

Histomorphological Evaluation of Lymph Node Lesions: A Two Year Study

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Abstract

Introduction: Lymph node pathology is complex as it can be affected by a variety of non-neoplastic and neoplastic diseases. Histopathological examination especially at low magnification gives considerable information and helps to arrive at a diagnosis. *Aims and Objectives:* To study diagnostic histopathological patterns of various lymph node lesions and to study in depth rare lymph node lesions. *Materials and Methods:* This was a retrospective study carried out in the department of Pathology, Topiwala National Medical College and BYL Nair Hospital, Mumbai, over a period of two years. A total of 255 lymph nodes were examined on routine histopathology and immunohistochemistry was done in a few cases of lymphomas. *Observations and Results:* There were 153 males and 102 females in the study and the age ranged from 1 year to 85 years. The non-neoplastic causes were common for lymphadenopathy and in specific causes, tuberculosis was most common. Incidence of metastatic malignancy was 9 % and of lymphomas was 11 %. *Conclusion:* Lymphadenopathy occurs more commonly due to non-neoplastic causes. Metastatic involvement of lymph nodes is mostly due to carcinomas. Histological evaluation of lymph nodes at low magnification helps to evaluate the architectural patterns of lymph nodes. These along with the identification of the cellular composition help in the diagnosis of lymph node diseases.

Keywords: Lymph Node Lesions; Lymphadenopathy; Immunohistochemistry.

Introduction

Lymph node pathology is complex because of the inherent complexity of the immune system and because of the various primary diseases and also the varied number of diseases that reach it via lymph [1]. Study of lymph node at low magnification gives considerable information and specific patterns help to formulate a list of differential diagnoses [2]. In lymphadenopathy, the lymph nodes increase in size and have an abnormal consistency. Cervical lymphadenopathy is defined as any enlarged cervical lymph node that is more than 1cm in diameter [3]. Lymphadenopathy

can have various causes and can affect all age groups. With increasing age and in older population the involvement of lymph nodes by metastatic malignancy becomes more common as compared to younger people. The detection of metastatic tumour in lymph nodes is very important as it gives clues for the primary tumour especially for occult primary tumors [4].

Aims and Objectives

1. To study diagnostic histopathological patterns of various lymph node lesions.
2. To study in depth rare lymph node lesions

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Materials and Methods

This was a retrospective study carried out in the

department of Pathology, Topiwala National Medical College and BYL Nair Hospital, Mumbai, over a period of two years. The study material included all the excisional lymph node biopsies that were received to the department. The tissue was fixed in 10% buffered formalin and submitted to histopathological processing. Sections 5-7 microns thick were cut from the blocks and were stained with routine hematoxylin and eosin stains. Special stains like Ziehl-Neelsen, Masson-Fontana, Reticulin and Prussian blue were performed when required. Immunohistochemistry was performed on the lesions that were reported as neoplastic on routine light microscopy examination. The clinical details on all the request forms were noted. Additional relevant clinical information was collected from the clinicians whenever required.

Inclusion Criteria

1. Excision biopsy tissue of lymph nodes was considered.
2. Trucut biopsy specimens of lymph nodes were included

3. Formalin fixed paraffin blocks of lymph nodes from other hospitals that had come for review

Exclusion Criteria

1. Inadequate samples were excluded
2. Incomplete clinical details

The lymphadenopathy cases were grouped into non-neoplastic and neoplastic categories. The non-neoplastic lesions were further divided into non-specific and specific lymphadenopathy. The non-neoplastic lesions included all primary and metastatic lesions of the lymph node. For this group immunohistochemistry was also performed for definite categorization.

Observations and Results

The total number of cases studied was 255. There were 153 males and 102 females in the study and the male to female ratio was 1.5:1. The age of the patients ranged from 1 year to 85 years.

Table 1: Distribution of lymphadenopathy according to the etiology

Etiology		No. of cases	Percentage
1. Non-neoplastic		-	-
Non-specific causes		111	43.5
Specific causes			
	Tuberculosis	82	32.1
	Typhoid	1	0.4
	Filarial	1	0.4
	HIV-related	1	0.4
Others			
	Necrotizing lymphadenitis	3	1.2
	Dermatopathic	2	0.8
	SHML	1	0.4
	ALHE	1	0.4
	Amyloidosis	1	0.4
2. Neoplastic			
	Metastatic	23	9.0
	Hodgkin's lymphoma	12	4.7
	Non- Hodgkin's lymphoma	16	6.3
Total		255	100

SHML- Sinus histiocytosis with massive lymphadenopathy, ALHE- Angiolymphoid hyperplasia with eosinophilia

Maximum number of cases was of non-specific lymphadenitis accounting for 43.5 %. The primary neoplastic lymphomas accounted to 11 %.

Table 2: Distribution of cases based on histopathology and age

Histopathology	Age in years									Total
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
Non-specific causes	19	48	24	7	4	6	1	1	1	111
Tuberculosis	24	19	23	8	3	3	1	1		82
Typhoid	-	-	1	-	-	-	-	-	-	1
Filarial	-	-	1	-	-	-	-	-	-	1
HIV-related	-	-	-	-	-	-	-	-	-	1
Necrotizing lymphadenitis	-	1	-	2	-	-	-	-	-	3
Dermatopathic	1	1	-	-	-	-	-	-	-	2

SHML	1	-	-	-	-	-	-	-	-	1
ALHE	-	-	-	1	-	-	-	-	-	1
Amyloidosis	-	-	-	-	-	-	-	1	-	1
Metastatic	-	1	-	9	5	5	1	2	-	23
Hodgkin's lymphoma	5	5	-	1	1	-	-	-	-	12
Non-Hodgkin's lymphoma	1	2	2	2	1	6	-	2	-	16
Total	51	78	51	30	14	20	3	7	1	255

Among the specific causes for lymphadenitis, tuberculosis was most common and was predominantly seen in the 1-30 years age group. Metastatic malignancy was most common between 30 to 60 years. Hodgkin's lymphoma was most common in the first and second decades.

Table 3: Distribution of cases according to the site

Site	No. of Cases	Percentage (%)
Cervical	122	47.8
Mesenteric	54	21.7
Axillary	34	13.3
Inguinal	10	3.9
Supraclavicular	10	3.9
Submandibular	8	3.1
Submental	3	1.1
Postauricular	2	0.7
Femoral	2	0.7
Iliac	2	0.7
Suboccipital	1	0.3
Intrapectoral	1	0.3
Periesophageal	1	0.3
Retrosternal	1	0.3
Peripancreatic	1	0.3
Celiac	1	0.3
Around common bile duct	1	0.3
Retroperitoneal	1	0.3
Total	255	100

Table 4: Histopathological type of metastatic tumor

Histopathology	No. of Cases	Percentage (%)
Invasive ductal carcinoma	8	34.8
Squamous cell carcinoma	6	26.2
Adenocarcinoma	4	17.4
Papillary carcinoma thyroid	2	8.7
Nasopharyngeal carcinoma	1	4.3
Small cell carcinoma of lung	1	4.3
Undifferentiated carcinoma	1	4.3
Total	23	100

Maximum number of metastatic cases belonged to primary breast carcinomas.

Table 5: Distribution of types of Lymphoma after immunohistochemistry

Lymphoma	Type	No. of Cases
Hodgkin's	Nodular sclerosis	6
	Mixed cellularity	4
Non-Hodgkin's	Diffuse large cell	7
	Small lymphocytic	2
	Anaplastic large cell	1
Total		20

Immunohistochemistry could be performed only in 10 cases each of Hodgkin's and non-Hodgkin's lymphoma. In NHL, Diffuse large cell type was the most common type encountered.

Discussion

Lymphadenopathy is more common in non-neoplastic conditions than neoplastic conditions. In the present study, 80% cases of lymphadenopathy were due to non-neoplastic lesions of various etiologies which is comparable to a study of 220 cases in which 84 % of lymphadenopathies were due to non-neoplastic causes [5].

In the present study, the major cause of lymphadenopathy with a specific etiology was tuberculous lymphadenitis. This was present most commonly in the 1-30 years age groups. Pandit et al [6] in their study, on cervical lymphadenitis of tuberculous etiology observed the mean age of presentation as 21-30 years. Narang et al [7] observed the mean age to be 25 years and Balkishan et al [8] reported it to be most common in the 11-30 years age. Our findings compare well with the above studies.

Lymphadenopathy due to typhoid infection was seen in one case of small intestinal perforation by typhoid infection. The lymph node showed small randomly scattered foci of necrosis with aggregates of phagocytic mononuclear cells (typhoid nodule) similar to histology described in literature [9].

Lymphadenopathy due to filariasis was seen in one case. The lymph node showed calcified adult worm of *Wuchereria bancrofti*, dilated and engorged lymphatics and fibrosis [9].

In the present study, there were three cases of Necrotising lymphadenitis of Kikuchi type. The incidence of Kikuchi disease was 0.4% in our study as compared to a study done by Kuo [10] from Taiwan where it was reported to be 5.7%. It occurs more commonly in women than men with most patients being under the age of 40 years as also seen in the present study. It commonly involves solitary or multiple lymph nodes in an anatomic region, particularly the cervical nodes are affected more frequently [11]. In the present study also the lymph nodes involved by Kikuchi's disease were solitary and cervical in location. There are three histological variants of this disease, proliferating, necrotizing and xanthomatous types and the necrotizing type is more common. In the study by Kuo [10] 42 out of 79 cases were reported as the necrotizing type. In the present study also all three cases were of necrotizing type. Histologically, this type of Kikuchi disease must be differentiated from lymphadenopathy due to systemic lupus erythematosus (SLE). Presence of Hematoxyline bodies and plasma cells favour the diagnosis of SLE [10].

In the present study there were two cases of dermatopathic lymphadenitis. The nodes showed expansion of paracortex with compression of the follicles and presence of brown pigment confirmed to be melanin by Masson-Fontana stain. This histology correlates with grade 4 of dermatopathic lymphadenopathy as per criteria given by Gould et al [12].

Although dermatopathic lymphadenopathy is known to be associated with dermatitis, mycosis fungoides and Sezary syndrome, in a study by Gould et al [12] the incidence of skin disease in patients with dermatopathic lymphadenopathy was reported to be low as was seen in the present study where both the cases had no evidence of skin lesions in the corresponding drainage sites.

SHML is known to present as painless massive lymph node enlargement in children. Our case also presented with similar features. Extranodal involvement especially of respiratory tract, skin and bone are known to occur in about 25% cases [13]. Such involvement was not apparent in the present case.

Lymphadenopathy is one of the manifestations in ALHE [14]. It should be differentiated from Kimura's disease by the presence of proliferation of thick walled muscular blood vessels and absence of folliculolysis [15]. Proliferation of thick walled blood vessels in the node was observed in our case.

Amyloid deposition in the lymph node is uncommon and is associated with plasmacytomas, NHL or long standing infections and inflammatory conditions [6]. In our study, there was a single case of amyloid deposition in lymph node and this patient also had multiple myeloma.

Any malignant tumor can metastasize to lymph nodes but the incidence varies depending on the tumor type. It is common with carcinomas, melanomas and germ cell tumors and rare with sarcomas and central nervous system malignancies [2].

Patients of nasopharyngeal carcinoma (NPC) often show initial sign of cervical lymphadenopathy without a readily apparent mass in the nasopharynx.^[1] Similar presentation was seen in one case in the present study. Nodal involvement by NPC may be misinterpreted as lymphoma [1].

The types of lymphomas most likely to be misdiagnosed as metastatic carcinoma are anaplastic large cell lymphoma, large cell lymphoma with sclerosis or sinusoidal pattern of growth and nodular sclerosis Hodgkin's disease with concentration of large mononuclear variants of Reed-Sternberg cells around areas of necrosis [2].

In our study, the incidence of metastatic tumors in lymph nodes was 9%. This compares well with the findings of Ahmed et al [17] who observed an incidence of 12% for secondaries in their study. Metastatic undifferentiated carcinoma can be confused with lymphoma. Features favouring metastatic tumors are focal nodal involvement, definite nesting, extensive necrosis, predominantly sinusoidal distribution and solid plugs of tumor cells in the lymphatic channels [2].

In the present study, cervical lymph nodes were involved in all cases of Hodgkin's disease and ten out of twelve cases (83.3%) occurred in the 1-20 years age groups. Ramani et al [18] in their study on Hodgkin's lymphoma observed the median age of presentation in India to be 34 years. In the study by Desforges et al [19] 60% and 30% of Hodgkin's disease was nodular sclerosis and mixed cellularity type respectively. In our study, nodular sclerosis and mixed cellularity type were 50% each.

Diffuse large cell lymphoma differs from immunoblastic lymphoma by the presence of lighter staining, less pyrinophilic cytoplasm, more peripheral location of the nucleoli and lack of plasmacytoid differentiation [2].

Small lymphocytic lymphoma usually shows extranodal extension in one-third cases. Here, the cells show a diffuse pattern with effaced architecture of the node. However, interfollicular pattern with some remaining lymphoid follicles [20] and involvement of the B cell zone are also known.

Conclusion

Lymphadenopathy occurs more commonly due to non-neoplastic causes than neoplastic conditions. Metastatic involvement of lymph nodes is mostly due to carcinomas. Histological evaluation of lymph nodes at low magnification helps to evaluate the architectural patterns of lymph nodes. These along with the identification of the cellular composition help in the diagnosis of lymph node diseases.

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