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Etiology and clinical pattern of cervical lymphadenopathy in Sudanese children

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ABSTRACT

Cervical lymphadenopathy (CLA) is a common childhood problem in clinical practice which poses diagnostic difficulties to pediatricians. The aims of this study were to determine the causes of CLA in Sudanese children and to evaluate the value of routine laboratory tests in determining the etiology. Demographic and clinical data were prospectively collected from eighty children with palpable cervical nodes. Children were then subjected to complete blood count, ESR, Mantoux test, aspiration cytology of a lymph node and serological tests for HIV agglutination test, ELISA for Epstein–Barr virus and toxoplasma gondii. The age ranged 1-13 years with a mean of 5.8 ± 3.1 SD years with no gender difference. Specific etiologies of CLA were determined in 62.5% of patients. Ninety five percent of the causes were due to non-specific reactive hyperplasia of lymph nodes (NSRH) (37.5%), toxoplasmosis (27.5%),

infectious mononucleosis due Epstein–Barr virus (13.8%), tuberculous adenitis (10%), acute adenitis (6.2%), whereas malignancy (Hodgkin's lymphoma) constituted 5% of causes of CLA. The clinical characteristics were insignificantly associated with the causes of lymphadenopathy ($p > 0.05$). However, mobile lymph nodes were significantly associated with inflammatory conditions ($P < 0.05$). Inflammatory causes accounted for the majority of the etiologies whereas Hodgkin's lymphoma was the only identified malignancy. Laboratory tests such as, ESR, TWBC, hemoglobin and Mantoux test should be used in adjunct with cytology and serology for diagnosis.

Key words: Lymphadenopathy, cervical lymphadenopathy, etiology, Sudan.

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INTRODUCTION

Lymphadenopathy is the disease process of the lymph nodes that rendering them abnormal in size and consistency. The etiologies are multiple; Infection is the most common trigger for lymph nodes enlargement in children [1]. Cervical lymphadenopathy (CLA) is a common problem in clinical practice during childhood [2] and usually poses diagnostic difficulties on the physicians and looked at with fear by parents. Approximately 38% to 45% of apparently normal children have palpable cervical lymph nodes [3]. The aims of this study were to determine the causes of CLA in Sudanese children and to evaluate the value of routine laboratory tests in determining the etiology.

PATIENTS AND METHODS

This cross-sectional, descriptive study was conducted in Khartoum Children Emergency Hospital during the period from January through December 1998. The population was children with CLA (lymph node of ≥ 10 millimetres) [1] aged 1-13 years attending the outpatient clinic. Patients with cervical abscess or who were previously investigated for lymphadenopathy were excluded. Parents of children were briefed about the study and a written consent was signed by them. This study was approved by the Research and Ethics Committee of the Department of Paediatric, University of Khartoum.

A total of 80 patients with CLA were included in this study following a pilot study. Demographic data and the clinical history and examination details were obtained using a questionnaire. For every child a thin-needle transcutaneous biopsy of a lymph node was performed by the author and the aspirate was evenly spread onto 2 glass

slides stained by H&E and Geimsa stain and then examined by a cytologist. Five millilitres of blood were obtained from a peripheral vein for determination of haemoglobin concentration, ESR, total and differential white blood cell count and centrifuged for sera. Sera were used for analysis for HIV using a particle agglutination test (Fujirebio inc., Tokyo, Japan), ORTHO Epstein-Barr virus VCA-IgM antibody ELISA. Furthermore anti-Toxoplasma gondii IgM and IgG antibodies were analysed by ELISA technology (in vitro test) using special kits by Alpha Diagnostic International (ADI) - 8491 Abe Lincoln Rd., San Antonio, Texas 78240, USA. All these serological tests were performed according to the standards of the manufacturer's guidelines.

Final diagnoses were set on the basis of clinical findings, cytology and serology.

Data were entered into SPSS software version 16. Chi square test was used to compare the difference between categorical data and one-way ANOVA to compare means of laboratory values in different causes of CLA. The Level of significance was set at $P \leq 0.05$.

RESULTS

We studied 80 children with CLA. The age of patients ranged 1-13 years with a median of 6 years and a mean of 5.8 ± 3.1 SD years. Males were 49 (61.2%) and females were 31(38.2%) with a ratio of 1.5:1. However, gender difference was statistically insignificant ($P=0.27$).

The presentation and the clinical findings including the affected groups of lymph nodes are shown in table 1.

Table 1- History and clinical examination findings in children with cervical lymphadenopathy.

	Patients (N)	%
History		
neck mass	68	85
Fever	57	71.3
Cough	45	57
Loss of weight	44	55
Sore throat	37	46.2
Loss of appetite	33	41.2
Headache	22	27.5
Malaise	15	18.8
Tuberculosis contact	13	16.2
Arthralgia	10	12.5
Earache	10	12.5
Dental caries	8	10
Skin rash	7	8.8
Skin infection	5	6.2
Haemoptysis	2	2.5
Physical examination		
Splenomegaly	15	18.8
Hepatomegaly	5	6.2
Mouth ulcers	3	3.8
Impetigo	3	3.8
Otitis media	2	2.5
Affected group of nodes		
Anterior cervical triangle	69	86.2
Submandibular	48	60
Posterior cervical triangle	46	57.5
Groups other than cervical	21	26.2
Preauricular	6	7.5

The number of palpable cervical lymph nodes in the patients ranged from 1-10 nodes with a mean number of 3.5 ± 2 nodes and a mean size of 3.4 ± 1.7 (ranged 1-6) centimeter. The majority of the patients; 96.2% (n=77) had firm, non-tender (83.8%, n=67) and mobile nodes (87.5%, n=70).

Specific etiologies of CLA in children in the present study were determined in 62.5% of patients. Ninety five percent of these causes were due to inflammatory conditions. These were, non-specific reactive hyperplasia of lymph nodes (NSRH) in 37.5% (n=30) patients, toxoplasmosis in 27.5%

(n=22) patients, infectious mononucleosis due to Epstein-Barr virus in 13.8% (n=11) patients, tuberculous adenitis in 10% (n=8) patients, acute adenitis in 6.2% (n=5), whereas malignancy (Hodgkin's lymphoma) constituted 5% of causes of CLA.

As shown in table 2, age is not an important determinant of any of the causes of CLA except for lymphoma where it was significantly found in the age group above 10years ($p < 0.001$). However, there was no significant gender difference within all causes of CLA ($p = 0.57$).

Table 2- Causes of cervical lymphadenopathy in children according to the age (N=80).

Diagnosis	Age groups						Total	P value
	0-5		>5-10		>10-15			
	Freq	%	Freq	%	Freq	%		
NSRH	13	43.3	17	56.7	0	0	30	0.057
Toxoplasmosis	10	45.5	10	45.5	2	9	22	0.995
Mononucleosis	4	36.4	6	54.5	1	9	11	0.767
Tuberculosis	5	62.5	2	25	1	12.5	8	0.487
Acute adenitis	4	80	1	20	0	0	5	0.284
Lymphoma	1	25	0	0	3	75	4	0.000
Total	37	46.25	36	45	7	8.75	80	0.003

NSRH - nonspecific reactive hyperplasia

The clinical characteristics of lymphadenopathy caused by the different causes, in this study, with special reference to the site, number, tenderness and the size of the involved lymph nodes in the cervical region were insignificantly associated with the causes of lymphadenopathy ($p>0.05$). However, mobile lymph nodes were significantly associated with acute adenitis ($p=0.002$) and toxoplasmosis ($p=0.031$).

A one-way ANOVA between subjects was conducted to compare the values of erythrocyte sedimentation rate, hemoglobin concentration, total and differential white cell count and mantoux test in causes of CLA in this study. Taken together, these laboratory values, as diagnostic tools, have no significant association with the causes of CLA ($p>0.05$) (Table 3).

Table 3- One way ANOVA comparing means of laboratory values in etiologies of cervical lymphadenopathy in children (N=80).

Causes of LA	Mantoux test (mean±SD) mm	ESR (mean±SD) mm/hour	Hb (mean±SD) Mg/dl	WCC** (mean±SD) Cells/mm ³	Differential WCC (% of total WCC)		
					Neutrophils	Lymphocytes	Eosinophils
NSRH	7.96±2.4	62.6±3.5	10.06±1.87	7790±4591	46	52	2
Tuberculosis	10.12±9.1	87±2.8	8.9±1.7	7275±2686	52	47	1
Acute adenitis	3.4±4.6	61.4±3.2	9.9±2.0	12200±1047	50	48	2
Toxoplasmosis	7.5±1.5	60.6±3.0	9.7±2.4	7141±3247	43	55	2
Mononucleosis	8.6±1.4	60.3±2.5	9.9±2.1	7672±3753	44	53	3
Lymphoma	5.5±1.0	50.7±8.3	9.8±0.6	5775±1629	64	36	0
F	1.987	1.140	0.449	1.253	1.639	1.599	0.865
P	0.09	0.34	0.81	0.29	0.16	0.17	0.87

ESR - erythrocyte sedimentation rate, F - F test value, Hb - hemoglobin, LA - lymphadenopathy, NSRH - Nonspecific reactive hyperplasia, P - P test value, WCC - white cell count

DISCUSSION

The workup of palpable lymph nodes is a common clinical task for the general practitioners and the pediatricians. Most of the causes of CLA are benign and may resolve spontaneously [4]. It can be, on the other hand, a sign of malignancy or systemic disease, thus understanding the differential causes is of paramount importance for evaluation and precise timely diagnosis for the possibility of a yield of around 15.8% for serious conditions in one series [5]. Specific causes of lymphadenopathy, in this study, could be determined in 62.5% of patients. Non-specific reactive hyperplasia of lymph nodes (NSRH) is defined as a benign reversible enlargement of the lymph node resulting from the proliferation of part or all of its cellular components [6]. NSRH was found in 37.5% of patients with CLA in this study, much less than the 60% reported by Citak et al. [7], and more than Ayugi et al. who reported 29%. Ranking as first as of the benign causes in this study, NSRH is known to be of unknown cause and the most common in literature [8]. The difference in occurrence is possibly attributed to different methods of identification and definition of NSRH.

Enlarged lymph nodes are the most frequently observed clinical form of toxoplasmosis in humans [9]. Almost 28% of patients with enlarged cervical lymph nodes had acquired toxoplasmosis in the present study, a much higher rate than the 10% rate reported in literature [1]. The seropositive prevalence of toxoplasma antibodies was historically high (61%) among Sudanese population [10]. In another African country it was found to be 46% [11]. This may be attributed to consumption of raw animal products and it is known that infection associated with cervical adenopathy is usually acquired via the oral route by consumption of meat- or milk-containing cysts or oocytes [1].

Infectious mononucleosis caused by Epstein-Barr virus was found in 13.8% of patients with CLA in

this series. This was similar to literature as Citak et al reported 13.4% among children with benign lymphadenopathy [7], whereas Abdel-Aziz et al reported a figure of 15% [12].

Lymphadenopathy due to tuberculosis was found in 10% of patients in this study which is lower than the report from Greece by Papadopouli et al who reported a rate of 12% and even much lower than the 21.4% rate of a similar study from Kenya [13]. This may be attributed to the low specificity of fine needle aspiration cytology for the diagnosis of the granulomatous lesion of tuberculosis that may have a false negative rate of 38%. FNAC would have been more yielding if combined with PCR, a costly tool of diagnosis in a developing country [14].

Cervical lymph node infection, acute or sub-acute is frequent and is usually due to viral causes and many bacteria. This study reported 6.2% acute adenitis as a cause of CLA. We did not include complications of acute adenitis, such as abscess in the sample nor did we ascertain bacteremia, viremia or aspirate culture. This may underestimate the prevalence of acute adenitis in pediatric population as Ayugi et al reported abscess as the commonest cause representing 33% of the inflammatory causes of lymphadenopathy [8]. However when cases of NSRH, as inflammatory causes, are added to the 6.2% of acute adenitis the figure will be 43.7% which is more or less comparable to literature reports [8].

Lymphoma cases in this study, all Hodgkin's, were found in 5% of patients with CLA. These cases were confirmed later by excisional biopsy and referred to the oncologist. Our figure is comparable to the report of Citak et al [7] but higher than the 2% reported by Papadopouli et al. [13], their low prevalence might be attributed to their method of diagnosis and not all patients underwent biopsy of any type.

Only lymphoma was associated with lymphadenopathy in children 10 years and older. Age and gender was not a determinant in any the other causes of CLA in

this study.

This study did not find any relationship between lymph nodes size, site, number, tenderness and etiology. However, mobile lymph nodes were associated with acute adenitis and toxoplasmosis. Srouji et al., reported an association of tenderness, mobility and fluctuating size of the nodes with NSRH but their sample was too small to draw conclusive guidelines [5].

The series of investigations done in this study i.e. ESR, hemoglobin concentration, total and differential white cell count showed great inconsistency with different means and ranges for each patient in the study. This observation is similar to Srouji et al results [5] but reported by Niedzielska et al [4] as helpful in the differential diagnosis.

CONCLUSION

Specific etiologies of CLA in children can be

determined in 62.5% of patients using FNCS and serological tests, indicating the usefulness of FNAC and serology, especially in limited-resource countries. Inflammatory causes accounted for the majority of the etiologies. These are NSRH, acquired toxoplasmosis, Epstein–Barr virus-infectious mononucleosis and tuberculosis. Hodgkin’s lymphoma was the only identified malignancy among the studied cases. Lymph node site and size are not helpful in diagnosis whereas mobility is associated with inflammatory causes.

Laboratory tests such as, ESR, TWBC, hemoglobin and mantoux Test should be used in adjunct with cytology and serology for diagnosis.

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