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DETERMINATION OF AETIOLOGY OF SUPERFICIAL ENLARGED LYMPH NODES USING FINE NEEDLE ASPIRATION CYTOLOGY
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ABSTRACT

Objective: To assess the causes and patterns of enlarged superficial lymph nodes.

Design: Cross sectional survey.

Setting: Jimma Teaching Hospital, Pathology Department, Jimma University, southwest Ethiopia for a study conducted between September 1999 and August 2001.

Participants: Eight hundred and eight patients presenting with enlarged superficial lymph nodes in cervical, axillary, inguinal etc. regions were included (456 males and 352 females) whereas non lymph node samples and deep-seated lymphoid lesions were excluded from the study.

Main outcome measures: Fine needle aspiration cytology (FNAC) technique and wright's staining procedure were utilized to diagnose the causes of enlarged lymph nodes.

Results: Of the 1693 patients attended to at the cytologic diagnostic service, 808(47.7%) had lymph node disorders with benign and malignant causes of lymph node enlargements comprising of 93.2% and 6.8% respectively. The most frequent cause of benign enlargement was tuberculous lymph adenitis (66.3%), followed by reactive lymph node hyperplasia (19.2%). Among malignant ones, non-hodgkin's lymphomas (2.7%) and metastatic carcinomas (2.2%) were most frequently diagnosed. The cervical region was the most frequent site for enlarged lymph node disorders accounting for more than three quarters of all cases.

Conclusion: This study revealed a huge burden of benign lymph node enlargements in general, and tuberculous lymph adenitis in particular. The latter was responsible for about two-third of lymph node enlargements in South Western parts of this country. It is recommended that health providers undertake intensive public health education and screening activities in order to help salvage our community from these potentially preventable and treatable causes of enlarged lymph node disorders.

INTRODUCTION

Lymph node aspiration cytology was first employed during the early 1900's for the identification of trypanosomes in sleeping sickness. Aspiration biopsy was practised at memorial Sloan Kettering during the 1930's in USA; however, aspiration cytology took hold in Europe and especially in Sweden in the 1950's and thereafter (1). Under normal conditions lymph nodes are small bean shaped structures even in their superficial locations (cervical, axillary and inguinal) and are seldom palpable (2). Lymph nodes, which are usually superficially, are easily accessible and frequently sampled and the findings of such samples are invaluable in the diagnosis, treatment and determination of prognosis of the disease (3). Enlarged lymph adenopathies may be primary or secondary manifestations of numerous disorders and it is a common clinical problem in Africa where cervical, axillary, inguinal and abdominal lymph nodes are most often enlarged (4-6). The limited

diagnostic facilities in rural hospitals of developing countries can make it difficult to distinguish tuberculous lymph adenitis from other forms of adenopathies (7).

Fine needle aspiration cytology (FNAC) is particularly helpful in the work-up of nodules because surgical biopsy of lymph adenopathies is a more invasive procedure. Furthermore FNAC represents an accurate, inexpensive and rapid technique for the elucidation of the etiology of lymph adenopathies (8-11). In health institutions where FNAC diagnostic techniques have been practised, its utility has expanded dramatically to encompass a spectrum of malignant disorders including malignant lymphoma, metastatic carcinoma as well as infections of patients presenting with persistent lymph adenopathy and reactive lymph node disorders (12). Even though, FNAC is a reliable diagnostic technique, its diagnostic utility for malignant lymphomas has been controversial as a result of problems related to sampling errors and inability of cytology to demonstrate histologic growth patterns.

Today cytologic evaluation of non-hodgkin's lymphoma remains a diagnostic challenge (8-13). Enlargements of lymph nodes are frequently seen in clinical practises and in many instances the causes of enlarged lymph adenopathies is obscure and the conditions that may produce such pictures are many. It is of great diagnostic and management value to know their relative frequencies, as experiences gained in other parts of the world may be different or misleading (14). Patterns of lymph adenopathies have not been reported extensively even in clinical text-books (14). Thus, the aim of this study was to asses the causes and patterns of enlarged lymph nodes, diagnosed by use of FNAC techniques in a teaching hospital.

MATERIALS AND METHODS

This cross-sectional study was conducted within Jimma teaching hospital (Pathology Department, Faculty of medical sciences, Jimma University) between September 1999 and August 2001. The department presently serves as the only referral center for all FNAC and surgical biopsy services covering a large catchment area of more than six million people in the southwestern part of the country. Patients with superficial enlarged lymph nodes (roughly more than 0.5 cm in diameter) in cervical, axillary, and inguinal etc. regions were investigated. The variables incorporated in the structured report forms were age, sex, site as well as cytologic diagnosis of lymph adenopathies. Non-specific abscesses and deep-seated adenopathies on cytologic examinations as well as cases with inadequate samples for cytodiagnoses were excluded from the study. The lymph node lesions were categorized into benign lymph node enlargements (granulomatous inflammation, tuberculous lymph adenitis, pyogenic lymph adenitis and reactive lymph adenitis) and malignant lymph node enlargements (non-hodgkin's lymphoma, hodgkin's lymphoma and metastatic tumours) based on their respective cytomorphologic features. Thus, granulomatous inflammation was entertained when epithelioid cell aggregates were seen with occasional multinucleated giant cells without caeous necrosis (2). Tuberculous lymphadenitis was diagnosed when cytology revealed oesinophilic granular debris (caeous necrosis) and/ or epithelioid cell aggregates with or without multinucleated giant cells (10). Reactive lymph node hyperplasia was entertained when all cellular components or any combination of lymphocytes, plasma cells, follicle center cells and mononuclear phacocytic cells that undergo proliferations in response to a variety of infectious, inflammatory and neoplastic disorders were identified (15). Pyogenic lymphadenitis was diagnosed when the lymph node aspirates were flooded with predominantly polymorphonuclear leukocyte and occasional lymphoid cells (10). When largely monotonous non-cohesive noeplastic lymphoid cells were observed the diagnosis of non-hodgkin's lymphoma was entertained whereas the presence of the Pathognomonic Reed-Sternberg cells with the characteristic background cells was diagnosed as hodgkin's lymphoma. However, metastatic carcinomas were diagnosed when loose to tight aggregates of epithelial cells were visualized in lymph nodes (12). Suspicious cases in this study were incorporated into their respective groups.

FNAC procedure: Patients presented with enlarged lymph nodes were subjected to the routine FNAC diagnostic

procedures by cleaning the node with 70% ethyl alcohol and the node was then fixed with the left thumb and index finger. Subsequently a 10 CC disposable plastic syringe plugged with a sterile disposable needle was inserted into the lump perpendicularly. The aspirated material was then dropped onto a dry and clean slide and the air-dried smear was stained with Wright's staining technique and finally these slides were diagnosed under light microscopy.

Data analysis: Data were coded, entered and analysed using SPSS/PC version 11.0 statistical package (SPCC inc. 233 S Wacker Drive Chicago, Illinois, 2001). Comparisons between age groups and between males and females were performed using Chi-square tests. P values less than 0.05 were considered statistically significant.

Pitfalls of the study: We lacked ancillary diagnostic services such as immunocytochemistry etc. that are helpful in confirming suspicious cases and also in sub-categorising some of difficult malignant neoplasms identified cytologically. Ultrasonically guided FNAC is not practised in our hospital hence the study failed to diagnose deep-seated lymph node disorders.

RESULTS

A total of 1693 patients were sent to the Department of Pathology for FNAC during the study period where 808 (47.7%) were disorders of enlarged lymph node origins with the median age of 24.0 years for all adenopathies (range 0.2-85 years).

Children and young adults less than 30 years of age were predominantly affected in benign enlargements 549 (67.9%) whereas adults more than 40 years of age more commonly affected in malignant nodal enlargements 28 (3.5%). The peak age group for benign enlargements was between 20-29 years comprising of 276 (34.2%) whereas, 40-49 years for malignant ones was 15 (1.9%). Tuberculous lymph adenitis was the most common 536 (66.3%) type of benign adenopathies followed by reactive lymph node hyperplasia 155 (19.2%). Among malignant nodal enlargements, lymphomas represented 37 (4.6%), of which 22 (2.7%) were non-hodgkin's lymphomas. Metastatic tumours however, were diagnosed in 18 cases (2.2%) ($p < 0.05$) as shown in Table 1. There were remarkable male dominances in tuberculous lymph adenitis 302: 234 (1.3:1) and non-hodgkin's lymphomas in 19:3 (6.3:1) moreover, the overall male to female ratio was 546: 352 (1.3:1) ($P > 0.05$) as shown in Table 2. Table 3 shows that the cervical region was common site for lymph adenopathies and was more commonly noticed in males than in females ($P > 0.05$). The cervical region was also the most common site for benign enlarged nodes 600 (74.3%) and for malignant enlargement in 27 (3.3%). Tuberculosis was the most common in 435 (53.8%) benign diagnosis compared to lymphomas which were the most frequent 12 (1.5%). The axillary regions were the second most common site 140 (17.3%) for all adenopathies and tuberculous lymph adenitis was the most frequent 81 (10%) cause of adenopathy in the region. This region was also a frequent site for

metastatic tumours in nine (1.1%) cases where all but one (melanoma) were secondary to breast carcinomas. Out of the remaining nine metastatic tumours five cases were found in the cervical region (one nasopharyngeal carcinoma, one oesophageal carcinoma, one mucoepidermoid carcinoma, one melanoma and one

unspecified adenocarcinoma), and there were also four metastatic cases identified in the inguinal region (three metastatic melanomas and one unspecified carcinoma) (Table 4). There were seven suspicious cases of lymphomas, (four non-hodgkin's lymphoma and three hodgkin's lymphoma's)

Table 1*Distribution of enlarged nodes by age*

Age in years	Granulomatous inflammation	Tuberculous adenitis	Reactive lymph node hyperplasia	Pyrogenic lymph adenitis	Non-hodgkin's lymphomas	Hodgkin's lymphoma	Secondary tumours	Total No. %
0-9	1	54	32	9	3	1	-	100(12.4)
10-19	11	114	39	3	2	4	-	173(21.4)
20-29	14	199	43	9	6	4	1	276(34.2)
30-39	4	101	29	5	2	1	3	145(17.9)
40-49	1	38	8	-	6	4	5	62(7.7)
50-59	3	21	4	1	2	1	4	36(4.4)
60+	1	9	2	-	1	-	5	16(2.0)
Total	35(4.3)	536(66.3)	155(19.2)	27(3.3)	22(2.7)	15(1.9)	18(2.2)	808(100)

 $\chi^2=161.51$; p-value=0.000
Table 2*Distribution of enlarged nodes by sex*

Type of node lesion	Males No. (%)	Females No. (%)	Total No. (%)
Granulomatous	22	13	35(4.3)
Tuberculous lymph adenitis	302	234	536(66.3)
Reactive lymph node hyperplasia	80	75	155(19.2)
Pyogenic lymph adenitis	16	11	27(3.3)
Non-hodgkin's lymphoma	19	3	22(2.7)
Hodgkin's lymphoma	9	6	15(1.9)
Metastatic tumours	8	10	18(2.2)
Total	456(56.4)	352(43.6)	808(100)

 $\chi^2=11.29$; p-value= 0.080
Table 3*Distribution of enlargement nodes by sites of occurrences versus sex*

	Cervical	Axillary	Inguinal	Epithrochlear	Total No. (%)
Male	358	71	26	1	456(56.4)
Female	269	69	12	2	352(43.6)
Total	627(77.6)	140(17.3)	38(4.7)	3(0.4)	808(100)

 $\chi^2=4.85$; p-value=0.183

Table 4

Distribution of enlarged nodes by sites of occurrences

Lymph node region	Granulomatous	Tb adenitis No. (%)	Reactive lymph node hyperplasia No. (%)	Pyogenic lymph adenitis No. (%)	Non-hodgkin's lymphoma No. (%)	Hodgkin's lymphoma No. (%)	Metastatic tumours No. (%)	Total No. (%)
Cervical	29(3.6)	435(53.8)	115(14.2)	21(2.6)	12(1.5)	9(1.1)	6(0.7)	627(77.6)
Axillary	5(0.6)	81(10.0)	29(3.6)	5(0.6)	7(0.8)	4(0.5)	9(1.1)	140(17.3)
Inguinal	1(0.1)	19(2.4)	9(1.1)	1(0.1)	3(0.4)	2(0.3)	3(0.4)	38(4.7)
Epithrochlear	-	1(0.1)	2(0.3)	-	-	-	-	3(0.4)
Total	35(4.3)	536(66.3)	155(19.2)	27(3.3)	22(2.7)	15(1.9)	18(2.2)	808(100)

 $\chi^2=82.69$; p-value =0.000

DISCUSSION

Nowadays, FNAC is the first line of investigation to confirm the diagnosis of lymph node lesions and lymph node excisional biopsy is entertained only when definitive diagnosis cannot be made with FNAC (8,9). About two-thirds of patients with lymph adenopathies in this study were children and young adults less than 30 years of age as were reported in various papers (3,5, 13,16). Forty seven point seven per cent of all patients diagnosed in our cytologic diagnostic service were of lymph node disorders and this finding discloses a high prevalence rate of the adenopathies on our catchment areas. 93.2% Benign lymph node enlargements and 6.8% malignant lymph node enlargements were reported in this study and there were similar studies with highly variable results such as 84% and 16%(3) as well as 70.0% and 30% (7) for benign and malignant nodal enlargements respectively.

These differences in frequency distributions from our study could be explained largely by epidemiological factors and these data depict the fact that experiences that are got at one center may be different from other studies (14). Among benign causes of adenopathies, tuberculous lymph adenitis was most frequently diagnosed and comparable results were found elsewhere (9,10,16). In areas where mycobacterial infection is common (like ours), the presence of granulomatous inflammations (as were seen in our 35 cases) in lymph nodes is strongly suggestive of tuberculosis (10). However, research conducted in Zimbabwe (3) and elsewhere (2,4) showed that reactive lymph node hyperplasia was the most common entity. In this study lymph adenopathies were more commonly encountered in males than in females as consistently reported by Khiery *et al.* (16) moreover, the converse described by others (17,18). Tuberculous lymph adenitis and malignant non-hodgkin's lymphomas were commonly encountered in males as were depicted in other studies (14,16). Benign lymph nodal enlargements were the more common patterns of enlargements than the malignant ones and among these benign lesions tuberculous lymph

adenitis were responsible for about three quarters of the adenopathies.

The cervical region was the most frequently involved site for tuberculous lymph adenitis (3,9,16,17). In the axillary region more than one-half of all lesions were of tuberculous origin and the axilla was also an important site for metastatic carcinomas in which the majority were secondary to breast carcinomas as similar patterns were reported in literatures (4,19). The prevailing high rates of enlarged lymph nodes could be ascribed to the surge of tuberculosis due to increasing profile of AIDS epidemics. Extra-pulmonary manifestations of tuberculosis may appear in over half of the patients who are dually infected. This has resulted in the rising incidence of tuberculosis in several parts of Africa (20,21). Suspicious cases of lymphoma detected in this study demonstrated the difficulties in diagnosing and categorizing low and intermediate degree lymphomas cytologically as reported in various papers (8,13,22). In conclusion, this study revealed a huge burden of enlarged lymph nodes disorders in southwestern part of this country where tuberculous lymph adenitis was identified in about two thirds of all cases. Health care providers are thus advised appropriate public health education and screening activities in order to save our community from this preventable and treatable health burden.

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