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CAUSES OF CERVICAL LYMPHADENOPATHY IN CHILDREN OF THE REPUBLIC OF UZBEKISTAN AND ITS CONNECTION WITH CHILDHOOD CANCER

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✓ ***Resume***

Objectives: Peripheral lymphadenopathy remains an extremely common clinical problem in Pediatrics. To define the causes of lymph node enlargement in children in this environment.

Methods: In period of January-December 2023, we conducted research on the problems encountered during the diagnosis of cervical lymphadenopathy (LAP) in children of Uzbekistan. Based on the obtained conclusions, we created a rapid diagnostic algorithm of children's dysphadenopathy in Uzbekistan and applied it to our practice.

Results: One hundred fifty-four (154) with a median age of six years (range two months-18 years) were included in our study. The majority of the patients (98%) had localized lymphadenopathy and the head and neck region was the most common site of involvement (87%). Twenty-four patients (15.6%) had lymph node biopsy. Four patients had ruptured epidermal cyst, lymphangioma, pilomatricoma and ectopic thymus. Of the other biopsies, nine patients were diagnosed with reactive LAP, four with lymphadenitis, and four with Hodgkin's disease. The lymphoma patients had lymph node size greater than 2.5 cm and the duration of lymphadenopathy was longer than four weeks. Three out of four patients had systemic clinical findings accompanying lymph node enlargement.

Conclusion: Enlargement of cervical lymph nodes in children can rarely occur in children's cancer and in most cases in benign tumors and common childhood infections. Lymph node biopsy can be avoided in many children based on previously studied treatment algorithms.

Keywords: cancer; children; lymphadenopathy.

ПРИЧИНЫ ШЕЙНОЙ ЛИМФАДЕНОПАТИИ У ДЕТЕЙ РЕСПУБЛИКИ УЗБЕКИСТАН И ЕЕ СВЯЗЬ С ДЕТСКИМ РАКОМ

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✓ ***Резюме***

Цели: Периферическая лимфаденопатия остается чрезвычайно распространенной клинической проблемой в педиатрии. Определить причины увеличения лимфатических узлов у детей в данной среде.

Методы: В январе-декабре 2023 года мы провели исследование проблем, возникающих при диагностике шейной лимфаденопатии (ШЛА) у детей Узбекистана. На основании полученных выводов мы создали алгоритм экспресс-диагностики детской дисфаденопатии в Узбекистане и применили его в нашей практике.

Результаты: В наше исследование были включены сто пятьдесят четыре (154) человека со средним возрастом шесть лет (диапазон от двух месяцев до 18 лет). У большинства пациентов (98%) наблюдалась локализованная лимфаденопатия, причем наиболее частой

локализацией поражения была область головы и шеи (87%). Двадцати четырем пациентам (15,6%) была проведена биопсия лимфатических узлов. У четырех пациентов наблюдался разрыв эпидермальной кисты, лимфангиома, пиломатрикома и эктопия тимуса. Из других биопсий у девяти пациентов был диагностирован реактивный ЛАП, у четырех – лимфаденит и у четырех – болезнь Ходжкина. У пациентов с лимфомой размер лимфатических узлов превышал 2,5 см, а продолжительность лимфаденопатии превышала четыре недели. У трех из четырех пациентов наблюдались системные клинические проявления, сопровождающие увеличение лимфатических узлов.

Заключение: Увеличение шейных лимфатических узлов у детей редко встречается при детском раке и в большинстве случаев при доброкачественных опухолях и распространенных детских инфекциях. Биопсии лимфатических узлов можно избежать у многих детей на основании ранее изученных алгоритмов лечения.

Ключевые слова: рак; дети; лимфаденопатия.

O‘ZBEKISTON RESPUBLIKASI BOLALARIDA BACHADON BO‘YNI LIMFADENOPATIYASINING KELIB CHIQISH SABABLARI VA UNING BOLALAR SARATONI BILAN BOG‘LIQLIGI

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✓ ***Rezyume***

Maqsadlar: Periferik limfadenopatiya pediatriyada juda keng tarqalgan klinik muammo bo'lib qolmoqda. Ushbu muhitda bolalarda limfa tugunlarining kengayish sabablarini aniqlash.

Usullari: 2023-yilning yanvar-dekabr oylarida O‘zbekiston bolalarida bachadon bo‘yni limfadenopatiyasi (LAP) diagnostikasi jarayonida yuzaga keladigan muammolar bo‘yicha tadqiqot o‘tkazdik. Olingan xulosalar asosida O‘zbekistonda bolalar disfadenopatiyasining tezkor diagnostika algoritmini yaratdik va amaliyotimizga tatbiq etdik.

Natijalar: Tadqiqotimizga o'rtacha yoshi olti yosh (ikki oydan 18 yoshgacha) bo'lgan bir yuz ellik to'rt (154) ishtirok etdi. Bemorlarning aksariyatida (98%) mahalliy limfadenopatiya bo'lgan va bosh va bo'yin mintaqasi eng ko'p uchraydigan joy (87%) edi. Yigirma to'rtta bemorda (15,6%) limfa tugunlari biopsiyasi o'tkazildi. To'rt bemorda epidermis kistasi, limfangioma, pilomatrikoma va ektopik timusning yorilishi bor edi. Boshqa biopsiyalardan to'qqizta bemorga reaktiv LAP, to'rttasida limfadenit va to'rttasida Xodgkin kasalligi tashxisi qo'yilgan. Limfoma bilan og'rigan bemorlarda limfa tugunlari hajmi 2,5 sm dan oshdi va limfadenopatiya davomiyligi to'rt haftadan ko'proq edi. To'rt bemordan uchtasida limfa tugunlarining kengayishi bilan birga keladigan tizimli klinik belgilar mavjud edi.

Xulosa: Bolalarda bachadon bo'yni limfa tugunlarining kengayishi kamdan-kam hollarda bolalar saratonida va ko'p hollarda yaxshi xulqli o'smalarda va bolalik davridagi keng tarqalgan infektsiyalarda paydo bo'lishi mumkin. Oldin o'rganilgan davolash algoritmlari asosida ko'plab bolalarda limfa tugunlarining biopsiyasidan qochish mumkin.

Kalit so'zlar: saraton; bolalar; limfadenopatiya.

Relevance

Lymphadenopathy is a common clinical finding in child- hood. The lymph node size above the expected limits and/or disruption of its structure is called LAP. Although it varies according to the region where the lymph node is located, lymph nodes that are generally greater than 1-1.5 cm, and in some resources larger than 2.5 cm and/ or deformed structure are considered pathological. LAP is most often seen in response to regional or systemic acute infections and has a good course. Severe diseases,

such as chronic infections, rheumatological diseases and rarely childhood cancers, can be included in its etiology. The frequency of cancer among patients who are followed up due to growth in lymph nodes varies according to the centers. In primary care centers, the proportion of patients diagnosed with cancer in all age groups generally does not exceed one percent.

The likelihood of malignancy is much lower in children, especially in acute conditions.[1–5] Referral of patients with- out adequate evaluation of cancer risk reduces the rate of cancer in reference centers. Directing patients with lymph node enlargement to outpatient clinics of pediatric oncology without investigating and monitoring other causes in its etiology may cause panic in patient and family and an increase in the burden of oncology outpatient clinics.

Purpose of the study: In our study, we planned to determine the clinical and laboratory features, biopsy and cancer diagnostic indicators in patients referred to our oncology clinic with a diagnosis of PAP.

Material and methods

Patients who were referred to pediatric oncology out clinic with the diagnosis of the LAP between January 2023 and December 2023 formed the study group.The patients were determined according to the diagnostic codes of ICD were examined prospectively. As diagnostic codes, R59 (enlarged lymph nodes), were chosen. Data wereobtained from the "Lympharegistry" created in online system of the patients determined according to thesecodes. Information about the center that sent these patients means of transportation, age, and gender of the patients' duration of their complaints, presence of systemic signs and symptoms, location and structure of the lymphnode; the results of the examinations performed in the center and hospital where the patient was first applied, and antibiotherapy administered (if any) were recorded.The proportion of patients who needed a biopsy and the frequency of malignancy were calculated, and the features that might be related to malignancy were investigated.

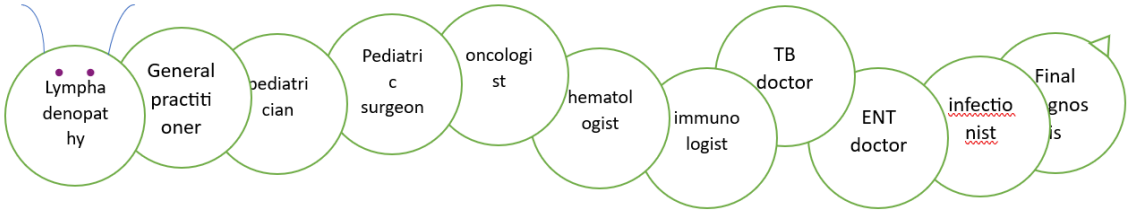
Result and discussions

A total of 154 patients who came to 3 clinics of Tashkent with the diagnosis of LAP formed the study group. Eighty percent of the patients with a male/female ratio of 31/123 and a median age of six years (2 months-18 years), were sent from General practitioners of local policlinics while 20% them were sent from the pediatric, pediatric surgery or ENT (ear nose, and throat) private hospitals for consultation.

In patients sent with the diagnosis of mesenteric LAP, lymph node size was determined on the ultrasonography (US) re- quested with the indication of abdominal pain. The median time elapsed between the first application to a physician and the referral to pediatric hospitals in the whole group was 43 days and ranged from one day to four years (picture 1. Caterpillar.).

Our patients had upper respiratory tract infection (URT: 60%), typical adenoid face and/or allergic rhinitis (22%). Dental caries were detected in 12% and skin infection in 3% of all cases, while 7% of them complained of abdominal pain. One patient was in the active period of chickenpox infection.

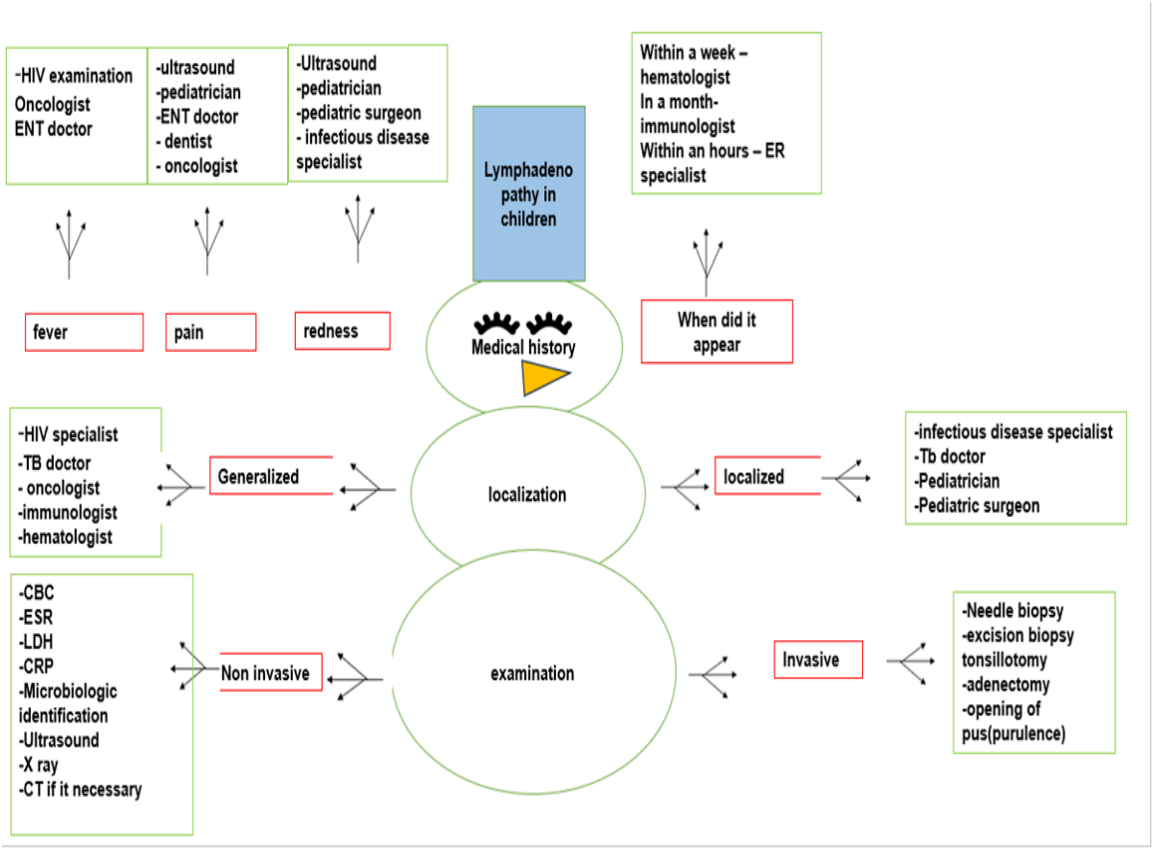
When the examinations performed before referrals to our outpatient clinic were reviewed, it was seen that the most requested examination was ultrasonography (US) for the enlarging lymph node. Information about the size of the lymph node was given in 62% of US reports, and findings of fatty hilus, bleeding, resistance and echogenicity that could be used in differential diagnosis were not specified.



Picture 1. Caterpillar.
Current situation on diagnosis of lymphadenopathy in Uzbekistan.

The lymph node sizes reported in the US reports of 90% of the patients were larger than patients measured during the examination. The rates of other examinations performed are shown in Table 2. There was microcytic anemia in four cases and positive EBV IGM in two of the blood tests. None of the patients were referred to the dentist or allergy out- patient clinic before referral to oncology.

Ninety-eight percent of the lymph nodes were regional and most commonly located in the cervical location. Their dimensions were found between 0.5-5 cm (median 2 cm) during physical examination (picture 2 snowman).



Picture 2. Snowman.

Survey for doctors

The lymph nodes had normal histology in 24.6% of the cases and they measured 1 cm or less in diameter. Since there were no serious accompanying systemic signs and symptoms, lymph nodes were not evaluated pathologically and removed from follow-up. One patient in the group had hepatosplenomegaly and two patients had splenomegaly. Organomegalies exceeded normal limits at most 2 cm. They had soft consistencies and regressed during follow-up; these organomegalies were thought to be due to infection.

The antibiotherapy was initiated in 90% of the patients, and treatment was continued in patients still taking anti- biotics. Among other patients, any treatment was not ad- ministered to any patient other than a patient with a dental abscess, who was considered to receive undertreatment.

A biopsy was performed in 21 (15.6%) of the cases. The pathological examination results are summarized in Table 3. The cancer detection rate was 19% among biopsied patients and 3% in the whole group. In patients diagnosed with Hodgkin lymphoma, the LAP size was greater than 2.5 cm, and the LAP was present for longer than four weeks. In addition, three of them had accompanying systemic findings (Table 1).

Swollen lymph nodes in the throat, itching and swelling	Chronically enlarged lymph nodes in frequently ill children	Enlarged neck lymphadeno pathy and long-term weight loss? Subfebrile fever	Supraclavicular/pos terior cervical or “uncommon” localized lymphadenopathy mass with unexplained weight loss or systemic intoxication	Progressivel y generalized lymphadeno pathy with pallor, hemorrhage, septic condition	Simple and mild generalized lymphadeno pathy	Painful unilateral lymphaden itis with fever and local redness	generalized lymphadenopat hy with severe immunodeficien cy, frequent opportunistic infectious episodes
ENT doctor	immunologist	TB specialist	Pediatric oncologist	hematologist	Infectious disease specialist	Pediatric purulent surgeon	HIV specialist
Profmedse rvice private ENT Clinic	De factum – private hospital	1.Republica n Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonolog y 2. intermed innovation	Center of pediatric Hematology and Oncology	Center of pediatric Hematology , Oncology	Clinic of the Research Institute of Epidemiolog y, Microbiolog y and Infectious Diseases	Clinic of the Tashkent Pediatric Medical Institute, Departmen t of Purulent Surgery	Center of Virology
Streptococc cal sore throat	Immunogram	Quantiferon gold Assey	Ultrasound, LDH, CBC, ESR	Spleen and hepar Ultrasound, CBC + bone marrow biopsy	PCR tests for Toxoplasmo sis Mononucleo sis Chickenpox Measles	Acute purulent lymphaden itis	AIDS, HIV
Streptatest , CRP	Primary Immunodeffcie ncy	TB infection	Malignant neoplasm such as Hodgkin or non hodgkin’s lymphoma or Neuroblastoma, sarcoma, carcinoma	Acute leukemia, Hemophago cytic histicytosis, Langerhans cell histicytosis	Infectious diseases	CBC CRP US	PCR test for HIV
Antibacter ial therapy	Specific therapy on PID guidelines	Specific treatment	Specific treatment	Specific treatment of Al	Ant infectious treatment	Purulent abscess opening	ARVT therpy

Discussion

Lymph nodes are often encountered in childhood. In a study conducted with children under the age of five, lymph nodes were found in 44% of healthy children and in 64% of the children examined for a disease [6]. In order for the pal- pated lymph node to be considered pathological, its size should be above normal limits and/or its structure should be deteriorated. In a significant portion of our cases (i.e., 24.6%), lymph nodes were not evaluated as LAP, the reason for referring to oncology could not be explained and these cases were not followed up.

Most of the enlargements in lymph nodes are reactive, have a benign course, and usually develop during viral infections. Since childhood cancers are considered in its etiology, the growth of lymph nodes worries families and even doctors, regardless of their size and structure. These concerns may cause patients to be referred to oncology without being adequately evaluated and monitored. The possibility of malignancy is low, especially in LAPs, present for less than 2-4 weeks or have not increased in size for more than a year. Cancerous tumor development is also less frequently seen in mobile, soft LAPs less than 2.5-3 cm in size, in the patients with cervical location, and without concomitant severe systemic signs and symptoms.[1–10]

Patients should be adequately evaluated for these features and oncology consultation should be requested in case of doubt. In our study, only three patients (2%) had extensive lymph node involvement and 85.5% of the regional lymph nodes were located in the cervical or submandibular regions. Only

6.7% of thepatients had lymph nodes measuring >2.5 cm in diameter. Sixty percent of patients had signs of upper respiratory tract infection at the time of diagnosis or previously. The time elapsed between noticing the lymph node and referral of the patient to us was less than two weeks in 61% and more than one year in 12% of the cases.

Conclusion

The following results were obtained from our interactive database: Each patient studied by marketing spent an average of 26 days to 3 months for diagnosis and visited at least 5 hospitals and 24 clinical centers with a coupon. 10 million soums (~800$) were spent on average for each patient after calculating the amount of money spent.

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