

LYMPHNODE ENLARGEMENT — MALIGNANT OR BENIGN

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SUMMARY

A total of 50 cases of lymph adenopathy were studied to know the incidence of malignant versus non-malignant disorders and assess the diagnostic yield of various investigations. A detail history, careful clinical examination, laboratory tests were done including tissue culture for Acid fast bacillus (AFB) and lymphnode biopsy. The causes of adenopathy included tuberculosis (50%), lymphoma (30%), leukemia (10%), sarcoidosis (02%), Kala-Azar (02%), rheumatoid arthritis (02%), metastatic carcinoma (02%) and reactive hyperplasia (02%). Surprisingly malignant diseases 21 (42%) were not uncommon than the non-malignant 29 (58%). The lymphnodes enlargement in the younger age group i.e. (14–20 years) involving anterior and posterior triangle of cervical region, cervical and axillary region or axillary region alone were non-malignant. In the older age group i.e. 21 years of age or above enlargement in the suboccipital area and posterior triangle of cervical region or generalized lymphnode involvement pointed to malignant disease. Petechial haemorrhages, weight loss and hepatosplenomegaly indicated malignancy. Characteristics of lymphadenopathy such as size, shape, tenderness, fixity and matting together were not helpful. Sex distribution showed a predominance of females in the younger age group i.e. non-malignant, versus a predominance of males in the older age group. ESR and tuberculin tests were generally inconclusive. Out of 25 (100%) cases of tuberculous adenopathy, AFB culture was only positive in 5 (20%). Histopathology was found to be the most reliable diagnostic test, in tuberculous adenopathy.

INTRODUCTION

Normal lymphnodes are impalpable except, in some very thin individuals. Palpable enlargement is referred to as lymphadenopathy¹. This article includes the nodes picked up by the physician clinically, detection by radiography was not involved. It applies mainly to adolescence and adults, a different array of diseases underlies enlarged lymphnodes in infants and children. It does not include therapy and the diagnostic evaluation of rare diseases.

The purpose of this study was to:

1. Find the causes of peripheral lymphadenopathy and the presentation in various disorders.
2. Assess the diagnostic yield of common investigations such as erythrocyte sedimentation rate and tuberculin test.
3. See the percentage of positive tissue cultures in tuberculous lymphadenopathy and point out the problems inherent in culturing Acid fast bacillus (AFB).
4. Compare the histopathologic report of tuberculous lymphadenopathy and the tissue culture.

MATERIAL AND METHODS

All patients of the age 14 years or above with enlarged peripheral lymphnode were admitted in "Medical B" Unit of PGMI. A total of 50 cases were included in this study. A comprehensive clinical history, complete physical examination of the relevant systems and such laboratory tests as haemoglobin (Hb), total leucocyte count (TLC), Differential (DLC), erythrocyte sedimentation rate (ESR) and tuberculin test (5TU I/C) were performed in all the patients. X-ray chest was done in all. Other investigations done in some of the cases were peripheral smear, S. calcium, R.A. factor, serum uric acid, barium studies, chest tomography, ultrasonography and bone marrow examination. Lymphnode biopsy was done on all excepts the leukemic patients. Each node removed was divided into two parts. One half was sent for histopathologic report, the other half was divided into small pieces and was preserved in a bottle containing saline. The culture was done only on tuberculous cases.

Tissue was ground and homogenized into a tissue grinder at 150 RPM in a universal Laboratory Aid type 309 (Mechanika Preczyjna- made in Poland). After grinding equal amounts of 5% oxalic acid was added to the homogenized material. It was kept at 37 C for 20 minutes and then was centrifuged at 3000 RPM using Hettich EBA 35 centrifuge, for 20 minutes. The supernatant fluid was discarded. Prior to culture a smear was made of the deposit and stained with Ziehl-Neelsen method. The deposit was cultured on to three tubes of Lowenstein Jensen medium of which one contained sodium Salicylate in quantity of one ng/ml. The tubes after inoculation were incubated at 37C and were examined at weekly intervals for upto 8 weeks for any growth. The growth when visible on the medium was confirmed by staining with Ziehl-Neelsen method.

RESULTS

Interesting facts emerged from this study. Twenty five (50%) cases were suffering from tuberculous lymphadenopathy, 15 (30%) had malignant lymphoma and 5 (10%) were leukemic. Besides rheumatoid arthritis (02%), metastatic carcinoma (02%) reactive hyperplasia (02%), and rare diseases such as sacroidosis (02%) and Kala-Azar (02%) were also documented. Looking at the above figures chances of finding the malignant diseases 21 (42%) are not uncommon than the non-malignant ones 29 (58%).

Out of 5 (100%) cases of Hodgkin's disease, 4 (80%) were modular sclerosing type and the remaining one of mixed cellularity. In non-Hodgkin's lymphoma (100%) the incidence (20%) of nodular lymphoma 5 (50%) was higher as compared to well differentiated lymphocytic lymphoma (WDLL) 2 (20%), Poorly differentiated lymphocytic lymphoma (PDLL) 2 (20%) and histiocytic lymphocytic 1 (10%). Of the 5 (100%) cases of leukemia, 2 (40%) had acute myelomonocytic leukemia (AML), 1 (20%) had acute lymphoblastic leukemia (ALL) and 2 (40%) chronic lymphocytic leukemia (CLL).

The age distribution was between 14-60 years (Table No. 1). The highest incidence was between the age group 14-20 years i.e. 22 (44%), with female predominance 12 (24%). In this group the incidence of non-malignant (38%) versus malignant disease (06%) remained higher. However, in the patients over 21 years of age this reversed itself i.e. malignancy 17 patients (34%) versus non-malignant disease 11 (22%) with male predominance 15 (30%).

Regarding the site of distribution (Table No. 2). Those who had lymphnode involvement in the anterior and posterior triangle of cervical region 10 (20%), cervical and axillary region 3 (06%) or axillary area

TABLE - 1
DISTRIBUTION OF VARIOUS CAUSES ACCORDING TO AGE AND SWX IN 50
PATIENTS WITH LYMPHADENOPATHY

Causes Sex	14-20 Years		21-30 Years		31-40 Years		41 + Years	
	Male	Female	Male	Female	Male	Female	Male	Female
Tuberculous Adenopathy	7 (14%)	11 (22%)	5 (10%)	1 (2%)	—	1 (2%)	—	—
Lymphoma	1 (2%)	1 (2%)	5 (10%)	1 (2%)	3 (6%)	—	3 (6%)	1 (2%)
Leukaemia	1 (2%)	—	2 (4%)	—	—	—	1 (2%)	1 (2%)
Sarcoidosis	1 —	—	— (2%)	1 —	—	—	—	—
Kala-Azar	1 —	—	— (2%)	1 —	—	—	—	—
Rheumaoid Arthritis	1 —	—	— (2%)	1 —	—	—	—	—
Metastatic Carcinoma	—	—	—	—	—	—	1 (2%)	—
Reactive Hyperplasia	1 (2%)	—	—	—	—	—	—	—

alone 4 (08%), had tuberculous adenopathy. Where as those in whom posterior triangle and suboccipital nodes were enlarged i.e. 3 (06%) lymphoma was the diagnosis. Generalized adenopathy was observed in 7 (14%) cases, all of whom were malignant. Among these cases 5 (10%) were lymphoma and 2 (04%) were chronic lymphocytic leukemia (CLL).

The nodes were tender in 6 (12%) patients with tuberculous adenopathy and in 2 (4%) cases of lymphoma. Matting together was observed in 15 (30%) cases of tuberculous and in 6 (12%) cases of lymphoma. Fixity of the tissues was noted in both, 3 (06%) in each. Hepato-splenomegaly was present in 2 (4%) cases of lymphoma and in all cases of leukemia. In one (2%) case of rheumatoid arthritis

splenomegaly was noted. Petechial haemorrhages 2 (4%) were only seen in leukemia. Weight loss 8 (16%) was documented in leukemia, lymphoma and metastatic carcinoma.

In 20 cases (40%) the ESR was between 0-20 mm mercury/hour. It ranged between 21 to 80 mmHg/hr in 22 (44%) cases and above 80 mmHg/hr in 8 (16%) case. Tuberculin test was positive in all patients of the non-malignant diseases and in 10 (20%) of lymphoma. Culture of the tissue was done in all 25 (100%) cases of tuberculous adenopathy. The smears from the tissue deposits were positive for AFB in 2 (8%) cases. Mycobacterial growth was documented in only 5 (20%) cases and it yielded typical mycobacteria in all of them.

TABLE - 2
DISTRIBUTION OF LYMPHADENOPATHY IN VARIOUS REGIONS

	Cervical			Cervical and axillary	Axillary	Axillary inguinal	Generalized
	PT	AT+PT	PT+SO				
Tuberculous Adenopathy	08 (6%)	10 (8%)	—	3 (6%)	4 (8%)	—	—
Lymphoma	7 (14%)	—	3 (6%)	—	—	—	5 (10%)
Leukaemia	1 (2%)	—	—	—	—	2 (4%)	2 (4%)
Sarcoidosis	1 (2%)	—	—	—	—	—	—
Kala-Azar	1 (2%)	—	—	—	—	—	—
Rheumaoid Arthritis	—	—	—	—	—	1 (2%)	—
Metastatic Carcinoma	1 (2%)	—	—	—	—	—	—
Reactive Hyperplasia	1 (2%)	—	—	—	—	—	—

PT: Posterior triangle

AT: Anterior triangle

SO: Soboccipital

DISCUSSION

Enlargement of the lymphnode occurs either due to simple inflammatory process or because of a dreadful disease like lymphoma. Lymphomas are relatively rare, and metastatic carcinoma is a more common cause, of malignant disorders. Of the non-malignant conditions the adenopathy is commonly due to infections. Other causes includes autoimmune diseases, granulomatous, drug induced and angioimmunoblastic lymphadenopathy (AIBL)^{1,2}.

Hodgkin's disease is believed to occur in families or by contact^{2,3}. Etiology of leukemia is not known and its higher incidence is related to radiation exposure or

chemical agents^{4,5}. B. Cell lymphomas of non-Hodgkin's type are common in the West whereas T-cell type are upto 70% in Japan and Taiwan⁶. Its incidence has increased since the AIDS epidemic began in 1981⁷. In relation to age, in Hodgkin's disease, the distribution curve is bimodial in contrast to non-Hodgkin's lymphoma, however nodular types are common in both^{8,9,10}.

In our patients Hodgkin's disease was not present in the families. The presence of radioactive materials in the close by range Himalayan may be the probable cause of leukemia? In view of the fact that thalassaemia (specially the beta type) is more common in this part of the subcon-

tinent¹. The origin of the people of this province is being traced to Greek blood from Alexander the Great. It is predicted that B-cell type of non-Hodgkin's lymphoma should also be more common than T-cell type, however no statistic exist to prove this fact. Similarly, nodular type of lymphomas were higher is Hodgkin's and non-Hodgkin's lymphomas.

Tuberculosis is the disease of Asians and Africans¹. Kala-Azar is prevalent in India, middle Asia, Middle East, Southern Europe and Africa^{11,12}. Sarcoidosis is common in the black population of USA, Africa, in the white population of Europe and is rare in Asia^{13,14}. Tuberculous adenopathy is the most common extra-pulmonary tuberculosis in Saudi Arabia. The lymphnode involvement is usually by the typical mycobacteria as it is in our country^{15,16}. However in USA and Europe the atypical type of mycobacteria involves the lymphnodes^{17,18}. The single patient of Kala Azar reported in this study had come from Bihar (India) where the vector is endemic.

Enlarged nodes confined to the neck may result from local infection, in the absence of which Epstein-Barr virus, Cytomegalo- virus, toxoplasmosis, Hodgkin's and non-Hodgkin's lymphoma, sarcoidosis, tuberculosis and fungal infections and leukemia should be considered^{19,20,21}. Localization of the node enlargement to the axilla represents cat-scratch-disease, staphylococcal or streptococcal infection, tuberculosis, tumours of extremities and breast^{22,23,24}. With regard to inguinal lymphadenopathy syphilis, lymphogranuloma venereum and malignant melanoma may be the cause besides local infections^{25,26}. Generalized lymphadenopathy is often caused by infections, drugs p73 and lympho or myeloproliferative disorders including autoimmune diseases^{27,28,29}.

The attribute of tenderness does not adequately discriminate between enlarged nodes of infected origin or that produced by

Hodgkin's disease. The tumours tissue may permeate the capsule and extend into the pericapsular tissues to produce interadherence and matted nodular tumour mass^{30,31,32}.

In our patients, involvement of lymphnodes in the posterior triangle of the neck including the suboccipital area (and cases where lymphadenopathy was generalized).lymphoma was the diagnosis. petecinal haemorrhages, weight loss and hepatosplenomegaly also indicated malignancy including leukemia.

Patients with tuberculous cervical adenopathy had classically lymphnode enlargement in the anterior and posterior triangle of the neck, other had cervical with axillary or axillary adenopathy alone. Various characteristics of enlarged lymphnodes such as the size, shape, tenderness, matting together and fixity were found both in malignant and non-malignant patients.

The ESR is taken to be of considerable value in patients suffering from infectious, malignant and connective tissue diseases³³. In this study although it was raised in many of cases yet in a significant number of cases it was within normal limits.

Tuberculin test become positive after infection. It becomes negative in few conditions including malignant disorders³³. In about 80% of all the patients tuberculin test was positive including malignant diseases. This is because of prevalence of pulmonary tuberculosis in this province. These patients cough and their sputum contaminates the atmosphere. Thus this test whether positive or negative has no significance in diagnosing or ruling out tuberculosis in patients having adenopathy.

It is ideal to culture the tissue specimen if it is infective in origin. Moreover, it is advisable to carry out the sensitivity of such organism to commonly used drugs. However many problems are faced when the tissue culture is done such as limited number of bacteriologist, contamination and minimal

number of successful growth of Acid fast bacilli e.g.⁵ out of 25 cases. Availability of adequate amount of tissue was on various occasion not possible due to difficult dissection in deeply seated lymphnode, providing half of the tissue for histopathology and excessive necrosis.

Because of non significant role of ESR and tuberculin test in the diagnosis and the above mentioned problems associated with tissue culture the histopathological parameter for the diagnosis (through not as ideal as tissue culture) becomes the most reliable and cost effective methods. In the follow-up of 15 patients with tuberculous adenopathy the response to therapy was 100% in all of them. Therefore, it is clear that there is no need to request for aforementioned three laboratory tests as a routine. However, a continuous search in the field of tissue culture for AFB should aim at,

- a) Creating a better method of tissue culture for AFB.
- b) Detecting the emergence of the resistant strains and atypical mycobacteria.

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