

## RESEARCH ARTICLE

# Metastatic Lymphadenopathy in Kashmir Valley: A Clinicopathological Study

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### Abstract

**Background:** Lymphadenopathy is a common presentation in both benign and malignant diseases which need to be diagnosed without delay. Fine needle aspiration cytology (FNAC) helps us diagnose a disease and follow its course, including the response to therapy. **Aim:** This study aimed to analyze the clinicopathological features of metastatic lymphadenopathy and the diagnostic utility of FNAC in our setting. **Materials and Methods:** This two-year prospective study included all the patients with metastatic lymphadenopathy, diagnosed with FNAC. **Results:** A total of 412 cases (male:female ratio, 1.3:1; age range, 3 to 90 years) were studied. Supraclavicular lymph nodes were involved most commonly (50.5%). The commonest metastatic tumor was squamous cell carcinoma in general (30.1%) and in males (37.6%), and infiltrating ductal carcinoma (25.3%) in females. Lung, with 64 (15.5%) cases followed by esophagus, 60 (14.6%) cases; breast, 49 (11.9%) cases; skin, 32 (7.8%) cases; and stomach, 25 (6.1%) cases were the most common primary sites of malignancy. In 69 patients, excision biopsy was performed. Histopathological findings correlated well with that of cytology in all these cases. **Conclusions:** FNAC is an important tool in the diagnostic work up of metastatic lymphadenopathy, which in the hands of an experienced and skilful cytopathologist can avoid the need for excision biopsy.

**Keywords:** Metastatic - lymphadenopathy - lymph nodes - FNAC - Kashmir valley

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### Introduction

Lymphadenopathy (abnormality in size, consistency or number of lymph nodes) occurs in response to foreign antigens or by invasion or propagation of either inflammatory or neoplastic cells into the node, depending upon the geographical conditions and socioeconomical set up (Darnal et al., 2005; Bhuyan et al., 2008; Ahmad et al., 2009). In developing countries, infective lymphadenopathy is quite common, mostly due to high prevalence of tuberculosis. However, still a large percentage of lymphadenopathies in adults turn out to be malignant (Ghartimagar et al., 2011). It is, therefore, necessary to evaluate a patient with lymphadenopathy of >3 weeks duration without any delay. The use of fine needle aspiration cytology (FNAC) for the diagnosis of metastatic malignancies in the lymph nodes is a well established method (Steel et al., 1995). FNAC is a very cost effective, simple procedure, free of complications, well tolerated by patients, done on an outpatient basis and repeatable (Bagwan et al., 2007). The purpose of this study was to analyze the clinical profile of lymph node metastasis in this part of North India (Kashmir valley) and determine the diagnostic accuracy of FNAC.

### Materials and Methods

This prospective study was conducted at our tertiary care institution over a period of 2 years (July 2011 to June 2013). All the patients of metastatic lymphadenopathy diagnosed on FNAC were studied. In all these patients, after talking consent, FNAC was performed using a 22-G needle and 20 ml disposable syringe, and the slides were stained with May-Grunwald Giemsa and Papanicolaou stains. All the relevant clinical details of the patients were noted. The slides were reviewed and their cytomorphological features were studied. Patients of haematological malignancy were excluded from the study.

### Results

Out of a total of 5129 cases of FNAC performed during this 2 year study period, 1314 FNACs (25.6%) were done from lymph nodes and among them, 412 nodal FNACs (31.4%) reported as 'metastatic' were studied. There were 234 males (56.8%) and 178 females (43.2%) with a male to female ratio of 1.3:1. The age of the patients ranged from 3 years to 90 years with a mean age of 52.5 years.

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The most common site of involvement was found to be supraclavicular lymph nodes, 208 (50.5%) cases followed by cervical region, 82 (19.9%) cases. Metastasis was also diagnosed in 11 (2.7%) cases of retroperitoneal lymphadenopathy in which image (CT or USG) guided aspiration was performed (Table 1).

The size of the lymph nodes ranged from 1-1.5 cm in 62 (15%) cases and >1.5 cm in the remaining 350 (85%) cases. Overall, squamous cell carcinoma (SCC), 124 (30.1%) cases followed by adenocarcinoma, 88 (21.3%) cases and poorly differentiated carcinoma (PDC), 72 (17.5%) cases were the most common metastatic tumors. In males, SCC, 88 (37.6%) cases, followed by PDC, 44 (18.8%) cases, and adenocarcinoma, 47 (20.1%) cases, were the most common metastatic tumors. However in females, infiltrating ductal carcinoma (IDC), 45 (25.3%) cases, was the most common metastatic tumor followed by adenocarcinoma, 41 (23%) cases and SCC, 40 (22.5%) cases (Table 2).

In the cervical lymph nodes, SCC was the most common metastatic tumor, 31 (37.8%) cases and these nodes were found to be the most common site for metastatic papillary carcinoma thyroid (PCT), 11(91.7%) cases. A wide variety of tumors were found to metastize supraclavicular lymph nodes. Besides being the most common site for the metastasis of SCC, 61 (47.3%) cases; adenocarcinoma, 58 (65.2%) cases; PDC, 39 (60%) cases; small cell carcinoma lung (SmCCL), 18 (75%) cases; germ

**Table 1. Site Distribution of Cases**

Lymph Nodes	Males	Females	Total Cases	%
Supraclavicular	125	83	208	50.5
Cervical	47	35	82	19.9
Axillary	27	35	62	15
Inguinal	21	13	34	8.2
Retroperitoneal	6	5	11	2.7
Submandibular	5	3	8	1.9
Postauricular	2	2	4	0.9
Preauricular	1	1	2	0.5
Submental	0	1	1	0.2
<b>Total</b>	<b>234</b>	<b>178</b>	<b>412</b>	<b>100</b>

**Table 2. Distribution of Different Metastatic Tumors in Males and Females**

	Males	Females	Total
Squamous cell Ca	88	41	129
AdenoCa	47	42	89
Poorly differentiated Ca	44	21	65
Infiltrating ductal Ca	4	45	49
Small cell lung Ca	21	3	24
Papillary thyroid Ca	3	9	12
Malignant melanoma	6	5	11
Sarcoma	5	5	10
Germ cell tumor	6	3	9
Small round cell tumor	5	2	7
Langerhans' cell histiocytosis	2	0	2
Trasitional cell Ca	2	0	2
Adenoid cystic Ca	1	1	2
Acinic cell Ca	0	1	1
<b>Total</b>	<b>234</b>	<b>178</b>	<b>412</b>

\*Ca=carcinoma

cell tumors (GCT), 5 (55.6%) cases; and transitional cell carcinoma (TCC), 2 (100%) cases, supraclavicular area was the second most preferred site for metastatic IDC following axillary lymph nodes, 25 (51%) cases. Inguinal lymph nodes were the most preferred site for the metastasis of malignant melanoma, 9 (27.3%) cases (Table 3).

Common primary sites of malignancy identified by FNAC and clinical data were: lung, 64 (15.5%) cases; esophagus, 60 (14.6%) cases; breast, 49 (11.9%) cases; skin, 32 (7.8%) cases; and stomach, 25 (6.1%) cases. In 81 patients (19.7%), the primary site was unknown (Table 4).

In 69 patients, excision biopsy was performed in addition to FNAC. In all these cases, histopathological

**Table 3. Distribution of Metastatic Tumors in Different Lymph Node Areas**

	CX	SC	AX	RP	Sub- Inguinal	Post- manar- dibul	Pre- auri- cular	Sub- auri- mental
Squamous cell Ca	31	61	15	15	2	2	3	-
AdenoCa	15	58	6	1	6	1	-	2
Poorly differentiated Ca	15	39	7	1	1	2	-	-
Papillary Ca thyroid	11	-	1	-	-	-	-	-
Infiltrating ductal Ca	2	20	25	2	-	-	-	-
Small round cell tumor	2	2	1	1	-	1	-	-
Small cell Ca lung	5	18	1	-	-	-	-	-
Germ cell tumor	1	5	-	1	2	-	-	-
Langerhans' cell histiocytosis	-	1	-	-	-	-	1	-
Sarcoma	-	1	5	4	-	-	-	-
Malignant melanoma	-	1	1	9	-	-	-	-
Transitional cell Ca	-	2	-	-	-	-	-	-
Adenoid cystic Ca	-	-	-	-	-	1	-	1
Acinic cell Ca	-	-	-	-	-	1	-	-
<b>Total</b>	<b>82</b>	<b>208</b>	<b>62</b>	<b>34</b>	<b>11</b>	<b>8</b>	<b>4</b>	<b>2</b>

Ca=Carcinoma; CX=cervical; SC=supraclavicular; AX=axillary; RP=retroperitoneal

**Table 4. Distribution of Primary Site Metastatic to Lymph Nodes**

	CX	SC	AX	RP	Sub- Inguinal	Post- manar- dibul	Pre- auri- cular	Sub- auri- mental
Lung	16	42	5	1	-	-	-	-
Esophagus	15	40	2	-	-	1	1	1
Breast	2	20	25	2	-	-	-	-
Skin	1	1	8	21	-	1	-	-
Stomach	2	22	-	-	-	1	-	-
Ovary	2	10	-	-	1	-	-	-
Thyroid	11	-	1	-	-	-	-	-
Bone/soft tissue	-	1	5	4	-	-	-	-
Gallbladder	-	10	-	-	-	-	-	-
Pancreas	-	3	-	-	5	-	-	-
Colorectum	1	4	-	1	1	-	-	-
Upper respiratory tract	6	1	-	-	-	-	-	-
GE junction	-	7	-	-	-	-	-	-
Testis	1	3	-	1	1	-	-	-
Small round cell tumor	2	2	1	1	-	-	-	-
Salivary gland	1	-	-	-	-	2	-	1
Endometrium	-	2	1	-	-	-	-	-
Oral cavity	-	-	-	-	-	2	-	-
LCH	-	1	-	-	-	-	1	-
Urinary bladder	-	2	-	-	-	-	-	-
Prostate	-	1	-	-	-	-	-	-
Cervix	-	-	1	-	-	-	-	-
Unknown	22	36	13	3	3	1	2	1
<b>Total</b>	<b>82</b>	<b>208</b>	<b>62</b>	<b>34</b>	<b>11</b>	<b>8</b>	<b>4</b>	<b>2</b>

LC=Langerhans cell histiocytosis; CX=cervical; SC=supraclavicular; AX=axillary; RP=retroperitoneal

diagnosis correlated with cytological diagnosis

## Discussion

Lymphadenopathy in an adult may be the first presenting clinical sign of a malignancy. FNAC not only confirms the presence of metastatic disease but also gives clues regarding the nature and origin of primary tumor (Bagwan et al., 2007; Ghartimagar et al., 2011). The diagnosis given on the cytological material is often the only diagnosis accepted and sometimes there is no further correlation with histopathology especially in cases of advanced malignancies. The value of FNAC besides making a diagnosis also lies in early direction of appropriate investigations (Khajuria et al., 2006). The frequency of metastatic lymphadenopathy was observed to be low, 3.8% and 8.7% in some studies (Khajuria et al., 2006; Fatima et al., 2011) whereas, a higher incidence of 19.7% and 24.7% was reported by other studies (Hafez et al., 2011, Ageep et al., 2012) respectively. However, in the current study, metastatic lymphadenopathy contributed to 31.3% of lymphadenopathies.

The incidence of malignancy rose steadily through the age groups to greater than 95% in patients above 60 years of age (Mitra et al., 2011). The youngest patient in our study was a 3 years old child and the oldest one was of 90 years. Similar, wide age range was also observed in other studies (Bagwan et al., 2007; Ghartimagar et al., 2011; Wilkinson et al., 2012). Males outnumbered the females in our study with a male to female ratio of 1.3:1, which correlated well with other studies (Steel et al., 1995; Alam et al., 2010). In contrast, another study (Ghartimagar et al., 2011) reported the incidence of metastasis to be more common in females than males with a male to female ratio of 1:1.25.

Supraclavicular lymph nodes were found to be involved in majority (50.5%) of our cases followed by cervical (19.9%) and axillary lymph nodes (15%). However, in other studies, cervical lymph nodes were the most common site of involvement (Alam et al., 2010; Ghartimagar et al., 2011; Wilkinson et al., 2012). The size of the malignant lymph nodes was >1.5 cm in most (85%) of our patients which is similar to that observed by another study (Wilkinson et al., 2012).

Most of the studies have reported SCC as the most common metastatic tumor (Hirachand et al., 2009; Fatima et al., 2011). In the present study, SCC was the most common metastatic tumor followed by adenocarcinoma and poorly differentiated carcinoma. Similar findings were reported in other studies (Ahmad et al., 2005; Khajuria et al., 2006; Hafez et al., 2011). In contrast, other study (Ghartimagar et al., 2011) found adenocarcinoma to be the most common tumor to metastasize lymph nodes followed by SCC.

In the current study, with the help of FNAC and other clinical data, primary site could be identified in 331 (80.3%) cases, while primary site was unknown in the remaining 81 (19.7%) cases. In a study, (Alam et al., 2010) primary site was identified in about 90% of cases, while as in another study, (Facundo et al., 2003) primary site was identified in 59% of cases. However, a higher

efficacy of 95% was achieved when immunocytochemistry was combined.

In our study, esophagus, 49 (38%) cases, followed by lung, 28 (21.7%) cases, was the most common primary site of malignancy in metastatic SCC. Other studies from India reported head and neck (particularly, mouth, larynx and pharynx) as the most common primary site in metastatic SCC (Bagwan et al., 2007; Alam et al., 2010; Ghartimagar et al., 2011; Wilkinson et al., 2012). The most common primary site of metastatic adenocarcinoma in our study was stomach, 17 (19.1%) cases followed by ovary 10 (11.2%) cases. Other study (Ghartimagar et al., 2011) found lung, stomach, colon and rectum as the most common primary sites for metastatic adenocarcinoma. In our study, primary sites of malignancy could not be identified in 21 (16.3%) cases of metastatic SCC and 26 (29.3%) cases of metastatic adenocarcinoma. Similar findings were observed in another study, (Alam et al., 2010) where primary site was unknown in 18.7% cases of metastatic SCC and 10% cases of metastatic adenocarcinoma.

In our study, lung (24, 20.2% cases), esophagus, (40, 19.2% cases), stomach, (22, 10.6% cases) and breast (20, 9.6% cases) were the most common primary sites of malignancy to metastasize to supraclavicular lymph nodes. In a study of supraclavicular lymph nodes, (Mitra et al., 2011) similar primary sites were found.

The sensitivity of FNAC for metastatic lesions to lymph nodes has varied from 97.9% to 100% whereas the specificity has been found to be 100% (Hirachand et al., 2009; Alam et al., 2010; Wilkinson et al., 2012). In our study also, FNAC was found to have a high sensitivity and specificity of 100% in the diagnosis of metastatic lymphadenopathy.

In conclusion, lymph node metastasis is one of the major adverse prognostic factors in all malignant tumors that influence not only the treatment plan but also the outcome of cancer patients. In our set up, supraclavicular nodes is the most common site of metastasis; squamous cell carcinoma is the most common type of metastatic tumor in general and in males, while in females, infiltrating ductal carcinoma is the most common type; and lung, esophagus, breast and stomach are the most common primary sites that metastasize to lymph nodes. Diagnosis of lymph node metastasis by FNAC helps in planning the initial management of newly diagnosed malignant cases, following the patients with known malignancy and assessing the response to therapy. Thus FNAC is an important tool in the diagnostic work up of metastatic lymphadenopathy, which in the hands of an experienced and skill full cytopathologist, can avoid the need for excision biopsy.

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