

Evaluation of Histopathological Patterns of Lymph Node Biopsies in a Tertiary Care Hospital -Three Year Observational Study

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Conflict of interest: Nil

Abstract:

Background: The causes of lymphadenopathy exhibit a wide range of spectrum from stereotypical patterns of treatable infectious etiology to deadly malignant neoplasms. Detailed investigations are required to reveal the underlying pathology, as clinical diagnosis is usually delayed because of nonspecific symptoms and radiological images may not be sufficient for diagnosis. Hence, excision biopsy of lymph node and its histopathological analysis are considered mandatory to arrive at a specific diagnosis for appropriate patient care and management.

Objectives: 1. To study the frequency of occurrence of diseases of lymphnode in relation to age, gender and site. 2. The study aims to analyse the various histopathological patterns of lymph node biopsies and classify them into major groups.

Materials and Methods: The present study was retrospective observational type, which included 137 cases presented with lymph node enlargement in a tertiary care hospital over a period of 3 years from December 2020 to November 2023.

Results: Out of total 137 lymphnode biopsies analysed in our study, the demographic most significantly impacted were those aged between 51-60 years with a female preponderance. 70 cases (51.09%) constituted non-neoplastic lesions, while 67 cases (48.91%) were observed to be neoplastic. Among 70 non neoplastic lesions (51.09%), majority of 55 cases (40.14%) constituted Reactive Lymphadenitis followed by 11 cases (8.03%) of Granulomatous lymphadenitis. Among 67 neoplastic lesions (48.91%), 7 cases (5.11%) were primary lymphomas and the other remaining 60 cases (43.80%) were metastatic lesions, in which majority of 37 cases (61.69%) turned out to be metastasis from carcinoma of breast presenting with axillary lymphadenopathy.

Conclusion: Lymphadenopathy is not so uncommon in our geographical area. Thus, excision biopsy of lymphnode and its histopathological analysis play a pivotal role in the clinical management by establishing the cause of lymphadenopathy for early definitive diagnosis and prognostic purpose. In our present study, non-neoplastic lesions were more frequent than neoplastic lesions. In specific, metastatic lesions were the major cause of lymphadenopathy followed by reactive lymphadenitis and the axillary lymphnodes were the most frequently biopsied group.

Keywords: Lymphadenopathy, Excision biopsy, Histopathological analysis, Reactive Lymphadenitis, Metastatic lesions.

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Introduction

Lymphnode is an integral component of the immune system because normal immune response leads to proliferation and expansion of the cellular components of lymphnode leading to its enlargement [1,2]. Normally in adults, only inguinal lymphnodes are palpable as multiple, firm 0.5 – 2 cm nodules below inguinal ligaments. Small, tiny 0.5 – 1 cm cervical lymphnodes may be normally palpable in children [3]. Lymphadenopathy is a term used to describe the condition in which they become abnormal in size, consistency or number caused by invasion of either

inflammatory or neoplastic cells into lymphnode [4]. It can be localized or part of generalized lymphadenopathy or asymptomatic. Specific anatomic locations are associated with certain etiologies [3]. Lymphnodes are most widely distributed, easily accessible and frequently obtained for diagnostic purposes [2]. Fine needle aspiration cytology is commonly used for diagnosis of lymphadenopathy but there are still many instances where excision biopsy is mandatory, especially in suspected and grey zone of various lesions and lymphoproliferative disorders or in

those cases where diagnosis cannot be reliably reached on clinical grounds or fine needle aspiration cytology [5]. Hence, excision biopsy of lymphnode and its histopathological examination remains the main stay for etiological diagnosis of lymphadenopathy [6]. The present study was an attempt to evaluate different histomorphological patterns of lymphnode biopsies in detail.

Materials and Methods: A retrospective, cross-sectional, descriptive, non-interventional observational type of study was carried out on 137 lymphnode biopsies received in the department of Pathology, Government Medical College and Hospital, Ananthapuramu, Andhra Pradesh for a period of three years from December 2020 to November 2023.

Specimen processing: All lymphnode biopsies were preserved in 10% neutral buffered formalin. The tissue blocks produced were embedded in paraffin wax and then sliced into 4-5 microns thin sections using a rotary microtome. Standard hematoxylin and Eosin staining was performed.

Inclusion criteria: All lymphnode biopsies received in the histopathological section during the study period, irrespective of age, gender, site and clinical diagnosis with definitive histopathological diagnosis were included.

Exclusion criteria: Autolysed, insufficiently fixed and inadequately lymphnode biopsy specimens were

excluded from the study. Final diagnosis was arrived after meticulous histopathological examination by two pathologists.

Ethical consideration: Ethical approval was obtained from the Institutional Ethics Committee of Government Medical College and Hospital, Ananthapuramu.

Statistical analysis: All collected data was systematically tabulated on an excel sheet. The percentage of distribution of lymphnode biopsies among various age groups, genders, sites in comparison to other studies were calculated using descriptive statistical analysis.

Results

In the present study, a total of 137 lymphnode biopsies were reviewed and grouped into four main categories namely 55 cases (40.14%) of reactive lymphadenitis, 11 cases (8.03%) of granulomatous lymphadenitis, 67 cases (48.91%) of neoplastic lesions and 4 cases (2.92%) of miscellaneous group [Table-1]. 70 cases (51.09%) of non-neoplastic lesions were more frequent in our present study followed by 67 cases (48.91%) of neoplastic lesions [Fig.1a]. Out of 67 neoplastic lesions, 7 cases (10.45%) included primary lymphomas and a majority of 60 cases (89.55%) included metastatic malignancies [Fig.1b].

Table 1: Distribution of Lymphnode lesions

Histological Diagnosis			Total Number of cases
Reactive Lymphadenitis			55 (40.14%)
Granulomatous Lymphadenitis	Caseating TB Lymphadenitis	10 (7.3%)	11 (8.03%)
	Non-Caseating TB Lymphadenitis	01(0.73%)	
Neoplastic	Primary Lymphomas	07(5.11%)	67(48.91%)
	Metastatic malignancies	60 (43.8%)	
Miscellaneous	Kikuchi disease	01 (0.73%)	04(2.92%)
	Kimura disease	03(2.19%)	
Total			137(100%)

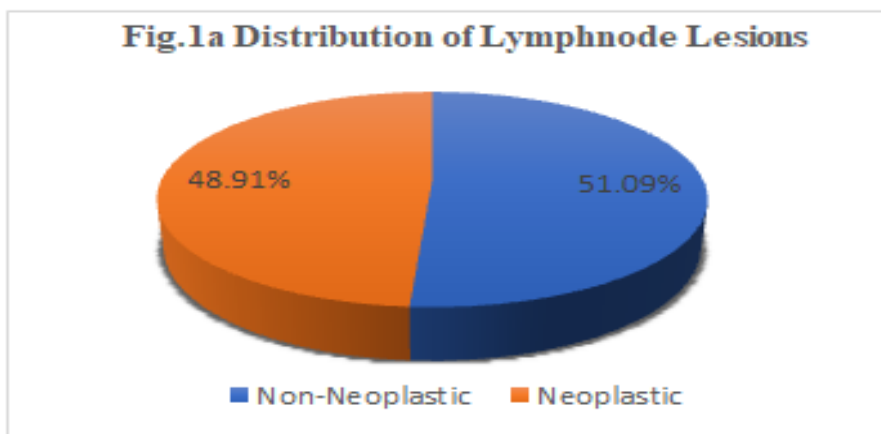


Figure 1a: Distribution of Lymphnode Lesions

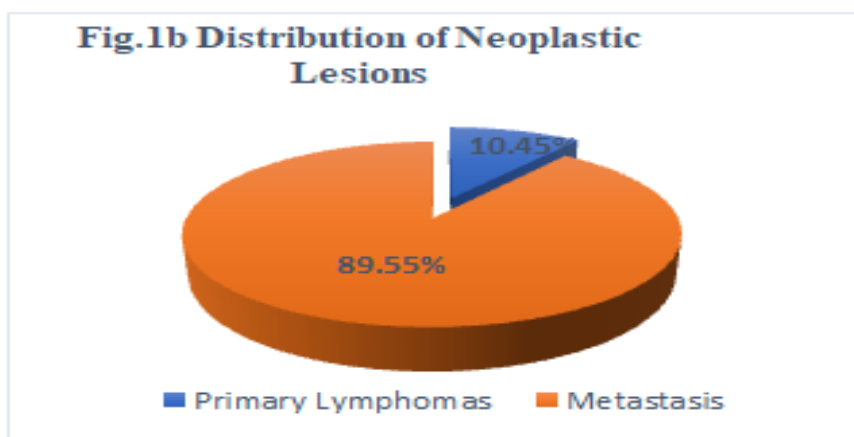


Figure 1b: Distribution of Neoplastic Lesions

In the present study, 96 cases (70.07%) were females and 41 cases (29.93%) were males with a male to female ratio of 1:2.3 [Table/Fig.2]. The range of age group of patients was between 2 years to 78 years. Majority of 40 cases (29.20%) were in the age group of 51-60 years, followed by 26 cases (18.98%) in the age group of 41-50 years and least number of cases were observed in the age group less than 10 years (3.65%) [Table-2].

Table 2: Age and Sex wise distribution of lymphnode lesions amongst the study population

Age group (years)	Female	Male	Total
<10	01	04	05 (3.65%)
11-20	01	07	08 (5.84%)
21-30	09	05	14 (10.22%)
31-40	18	06	24 (17.51%)
41-50	24	02	26 (18.98%)
51-60	30	10	40 (29.20%)
61-70	10	04	14 (10.22%)
>71	03	03	06 (4.38%)
Total	96(70.07%)	41(29.93%)	137(100%)

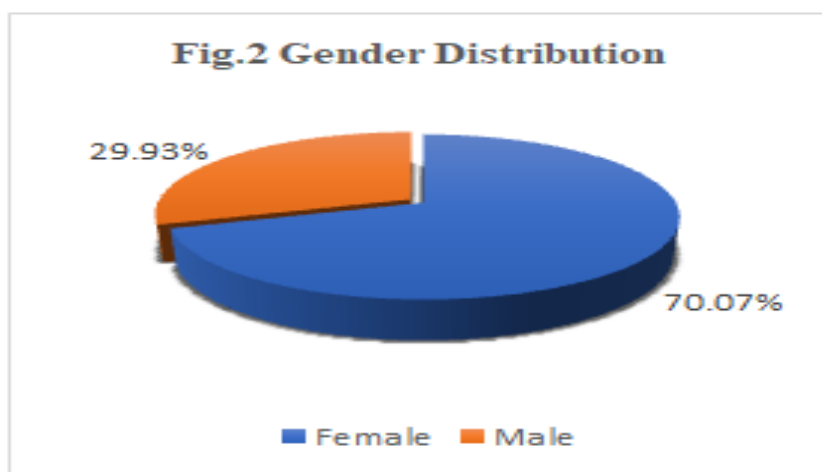


Figure 2: Gender Distribution

Amongst non-neoplastic lesions, majority of 55 cases (40.14%) were reactive lymphadenitis with the maximum number of 15 cases (10.95%) observed in the age group of 51-60 years. 11 cases (8.03%) of Granulomatous lymphadenitis included the next common non-neoplastic lesions, with the

most common age group being impacted between 21 to 30 years with a maximum of 4 cases (2.92%). Out of total 11 cases, 10 cases (7.3%) constituted tuberculous lymphadenitis and 1 case (0.73%) included non-caseating tuberculous lymphadenitis [Table-3/Fig.3].

Table 3: Distribution of lymphnode biopsies based on histological diagnosis and age amongst the study population

Age group (years)	Reactive Lymphadenitis	Granulomatous Lymphadenitis		Primary Neoplasms		Metastasis	Miscellaneous		Total
		Casating TB	Non-casating TB	Hodgkin's Lymphoma	Non-Hodgkin's		Kikuchi disease	Kimura disease	
<10	02(1.46%)	02 (1.46%)	-	01 (0.73%)	-	-	-	-	05 (3.65%)
11-20	06(4.38%)	01 (0.73%)	01 (0.73%)	-	-	-	-	-	08 (5.84%)
21-30	05(3.65%)	04 (2.92%)	-	02 (1.46%)	-	01 (0.73%)	1 (0.73%)	01 (0.73%)	14 (10.22%)
31-40	13(9.48%)	01 (0.73%)	-	-	-	10 (7.3%)	-	-	24 (17.51%)
41-50	10(7.3%)	01 (0.73%)	-	-	01 (0.73%)	12 (8.76%)	-	02 (1.46%)	26 (18.98%)
51-60	15(10.95%)	-	-	-	02 (1.46%)	23 (16.79)	-	-	40 (29.20%)
61-70	03(2.19%)	01 (0.73%)	-	-	-	10 (7.3%)	-	-	14 (10.22%)
>71	01(0.73%)	-	-	01 (0.73%)	-	04 (2.92%)	-	-	06 (4.38%)
Total	55 (40.14%)	10 (7.3%)	1 (0.73%)	04 (2.92%)	03 (2.19%)	60 (43.8%)	1 (0.73%)	3 (2.19%)	137 (100%)

In the present study, amongst 67 neoplastic lesions, 7 cases (5.11%) were primary lymphomas with 4 cases (2.92%) comprising of Hodgkin's lymphoma, out of which 2 cases (1.46%) were observed in the age group of 21-30 years of male and female patients respectively. The remaining 2 cases (1.46%) of Hodgkin's lymphoma were observed in

8 years and 75 years of male patients respectively, supporting the evidence of bimodal age distribution with overall male preponderance. There were 3 cases (2.19%) of Non-Hodgkin's lymphoma diagnosed after the age group of 40 years, peak between 51-60 years with slight female preponderance [Table-3/Fig.3].

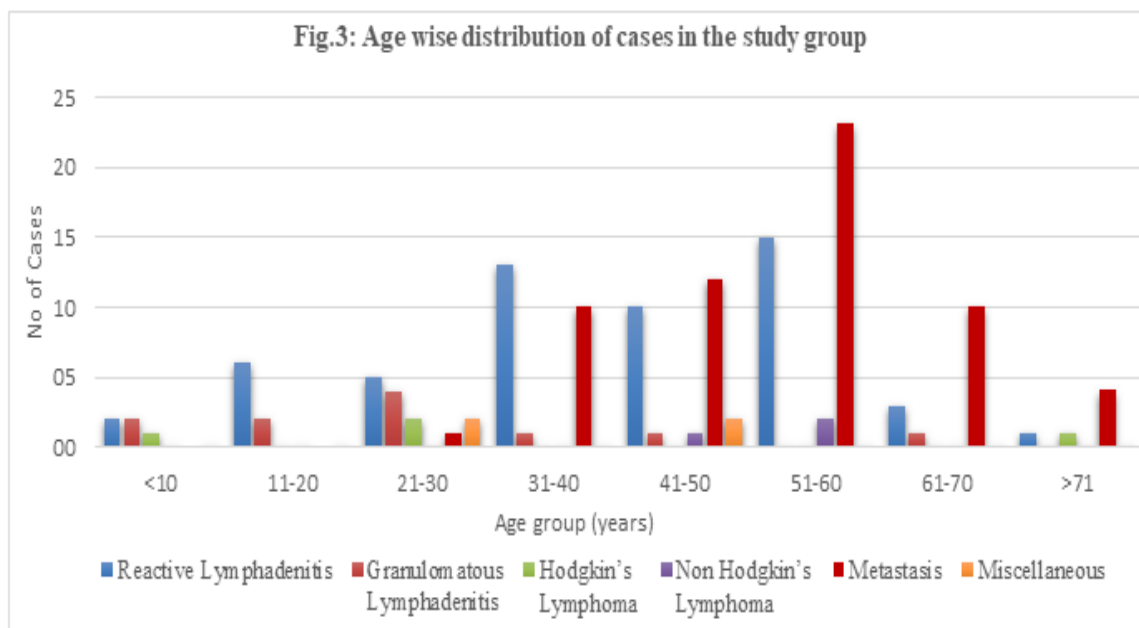


Figure 3: Age wise distribution of cases in the study group

In the present study, 60 cases (43.8%) included metastatic neoplasms, of which 14 were males and 46 were females, with the majority of 23 cases (16.79%) being affected between the age group of 51-60 years, followed by 12 cases (8.76%) in the age group of 41-50 years [Table-3/ Fig.3]. Overall, the most common sites of presentation of lymphadenopathy were axillary (45.98%) followed by cervical (29.93%) [Table-4/ Fig.4]. Out of these 60 metastases, 37 cases (61.69%) included

carcinoma of breast, 11 cases (18.33%) included squamous cell carcinoma, 10 cases (16.66%) included adenocarcinoma and 1 case (1.66%) each included in papillary carcinoma of thyroid and high-grade serous carcinoma of fallopian tube respectively. Miscellaneous lesions diagnosed of all cases were 1 case (0.73%) of Kikuchi disease in a female patient of 21-30 years of age and 3 cases (2.19%) of Kimura disease between 21-50 years of age with male predominance [Table-3/ Fig.3].

Table 4: Distribution of lymphnode biopsies based on histological diagnosis and location amongst the study population

Histological Diagnosis	Axillary	Cervical	Abdominal	Inguinal	Total
Reactive Lymphadenitis	19(13.86%)	18(13.14%)	15(10.95%)	3(2.19%)	55(40.14%)
TB Lymphadenitis	1(0.73%)	7(5.11%)	1(0.73%)	1(0.73%)	10(7.30%)
Non-caseating TB Lymphadenitis	-	-	-	1(0.73%)	1(0.73%)
Hodgkin's lymphoma	-	3(2.19%)	-	1(0.73%)	4(2.92%)
Non-Hodgkin's lymphoma	2(1.46%)	1(0.73%)	-	-	3(2.19%)
Metastasis	41(29.93%)	8(5.84%)	11(8.03%)	-	60(43.8%)
Kikuchi disease	-	1(0.73%)	-	-	1(0.73%)
Kimura disease	-	3(2.19%)	-	-	3(2.19%)
Total	63(45.98%)	41(29.93%)	27(19.71%)	6(4.38%)	137(100%)

FIG 4 SITE OF LYMPH NODE BIOPSIES

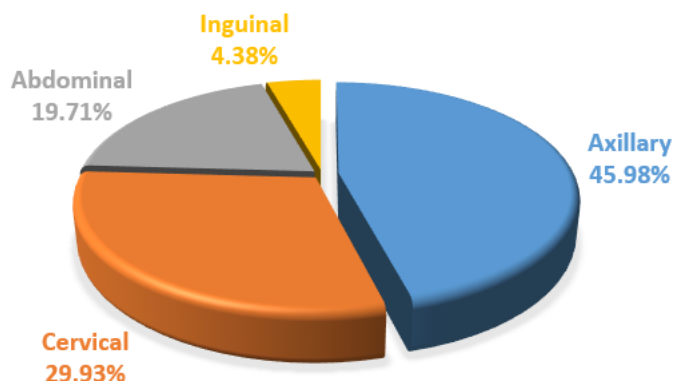


Figure 4: Site of Lymph Node Biopsies

Discussion

The present study is carried out for over a period of 3 years to evaluate the different histopathological patterns of lymphnode biopsies and its clinicopathological correlations. In our study, majority of patients were females with male to female ratio of 1:2.3. Age group of patients ranged between 2 years to 78 years. Similar results of female preponderance were also reported by Rehman Md A [4], Kim LH [7], Tiwari M [8] and Kamat GC [9]. In the present study, non-neoplastic lesions (51.09%) were more common than neoplastic lesions (48.91%) and these results were consistent with Rehman Md A [4] i.e., 70.2%, Rao MN et al [10] i.e., 56%, Vacchani A et al [11] i.e., 75%. Reactive Lymphadenitis (40.14%) constituted the predominant non-neoplastic pattern, which was consistent with the study of Damle R et al [2] i.e., 52.87% and Moore SW et al [5] i.e., 47.8%. Higher percentage of this might be due to reactive hyperplasia in lymphnodes, which do not show the metastatic deposit due to early diagnosis and surgical excision [2] [Table-5].

In our present study, Granulomatous Lymphadenitis was the next most common non-

neoplastic pattern constituting 8.03% of all cases but several authors reported Tuberculosis as the major cause of lymphadenopathy, since India being a developing country with low socio-economic and poor living conditions [4,8]. In our present study, amongst 67 neoplastic lesions (48.91%), there were 7 cases (5.11%) of primary lymphomas, in which 4 cases (2.92%) were Hodgkin's lymphoma and 3 cases (2.19%) were non-Hodgkin's lymphoma. The other remaining 60 cases (43.8%) accounted for metastatic lesions.

A study conducted by Sibanda EN et al [6], Tiwari M et al [8], and Kamat GC et al [9] reported 7%, 2% and 3.6% of lymphomas respectively, which were comparable with our study. Primary malignancies have been reported to be the major cause of lymphadenopathy in developed countries because of racial and genetic factors.

To the contrary, studies by Mohan A et al [12], Roy A et al [13] and Sinclair S et al [14] reported 25.9%, 44.5%, 63.29% cases of primary lymphomas respectively with very higher incidence than the current study, since they included large number of cases conducted in research center or Onco institutes.

Table 5: Comparison of histopathological diagnosis of lymphnode lesions among various studies

Names of authors	Reactive lymphadenitis (%)	Granulomatous lymphadenitis (%)	Hodgkin's lymphoma (%)	Non-Hodgkin's lymphoma (%)	Metastasis (%)	Miscellaneous (%)
Present Study	40.14	8.03	2.92	2.19	43.8	2.92
Damle R et al., 2017 [2]	52.87	20.24	1.2		2.4	16.31
Egejuru RO et al., 2018 [15]	17.86	14.29	8.9		50	-
Melkundi R et al., 2017 [16]	24	52	2	2	20	-
Shivamurthy A et al., 2016 [17]	15	16	2	22	38	1
Hemant B et al., 2017 [18]	-	32.1	11	9	-	

In the present study, 60 cases (43.8%) were metastatic malignancies, out of which 37 cases (61.69%) were metastases from carcinoma of breast, 11 cases (18.33%) were metastatic squamous cell carcinoma, 10 cases (16.66%) were metastatic Adenocarcinoma, 1 case (1.66%) was Papillary carcinoma of thyroid and 1 single case (1.66%) included High-grade serous carcinoma of fallopian tube [Table 6]. Majority of 23 cases (16.79%) of metastases were seen in the age group

of 51 to 60 years. Our findings were similar to various studies in literature like Tiwari M et al [8] i.e., 11% and Vachhani A et al [11] i.e., 23%. Metastasis of squamous cell carcinoma in lymphnode was due to intake of various forms of tobacco in our geographical area, leading to malignancy in aero-digestive tract.

Lifestyle modification and cultural factors accounted for carcinoma of breast metastasis in lymph node.

Table 6: Distribution of different types of metastatic tumours in present and other studies

Metastatic Tumours	Present study (%)	Damle R et al., 2017 [2]	Hemant B et al., 2017 [18]
Carcinoma of breast	37 (61.69%)	34 (62.9%)	8 (34.8%)
Squamous cell carcinoma	11 (18.33%)	12 (22.2%)	6 (26.2%)
Adenocarcinoma	10 (16.66%)	8 (14.8%)	4 (17.4%)
High grade serous carcinoma of fallopian tube	1 (1.66%)	-	-
Papillary carcinoma of thyroid	1 (1.66%)	-	2 (8.7%)
Miscellaneous tumours	-	-	3 (12.9%)
Total	60(100%)	54(100%)	23(100%)

In the present study, axillary lymphnodes [45.98%] were the predominant biopsied group. Contrary to the previous belief that cervical lymphnodes being the most common site of presentation due to their easy accessibility and drainage, axilla is taking a pride of place in lymphadenopathy in our geographical area. Clinicians use FNAC as the initial diagnostic test in daily practice and treat accordingly.

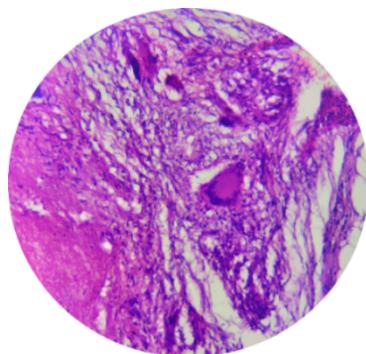


Figure 5: Tuberculous Lymphadenitis: Microphotograph showing well-formed epithelioid cell granulomas comprising of epithelioid cells, Langhan's giant cell and lymphocytes (H&E, 10x)

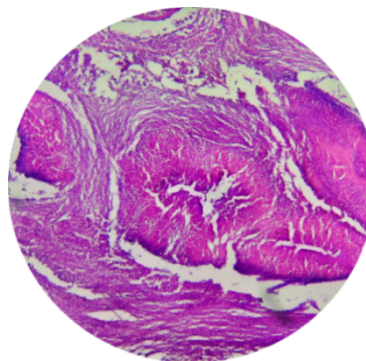


Figure 6: Kikuchi's disease: Microphotograph showing large areas of necrosis along with apoptotic cells and nuclear debris (H&E, 10x)

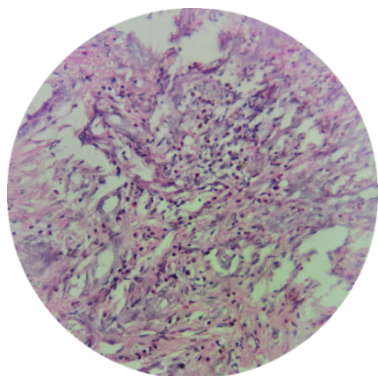


Figure 7: Kimura disease: Microphotograph shows eosinophilic abscess in the interfollicular area. (H & E, 10x)

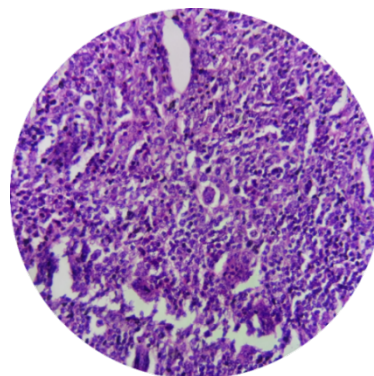


Figure 8: Hodgkin's Lymphoma: Microphotograph showing Reed-Sternberg cells against a polymorphous background (H&E, 10x)

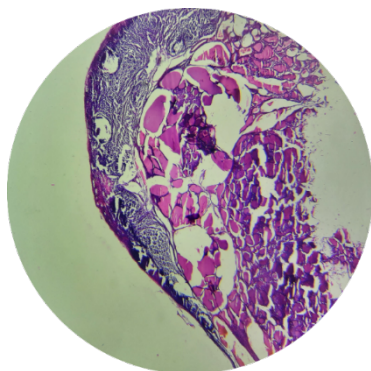


Figure 9: Metastatic papillary carcinoma of thyroid showing tumour cells arranged in papillary pattern within lymphnode [H&E,10x]

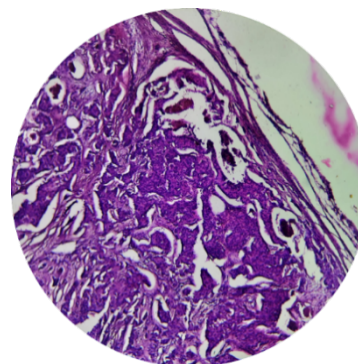


Figure 10: Metastatic invasive ductal cell carcinoma showing tumour cells arranged in nests and diffuse sheets within lymphnode (H&E,10x)

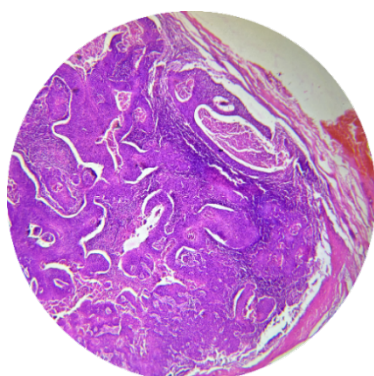


Figure 11: Metastatic squamous cell carcinoma shows nests of atypical Keratinised squamous cells within lymphnode (H&E,10x)

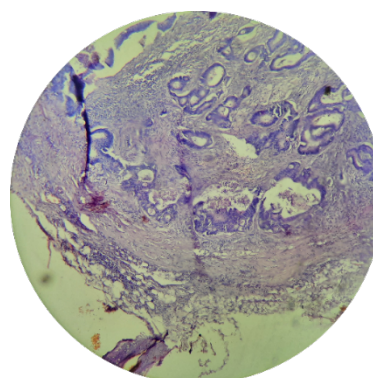


Figure 12: Metastatic Adenocarcinoma showing tumour cells arranged in glandular pattern within lymphnode (H&E,10x)

Conclusion

The present study highlights the usefulness of lymphnode biopsy as a simple and cost-effective

tool for patients presenting with lymphadenopathy. It also further aids to establish the etiological causes and classification for early disease

detection, thereby reducing mortality and positively influencing the overall prognosis of patients.

In the present study, non-neoplastic lesions were the predominant ones compared to neoplastic lesions. Metastatic neoplasms were the most dominant cause of lymphadenopathy followed by reactive lymphadenitis, both showing peak incidence in the age group of 51-60 years. The most frequent malignant condition was metastasis of breast carcinoma in axillary lymphnode.

This trend is implicating the clinicians to think more in lines of malignancy rather than benign or reactive in older adults. More comprehensive investigations like special stains and immunohistochemistry performed will aid in further diagnostic evaluation.

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