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Etiology of Childhood Lymphadenopathy: A Report by a Single-center (2016-2018)

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Abstract

Background: Lymphadenopathy is an enlargement of a lymph node. Pathologic Lymphadenopathy is when there is a symptom of infectious and noninfectious abnormalities or malignant diseases. Most Lymphadenopathies are benign and are associated with a short period of symptoms. Concerning diagnosis and management of adenopathy, especially in the case of children, research is still underway. For this reason, our study investigated and analyzed the causes of lymphadenopathy in children.

Materials and Methods: This is a retrospective study conducted at the Pediatric Department of children's medical center of Tehran University of medical science. In this study, 130 children with cervical lymphadenopathy aged under 12 years underwent lymph node biopsy. Then under general anesthesia and evaluation of a senior pathologist, the lymph node was excised and biopsied.

Results: During the study, twenty-five cases were excluded. Fifty-three patients (50.47%) demonstrated infection history, 22 cases (21%) had neoplasia, and reactive inflammatory changes with nonspecific origin were seen in 42 cases (40.0%). We observed chronic lymphadenitis in 3(2.9%) cases, and finally, 1(1.0%) case was metastatic. Mean lymph node size proved to be greater than two cm in metastatic (2.22cm), lymphoma (2.33cm), and granulomatous (3.17cm) lymphadenopathies. The average lymph node size turned out to be 1.53 cm in reactive lymph nodes (P =0.021). The diagnosis was obtained by excisional biopsy and histopathology.

Conclusion: Acute infections are the most common reason for lymphadenopathy in pediatric conditions. It is better to be suspicious of malignancy with a high index in cases of cervical lymphadenopathy, especially if the lymph node size is higher than 2 cm. History, clinical features, and paraclinical tests can be used for lymphadenopathy in children.

Keywords: Children, Etiology, Lymphadenopathy

Introduction

Common among the children are the enlarged cervical lymph nodes. A palpable lymph node is seen in 38% to 45% of the average population among children due to lymphoid tissue increment (1). The augmented incidence of congenital conditions and infectious diseases, along with the relative absence of malignant disorders, can contribute to this condition (2). For this reason, lymphadenopathy can, in some cases, project the existence of the more severe disease, i.e., malignancy (3). Lymphadenopathy can be defined as an enlargement or a change in the features of a lymph node. Pathologic Lymphadenopathy is usually a manifestation of infectious or noninfectious conditions, or in rare situations, malignant diseases. Most lymphadenopathies are benign that generally trigger a short period of symptoms (4). Enlargement of more than two noncontagious lymph nodes is defined

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as generalized lymphadenopathy. In evaluating lymphadenopathy, an accurate history, physical examination, appropriate laboratory evaluation, and mind full imaging help decide tissue sampling accurately. Antibiotic therapy often improves acute lymphadenopathy or may resolve spontaneously due to viral illnesses (5, 6).

A surgeon should consider key historical questions such as location, duration, progression, associated symptoms, including pain, fever, weight loss, and night sweat, during examing a child (7). Additional data include recent illness, upper respiratory tract symptoms, infections, trauma, bites, and dental problems. Current vaccination should be evaluated as bacillus Calmette-Guerin (BCG) (8, 9). An excisional biopsy may obtain adequate tissue to conduct flow cytometry, chromosomal analysis, and the use of special stains. Excisional biopsy is accommodated for the following cases: hard, matted, or fixed lymph nodes extended to the surrounding tissues, progressively enlarging supraclavicular, epitrochlear, mediastinal areas hepatosplenomegaly condition. Lymph nodes are typical structures, and a given type of it may be palpable in a healthy patient, especially in a young child.

The presence of abnormally enlarged lymph nodes may describe a severe underlying systemic disease, so the differential diagnosis of lymphadenopathy can be broad. Therefore, developing an approach to lymphadenopathy is challenging for a pediatrician to differentiate between pathologic and nonpathologic lymph nodes(10, 11). The disease can also be a source of parental anxiety associated with malignancy. Therefore, it is necessary to know when the patient should be referred to a subspecialist. This study aimed to determine the causes of childhood lymphadenopathies to take a systematic attitude to these lesions based on anatomy, history, and clinical features to decrease some unnecessary investigations and reduce the parents' anxiety (12, 13).

Materials and Methods

This is a retrospective study carried out at the Pediatric Department of children's medical center of Tehran University of medical sciences for three years from January 2016 till December 2018. Collected information for this study included age, gender, location of lymphadenopathy (cervical, axillary, or inguinal), lymph node size (cm), and the pathologist's report. All the children under 12 years old with lymphadenopathy who had undergone lymph node biopsy were entered into the study. Notably, lymph node examining is a critical aspect of physical examination in both well and diseased children and adolescents. We addressed lymphadenopathy with the lymph nodes that were more than 10 mm in size and any persistent lymphadenopathy existing for more than three weeks. The lymph nodes were excised under general anesthesia to be biopsied and evaluated by a senior pathologist.

Statistical analysis

All data were analyzed by PASW 22 (IBM Corporation Company, USA). Chi-square, student t-test, and Fisher exact test were used for data analysis. P values less than 0.05 were considered significant.

Ethical Consideration

The Ethics Committee of Tehran University of medical sciences approved the study protocol (Research project number IR.TUMS.CHMC.REC.1398.117).

Results

In total, 130 patients were enrolled in the research, their mean age was 6.5 years (range, two months to 12 years), and 65.7% of the cases were male. Twenty-five patients were excluded from the study due to carrying insufficient data. Therefore, the

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cases of lymphadenopathies who underwent lymph node biopsy amounted to 105. The abnormal locations were 62.9% cervical, 24.8% axillary, and 12.4% inguinal. In 22 cases (21%), lymphoma diagnosis was proved. Reactive nonspecific origin (NAS) changes were discerned in 42(%) of the children. Granulomatous inflammation was seen in 32 (30.5%) patients. Chronic lymphadenitis was observed in 3(2.9%) cases, and finally, 1(1.0%) of the cases was metastatic. Mean lymph node size was more significant than 2 cm in metastatic (2.22cm), lymphoma (2.33cm), and granulomatous (3.17cm) lymphadenopathies. Average lymph node size showed to be 1.53 cm in reactive types (P= 0.021). The diagnosis was obtained by utilizing excisional biopsy and histopathology. Ninety percent of malignant lymphadenopathies were cervical. Cervical lymphadenopathy, therefore, needs to be addressed as highly possibly a malignant case.

Discussion

Male patients were more prominent than females. Our study aligns with Oguz and colleagues' results on 457 patients within the age range of 2 months to 19 years (14). Although relevant management algorithms have been determined to diagnose generalized lymphadenopathy, a general agreement in the international pediatric literature for appropriate examinations of lymphadenopathy in children remains known. Reactive lymphadenopathy is defined as lymph node enlargement due to hyperplasia of cellular components, benign and reversible process with no clonal process, and no cytologic or architectural atypia (15-17). A comprehensive review of adenopathy in pediatrics has recently been published (3, 18, 19). However, our study showed more malignant cases (21% vs. 2.7% and 1.15%), which contrasts with other investigations likely arising from the more significant number of patients participating in our study. We explain this contrast as our unit is a hemato-oncology children's center. Additionally, our research's common cause of cervical lymphadenopathy was lymphoma, hence being consonant with some previous inquiries (20). Drs Weinstock et al. in 2018 reported the most common reason for cervical lymphadenopathy in children as reactivity to known and unknown viral agents. The next most common cause of the disease included bacterial infections ranging from aerobic to anaerobic to mycobacterial infections. Malignancy was identified to be the most projected cause of cervical lymphadenopathy (21, 22). The prevalence of idiopathic cervical lymphadenopathy in other studies was 45% to 60% (23, 24). In the present study, 40.0% of patients showed reactive benign lymphadenopathy. It is worth noting that the occurrence of other masses similar to lymph nodes is possible in pediatric cases so that they are likely to be mistaken for enlarged cervical lymph nodes such as thyroglossal duct cyst, dermoid cyst, lipoma, and the like. Ankita Deosthali and colleagues in 2019 investigated 2687 patients and demonstrated that two-thirds of cases appear to have no identifiable etiology. Epstein-Barr virus, malignancy (3.3%), and granulomatous disease were the most common etiologies in patients with definitive diagnosis (25); this is inconsistent with our study. The authors believe that planning an approach to cervical lymphadenopathy can allow an accurate diagnosis. Recording patients' clinical data implementing diagnostic tests such as complete blood count (CBC), C-reactive protein(CRP), Chest X-ray, and CT scan is required (26, 27). Assessment of the location, size, presence of inflammation characteristics such as redness, tenderness, elevated skin heat, relation with peripheral tissue, including fixed or otherwise, are clinical approaches to cervical lymphadenopathy. A diameter of <2 cm, an ovoidal shape, and elastic texture characterize a normal lymph node (28). In contrast, lack of acute

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inflammation, rigid and fixed state of the lymph node to the underlying tissue, showing a diameter >2.5 cm, or being located in high-risk sites are features that project the likelihood of malignancy (29). In addition, the lymph node long /short axis ratio (L/S), vascular pattern, and hilum echogenicity need to be examined on ultrasonography evaluation, even if for the benign or malignant condition of the disease, no single ultrasound feature is specific. Incompatibility with malignancy, usually, L/S being around one, echogenicity exhibiting deformation, lack of hilum, irregular margins, extracapsular involvement, and chaotic vascular patterns need to be addressed (30). Establishing diagnosis also appears to be urgent in the following cases: symptoms or signs of malignancy exist, lymphadenopathy persists or enlarges, and the diagnosis remains in doubt. We suggest excisional biopsy in accord with other researchers. Results of FNAB in children are not sensitive and specific. Implementation of FNAB in children is not recommended (31). Bone marrow biopsy (BMB) is also one of the most crucial steps in treating lymphadenopathy. In case the serum lactate dehydrogenase(LDH), uric acid, or erythrocyte sedimentation rate (ESR) appear to elevate, or there are signs of leukopenia, leukocytosis, anemia, thrombocytopenia, thrombocytosis, fever (core T>37.8), sweating, weight loss>10% since the last three months, or mediastinal lymph node in CXR, we perform BMB (32).

In some cases, a lymph node itself becomes infected by bacteria, and if the gland appears to be large, the skin around it will become red, very painful, and tender. Immediate medical treatment and antibiotics are necessary, and there might be a need for drainage (5, 33). Notably, an accurate history, prominent physical examination findings, and laboratory results can contribute to a procedure, endorsing the malignant etiology. In many cervical lymphadenopathies, the etiology is benign rather than malignant. Due to this issue, the clinical providers should reassure the pediatric patients and their families.

Conclusion

Acute infections are the most common reason for lymphadenopathy in pediatric conditions. It is better to be suspicious of malignancy with a high index in cases of cervical lymphadenopathy, especially if the lymph node size is higher than 2 cm. History, clinical features, and paraclinical tests can be used for lymphadenopathy in children.

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Conflict of interest

There is no conflict of interest.

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