious agents. This makes them the most commonly involved nodes, and as expected reactive hyperplasia occurred most frequently in the cervical lymph nodes.
- The M:F ratio in our study was 1.18:1. This is accordance with the study by Mona-Al-Nazer et al (1.96:1) and Maria B (1.67:1) et al which also showed similar ratios.[15,16]
- Patients belong maximally to the age group 4-6 years of age which is similar to study by Mona Al-Nazer et al.[12,13,16] Benign disease is seen most commonly in younger age group (4-6 years) and the malignant disease is seen more commonly in the older children around 37.5% cases (8-10 years) which is seen in a similar study by Maria B et al.[15]
- The most common etiology was reactive lymphadenopathy (63.18%) in our study. This was similar to the findings Shilpa G et al and Maria B et al and other studies.[4,7,15]
- Our institute showed 130 cases of tuberculous lymphadenopathy which is similar to the study carried out by Shilpa G et al.[4] In India lymphadenopathy is the common presentation of extra pulmonary tuberculosis with massive economical implication on the health care system. It is also resurging due to the increasing incidence of Human Immunodeficiency Virus. In our study, the most common lymph node involved in tuberculosis was cervical (67.18%) followed by inguinal (16.9%) and the most common age group was 4-6 years (25%). This is similar to the article by Sarma PK et al.[14]
- Malignancy is seen in 2% cases which is similar to the study by Shilpa et al. [4] The most common malignancy seen is Hodgkin's lymphoma (87% of total malignancies) followed by Non-Hodgkin's lymphoma. The most common lymph node involved in malignancy is cervical (50%). Malignancy is most commonly seen in the age group of 8-10 years.[3,11]
- The diagnostic yield of a procedure is defined as the number of cases detected which can be estimated from the positive predictive value of the procedure. The incidence of specific pathological yield in our study was 35.58% which was found statistically significant at $p<0.05$ using the Z-test. This was similar to the findings of Ashish et al who obtained similar diagnostic yield in their study.[17]
- The highest yield is seen in inguinal group (56%) and the least seen with cervical group (30.55%) reflecting their frequent non-specific enlargement. The yield is seen maximum in the age group of 10-12 years (45.5%).[9,10]
- Had the biopsy been not done, the likelihood of missing these specific findings would have been high increasing the morbidity and further the mortality. The over-all end conclusion being that peripheral lymph node biopsy is considered favorable in eliminating diagnostic doubt.[17]
- The limitations of our study include the bias associated with a retrospective observational study.

CONCLUSION:

Lymphadenopathy in pediatric population is always a diagnostic challenge. While FNAC tends to be investigation of choice for adults, in a developing country like India with limited resources and high prevalence of tuberculosis, peripheral lymph node biopsy is the gold standard and should always be considered for patients with persistent lymphadenopathy.

In view of the simplicity and good diagnostic yield of peripheral lymph node excision biopsy, it is an indispensable tool for diagnosis in a tertiary care centre to diagnose benign as well as sinister causes of peripheral lymphadenopathy in children.

Conflict of Interest: Nil

Declaration: Nil

Sponsor: None

Ethical approval: Institutional Ethical Committee approval was obtained at the beginning of the project.

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