CYTODIAGNOSTIC SPECTRUM OF METASTATIC LYMPH NODES - A PROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

Malignancies in lymph nodes in our country are mostly metastatic in nature and sometimes constitute the first clinical manifestation of the disease with an incidence ranging from 65.7% to 80.4% and lymphomas from 2% to 15.3% among lymph nodes aspirated from all sites. Enlarged lymph nodes are often easily accessible, which makes Fine Needle Aspiration Cytology (FNAC) a very simple and important diagnostic tool for lymph node lesions.

MATERIALS AND METHODS

Fine Needle Aspiration Cytology (FNAC) is a very simple and rapid diagnostic tool. The present study is a prospective cross-sectional over a period of 2 years from June 2014 to May 2016 to find out cytodiagnosis of clinically suspected malignant lymphadenitis.

RESULTS

A total of 150 cases clinically suspected for malignancy were evaluated, out of which 121 (80.66%) were metastatic and rest 4 (2.66%) cases were lymphoma and 25 (16.66%) cases turned out to be reactive lymph nodes and benign cystic and were excluded from the study for further analysis. The peak age of incidence of metastatic lymphadenitis was in the 5th decade amounting to 58 (47.93%) cases followed by 6th and 4th decade with an age range varying from 23 to 84 years with a male-to-female ratio of 2.78:1. Out of these 121 cases, 76 (62.80%) were metastatic Squamous Cell Carcinoma (SCC) followed by adenocarcinoma in 27 cases (22.31%), breast carcinoma in 6 (4.95%), small cell carcinoma of lung and undifferentiated carcinoma in 5 cases each (4.13%) and papillary carcinoma of thyroid in 2 (4.95%). The maximum number of lymph nodes involved were the cervical group in 98 (80.99%) followed by axillary in 9 (7.43%), supraclavicular in 9 (7.43%) inguinal in 4 (3.30%) and mesenteric in 1 (0.82%) case. The primary tumours could be identified in 110 out of 121 cases of metastatic lymphadenitis. The common sites were head and neck region, nasopharynx, other parts of GIT, breast, lung and genital areas.

CONCLUSION

It has been concluded that FNAC helps in diagnosing and categorisation of the tumour type, while detailed clinical history and investigations help in identifying the primary tumour site and further management.

KEYWORDS

Fine Needle Aspiration Cytology (FNAC), Cytodiagnosis, Metastatic Malignancy, Metastatic Lymphadenitis.

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BACKGROUND

The Fine Needle Aspiration Cytology (FNAC) is one of the most commonly practised investigative procedures for the diagnosis of various conditions including metastatic malignancies. In 1930, Martin and Ellis of Memorial Hospital for Cancer included tumours that had metastasised to lymph node among targets of aspiration biopsy.¹ Since then, it is a well-established and accepted method because of simplicity of the procedure, easy repeatability if necessary, a very reasonable sensitivity and specificity, fast and cost effectiveness with very minimal complications if at all.

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FNAC not only confirms the presence of metastatic disease, but also gives the clue regarding the nature and origin of primary malignancy. It is useful for the detection of recurrence and new metastases. Hence, it is a very good tool in followup of malignant conditions as well. Although, histopathological examination is considered as the gold standard in diagnosis, especially in lymphomas, FNAC may be the only tool for diagnosis and further management of the patients in some instances of metastatic malignancy.

In developing country like India, infective lymphadenopathy is also quite common, mostly due to high prevalence of tuberculosis and other granulomatous conditions. However, still a large percentage of cervical lymphadenopathy in adults turn out to be cysts or abscesses, benign and malignant conditions may mimic lymph node metastasis, especially with a case of known tumour.² Hence, clinical recognition and urgent diagnosis of palpable lymphadenopathy is of immense importance, especially to differentiate between inflammatory or metastatic or primary neoplastic lesion. The present study undertaken at Tripura Medical College and Dr. BRAM Teaching Hospital from June 2014 to May 2016 (2 years) was to unravel the spectrum of

cytomorphological patterns of metastatic lymph nodes in different areas of the body in this part of country.

MATERIALS AND METHODS

Study design was a prospective and a cross-sectional one. The duration of the study was 2 years from June 2014 to May 2016. The study was approved by Institutional Ethics Committee of Tripura Medical College and Dr. BRAM Teaching Hospital, Hapania.

All patients with metastatic lymphadenopathy reported from Dept. of Pathology, TMC and Dr. BRAM Teaching Hospital was analysed for the study. An informed consent of all the patients has been taken and the pros and cons of the said procedure were explained to the patients and their guardians.

A detailed history, clinical examination and relevant investigations were documented. Under aseptic precaution, node was held between left index finger and thumb followed by insertion of 22 - 23 gauge needle fitted with 10 mL syringe for aspiration. The needle with syringe was introduced in node, plunger of syringe pulled to create negative pressure. With the negative pressure, maintained needle was moved to and fro within node to aspirate the material. The negative pressure was released and needle with syringe was withdrawn from node. Pressure with cotton swab was applied to node after withdrawal of needle. Needle was detached from syringe, air drawn into syringe, needle reattached and material pushed on slides. Multiple smears were made; few of them air dried for Romanowsky stain like May-Grunwald-Giemsa stain (MGG), Leishman Giemsa and few were fixed with ethyl alcohol for staining with Haematoxylin and Eosin (H and E) stain and Periodic-Acid Schiff (PAS) stain. Special stain such as Ziehl-Neelsen's stain (Z-N) was used wherever indicated.

In few cases where the glands were deeper and accessibility was difficult, Ultrasonography (USG) guided FNAC was performed. All the clinical and pathological data were collected and analysed.

RESULTS

A total of 150 cases clinically suspected for malignancy were evaluated, out of which 121 (80.66%) were metastatic tumours of lymph node. Rest 4 (2.66%) cases were lymphoma and 25 (16.66%) cases clinically suspected for malignancy turned out to be reactive lymph nodes and benign cystic lesions and were finally excluded from our study.

Sl. No.	Age Group(yrs.)	No.	Percentage (%)
1	21 - 30	2	1.65
2	31 - 40	11	9.09
3	41 - 50	19	15.70
4	51 - 60	58	47.93
5	61 - 70	25	20.66
6	71 - 80	4	3.30
7	81 - 90	02	1.65
Total		121	100

Table 1. Age Distribution

The peak age of incidence of metastatic lesions were in the 5th decade amounting to 58 (47.93%) cases followed by 6th and 4th decades in 25 (20.66%) and 19 (15.70%) respectively. The youngest and oldest patient of our study was 23 years and 84 years respectively (Table 1).

Sex	No.	Percentage (%)	Ratio
Male	89	73.55	2.78:1
Female	32	26.44	

Table 2. Sex Distribution

Males outnumber the females in our study amounting to 89 (73.55%) and 32 (26.44%) cases respectively, with a male-to-female ratio of 2.78:1 (Table 2).

Type of Malignancy	No. of Cases	Percentage (%)
Squamous cell carcinoma	76	62.80
Adenocarcinoma	27	22.31
Breast carcinoma	6	4.95
Small cell carcinoma	5	4.13
Undifferentiated carcinoma	5	4.13
Papillary carcinoma of thyroid	02	1.65
Total	121	100

Table 3. Distribution of Pathological Subtypes of Metastatic in Lymph Nodes

Out of these 121 cases, 76 (62.80%) were metastatic Squamous Cell Carcinoma (SCC) followed by adenocarcinoma in 27 cases (22.31%). The rest of the cases were breast carcinoma in 6 (4.95%), small cell carcinoma of lung and undifferentiated carcinoma in 5 cases each (4.13%) and Papillary carcinoma of thyroid in 2 (4.95%) (Table 3, Fig. 1 - 6).

Site	No. of Cases	Percentage (%)	Primary Site Identified	Primary Site
Cervical	98	80.99	89	Head and neck, lung, nasopharynx, other parts of GIT, breast, thyroid
Axillary	9	7.43	8	Breast and lung
Supraclavicular	9	7.43	8	GIT, lung, breast
Inguinal	4	3.30	4	Vulva, penis, cervix
Mesentery primary site unknown	1	0.82	1	GIT
Total	121	100	121	

Table 4. Metastatic Sites showing the Origin of Primary Tumours

The maximum number of lymph nodes involved were the cervical group in 98 (80.99%) followed by axillary in 9 (7.43%), supraclavicular in 9 (7.43%), inguinal in 4 (3.30%) and mesenteric in 1 (0.82%) case.

The primary site of lesions could be identified in 110 out of 121 cases of metastatic lymphadenitis. The common sites were head and neck region, nasopharynx, other parts of GIT, breast, lung and genital areas. In spite of repeated search in 7 cases of cervical, 2 cases of axillary and one case of supraclavicular lymphadenitis we failed to find out the primary tumour.

Figure 1. Metastatic Squamous Cell Carcinoma showing Clear Blue Cytoplasmic Staining, indicating Squamous Differentiation (May-Grunwald-Giemsa: 40X)

Figure 2. Metastatic Adenocarcinoma showing Glandular Cells, Pleomorphic in Nature and Arranged in Monolayer Sheets (May-Grunwald-Giemsa: 40X)

Figure 3. Metastatic Undifferentiated Carcinoma showing Pleomorphic Cell Populations with High Nuclear Cytoplasmic Ratio. Background shows Mature Lymphocytes (Leishman Giemsa; 40X)

Figure 4. Cytological Smear showing Metastatic Small Cell Carcinoma: (May-Grunwald-Giemsa 40X)

Figure 5. Cytological Smear showing Malignant Ductal Cells with Lymphoid Cells in the Background (Giemsa Stain: 40X)

Figure 6. Cytological Smear of Metastatic Papillary Carcinoma of Thyroid showing Papillary Pattern and Nuclear Grooving (May-Grunwald-Giemsa: 10X)

DISCUSSION

Malignancies in lymph nodes in our country are mostly metastatic in nature with an incidence ranging from 65.7%² to 80.4%³ and lymphomas from 2%⁴ to 15.3%³ among lymph nodes aspirated from all sites. So, lymph node aspiration plays a very vital role in the diagnosis of malignant lymphadenopathies, especially in a developing country like India considering the economic and health scenario.

The diagnosis given by FNAC is often the only diagnosis accepted and there is no further correlation with histopathology, especially in cases of advanced malignancies which provides clues for occult primaries. FNAC sometimes also surprises the physician, where there were no clues to suspect a malignant condition at all.

Our study showed metastatic malignancy of lymph nodes to be 80.66% and lymphomas in 2.66%. This observation very closely correlates with other Indian studies by Alam K et al³ and Khajuria R et al,⁴ who also confirmed that metastatic malignancy of lymph nodes were far more commoner than lymphomas, although there were variations in the percentage involved depending on the number of cases studied. However, little deviations were also observed in comparison with another Indian study by Arora B et al,⁵ where they documented little higher number lymphomas as compared to our study. It was noted that metastases and lymphomas were 68% and 32% respectively. A published data on the same from Brazilians revealed as 79.4% metastases and 14.2% lymphomas.⁶

The peak age of incidence was in the 5th decade followed by 6th and 7th decades. It correlates with the study by Kamat GC.⁷

In our study, the frequency of malignancies in males outnumber the females with a male-to-female ratio of 2.78:1. This may be due to higher prevalence of different addictions in males than their female counterparts, which are suspected to be one of leading causes of malignancy. Similar observations were made by Haque and Talukder⁸ and Steel et al.⁹

The cervical groups of lymph nodes were the most common group of lymph nodes to be involved in the present study and the primary is mostly noted from the oral cavity and other parts of upper GIT. Similar observations were noted by Hirachand et al¹⁰ and Hoft S et al.¹¹

The commonest cytodiagnosis were squamous cell carcinoma followed by adenocarcinoma. Squamous cell carcinoma was also highest in cervical group of lymph nodes, as majority of suspected nodes were in the cervical group of nodes as well. Similar observations noted by Alam K et al³ and Hoft S et al.¹¹

Rates of malignancy in oral cavity/pharynx, oesophagus and male larynx are highest in India, probably due to the use of multiple tobacco products as reported by Rastogi T et al.¹² Also our study is based in North Eastern part of the country, where chewing habits of tobacco and beetle nuts are quite high.

Metastatic squamous cell carcinoma was predominantly seen in 5th decade of life, whereas metastatic adenocarcinoma does not show any specific age dominance which correlates with the previous studies.^{3,4} On the contrary to our observations, few other studies where metastatic adenocarcinoma was the most common subtype than squamous cell carcinoma.^{13,14} However, often it becomes difficult to distinguish between adenocarcinoma and poorly differentiated squamous cell carcinoma when the cell clusters show thick nuclear membrane and prominent nucleoli.

Also, as over all male predominance is noted in metastatic tumours in the present study, which reflects in case of metastatic squamous carcinoma as well. Similar observations

were documented by Khajuria R et al,⁴ Qadri SK et al¹³ and Mohanty R et al.¹⁴

The primary sites of tumours in each group of enlarged suspected malignant lymph nodes in our study correlated well with other similar studies.^{2,15} A detailed history, radiological investigations and immunohistochemistry in difficult cases may help to arrive at a definitive diagnosis.¹⁵

The improved diagnostic accuracy of FNAC in the diagnosis of malignant lesions of the lymph nodes is probably due to a combination of factors, such as availability of using and guidance of imaging technique as well many other cytodiagnostic assistances like immunohistochemistry, trained and qualified manpower over the years.

CONCLUSION

The present study highlights cytological spectrum of metastatic lesions presenting as lymphadenopathy over a period of 2 years at the Department of Pathology, TMC and Dr. BRAM Teaching Hospital. FNAC is a very convenient extension of the more invasive biopsy procedure, lending itself to saving of time and cost, and a better compliant procedure for both patients and physicians in the management and followup of lymphadenopathies. FNAC helps in diagnosing and categorisation of the tumour type, while detailed clinical history and investigations help in identifying the primary tumour site and further management.

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