

A Retrospective Histological Evaluation of Non-neoplastic Superficial Lymphadenopathy

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Abstract

Background: Lymphadenopathy is a common presenting symptom in various diseases. The lymph nodes react to various known and unknown stimuli and undergo reactive changes leading on to vast array of non neoplastic lymphoid proliferations or hyperplasias. The involvement of lymph node by these non neoplastic conditions is much more common. From a topographic and functional standpoint, the major patterns of reactive non neoplastic lymphoid proliferations are follicular, nodular, interfollicular, paracortical, diffuse, sinusal and mixed.

Aim: To analyze pathological spectrum of involvement of lymph nodes by various non neoplastic conditions.

Setting and design- Retrospective study done at Government Medical College, Sector-32, Chandigarh.

Materials and Methods- Successive superficial lymph node biopsies received between 1999-2004 were archived from records and were divided into 2 broad categories: neoplastic and non-neoplastic. The latter group comprised the material for present study. Age, sex and site of biopsy were also recorded. The diagnoses were made on morphological grounds. Wherever required special histochemical stains were employed and the cases were reclassified.

Results: Out of a total of 370 lymph nodes examined, 120 cases (32.4%) were neoplastic and 250 cases (67.6%) were non-neoplastic. The most common site involved was neck as seen in 173 cases (69.2%). Out of 250 cases of non-neoplastic lymphadenopathy, 164 cases (65.6%) were of non-infectious etiology. Non-specific reactive lymphadenopathy was the most common lesion, seen in 124 cases (75.6%). In 35 cases a variety of specific histologic diagnoses were given. Tuberculosis was the most common infectious cause diagnosed in 85 cases (34%). One case (0.4%) showed cryptococcal lymphadenitis while one case showed presence of atypical mycobacteria.

Conclusion: Non-neoplastic lymphoid proliferations or hyperplasias show vast array of morphologic patterns on biopsy. One should be aware of these morphologic changes for definite and specific categorization of lesions for diagnostic and therapeutic purposes.

INTRODUCTION

Lymphadenopathy may be an incidental finding in patients being evaluated for various reasons or it may be a presenting sign or symptom of the patient's illness. Lymphadenopathy is defined as an abnormality in the size or character of lymph node caused by a vast array of disease processes, whose broad categories are easily recalled as the mnemonic acronym "MIAMI", representing Malignancies, Infections, Autoimmune disorders, Miscellaneous and unusual conditions, and Iatrogenic causes¹. A common finding in the primary outpatient setting, lymphadenopathy, is typically explained by identifiable regional injury or infection.

The basic question pathologist first attempts to answer when studying lymph node biopsies is to comment whether the process is reactive or neoplastic^{2,3}.

The involvement of lymph node by non neoplastic conditions is much more common than the neoplastic processes. The primary aim of this retrospective study was to analyze the pathological spectrum of involvement of lymph nodes by various non-neoplastic conditions.

MATERIALS AND METHODS

In the present study, successive superficial lymph node biopsies received in the Department of Pathology, GMCH, Chandigarh were archived from the records for the 6 year

period (1999-2004) and were divided into 2 broad categories: neoplastic and non-neoplastic. The latter group comprised the material for the present study. Age, sex and site of biopsy were also recorded. Biopsies from superficial lymph nodes (i.e. cervical, axillary, inguinal, pectoral and intra-parotid) were included in the present study. However lymph nodes removed as part of main specimen such as in surgery of bowel, gall bladder, breast, thyroid and larynx etc. and mesenteric and retroperitoneal lymph nodes were excluded from the study. The diagnosis was made on morphological grounds.

Wherever required histochemical stains like Ziehl Neelson stain, periodic acid Schiff (PAS) stain, Grocott's stain and mucicarmine stains were employed and cases were reclassified.

RESULTS

A total of 370 successive superficial lymph node biopsies received were divided into 2 broad categories: neoplastic (120 cases, 32.4 %) and non-neoplastic (250 cases, 67.6%). The latter group comprised the material for the present study. There were 126 male patients and 124 female patients with male: female ratio of 1.01:1. Maximum number of patients (138 cases, 55.2%) was seen in 10-30 years of age group followed by 31-50 years of age group (58 cases, 23.2%). Thirty two cases (12.8%) were less than 10 years of age and only 22 cases (8.8%) were more than 50 years of age. The most common site involved was the neck, comprising of 173 cases (69.2%), followed by the axilla (49 cases, 19.6%), and the inguinal region (23 cases, 9.2%). Intraparotid lymph node involvement was seen in 4 cases (1.6%) while pectoral lymph node was involved only in one case (0.4%) (Table 1).

Figure 1

Table 1: Site distribution of lymph nodes biopsied (n=250)

Site	Number of cases	Percentage
Neck	173	69.2 %
Axillary	49	19.6 %
Inguinal	23	9.2 %
Parotid	04	1.6 %
Pectoral	01	0.4 %

Out of 250 patients with lymphadenopathy, on morphological evaluation of biopsies 164 patients (65.6%) had a non-infectious etiology and remainder 86 cases (34%) had a specific infectious cause. Tuberculosis was the most

common infectious cause diagnosed, seen in 85 cases(34%) while there was only one case (0.4%) of cryptococcal lymphadenitis (Table 2). Out of 85 cases of tuberculous lymphadenitis stain for acid fast bacilli was positive in 13 cases only. Diagnosis of tuberculosis in remaining cases was furnished on the basis of caseating epithelioid cell granulomas. One case showed the presence of atypical mycobacteria consistent with the morphology of *Mycobacterium avium-intercellulare*. Histology of this case did not reveal caseation necrosis instead the lymph node was extensively replaced by histiocytes with foamy cytoplasm.

Figure 2

Table 2: Broad categorization of non- neoplastic lymph node lesions (n = 250)

Category		Number of cases	Percentage
Infectious	Tuberculous	85	34%
	Non-tuberculous	1	0.4%
Non-infectious		164	65.6 %

Out of 164 patients placed under the category of non-infectious, non-neoplastic conditions, 124 cases (75.6%) showed non-specific reactive lymphadenopathy. In these 124 lymph node biopsies follicular hyperplasia was seen in 115 cases, sinus histiocytosis in 7 cases and both follicular hyperplasia and sinus histiocytosis in 2 cases only. Three cases (1.8%) showed non-specific granulomatous inflammation, one case (0.6%) was described as necrotic lymph node, while one case (0.6%) was given as descriptive. In the remainder 35 cases (21.3%), a variety of specific histologic diagnoses were given (Table 3).

Figure 3

Table 3: Disease pattern in non-infectious, non-neoplastic lesions (n=164 cases)

Lesion	Number of cases N= 164	Percentage
Reactive lymphoid hyperplasia	124	75.6
Dermatopathic lymphadenitis	15	9.2
Kikuchi's disease	7	4.3
Sarcoidosis	4	2.5
Non-specific granulomatous inflammation	3	1.8
Kimura's disease	3	1.8
Castleman's disease	3	1.8
Langerhans' cell histiocytosis	1	0.6
Angio-immunoblastic lymphadenopathy	1	0.6
Necrotic lymph node	1	0.6
Reactive eosinophilic lymphadenitis	1	0.6
Descriptive	1	0.6

One case was diagnosed as necrotic lymph node where histology showed necrosis only with focal areas of dystrophic calcification. In other case histological findings were inconclusive since most of the nodal tissue was non-viable and a definite diagnosis was not possible. Both these cases were negative for AFB stain.

DISCUSSION

Lymph node enlargement may occur because of proliferation of cells of the lymphocyte and monocyte-macrophage system usually in response to antigenic stimulus or infiltration by inflammatory cells in infections involving lymph nodes (lymphadenitis), in situ proliferation of malignant lymphocytes or macrophages, infiltration of lymph nodes by metastatic malignant cells or infiltration of lymph nodes by metabolite laden macrophages in lipid storage diseases.

Analysis of lymphadenopathy in primary care practice has shown that more than two-third of patients have non-specific causes or upper respiratory illnesses (viral or bacterial), and less than 1% have malignancy₄. In one study, 186 of 220 patients (84%) referred for evaluation of lymphadenopathy had a benign diagnosis. One hundred and twelve of 186 (63%) patients with benign lymphadenopathy had a non-specific or reactive etiology (no causative agent found) and the remainder had a specific cause demonstrated₅.

In the present study 164(65.6%) lymph node biopsies

showed non-neoplastic non infectious reactive lymphadenopathy while in the remaining 86 (34.4%) cases an infectious cause was demonstrated.

Tuberculosis was the second most common disease seen involving the lymph nodes. Tuberculosis constituted 85 cases (34%) of all 250 cases and 99% of all infectious cases. Some previous studies revealed high prevalence of tuberculous lymphadenitis in countries like Pakistan, India and Bangladesh₆. Study by Danpat et al revealed tuberculosis in 51% of cases₇. In our study this %age is 34% which is lower than these studies. This could be due to improved living standard in general in this part of country, and secondly anti-tubercular treatment was started on the basis of FNA diagnosis. Staining for acid fast bacilli was positive in 13 cases only.

The next most common lesion identified was dermatopathic lymphadenitis seen in 15 cases (6%). Histologically all the cases showed expansion of paracortical zone by masses of pale staining cells, compressing and obscuring the germinal centres. Many of these histiocytes contained phagocytosed melanin pigment, positive for Masson Fontana in their cytoplasm. The differential diagnosis with mycosis fungoides was of particular concern because of the fact that mycosis fungoides is one of the cutaneous disorders that can be associated with dermatopathic lymphadenitis₉.

Kikuchi's disease was seen in 7 cases (2.8%) in the present study. Histologically all the nodes showed partial architectural effacement by large discrete areas of necrosis with abundant nuclear debris surrounded by lymphocytes, histiocytes and plasmacytoid monocytes. The absence of granulocytes in areas of necrosis and lack of follicular hyperplasia differentiated these cases from lymphadenitis caused by cat-scratch disease and other bacterial infections₁₀. Differentiation from lupus adenitis is problematic. However, absence of more numerous plasma cells, haematoxyphilic bodies, serum DNA antibodies favours Kikuchi's lymphadenitis.

Four cases were diagnosed as sarcoidosis, histologically showing diffuse architectural effacement of lymph node by compact, sharply demarcated, lymphocyte poor, reticulin rich epithelioid cell granulomas with Langhans' giant cells containing asteroid and conchoid bodies. All these nodes were negative for AFB staining. It is difficult to differentiate tuberculosis from sarcoidosis as AFB positivity rate is very low on tissue sections; so clinical correlation is of prime importance in such cases.

Kimura's disease was seen in 3 cases. Histologically all 3 cases showed follicular hyperplasia with variable interfollicular eosinophilia and proliferation of thin walled vessels. The major differential diagnosis was angiolymphoid hyperplasia with eosinophilia, a disease that is characterized by thick walled vessels, lined by epithelioid endothelial cells^{11, 12}.

Diagnosis of angiofollicular lymphoid hyperplasia (Castleman's disease)-hyaline vascular type was given in 3 lymph nodes – one each in cervical, intra-parotid, and axillary lymph nodes. Histologically these 3 cases showed partial effacement of lymph node architecture by large follicles having atrophic germinal centres. The centre of follicles and interfollicular areas showed increased vascularity with hyalinization of vascular walls, at places vessels were seen entering the germinal centres from interfollicular zone¹³.

Other rare lesions encountered were angioimmunoblastic lymphadenopathy¹⁴ (1 case), Langerhans' cell histiocytosis (1 case), reactive eosinophilic lymphadenitis (1 case).

One case was diagnosed as necrotic lymph node where histology showed necrosis only with focal areas of dystrophic calcification. In other case histological findings were inconclusive since most of the nodal tissue was non-viable and a definite diagnosis was not possible. Both these cases were negative for AFB stain.

Changes in lymph nodes of different individuals vary according to person's age, immunologic make-up, offending antigen and the duration of the proliferation. Histologically these events lead to a vast array of benign lymphoid proliferations or hyperplasia. So biopsy is mandatory. One should be aware of different non neoplastic morphologic changes for a definitive and specific histologic typing from diagnostic and as well as therapeutic point of view¹⁵.

CORRESPONDENCE TO

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