

Original Research Article

A Retrospective study of malignant lymphadenopathy diagnosed by Fine needle aspiration cytology (FNAC) at Tertiary health care hospital**Dipti R. Patel^{1*}, Shiv N. Chawla²**¹Assistant Professor, Department of Pathology, Zydus Medical College and Hospital Dahod, Gujarat, India²Professor & Head of Department, Department of Pathology, American International Institute of Medical sciences, GBH General & Cancer hospital, Bedwas, Udaipur, Rajasthan, India

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Abstract

Background: FNAC easily access enlarged lymph nodes and therefore, this procedure is of immense importance in the diagnosis of secondary or primary malignancies. **Aim:** The study was done to find out the frequency of various types of lymph node malignancy as well as to find out incidence of various pathological subtypes of metastatic lymphadenopathy and to test the utility of FNAC in diagnosis of malignant Lymphadenopathy. **Material & Methods:** This retrospective study of malignant lymph node aspirates diagnosed by FNAC in palpable lymphadenopathy. The study was conducted over a period of 1 & ½ years from Sept 2017 to Feb 2019 in Department of Pathology at American International institute of Medical Sciences (AIIMS), GBH General & cancer hospital, Udaipur, Rajasthan. All age group (1-90 years) of patients of malignant enlarged lymph nodes were included in study. All cytological smears were studied, analyzed, correlated with clinical and radiological data. **Results:** Out of 200 enlarged lymph nodes, 122 (61%) were identified as malignant lymph nodes, males 79 (64.8%), Females 43 (35.2%). M: F ratio 1.8:1. Cervical lymph node 73(59.8%) was commonly involved node. Metastatic malignancy 107(87.7%) was more common than lymphomas 15(12.2%). Squamous cell carcinoma 58(47.5%) was commonest metastasis followed by duct cell carcinoma 18(14.8%) and adenocarcinoma 13(10.7%). Oral cavity 39 (36.4%) were common primary site followed by breast 18(16.8%). Non Hodgkin Lymphoma was commonest 12(9.8%) out of 15 primary lymphoma. **Conclusions:** FNAC is simple, reliable, cost-effective and rapid technique in making diagnosis of lymph node malignancies, especially to confirm or to exclude the metastatic malignancy. **Keywords:** Fine Needle Aspiration Cytology (FNAC), Malignant Lymphadenopathy, Metastatic malignancy, Squamous cell carcinoma.

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Introduction

Lymphadenopathy is the term to describe the conditions in which lymph nodes become abnormal in size, consistency, and number. It is one of the most common clinical presentations of patients, attending the outdoor clinics in most of the hospitals.

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The aetiology varies from an inflammatory process to a malignant condition. [1]In our country, lymph nodes malignancies are predominantly metastatic in nature with an incidence ranging from 65.7% to 80.4% and lymphomas range from 2- 15.3% among lymph nodes aspirated from all sites.[2] In 1904, the Greig and Gray and Martin and Ellis had first used FNAC as diagnostic tool. They developed its use in the diagnosis of malignancy. [3] Fine needle aspiration cytology is a simple, cheap and accurate first line investigation in diagnosis of lymphadenopathy. Enlarged lymph nodes are easily accessible for FNAC and therefore, these procedure is of immense importance in the diagnosis of secondary or primary malignancies Because of its simplicity, cheapness, early availability of results and

with minimal trauma and complication, this aspiration cytology is now studied as a valuable diagnostic aid. [4, 5]FNAC can avoid the need for excisional biopsy in most of the cases and allow rapid onset of therapy. [6] This method also helps to sorting the selective cases like malignancies which need further work up for characterization of malignancies or work up to identify the primary malignancy site. It also plays an important role to confirm or exclude metastasis in a lymph node in a known case of malignancy, thereby avoiding unnecessary surgery. [2] This technique is important in advanced stage patients where exposure to anaesthesia or excision biopsy cannot be performed due to health constraints. [7] FNAC may be the first investigation to clinch a diagnosis of an occult malignancy in many other situations. [2] If FNAC is accompanied by radiological guidance like ultrasonography and computed tomography scan, the diagnostic yield of FNAC can be improved. [8] FNAC is a popular method used in lymph nodes evaluation for the diagnosis of lymphomas. In concurrence with Immunophenotyping and molecular studies, this method has gained acceptance in many centres as an initial diagnostic tool. [9] The aim of the present study is find out the frequency of various types of lymph node malignancy as well as to find out incidence of various pathological subtypes of metastatic lymphadenopathy and to test the utility of FNAC in diagnosis of malignant Lymphadenopathy.

Materials and Methods

Study setting: The present study is Retrospective study of malignant lymph node aspirates in palpable lymphadenopathy. The study was conducted as an outdoor procedure over a period of 1 & ½ years from Sept 2017 to Feb 2019 at American International institute of Medical Sciences (AIIMS), GBH General & cancer hospital, Udaipur, Rajasthan. The study was approved by the ethics committee of the institution.

Study period: A period of 1 & ½ years from Sept 2017 to Feb 2019.

Inclusion criteria: All age group (1-90 years) of patients of malignant enlarged lymph nodes having details like age & gender, site of lymph nodes, cytological findings & other investigations included in this study.

Exclusion criteria: Patients with inadequate aspirates and incomplete demographic details were excluded from this study.

Sample size: The study material was taken from 122 malignant lymph node aspirates out of a total of 200

superficial palpable lymph nodes aspirated during that period in our hospital.

Sampling method: A detailed history has been taken from all patients related to palpable lymphadenopathy and relevant questions were asked related to the etiological cause like present, past and family history of cancer and history of consumption of tobacco related products, history of any radiotherapy or chemotherapy taken or not. Clinical examination like site, size, consistency of enlarged lymph nodes and other investigations like radiological and laboratory investigations were also noted. Then patients were explained about the procedure and its indication. Their written consent was taken.

The area of palpable enlarged lymph node was cleaned with spirit & then it was fixed with the thumb and index finger of one hand. With all aseptic precautions, 22-23G needle with 10ml syringe was inserted into the swelling and a negative pressure was applied. The needle was moved briskly in different directions in the swelling till sufficient material was visualized into the hub of needle. The negative pressure of the syringe was released and the needle was taken out. The aspirated material was blown out on clean glass slides. At least 4 good aspirate smears were prepared. Two slides were immediately fixed in 90% alcohol and stained with Haematoxylin and Eosin (H and E) stain and Papanicolaou Stain (PAP stain) each. Another Two slides were air dried and stained with May Grunwald Giemsa (MGG) stain. All stained slides were mounted by DPX and examined under the light microscope. Fine Needle Aspiration Diagnosis was based on cytomorphology. All cytological smears were evaluated for adequacy, cellularity, type of cells, arrangement of cells and nuclear as well as cytoplasmic features. Background was evaluated in all smears for any specific findings like necrosis or presence of mucin or presence of keratin etc. And FNAC diagnosis was correlated with details of relevant clinical findings and other investigations like Ultrasonography (USG) or Computed Tomography (CT scan) and previous any excision biopsy report. Cytological findings were recorded and patients were advised follow up or biopsy and surgical intervention depending upon the pathology.

Statistical analysis: Data was recorded in Microsoft Excel 2007 sheet and analyzed according to age & gender, different groups of lymph nodes, Cytological types of malignancy in lymph nodes and primary sites of origin in metastatic malignant lymph node aspirates. Percentages were calculated for estimating frequency of all these conditions.

Results

A total of 200 lymph nodes were aspirated during the study period at American International institute of Medical Sciences (AIIMS), GBH General & cancer hospital, Udaipur. Out of total 200 lymph nodes aspirates, 122 cases (61%) were identified as malignant lymph node aspirates and they were taken as our study material. In our study, out of 122 malignant lymph node aspirates, Males were 79(64.8%) and females were 43(35.2%). Male: Female ratio was 1.8:1. Thus males constituted maximum number cases of malignant lymphadenopathy. The age of patients in malignant lymph node aspirates ranged from 15 years to 90 years. Mean age was 55.38 years. Maximum no. of cases were seen in age group of 51 – 60 years accounted 41(33.6%) followed by 41-50 years 30(24.6%) and 61-70 years 26(21.3%) [Table-1]. In present study, Cervical lymph nodes 73 (59.8%) were the highest group of enlarged lymph nodes identified among malignant lymph node aspirates, followed by axillary 27(22.1%), supraclavicular 17(13.9%) and inguinal 5(4.1%) cases respectively. In cervical lymphadenopathy, Male were common affected 58(73.4%) than female 15 (34.9%). In axillary group of enlarged lymph nodes, female were common affected in 16(37.2%) and male in 11(13.9%) [Table-2]. Most common lymph node malignancy noted was metastatic malignancy 107(87.7%) cases while primary lymph node malignancy was 15(12.2%) cases [Table-3]. Among metastatic malignancies, squamous cell carcinoma 58 (47.5%) cases was commonest malignancy identified followed by duct cell carcinoma 18(14.8%) cases and adenocarcinoma 13(10.7%) [Fig-1, 2, 3]. Rest of the metastatic lymph node malignancy were poorly differentiated carcinoma 8(6.6%) cases, Malignant melanoma 4 (3.3%) cases, papillary carcinoma 3(2.5%) cases [Fig -4], small cell carcinoma 2(1.6%) cases and Chondrosarcoma in 1(0.8%) case respectively. Cervical lymph nodes groups were commonly involved by squamous cell carcinoma in 53 cases, followed by Axillary 03 cases and Supraclavicular 02 cases. In duct cell carcinoma, axillary lymph nodes group was most involved 16 cases followed by supraclavicular 02 cases. There were 15 (12.2%) cases of primary lymphomas were noted on FNAC [Table-4]. Non-Hodgkin's lymphoma was commonest primary lymph node malignancy 12(9.8%) cases followed by Hodgkin's lymphoma 3(2.5%) cases [Fig 5]. In this study, primary sites of malignancy identified in 95 (88.7%) cases while primary site was unknown in remaining 12 (11.2%) cases [Table-5]. Out of 12 unknown primaries, 06 were metastatic Squamous cell

carcinoma, 01 melanoma and 05 poorly differentiated carcinoma. In our study, Oral cavity was the most common primary site noted in 39 (36.4%) out of 107 metastatic malignant cases. In oral cavity malignancies, all 39 cases were Squamous cell carcinoma noted. Breast was the second commonest primary malignant site of tumour comprising 18(16.8%) cases out of 107 metastatic malignancies. All 18 cases of breast were noted duct cell carcinoma. Lung was the third common primary site noted in 16 cases (14.9%). These 16 cases of lung malignancies were classified as adenocarcinoma (08 cases), Squamous cell carcinoma (05 cases) and small cell carcinoma (02 cases) and poorly differentiated carcinoma (01 case). Other primary malignant sites were larynx 05(4.6%), oesophagus 05(4.6%), Ovary 03 (2.8%), Thyroid 03(2.8%), Prostate 01(0.9%), salivary gland 01(0.9%), Bone (scapula) 01(0.9%) and 03(2.8%) cases were from skin of toe, foot and left leg each identified out of 107 metastatic malignancy [Table-5]. Out of 05 laryngeal malignancies, all cases were identified as Squamous cell carcinoma. Out of 05 oesophageal metastatic malignancies, 03 were identified as Squamous cell carcinoma and 02 were noted as adenocarcinoma. Out of 03 ovarian malignancies, 02 were adenocarcinoma and 01 case was of poorly differentiated carcinoma. All 03 cases of thyroid metastatic malignancies were identified as papillary carcinoma thyroid. And all 03 cases of malignant melanoma arised from primary sites of skin of toe, foot and left leg each. 01 case of Prostate primary site was identified as Adenocarcinoma. 01 case of salivary gland primary site was identified as poorly differentiated carcinoma and 01 case of bone (scapula) primary site was identified as chondrosarcoma [Table-5].

Discussion

Lymphadenopathy is the most common clinical presentations of patients with its aetiology varies from an inflammatory process to a malignant condition. [1] FNAC is a reliable diagnostic tool for lymphadenopathy who are suspected for malignancy because, it is simple procedure, has less complications and can be repeated easily. [10] In our study, out of 122 malignant lymph node aspirates, Males 79(64.8%) cases and females 43(35.2%) cases. Male: Female ratio was 1.8:1. Maximum no. of cases was seen in 51 – 60 years age group (33.6%) followed by 41-50 years (24.6%) and 61-70 years (21.3%) respectively. This study was comparable to study of Anne R. Wilkinson et al. [2] who noted males (30 cases, 60%) being more involved than females (20 cases, 40%) and M:F ratio 1.5:1. The study was also correlated with the study of

Danish Rafiq et al. [10] who reported Males 436 (61.4%) cases and females 274 cases (38.59%) out of 710 cases. M:F ratio was 1.59:1 and Maximum number of cases was seen in the age group 51-60 years (29.01%) followed by 61-70 years (28.30%). Another study of Manupriya Sharma et al.[11] noted 145 males (77%) and 43 females (23%) and M:F ratio was 3.5:1. The studies of Pramod Chandra Pathy et al.[12] and Ahmad et al.[13] who were observed that peak incidence of malignant lymphadenopathy was in the 5th decade which is similar with our study. Table-6 shows comparison of our study with other studies on the basis of distribution of groups of lymph node. It is noted that maximum aspirates were from cervical lymph nodes followed by axillary, supraclavicular and inguinal. In present study, metastatic malignancy was commonest lymph node malignancy 87.7% as compared to primary lymphoma 12.2%. This is similar to studies of Alam K et al.[14], Sravani P et al.[15] and Martins MR et al.[16] who were noted metastatic malignancy 80.4%, 89.47%, 79.4% respectively and Lymphomas 15.3%, 10.53%, 14.2% respectively. In this study, Squamous cell carcinoma was higher in number (47.5%) in metastatic malignancy followed by duct cell carcinoma (14.8%) and adenocarcinoma (10.7%). Rest of the metastatic malignancy were poorly differentiated carcinoma (6.6%), malignant melanoma (3.3%), papillary carcinoma (2.5%), and Small cell carcinoma (1.6%). Non Hodgkin's lymphoma (9.8%) was commonest in primary lymphoma than Hodgkin's lymphoma (2.5%) which is comparable to other studies shown in table-7. [2, 14, 15, 17] Out of 58 metastatic Squamous cell carcinoma, 10 cases shown cystic degenerative changes in our study. In these cases cytomorphological features shown abundant neutrophils, histiocytes, necrotic debris and stray individually scattered keratinized cells. Careful search was required for malignant cells for making diagnosis in these cases. In present study, cervical group is the most common group to be involved and the primary was most often arisen from oral cavity commonly from buccal mucosa with squamous cell carcinoma being the most common cytological type in this region. This may be due to usage of multiple tobacco products in this region. This is similar to other studies of Anne R. Wilkinson et al. [2] and Shamim sheikh. [17] Rates for oral cavity/pharynx, esophagus, and male larynx are highest in India, probably due to the use of multiple tobacco products. [18] Breast was the second common primary site 18(16.8%) which was similar to study of Alam K et al. [14] and Shamim sheikh. [17] 16 out of 18 cases of metastatic duct cell carcinoma were mainly identified in axillary lymph

nodes and 02 seen in supraclavicular lymph node. Our study also noted 14 cases had palpable breast lumps diagnosed as duct cell carcinoma breast on FNAC and 04 cases were of operated MRM cases. Diagnosis of metastatic deposit by FNAC can help the surgeon to assess the staging of tumour and helps for planning surgery. In this study, the most common primary site of metastatic adenocarcinoma was lung in 8 cases out of 13. Which was correlated with study of Ghartimagar et al. [19] Out of 8 cases of metastatic poorly differentiated carcinoma, 05 cases had unknown primary. FNAC has become first investigation to clinch a diagnosis of this unknown malignancy. [2] In 04 cases of melanoma deposits, Presence of fine granular melanin pigment in cytoplasm of tumour cells become a helpful identifying point for melanoma. In our study, cytological feature of metastatic deposit of papillary carcinoma thyroid showed papillary configuration of cells with and without fibrovascular cores with mild pleomorphic cells, ground glass nucleus and intranuclear inclusions with colloid in background [Image-4]. This point helps in giving diagnosis. So, FNAC not only confirms the presence of metastatic disease but also gives clues regarding the nature and origin of primary tumour. [7] 02 (1.6%) cases of metastatic small cell carcinoma were arisen from primary site of lung and involved axillary lymph nodes which were correlated with study of Sumit Mitra et al. [20] In our study, primary sites of malignancy were identified in 88.7% of metastasis with the help of cytological features of FNAC and clinical data. This was correlated with studies of Pramod Chandra Pathy et al. [12] and Alam K et al. [14] who identified primary site 85.59% and 90% respectively. The primary site was unknown in 11.2% cases and the malignancy was first diagnosed on FNAC which is similar to study of Pramod Chandra Pathy et al (14%). [12] Thereby, FNAC would be the single indicator for searching the primary tumour, especially in cases of occult carcinoma and this method can be used for patient's follow up where there is known primary tumour. [15] In our study 12(9.8%) Non Hodgkin's lymphoma and 3(2.5%) Hodgkin's lymphoma were identified. Cytologically, our study found monotonous population of atypical malignant lymphoid cells in making diagnosis of NHL [Fig-5] and for Hodgkin's lymphoma, characteristic Reed Sternberg cells found in a background of pleomorphic mature lymphocytes, eosinophils and plasma cells. Our study advised all these cases of lymphoma for excision biopsy for confirmation and immunohistochemistry for further characterization of lymphoma. The treatment protocols may vary in different subtypes of lymphoma, so it is

important to subtype the lymphomas based on WHO classification. [21, 22] So, importance of FNAC in

lymphomas is to triage such cases which needs further work up.

Table 1: Age and Sex wise Distribution of cases

Age Groups	Male (%)	Female (%)	Total (%)
1-10	0	0	0
11-20	1(1.3%)	0	1(0.8%)
21-30	0	2(4.7%)	2(1.6%)
31-40	5(6.3%)	4(9.3%)	9(7.4%)
41-50	20(25.3%)	10(23.3%)	30(24.6%)
51-60	27(34.2%)	14(32.6%)	41(33.6%)
61-70	15(19.0%)	11(25.6%)	26(21.3%)
71-80	9(11.4%)	1(2.3%)	10(8.2%)
81-90	2(2.5%)	1(2.3%)	3(2.5%)
	79(64.8%)	43(35.2%)	122

Table 2: Distribution of various groups of lymph nodes

Gender	Various groups of lymph nodes			
	Cervical	Axillary	Supraclavicular	Inguinal
Male	58	11	8	2
Female	15	16	9	3
Total(122)	73(59.8%)	27(22.1%)	17(13.9%)	5(4.1%)

Table 3: Distribution of types of lymph node malignancy

Malignancy	Total (%)
Metastatic malignancy	107(87.7%)
Primary lymph node malignancy	15(12.2%)

Table 4: Distribution of cytological diagnosis of malignant lymphadenopathy according to various group of lymph node.

Sr. No	Malignancy	Total (%)	Lymph node groups			
			Cervical	Supraclavicular	Axillary	Inguinal
Metastatic malignancy						
1	Squamous cell carcinoma	58(47.5%)	53	2	3	0
2	Duct cell carcinoma	18(14.8%)	0	2	16	0
3	Adenocarcinoma	13(10.7%)	7	1	3	2
4	Malignant melanoma	4(3.3%)	0	2	0	2
5	Chondrosarcoma	1(0.8%)	0	0	1	0
6	Small cell carcinoma	2(1.6%)	0	0	2	0
7	Poorly differentiated carcinoma	8(6.6%)	5	1	1	1
8	papillary carcinoma	3(2.5%)	3	0	0	0
Primary lymph node malignancy						
1	NonHodgkins lymphoma	12(9.8%)	3	8	1	0
2	Hodgkins lymphoma	3(2.5%)	2	1	0	0

Table -5: Distribution of primary sites in metastatic malignant lymph node aspirates.

Sr. No	Malignancy	Lymphnode groups	Primary sites
1	Squamous cell carcinoma (58)	Cervical (53)	Oral cavity-39(Buccal mucosa-19,Tongue-13, Lower lip-4, Floor of mouth-3), Larynx- 5, Oesophagus- 3, Unknown-6
		Supraclavicular (2)	Lung-2
		Axillary (3)	Lung-3
2	Duct cell carcinoma (18)	Supraclavicular (2)	Breast- 02
		Axillary (16)	Breast- 16
3	Adenocarcinoma (13)	Cervical (7)	Lung-05, Oesophagus-2
		Supraclavicular (1)	Ovary-1
		Axillary (3)	Lung-03
		Inguinal (2)	Ovary-1, Prostate-1
4	Malignant melanoma (4)	Supraclavicular (2)	Skin of left leg-1, Unkown-1
		Inguinal (2)	Skin of Toe-1, skin of Foot-1
5	Chondrosarcoma (1)	Axillary (1)	Bone(Scapula)-1
6	Small cell carcinoma (2)	Axillary (2)	Lung-2
7	Poorly differentiated carcinoma (8)	Cervical (5)	Salivary gland-1,Unknown-4
		Supraclavicular (1)	Unknown-1
		Axillary (1)	Lung-1
		Inguinal (1)	Ovary-1
8	Papillary carcinoma (3)	Cervical (3)	Thyroid-3

Table 6: Comparison of various group of lymph node distribution between our study and other studies.

Studies	Cervical	Axillary	Supraclavicular	Inguinal
Our study	59.8%	22.1%	13.9%	4.1%
Anne R. Wilkinson et al. ^[2]	62%	22%	6%	10%
Alam K et al. ^[14]	74.20%	9.50%	9.50%	4.97%
Sravani P et al. ^[15]	61.84 %	14.47%	19.74%	2.63%

Table-7 Comparison of our study with other studies on the basis of lymph node malignancy

Types of malignancy	Our Study	Study of Anne R. Wilkinson et al. ^[2]	Study of Sravani P et al. ^[15]	Study of Alam K et al. ^[14]	Study of Shamim sheikh ^[17]
Metastatic Squamous cell carcinoma	47.5%	46%	53.95%	67.87%	43.0%
Metastatic Duct cell carcinoma	14.8%	20%	15.79%	11.31%	20.8%
Metastatic Adenocarcinoma	10.7%	4%	10.53%	9.04%	13.8%
Metastatic Malignant melanoma	3.3%	4%	2.63%	0.90%	-
Metastatic Small cell carcinoma	1.6%	-	2.63%	1.80%	4.1%
Metastatic Poorly differentiated carcinoma	6.6%	-	-	4.07%	-
Metastatic Papillary carcinoma	2.5%	8%	3.95%	-	-
Non Hodgkins lymphoma	9.8%	6%	2.63%	-	11.1%
Hodgkins lymphoma	2.5%	4%	7.89%	-	4.1%

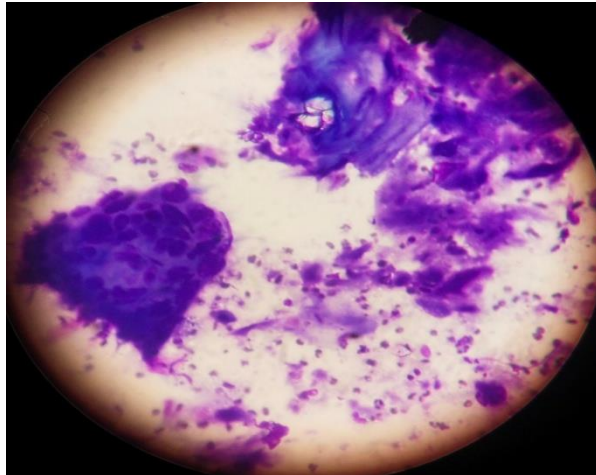


Fig 1:Metastatic squamous cell carcinoma [Giemsa stain (10x)]

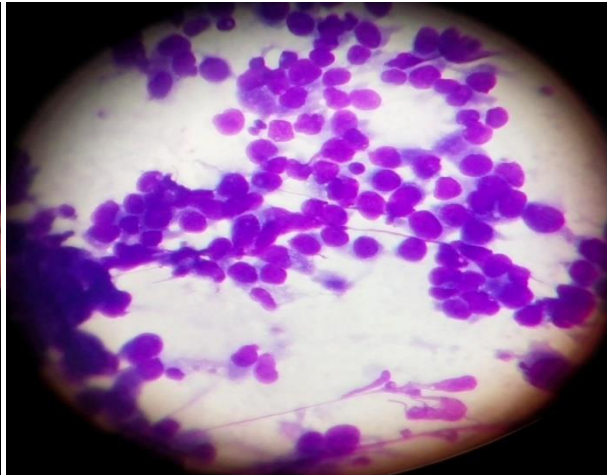


Fig 2: Metastatic duct cell carcinoma of breast [Giemsa stain (40x)]

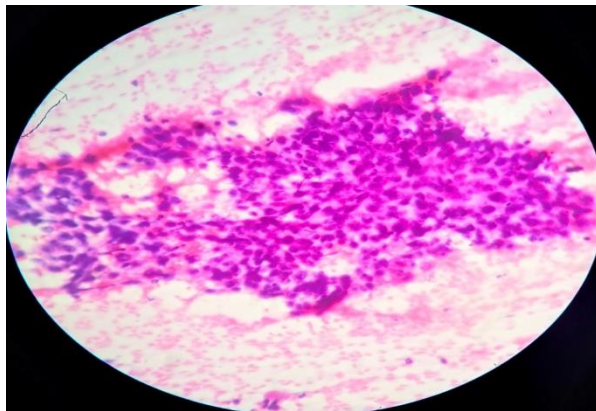


Fig 3 :Metastatic adenocarcinoma [H&E stain (40x)]

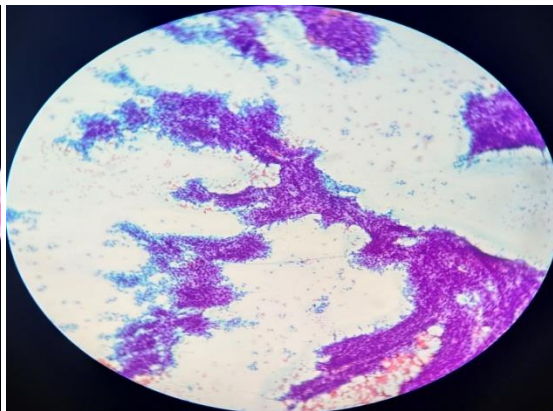


Fig 4:Metastatic papillary carcinoma[Pap stain (10x)]

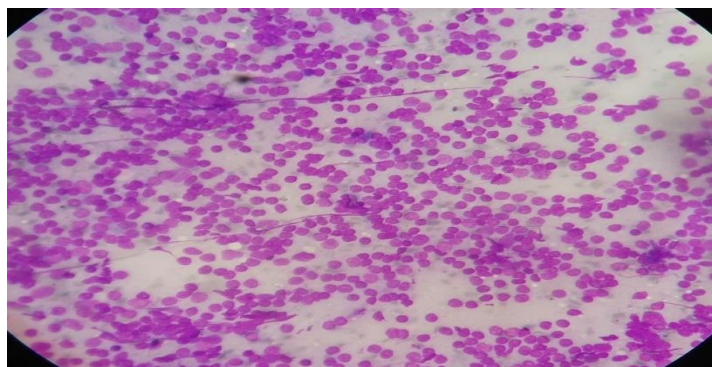


Fig 5:Non Hodgkin lymphoma [Giemsa stain (40x)]

Conclusion

From our present study, we have found wide range of lymph node malignancy and their pathological subtypes which can be diagnosed by fine needle aspiration cytology. Cervical lymph node groups was more common in lymph node malignancy in which metastatic malignancy was common than primary lymphoma. Metastatic squamous cell carcinoma and metastatic duct cell carcinoma of breast were high in number at this Center. It may be due to higher consumption of tobacco related products and unawareness or lack of knowledge related to breast cancer in female at this region relatively. Our study also concluded that FNAC is simple, reliable, cost-effective and rapid technique in making diagnosis of lymph node malignancies, especially to confirm or to exclude the metastatic malignancy. With the help of clinical history, relevant investigations and cytological features, this method become helpful for defining tumor type as well as identifying primary site of metastasis. This method can be used for patient's follow up where the primary tumour is known thereby it helps the surgeon to assess the staging of tumour and for planning surgery. We recommended FNAC can be used as reliable diagnostic specific tool for early detection of primary malignancy and metastatic lesions in our developing country where financial source and diagnostic modality are limited which become helpful to patients.

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