Original Article

Metastatic Lymphadenopathy by Fine-needle Aspiration Cytology

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Abstract

Introduction: Fine-needle aspiration cytology (FNAC) plays an undeniably important role in the diagnostic approach to lymphadenopathy. Our aim was to study the distribution and cytomorphology of metastatic lymphadenopathy and understand the approach to diagnosis.

Materials and Methods: This was retrospective study including all cases of lymph nodes involved by metastatic malignancy which was referred for FNAC over a period of 1-year.

Results: During the study period, 104 (4.8%), out of total 2140, lymph nodes aspirated showed evidence of metastatic malignancy. The age of the patients ranged from 19 to 90 years with the mean age being 55.8%. Male to female ratio was 1.8:1. The submandibular lymph nodes were the most commonly involved, 35 cases (33.6%) and closely followed by anterior cervical nodes 33 cases (31.7%). The most common primary site of malignancy was the oral cavity, and squamous cell carcinoma was the most commonly detected malignancy. Poorly differentiated epithelial malignancy was reported in 18 cases (17.3%).

Conclusion: Lymphadenopathy due to metastatic malignancy can be efficiently diagnosed by FNAC using a systematic approach combined with clinical information. Such an approach should be based on the characteristics of lymphadenopathy and the cytomorphology.

Key words: Fine-needle aspiration cytology, Lymphadenopathy, Metastasis

INTRODUCTION

Lymphadenopathy is a common clinical presentation which must be investigated thoroughly. It could be regional or generalized, and is seen in various benign and malignant conditions. To diagnose the cause of lymphadenopathy different diagnostic modalities are used, which include fine-needle aspiration cytology (FNAC), flow cytometry, radiologically guided core needle biopsy, and open biopsy. Among these FNAC is the cheaper, safer and faster technique for diagnosing the type of lymphadenopathy with a high degree of accuracy. FNAC also helps to diagnose metastases or recurrences in cases of known primary malignancies. It also plays a role in identifying an unknown primary tumor. Since FNAC is a minimally invasive procedure and can be performed in an outpatient department, FNAC also serves as an ideal follow-up tool.

The aim was to study the distribution and cytomorphology of lymph node metastases.

MATERIALS AND METHODS

This study included 104 cases of lymph nodes involved by metastatic malignancy which were referred for FNAC to Pathology Department of our institute over a period of 1-year. In 10 cases, ultrasonography (USG)-guided FNAC was performed and smears were sent with clinical details of the respective patients for cytological evaluation.

In all cases, a thorough evaluation was done and clinical details including history, physical examination, and

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laboratory studies were recorded. Findings of chest radiography, computed tomographic scans, USG, and mammography in women were duly recorded wherever available. The patients were explained about the procedure and an informed consent was taken.

Fine-needle aspiration was performed with disposable equipment, a 22-gauge, 1" needle attached to a 5 cc disposable syringe. Two or three separate passes were made for adequate sampling. The samples were ejected onto glass slides, evenly spread, fixed immediately in 95% alcohol, and stained with the Papanicolaou stain.

Slides were screened and those positive for malignant cells were further typed based on cytomorphology as metastasis of squamous cell carcinoma (SCC), adenocarcinoma, and other distinctive tumor types.

Those cases which showed features of malignancy but could not be placed into any definite group were reported as per their predominant cytomorphology. Inadequate smears were excluded from the study.

RESULTS

This study was a retrospective analysis of cases diagnosed over a period of 1-year. During this period, 104 (4.8%), out of total 2140, lymph nodes showed evidence of metastatic malignancy and were included in this study.

The age of the patients ranged from 19 to 90 years, with males 68 (65.4%) and females 36 (34.6%). The lymph node metastases were the most common in the age range of 45-54 years with the mean age being 55.8 years.

In 54 (51.9%) cases, the lymph node to be aspirated was the presenting symptom. Other common symptoms were dysphagia, change in voice, loss of appetite, and weight loss. The symptoms varied with the site of primary malignancy.

The submandibular lymph nodes were the most commonly involved nodes (Table 1), 35 cases (33.6%). This was closely followed by anterior cervical nodes 33 cases (31.7%) and supraclavicular nodes were involved in 13 cases (12.5%).

The size of the involved lymph nodes ranged from 0.5 to 7 cm in largest dimension. The majority of them, 37 (35.5%), were in the size range of 1.5-2.4 cm.

The most common primary site of malignancy was the oral cavity (Table 1), followed by larynx, hypopharynx, and oropharynx. In females, apart from these, primary in the breast was also common. Metastasis of SCC was most commonly reported (Table 2), 69 cases (66.3%), followed by

adenocarcinoma metastasis in 6 cases (5.7%) and metastasis of infiltrating duct carcinoma was seen in 4 cases (3.8%). SCC was the most common metastatic malignancy detected in submandibular (27 cases), anterior cervical (24 cases), posterior triangle (7 cases), and submental (2 cases) nodes (Table 3). The cases, where cytological features, were not typical of any particular malignancy; they were included in poorly differentiated epithelial malignancy (18 cases) and papillary epithelial malignancy (2 cases)(Figures 1-5).

DISCUSSION

Lymph nodes are the most common site of metastatic malignancies and sometimes, constitute the first clinical manifestation of the disease.
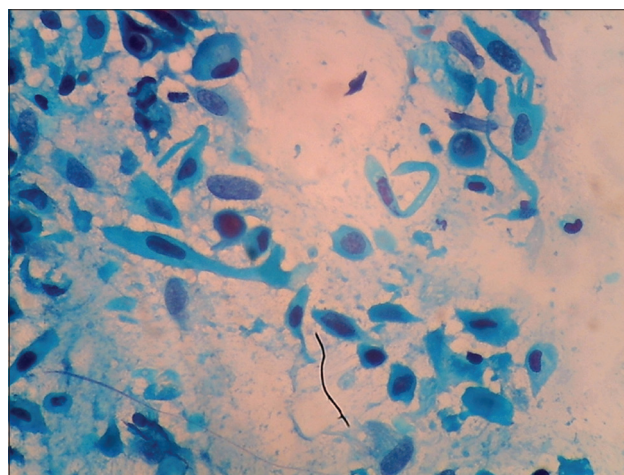
Figure 1: Metastases of squamous cell carcinoma (Papanicolaou, ×400) show malignant squamous cells in clusters and scattered singly with hyperchromatic nuclei and cytoplasm which is cyanophilic. Few cells with bipolar and unipolar cytoplasmic extensions are also seen. Background shows necrosis
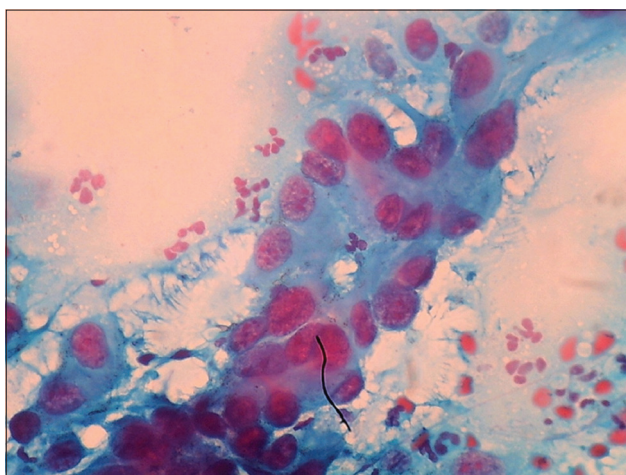
Figure 2: Metastasis of adenocarcinoma (Papanicolaou, ×400): Tumor cells in glandular arrangement with vesicular nuclei, conspicuous nucleoli and moderate amount of cytoplasm
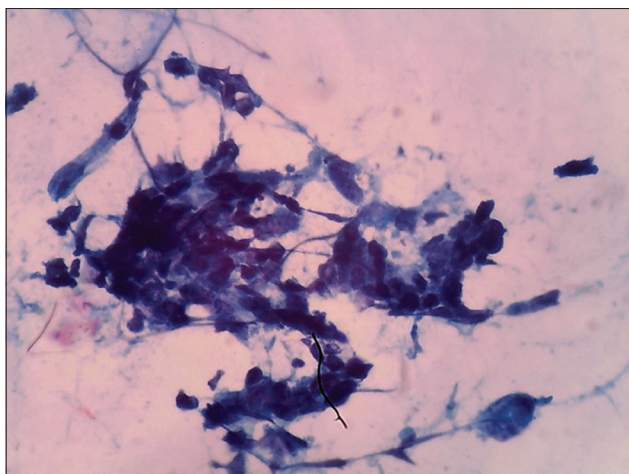
Table 1: Distribution of primary malignancies in lymph node groups

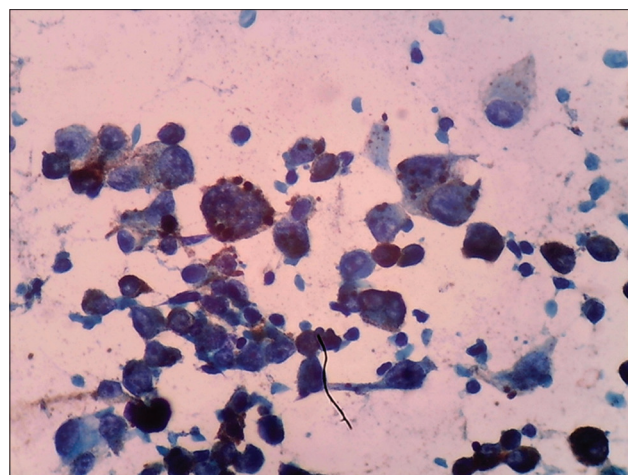| Primary sites	Distribution of metastatic lymph nodes							Periportal	Total
	Submandibular	Anterior cervical	Supraclavicular	Posterior triangle	Inguinal	Sub-mental	Axillary		
Oral cavity	13	6	2	1	0	2	0	0	24
Larynx	6	4	0	1	0	0	0	0	11
Hypopharynx	2	2	1	0	0	0	0	0	5
Breast	0	1	2	1	0	0	1	0	5
Oropharynx	1	2	0	1	0	0	0	0	4
Skin	0	1	1	0	1	0	0	0	3
GIT	1	1	1	0	0	0	0	1	4
Penis	0	0	0	0	3	0	0	0	3
Lung	1	0	1	0	0	0	0	0	2
Bladder	0	0	1	0	1	0	0	0	2
Ovary	0	0	0	0	1	0	0	0	1
Thyroid	0	0	1	0	0	0	0	0	1
Kidney	0	0	0	0	1	0	0	0	1
Salivary gland	1	0	0	0	0	0	0	0	1
Unknown	10	16	3	6	1	0	1	0	37
Total	35	33	13	10	8	2	2	1	104

GIT: Gastrointestinal tract

Table 2: Distribution of metastasis according to cytological diagnosis

Type of malignancy	Number
Squamous cell carcinoma	69
Adenocarcinoma	6
Infiltrating duct carcinoma	4
Mucoepidermoid carcinoma	2
Papillary carcinoma thyroid	1
Melanoma	1
Malignant germ cell tumor	1
Poorly differentiated epithelial malignancy	18
Papillary epithelial malignancy	2
Total	104

Figure 4: Metastasis of malignant melanoma (Papanicolaou, ×400) with dispersed single cells, eccentrically placed nuclei, few were binucleated with prominent nucleoli and cytoplasm showing melanin pigment

Figure 3: Metastasis of poorly differentiated epithelial malignancy (Papanicolaou, ×400) showing cells in loose clusters with marked nuclear hyperchromasia and anisonucleosis

This variation originates largely from the type of services and clinical expertise in oncological management provided by the place of study as well as the socioeconomic status of the patients.

Male to female ratio was 1.8:1. Male predominance was seen consistently in most of the Indian studies. This has been attributed to the use of tobacco, alcohol, etc., which is more prevalent in the male population.

The majority of cases, in our study, were in the age range of 45-54 years with the mean age being 55.8 years, which is consistent with other studies. However, with increasing consumption of tobacco (in various forms), paan and areca nut, the younger age group is also being affected. There were 23 patients below 45 years in our study.

In our study of 1-year duration, 4.8% cases of metastatic lymphadenopathy were diagnosed which is similar to few reports but considerably lower than other studies (Table 4).

Table 3: Distribution of metastases in lymph node groups

Type of malignancies	Sub-mandibular	Anterior cervical	Supraclavicular	Posterior triangle	Inguinal	Sub-mental	Axillary	Periportal	Total
Squamous cell carcinoma	27	24	6	7	3	2	0	0	69
Adenocarcinoma	2	2	2	0	0	0	0	0	6
Infiltrating duct carcinoma	0	1	1	1	0	0	1	0	4
Mucoepidermoid	2	0	0	0	0	0	0	0	2
Papillary carcinoma thyroid	0	0	1	0	0	0	0	0	1
Melanoma	0	0	0	0	1	0	0	0	1
Malignant germ cell tumor	0	0	0	0	1	0	0	0	1
Poorly differentiated epithelial malignancy	4	5	3	1	3	0	1	1	18
Papillary epithelial malignancy	0	1	0	1	0	0	0	0	2
Total	35	33	13	10	8	2	2	1	104

Table 4: Different studies and their corresponding findings

Author	Frequency of metastatic lymph nodes	Age predominance	Gender predominance	Common site of lymphadenopathy	Common site of primary malignancy	Common type of malignancy
Fatima et al.[1]	8.7	50-60	-	-	-	SCC
Ghartimagar et al.[2]	18	Mean 60.4	-	Anterior and posterior triangle cervical	Lung	Adeno-carcinoma
Rathod and Shah[3]	-	>40	Male	Cervical	-	SCC
Qadri et al.[4]	38.2	-	Male	-	-	SCC
Patel et al.[5]	27.06	41-50	Male	Cervical		SCC
Sheikh and Parmar[6]	26.4	41-60	Male	Cervical	Oral cavity, pharynx, larynx	SCC
Qadri et al.[7]	31.4	Mean 52.5	Male	Supraclavicular	Oesophagus	SCC
Pavithra and Geetha[8]	20.06	-	--	Cervical	-	SCC
Yadav et al.[9]	14.6	40-60	Male	Cervical	-	SCC
Mehdi et al.[10]	-	51-60	Male	Cervical	Larynx, tongue	SCC
Rathod and Singla[11]	20.46	-	-	Cervical	Oral cavity	SCC
Anila et al.[12]	48.2	50-80	-	Cervical	Head and neck	SCC
Sharma et al.[13]	6.38	-	-	Cervical	-	SCC
Present study	4.8	45-54	Male	Submandibular	Oral cavity	SCC

SCC: Squamous cell carcinoma
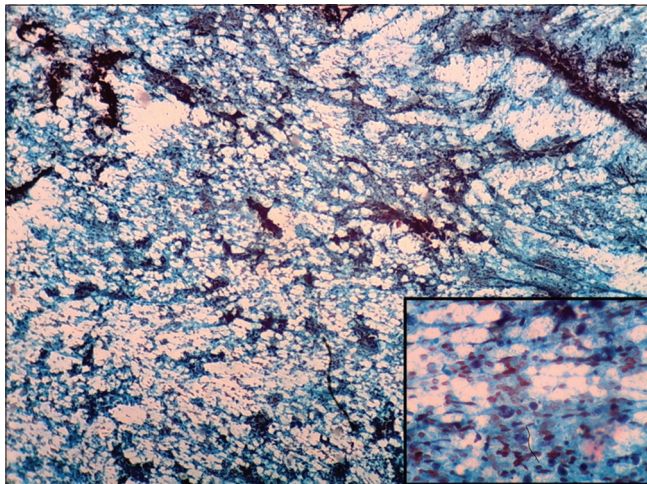
Figure 5: Metastasis of malignant germ cell neoplasm (Papanicolaou, ×100) showing dispersed large cells with macronucleoli and moderate amount of cytoplasm in a tigroid background with abundant lymphocytes. Inset showing the large cells with macronucleoli

The presenting symptom varied in different studies but palpable lymph node enlargement[14] and weight loss were at the top of the list, similar to our observations. However, pleural and pulmonary metastases were common in the study by Didolkar *et al.*[15]

In this study, submandibular nodes 35 (33.6%) were the most commonly involved group followed closely by the anterior cervical group 33 cases (31.7%). SCC was the most common malignancy in these groups.

The groups of lymph nodes with the most diverse set of primaries were supraclavicular and inguinal nodes. Supraclavicular nodes were involved in 13 cases (12.5%) and apart from aerodigestive tract, received metastases from lung, breast, thyroid and bladder, while inguinal nodes were involved in carcinoma penis, bladder, kidney, ovary, melanoma of right lower limb and germ cell neoplasm from unknown primary. Ahmad *et al.*[16] and

Sinha *et al*.[17] have observed that lung is the most common primary for metastases to supraclavicular nodes, along with colorectum and breast. As for the Inguinal nodes, malignant lesions arising in the lower extremity, perineum, male and female genital tracts have been reported to be important primary sites by Copeland and McBride[14] and Ahmad *et al*.[16]

SCC was the most common malignancy diagnosed in this study and was observed in 66.3% cases. This is consistent with most studies; however, Ghartimagar *et al*.[2] and Didolkar *et al*.[15] have found adenocarcinoma to be the most common metastatic malignancy. This can be attributed to various geographic, demographic and lifestyle factors.

Adenocarcinoma was detected in 6 (5.7%) cases in this study. The primaries were from lung in 2 cases, from esophagogastric junction (1 case), rectum (1 case) and 2 were unknown. Infiltrating duct carcinoma was found in 4 cases (3.8%) and all were known cases of breast carcinoma. In only 1 case, axillary lymph node was involved. In rest of the cases metastasis was detected in posterior cervical, supraclavicular and anterior cervical nodes.

Poorly differentiated epithelial malignancy was reported in 18 cases (17.3%) when the features were not typical of any of the malignancies. In 2 cases, the tumor cells were arranged in papillary clusters with fibrovascular cores and lacked any characteristic microscopic features. Histopathological correlation was not performed because tissue diagnosis was not sought for the majority of the patients.

On the other hand, the cytology of primary malignancy could be determined in 26 out of 37 (35.5%) cases in which primary was not known or suspected. These included SCC (59.4%), adenocarcinoma in 5.4%, 1 (2.7%) case of mucoepidermoid carcinoma, and 1 (2.7%) case of malignant germ cell tumor. Remaining were poorly differentiated epithelial malignancy in 9 (24.3%) cases and papillary epithelial malignancy in 2 (5.4%) cases. These findings are consistent with those in the study of efficacy of aspiration cytology by Prasad and Mohan,[18] where primary was not known in 37.3% cases and a cytological diagnosis of SCC was given in 12.7% cases, adenocarcinoma in 32.4% cases, and poorly differentiated carcinoma was given in 54.9% cases.

CONCLUSION

Lymphadenopathy due to metastatic malignancy can be efficiently diagnosed by FNAC using a systematic approach combined with clinical information. Such an approach should be based on the characteristics of lymphadenopathy and the cytomorphology. FNAC is cheap, non-invasive and is preferable for the patient. However, wherever it is required, tissue diagnosis must be performed.

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