Distribution of Various Malignant Lesions in Lymph Node Cytology – A 1 Year Population Based Study from a Tertiary Care Centre in North-East India

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ABSTRACT

BACKGROUND

Lymph nodes (LN) are an integral component of the immune system. Enlarged lymph nodes are a prime target for fine needle aspiration (FNA). Lymph nodes greater than 1 to 2 cm are an immediate source of concern. Lymphadenopathy is a common presenting symptom in various diseases. Fine needle aspiration cytology (FNAC) confirms the presence of metastatic disease and gives a clue regarding its nature and origin of primary malignancy. In many metastatic malignancies, FNAC may be the only tool for diagnosis and further management of the patients. We intend to assess the cytomorphological patterns of both primary tumour and metastatic tumour in a lymph node.

METHODS

A retrospective study was conducted in the Department of Pathology, RIMS, Imphal, over a period of one year from January 1, 2018 to December 31, 2018. Five hundred and fifty-five lymph nodes were aspirated, out of which 99 cases turned out to be malignant lesions. Giemsa and PAP stained FNAC slides were collected and reviewed. Data entry and analysis were done by using SPSS version 21.

RESULTS

Out of 99 cases, 88.9 % were metastatic tumours and 11.1 % were of primary lymphoproliferative disorders. Thirty three percent of malignant lymphadenopathy were found in fifth decade. Undifferentiated carcinoma constituted around 32.3 % of all the cases of malignant lymphadenopathy. Cervical group of lymph nodes were involved in 46.5 % of cases.

CONCLUSIONS

FNAC has proved to be a useful tool in diagnosing malignancy with good certainty. FNAC of lymph nodes prevents complications associated with lymph node biopsy.

KEYWORDS

FNAC, Lymph Node, Undifferentiated Carcinoma, Squamous Cell Carcinoma

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BACKGROUND

Lymph nodes are an integral component of the immune system and are affected by a multitude of pathological lesions which manifest most commonly as lymphadenopathy in clinical practice.[1] Lymph nodes are small, oval or reniform bodies, 0.1 - 2.5 cm long, lying in the course of lymphatic vessels. A LN is essentially a continuous framework consisting of the capsule, trabeculae and the reticulum, with cells enmeshed in it.[2] Enlarged lymph nodes are a prime target for fine needle aspiration (FNA). In an adult, lymph nodes greater than 1 to 2 cm are an immediate source of concern and unless the cause is evident, the enlarged node should be aspirated.[3] Lymphadenopathy is a common presenting symptom in various diseases. Key risk factors for malignancy include older age, firm, fixed nodal character, duration of greater than 2 weeks and supra clavicular location. The prevalence rate of malignant aetiologies of lymphadenopathy is very low in childhood but increases with age. The cytomorphological features obtained in fine needle aspiration, frequently correlate very well with histological appearance of the same lesion and in some situations, it has qualities of a micro biopsy.[4] FNA is accepted by most patients as it is a minimally invasive method for evaluating lymphadenopathy. It has advantages compared to surgical excision and preserves lymph node architecture should an excision be necessary. FNA is particularly useful in patients with deep seated lymphadenopathy. Even with superficial lymphadenopathy, using FNA avoids uncommon but serious morbidity associated with lymph node excision, like spinal nerve injury.[2] It is simple, cost effective procedure that is minimally invasive with almost no complications. FNA can also be of therapeutic use in a cystic swelling. FNA of superficial lesions need no anaesthesia eliminating the risk of complications associated with anaesthesia.[5] Fine needle aspiration cytology has a significant role in neck lymph nodes, particularly those with metastasis. FNAC confirms the presence of metastatic disease and gives a clue regarding its nature and origin of primary malignancy. It is very useful in detecting recurrence and new metastasis. It is important and reliable tool in follow up of malignant conditions.[6] Metastasis, the spread of tumour cells to the distant lymph node groups is the most fearsome aspect of cancer. Patients presenting with metastatic disease or those developing metastases after successful management of primary tumour carry a universally grave prognosis.[2] Tumour cells invade either the blood or the lymphatic vessels to assess the general circulation and then establish other tissues. Nodal status is a significant predictor of survival of patients with malignant tumour. Metastasis is the cause of 90 % of cancer death.[7]

The probability of having metastatic disease at presentation highly depends on the site of the primary tumour. Patients with squamous cell carcinoma (SCC) of buccal mucosa, lip usually present with only local disease, while the majority of tongue cancer patients present with advanced stage disease with regional and / or distant metastasis. Bilateral metastases are frequently encountered in tumours of the base of tongue.[2] Detection of lymphatic metastases of malignant tumours of the head and neck is pivotal for the management of the neck. Ultrasound-guided FNAC (USG-FNAC) has been shown to improve staging of the neck. A USG-FNAC is performed on lymph nodes that suggest malignancy on ultrasound examination. Ultrasonographic criteria for suspected malignancy are size > 8 mm in diameter for sub digastric nodes and > 7 mm for other nodes. However, these criteria do not work if metastatic disease has not yet resulted in an enlargement of the lymph node. Therefore, a lymph node with a small volume of metastatic cells may be missed by ultrasound and other higher imaging modalities as well.[8]

However, histopathological examination will always be considered as the gold standard in diagnosing various lymphadenopathy aetiologies, especially in lymphomas but in many metastatic malignancy FNAC may be the only tool for diagnosis and further management of the patients.[6]

The causes of lymphoma are largely unknown. Severe immunodeficiency, various infectious agents, familial aggregation, blood transfusion and occupational exposure to pesticides and solvents have been consistently reported to increase the risk of lymphoma. Perhaps, some of these risk factors are more strongly associated with specific subtypes of lymphoma.[9] In cases of highly proliferative lymphomas such as Burkitt's and lymphoblastic lymphoma, FNAC can provide a rapid and accurate diagnosis with minimal invasiveness that would be of critical importance. Fine needle aspiration yields smaller amounts of sample with partial or complete loss of histological structures, potentially causing its diagnostic limitations. In these cases, cell block preparation may be helpful. As morphology and immunophenotype are necessary for the diagnosis of most lymphoid neoplasms, FNAC alone is not sufficient, which can be overcome by cell block preparation.[10]

Cell blocks are typically prepared from fine needle aspirations, particularly deep-seated lesions. The residual materials from fine needle aspiration are routinely processed into cell blocks, which are composed of random cells and tissue fragments, which could provide morphology and partial histological structures and can be sectioned for immuno-histochemical staining, which offers reliable and stable results. Cytological features from the conventional smear along with the morphology and immunophenotype of cell blocks aid in the diagnosis and classification of lymphoma. Cell blocks maintain architecture which closely resembles that seen on surgical specimens, which are useful for diagnosis, pattern recognition and identification of features that may otherwise be difficult to appreciate on non-cell block cytology preparations. When adequately cellular, cell blocks serve as a source of multiple additional sections that are valuable in the evaluation of more cells and for performing ancillary studies. The diagnostic accuracy of fine needle aspiration cell block for sub classification of lymphoma was 86.6 %, with 77.8 % for classical Hodgkin's lymphoma (HL) and 87.5 % for non-Hodgkin's lymphoma (NHL).[11]

Immuno-histochemistry (IHC) is essential for the diagnosis and sub-typing of lymphoma. The basic IHC panel for suspected NHL includes antibodies against B cell (CD 20) and T cell (CD3) antigens and for suspected HL includes antibodies against CD 45RB, CD15 and CD30.[12]

The purpose of the study was to assess the cytomorphological patterns of both primary tumour and metastatic tumour in a lymph node.

METHODS

The present study is a retrospective review of malignant lymph node aspirates in superficial lymph nodes over a period of one year from January 1, 2018 to December 1, 2018. FNAC was performed following strict aseptic precautions. Inadequate aspirates were excluded from the study. Patients attending cytology outpatient department (OPD) with lymph node enlargement were the study population. Consent was obtained from each patient before the procedure.

Procedure

The site and size of the lymph nodes being aspirated was noted. A 22 / 23 gauge needle attached to 20 ml syringe mounted on Cameco handle was used for obtaining the material. The needle was inserted into the swelling and full suction pressure was applied. The needle was moved briskly in different directions in the swelling till sufficient material was visualised in the stem of the needle. The negative pressure of the syringe was released, and the needle was taken out. The aspirated sample was blown on clean glass slides and smears were made using squash preparation. Smears were fixed using air dried and alcohol fixation method. 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.

Statistical Analysis

The result was collected and analysed on SPSS version 21 and percentages were calculated.

RESULTS

A total of 535 lymph node cases were aspirated out of which 99 cases were of malignant lesions. Of the 99 cases the maximum number of cases were of metastatic origin, 88.9 % and 11.1 % were of primary lymphoproliferative disorders.

Age Group in Years	Percentage of Cases
31 – 40	6 (6 %)
41 – 50	17 (17.10 %)
51 – 60	33 (33.3 %)
61 – 70	28 (28.2 %)
71 – 80	15 (15.15 %)

Table 1. Age Wise Distribution of Cases (N = 99)

As shown in Table 1, the maximum number of malignant lymphadenopathies found during the fifth decade were around 33.3 % followed by 28.2 % during the sixth decade.

As shown in Table 2, 57.5 % were males and 42.5 % were females out of the 99 malignant cases identified during the study period.

Sex	Total Number of Cases
Male	57 (57.5 %)
Female	42 (42.5 %)

Table 2. Sex Wise Distribution of Cases (N = 99)

Lymph Node Groups	Percentage of Cases
Cervical	46 (46.5 %)
Supra-clavicular	30 (30.3 %)
Axillary	8 (8 %)
Generalised lymphadenopathy	8 (8 %)
Inguinal	7 (7 %)

Table 3. Distribution of Cases among Various Lymph Node Groups (N = 99)

As shown in Table 3, the maximum number of malignant lymphadenopathies were found in the cervical region around 46.5 % followed by supra clavicular region around 30.3 %. Eight percent of malignant cases presented with multiple lymph node enlargement.

Age Groups in Years	SCC	AC	Met NET	Met MM	UC	Nodal Lymphoma
31 - 40	2 %	1 %	-	-	3 %	-
41 - 50	2 %	4 %	-	-	8 %	3 %
51 - 60	7 %	10.1 %	1 %	1 %	1 %	5 %
61 - 70	6 %	7 %	3 %	-	9 %	3 %
71 - 80	5 %	5 %	1 %	1 %	3 %	-

Table 4. Distribution of Various Cases among Each Age Group (N = 99)

SCC: Squamous Cell Carcinoma, AC: Adenocarcinoma, Met NET: Metastatic Neuroendocrine Tumour, Met MM: Metastatic Malignant Melanoma, UC: Undifferentiated Carcinoma.

As shown in Table 4, lesions metastasizing to the lymph node constituted around 88.9 % and out of the metastasizing tumour undifferentiated carcinoma (Figure 5b) constituted around 32.3 % followed by the adenocarcinoma (Figure 5f) around 27.2 %. Primary lymphoproliferative disorder of lymph node (Figure 5a) constituted around 11.1 % out of which 5 % of cases were found during the fifth decade.

Cytological Features

The characteristic cytological features seen in making a diagnosis of undifferentiated carcinoma consisted of malignant cells in clusters with malignant cells having pleomorphic vesicular hyperchromatic nuclei with some having prominent nucleoli and scanty cytoplasm. Diagnosis of SCC consisted of clusters and scattered population of malignant cells with hyperchromatic nuclei and dense blue cytoplasm. Certain cells on PAP smear revealed orangeophilia. Background revealed necrosis and keratin debris. For diagnosing AC, the diagnostic features were clusters of malignant cells with coarse nuclear chromatin, prominent nucleoli and moderate cytoplasm with vacuolations in many. Many cells revealed acinar formation as shown in Figure 1f. Five percentage of cases were diagnosed as metastatic small cell carcinoma of lung. These cases revealed dispersed cell population and few clusters of tumour cells. The cells had higher nuclear cytoplasmic ratio and salt and pepper nuclear chromatin. The cells in clusters

revealed nuclear moulding as shown in Figure 1d. Two percentage of cases were diagnosed as malignant melanoma metastasizing to lymph node. The cytological features for diagnosis were malignant pleomorphic plasmacytoid malignant cells with some showing nuclear inclusion and cytoplasmic melanin pigmentation and cytoplasmic vacuoles. Cytological features for diagnosis of lymphoproliferative disorders were monotonous population of atypical lymphoid cells in dispersed singles.

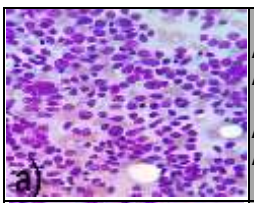

Figure 1a. Lymphoproliferative Disorder in Which Malignant Lymphoid Cells Are in Dispersed Singles [Haematoxylin & Eosin, 400X]

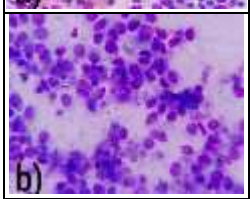

Figure 1b. Metastatic Undifferentiated Carcinoma of Lymph Node Showing Highly Malignant Pleomorphic Nuclei [Haematoxylin & Eosin, 400X]

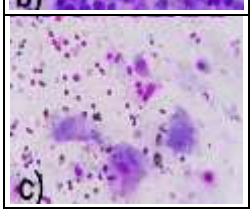

Figure 1c. Metastatic Squamous Cell Carcinoma of Lymph Node Showing Malignant Squamous Cells with Abundant Cytoplasm [Haematoxylin & Eosin, 400X]

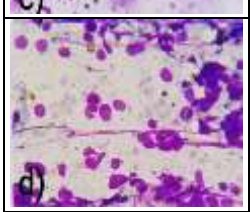

Figure 1d. Small Cell Carcinoma of Lung Metastasizing to Lymph Node with Scanty Cytoplasm Showing Nuclear Moulding [Haematoxylin & Eosin, 400X]

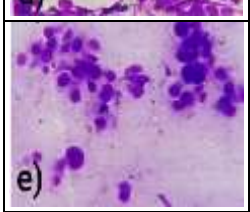

Figure 1e. Malignant Melanoma Metastasizing to Lymph Node Showing Pleomorphic Plasmacytoid Cells [Haematoxylin & Eosin, 400X]

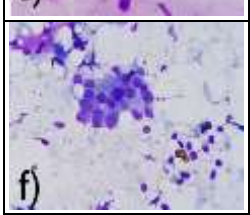

Figure 1f. Metastatic Adenocarcinoma of Lymph Node Showing Vague Acinar Pattern [Giemsa, 400X]

Figure 1. Photomicrograph of Cytomorphology

DISCUSSION

Lymphadenopathy is one of the common clinical presentation of various ongoing disease process inside the body. The lesions arising in the lymph node can be found in patients ranging from early to advanced age. Family history may raise suspicion for certain neoplastic causes of lymphadenopathy such as melanoma.[4] In many cases, lymphadenopathy may be the first presenting sign of an underlying malignancy. FNAC plays a pivotal role in making diagnosis in the superficial, easily accessible lymph nodes. The main importance of FNAC is that this simple diagnostic procedure can be easily performed in any peripheral centre with minimal resources. The set up does not require any sophisticated machinery and can be performed in day care settings. This way majority of cases can be easily diagnosed and managed on FNAC. Appropriate cases which need further evaluation can be easily identified by this procedure. This is important in advanced stage patients where exposure to anaesthesia or excision biopsy cannot be performed due to health constraints.[13]

In our study, the age range of the patients diagnosed with malignant lymphadenopathy spans from 31 - 80 years which is in contrast to the study conducted by Mallappa LB et al.[4] and Hirachand S et al.[14] in whose study the age group of the patient spans from 5 - 95 years. No malignant lymphadenopathy was encountered in the paediatric age group.

In this study, we recorded more cases of metastatic carcinoma than primary lymphoma. The maximum number of malignant cases were reported after the fourth decade with a peak of 33.3 % around the fifth decade which is similar to the study conducted by Mallappa LB et al.[4] and Ahmad SS et al.[15] Surprisingly, malignant lymph node aspirate identified in males (57.5 %) were higher than in females (42.5 %) with a male is to female ratio of 1.3:1, which is in concordance with the study conducted by Mallappa LB et al.[4] and Khajuria R et al[16] in whose study male predominance was there but the ratio is in the higher range of 2:1.

The predominant group of lymph nodes involved in this study was cervical region around 46.5 % which is similar to the study conducted by Mallappa LB et al[4] and Ahmad SS et al[15] in whose study the cervical group of lymph nodes were predominantly involved. The second most common group of lymph nodes involved in this study is from supra clavicular region which is similar to the study conducted by Vimal S et al.[17] Patro P et al.[1] and Ali MB et al[18] in whose study also supra clavicular lymph node was the second most common lymph node group involved, where as it is dis similar to the study conducted by Mallappa LB et al.[4] were inguinal group of lymph nodes were second most common group of lymph nodes involved.

In the study conducted by Khajuria R et al.[16] around 13 cases of lymphoproliferative disorder were reported which is similar to the current study were 11 lymphoproliferative cases were found during the study period. In this study the most common malignant tumour metastasizing to the lymph node was undifferentiated carcinoma constituting around 32.3 % followed by adenocarcinoma around 27.2 % which is in contrast to the study conducted by Mallappa LB et al.[4] and Ali MB et al[18] where squamous cell carcinoma was the predominant malignant tumour metastasizing to the lymph node.

The high rate of metastatic undifferentiated carcinoma in our study may be related to the increased incidence of nasopharyngeal carcinoma (NPC) in this part of the country. The striking feature of NPC in North East India is that its incidence can go as high as approximately 20 / 100000 population. A recent study in North East India has identified the association of NPC with a susceptibility locus in the (HLA)

human leukocyte antigen class I region, which has complex interactions with viral deoxyribonucleic acid (DNA) and environmental factors.[19]

CONCLUSIONS

FNAC has proved to be a useful tool in diagnosing malignancy with good certainty. Cytological morphology of malignant cells along with clinical correlation helps in identifying the site of primary tumour. FNAC of lymph nodes prevents complications associated with lymph node biopsy like lymphedema. FNAC of lymph node from already diagnosed malignant case helps in staging of the tumour.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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