



Streptococcal carriage in children with cervical lymphadenopathy

Cervical lymphadenopathy

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Abstract

Aim: To demonstrate the rate of streptococcal carriage in children with unexplained cervical lymphadenopathy (LAP) with clinical examination and ultrasonographic findings as well as by throat culture. **Material and Method:** A total of 90 children (45 patients and 45 control groups) were included in the study. All the patients were diagnosed radiologically on the basis of ultrasonographic evaluation. Pediatric patients who were followed up for at least 6 weeks for cervical LAP and whose LAP size was greater than 1 cm were studied. Throat culture and anti-streptolysin O titer (ASOT) was ordered for the patient and control groups. **Results:** LAP size was measured as minimum 20*5 mm and maximum 35*8 mm in US guided measurements. Bacterial reproduction was detected in 13 (28.9%) patients and only in one control subject (2.2%), which was statistically significant. The mean ASOT was found to be lower in the study group (ASOT: 90.70 IU/mL) and higher in the control group (ASOT: 208.00 IU/mL), but no significant difference was found between the groups ($p=0.113$). **Discussion:** Throat culture is a non-invasive test, but requires other tests for definitive diagnosis. In our study, bacterial reproduction detected in throat culture correlated with unexplained cervical LAP.

Keywords

Cervical Lymphadenopathy; Throat Culture; Anti-Streptolysin O; Bacterial Reproduction

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Introduction

Cervical LAPs are common in childhood and are usually benign. While LAP is fairly rare in healthy children under 1 year of age without adenitis and severe systemic diseases, it is frequently seen above 1 year of age [1]. However, when is detected over two years of age, a clarifying diagnostic finding is quite rare [2]. The most common are infective or inflammatory LAPs; malignancy is very rare. LAPs of large diameters (greater than 1 cm), supraclavicular LAPs, presence of hepatosplenomegaly, and a history of malignancy are the findings that increase the risk of malignancy [3,4]. Chronic cervical lymphadenopathy (greater than 6 weeks duration) has an unclear cause and does not respond to observation or medical treatment [5].

Approximately 15-30% of acute tonsillopharyngitis cases are of bacterial origin. The bacterial microorganism of clinical significance is group A beta hemolytic streptococcus (GABHS), namely streptococcus pyogenes [6,7]. Acute GAS infections cause development of skin sores and pharyngitis in children. Culture by throat swab in a sheep blood agar plate (BAP) first described in 1954 by Breese and Disney, is the standard method for the diagnosis of GAS pharyngitis [8,9,10]. The only disadvantage of the highly reliable throat culture is the delayed results. The measurement of streptococcal titres, particularly anti-streptolysin O titre (ASOT), is important in the diagnosis of acute rheumatic fever, and for distinguishing GABHS pharyngitis from asymptomatic GABHS throat carriage [11,12].

The objective of this study was to demonstrate the rate of carriage in children with unexplained cervical LAP diagnosed as having pathologic dimensions through throat culture and to shed light on the etiology of this pathology.

Material and Method

The study consisted of patients presented to the Department of Otolaryngology between 2016-2017 due to cervical LAP. A total of 90 children aged between 3 and 15 years were enrolled in the study. The study group consisted of 45 pediatric patients and the control group included 45 healthy pediatric controls. The patients were referred to the clinic with swelling in the neck. Medical histories were taken and the patients were examined. Age and gender were recorded and accompanying diseases were assessed. After carefully considering the medical history, epidemiologic clues, a physical examination, laboratory testing, and imaging, the cause of the cervical lymphadenopathy remained unclear.

Cervical regions were divided into eight levels on each side (IA, IB, IIA, IIB, III, IV, VA, VB) according to consensus definitions set forth by the American Head and Neck Society [13,14]. All of the patients were diagnosed radiologically by ultrasonographic (US) evaluation using a high-resolution Doppler ultrasonography system (Aplio™ 400 Platinum, Toshiba Medical Systems Corporation, Tochigi, Japan). Ultrasound examination was applied to determine the number of involved regions and the location and size of the largest node. Assessment of node morphology comprised evaluation of the nodal shape by measuring the long-to-short axis ratio (L/S), US hilum, homogeneity of echo-texture, clarity of margins, and intranodal vascularity. Final diagnoses were based on clinical findings or histology, laboratory testing, and US evaluation. We followed the patients at certain intervals.

Inclusion and exclusion criteria

Patients with a LAP size greater than 1 cm were routinely followed. Patients who were followed up for at least 6 weeks for cervical LAP and whose LAP size was greater than 1 cm were considered as chronic LAP and were included in the study. Throat culture and anti-streptolysin O titer (ASOT) were followed the patients at certain interval obtained from patients with chronic LAP and from the control groups. An ASOT level above 200 IU/mL was considered as high.

The control group consisted of patients who presented to the Phoniatory Unit due to speech disorders, with no history of chronic tonsillitis or cervical LAP and with normal acute inflammation parameters. Parents of the children in both groups were asked whether their child exhibited clinical symptoms such as sore throat, fever, chills, or malaise within the previous four weeks. Those who had any such symptoms or signs were excluded from the patient and control groups. The children who were on antibiotic treatment were also excluded. If the node was smaller than 1 cm or the node was fluctuating in size without any other concerning features, then the patient was excluded from the study. Children in the patient group with suspicious malignant were referred to the Pediatric Hematology Department. We conducted a plan biopsy for non-oval lymph node masses, extra articular or eccentric hilum, central nodal necrosis without peripheral inflammation, hypoechoic parenchyma, and displaced hilar vasculature by US. Considering the recommendation of the pediatric hematology department, a fine needle biopsy was performed on some of the patients and an excisional biopsy was performed on the others. Patients with biopsy results compatible with the inflammation were included in the study, while the patients with malignant outcomes were excluded.

GABHS detection

Throat swabs sent to the microbiology laboratory were incubated for 24 hours at 37 °C with 5% sheep blood agar. At the end of the incubation, Gram staining of the colonies that had undergone beta hemolysis was performed. The catalase tests of the colonies identified as gram-positive-chain cocci were studied. Strains identified as beta hemolytic streptococcus with a negative catalase test were further tested for group determination. For Lancefield group determination of the isolated beta hemolytic streptococci, Groups A, C, and G were distinguished using BD BBL™ Streptocard™ Enzyme Latex Test (Becton Dickinson, Diagnostic Instrument System, Sparks, USA).

Statistical analyses

Normality of the data was evaluated by the Kolmogorov-Smirnov test. The Mann-Whitney U test was applied for the comparisons of the groups. Chi-square test and exact test were used in examination of categorical variables. The statistical parameters are expressed as Median (Min-Max). Statistical significance was considered as $p < 0.05$. A power analysis of 0.80 test was applied at a significance level of $\alpha = 0.05$ and the number of persons taken into the study was determined. Statistical analysis of the data was performed using SPSS version 22 (IBM SPSS for Windows version 22, IBM Corporation, Armonk, New York, United States).

Results

The mean age was 7.69 ± 3.21 in the study group and 7.93 ± 2.92 in the control group, 29 (64.4%) were male and 16 (35.6%) female in the study group, and 33 (73.3%) were male and 12 (26.7%) female in the control group. LAP size was measured as min 20×5 mm and maximum 35×8 mm in US guided measurements. The ultrasonographic evaluation revealed oval-shaped lymph nodes with the domination of long axis in 42 patients (78.2%). The proper width of hilus and their proper vascularization were observed in 40 children (72.7%). The cervical classification was IB, IIA, or IIB in 80% of the study group.

Bacterial growth was identified in 13 (28.9%) of the 45 study group samples, while only one child in the control group showed growth (2.2%); this result was statistically significant ($p < 0.001$). In the patient group, GABHS bacteria colonization was detected in 10 cases (76.9%) and group G streptococcus (GGBHS) was detected in 3 cases (23.1%). In a patient with GGBHS detected by throat culture, staphylococcus aureus was also isolated. No streptococcus was isolated in the control group. Staphylococcus aureus was only isolated in one patient (Table 1). The bacterial growth distribution in the patient and control groups is shown in Figure 1. The median ASOT was 90.70 IU/mL (51.60-1220.00) in the patient group and 208.00 IU/mL (52.00-603.00) in the control group, but no significant difference was found between the groups ($p = 0.113$) (Table 2).

Discussion

GABHS are a common seen the Gram positive coccis. GABHS can be colonized in the pharynx of asymptomatic people. But the mechanism of invasive disease development is not fully clear. The present data suggest that chronic pharyngeal carriers create a low risk for poststreptococcal complications (acute rheumatic fever, acute glomerulonephritis), because carriers are thought to have no active immune response to GABHS. In this study, patients with bacterial colonization were asymptomatic but had a positive throat culture.

The most common bacterial factor responsible for acute throat infections is GABHS. Staphylococcus aureus, Groups C and G streptococci, and Gram negative bacilli are other bacteria causing upper respiratory tract infections. Some of the patients with GABHS growth in throat culture may be carriers. In the studies performed on the school age children, the rate of carriage ranges from 10% to 20% [15,16,17]. In our study, 28.9% of pathological cervical LAP patients were found to have bacterial growth in the throat culture. When we looked at the clinical characteristics of the patients, none of them had recurrent chronic tonsillitis. We detected 76.9% of the bacterial growth in our patient group as GABHS. This result suggests that an estimated subclinical infection in our patient group might stimulate lymphoid proliferation as an immunological response. Furthermore, we think that the degree of colonization and invasion might be affected depending on the balance between the natural and acquired immune system of the host and the bacteria present in the oropharynx. There have not clinical symptoms or findings in the carrier persons. The greatest risk of the carriers is that they will transmit GABHS to the persons they contact.

However, to date there is no evidence for any other risks. Studies show that carriers do not need to be treated because of the low risk of the development of rheumatic fever and contagiousness [18].

The normal values of ASOT vary and are usually dependent on the age of the patient, geographical location, epidemiological setting, and the season of the year [19]. ASOT is detected as high in recurrent tonsillitis episodes. Elevation of ASOT is an immunological response. The absence of an active immunological response in GABHS carriers also prevents a rise in ASOT. But, in our study, we found that ASOT was lower in patients than in the control group.

Reactive lymphadenitis due to underlying acute bacterial or viral infection is the most common cause of significant cervical lymphadenopathy in children. Management algorithms in patients with generalized lymphadenopathy have been established. On the other hand, there are still no formal guidelines for chronic cervical lymphadenopathy in the pediatric population. US has better resolution in the pediatric neck than in adults [20]. It can determine the shape, size, internal composition, vascularity, and status of surrounding soft tissues of an enlarged lymph node [20]. Benign reactive lymph nodes tend to be solid, oval structures with a fatty echogenic hilum and minimal to no hilar vascularity [21]. When suspicious characteristics are seen on US, computed tomography (CT) and/or MRI can provide additional information and confirm the sonographic findings [21]. Reactive benign LAPs detected in the patient may occur due to upper respiratory tract infections, pharyngitis, tonsillitis, or otitis media (viral or bacterial). However, it is often difficult to establish the etiologic cause of LAPs that persist for longer than 1 month and that reach pathological dimensions. Concerning findings that may suggest malignancy include nodes that are rapidly enlarging, are nontender, and are fixed to the skin or underlying structures. Also, generalized lymphadenopathy, supraclavicular nodes regardless of size, lower cervical nodes, increased patient age, lymph nodes greater than 2 to 3 cm, and hepatosplenomegaly are associated with increased risk of malignancy [3,22,23,24]. Associated systemic symptoms, such as weight loss, night sweats, unexplained fever, or fatigue should initiate further workup for possible malignancy or chronic inflammatory conditions [25,26]. None of these symptoms were present in our subjects.

Studies have shown that the Epstein-Barr virus helps in the identification of Cytomegalovirus, Toxoplasma, and Bartonella infective cases [27,28]. It has also been shown that the complete blood count is abnormal in some malignant conditions [3]. The specificity of fine needle aspiration cytology (FNAC) is high, between 92-94.4%, but its sensitivity varies between 67-97.1%. For this reason FNAC is not completely reliable [29,30]. The most reliable method for excluding malignancy in children is excisional biopsy. However, this process has morbidity.

In our study, we think that performing throat culture, a non-invasive method and routine examinations may help to reveal the etiologic factor in cases of LAPs with suspected malignancy. Finally, we think that more comprehensive studies are needed to understand what causes LAP, which is an immune response, to reach pathologic dimensions.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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