

Correlation of Imprint Cytology of Axillary Lymph Nodes in Breast Carcinoma with the Histopathological Diagnosis

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Abstract

Introduction Conventionally, at least ten axillary lymph nodes are dissected and examined for metastases in every breast carcinoma patient to find out the metastatic status. Recently however, with the use of intraoperative imprint cytologic examination of a single sentinel lymph node, presence or absence of metastases in axillary lymph nodes can be detected within five minutes.

Objectives The objective of this study was to determine sensitivity and specificity of imprint cytology in detecting metastases in axillary lymph nodes in breast carcinoma patients taking histopathological examination as the gold-standard. This is the first study of such kind done in Nepal so far. If it is done in other countries, why it is needed for Nepal?

Methods 34 female patients with breast cancer who had undergone lumpectomy/mastectomy with axillary lymphadenectomy were included in the study. Imprint smears of the axillary lymph nodes of each case were prepared. The smears were interpreted as positive or negative on the basis of whether metastases were present or absent respectively. Sensitivity and specificity of imprint cytology were calculated taking histopathologic diagnosis as the standard.

Results Of the 34 cases, 30 were found to have positive lymph node status in final histopathologic examination. Twenty six among the thirty cases were correctly identified by imprint cytology, resulting in its sensitivity rate of 86.66 percent. There were no false positive cases leading to the specificity rate of 100 percent.

Conclusion Imprint cytology has been found to be highly sensitive and specific method for detecting metastases in axillary lymph nodes of breast carcinoma patients.

Keywords Imprint cytology; Micrometastasis; Specificity; Sensitivity; Sentinel lymph node

Introduction

Among women, breast cancer is the most commonly diagnosed cancer after nonmelanoma skin cancer, and is the second leading cause of cancer deaths after lung cancer in the developed countries¹. The records of the year 2002 in Tribhuvan University Teaching Hospital showed that breast cancer is the second most common cancer in Nepalese women with 11.07 percent of the total².

The single most significant predictive factor of 10 and 20-year survival in breast cancer is the absolute number of axillary lymph nodes involved with metastases³. Traditionally, axillary lymph node

metastatic status has been evaluated by routine full axillary lymph node dissection in every breast carcinoma patient. The information thus obtained is used for staging the malignancy in an individual patient and for the selection of adjuvant therapy³. However, the only patients who are likely to derive therapeutic benefits from axillary lymph node dissection are those with positive nodes, approximately only 40 percent of those undergoing axillary dissection. In addition, axillary lymph node dissection is often associated with considerable chronic morbidity including lymphedema, neurologic damage to the brachial plexus and joint stiffness^{4,5}.

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These shortcomings of axillary lymph node dissection could be avoided if evaluation of a single or, at the most, a few lymph nodes could predict involvement of the axillary lymph nodes by tumor metastases. This has been possible exactly with the introduction of imprint cytology of the sentinel lymph node. A sentinel is the first lymph node which receives all the lymphatic drainage from an organ or a region of the body. This method is highly sensitive and specific for the aforementioned purpose. Moreover a number of studies have already proved that imprint cytology allows most patients who require an axillary clearance to be identified intra-operatively^{6,15}. Histological analysis of biopsy of breast lesions takes a minimum of 24 hours, but imprint cytology of a biopsy can be reported within about 5 minutes^{6,8}. The huge benefit breast cancer patients thus get is: axillary dissection can be done at the same time as the primary breast operation in node-positive cases without the need for a second trip to the operation theatre, whereas node-negative patients are spared of unnecessary total axillary lymphadenectomy⁴.

Material and Methods

Study type: This study was, cross-sectional comparative type. Department of Medicine, Dialysis Unit, Nepalgunj Medical College, Kohalpur

Study site: It was conducted in the Department of Pathology at Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal. Department of Medicine, Dialysis Unit, Nepalgunj Medical College, Kohalpur

Study population and specimen processing: 34 cases of breast cancer were collected in 12 months from February 15th, 2004 to Feb 14th, 2005. All female patients with breast carcinoma who had undergone tumor excision with axillary lymph node dissection were included in the study. Male patients with breast cancer were excluded. Those female patients in whom breast cancer excision was done but axillary lymph node dissection was not performed were also excluded from the research. Data were collected with the help of pre-formatted questionnaires.

Specimens of lumpectomy or mastectomy and axillary clearance were collected from the operation theatre before the specimens were immersed in the formalin solution. Easily palpable lymph nodes measuring, at least 0.5 cm in greatest dimension, up to seven in number per case, were examined in the study. A total of 174 lymph nodes were examined in thirty four cases. Each lymph node was bisected using sharp and clean scalpel along the longitudinal axis. Imprint (touch) smears were made from each of the cut surfaces. These imprint smears were stained with Giemsa staining solution. The corresponding lymph nodes were labeled separately, fixed in formalin and subjected to routine paraffin sectioning and staining with hematoxylin and eosin solution. Mastectomy specimens were similarly fixed in 10 percent buffered formalin for 24 hours before making histologic sections.

The imprint smears were interpreted as negative or positive on the basis of whether metastatic tumor cells were absent or present respectively. All cytopathology assessments were carried out without the previous knowledge of histopathological diagnosis. Correlation study between imprint cytological and histopathological diagnosis was carried out in order to find out sensitivity, specificity, positive and negative predictive values of imprint cytology method taking histopathological diagnosis as the gold standard.

Data analysis

The specificity and sensitivity values were calculated and interpretation was made in comparison with reference value.

Results

Among the study population, the age of patients ranged from 29 to 75 years with the mean of 44.6 years. Nearly two third (61.76%) of breast carcinoma occurred in the age group of 36 to 55 years. The most common histologic type of breast carcinoma was Infiltrating ductal carcinoma- not otherwise specified which constituted 73.53 percent of the total (Table no: 1).

Table 1: Histologic types of breast carcinomas in descending order of frequency

Histologic Type of Breast Carcinoma(WHO)	Number	Percentage
Infiltrating ductal carcinoma-NOS	25	73.53
Medullary carcinoma	4	11.77
Metaplastic carcinoma	2	5.88
Infiltrating tubulo-lobular carcinoma	1	2.94
Infiltrating papillary carcinoma	1	2.94
Mixed invasive ductal and lobular Ca	1	2.94
Total	34	100.00

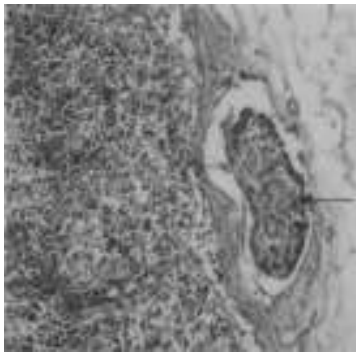
As the size of the tumor increased the number of lymph nodes with metastatic tumor cells also increased (Table no:2).

Table 2: Correlation of imprint cytology of lymph nodes with the histopathological finding

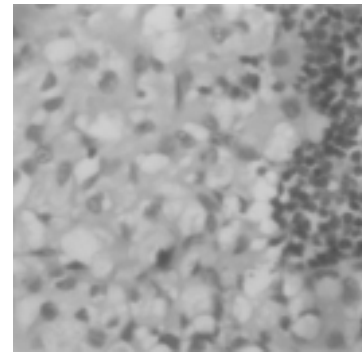
Metastatic Status	Imprint Cytology Number of Cases	Histopathological Diagnosis Metastatic Status		Total
		Positive	Negative	
Positive	26	30	04	34
Negative	08	-	-	-
Total	34	-	=	34

Out of the total 34 cases, thirty patients had metastatic carcinoma in their axillary lymph nodes on the basis of histopathological examination of the sections made from the lymph nodes. In other words, four patients did not have metastases in their lymph nodes. Imprint smears prepared from the sectioned surfaces of the lymph nodes correctly revealed metastases in 26 patients. In four patients who had

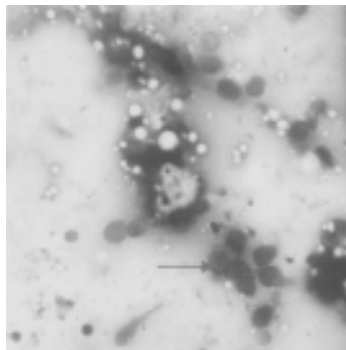
metastatic breast carcinoma cells in the histopathological sections, imprint smear gave negative result (Table no:3). Thus, the number of false negative cases was four but there was not a single case of false positive result. Among metastases missed by imprint cytology, two were micrometastases (size less than 2mm in maximum diameter) and two were macrometastases. (Photomicrograph: 1)



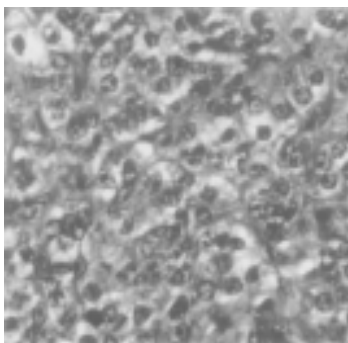
Photomicrograph 1: Micrometastasis located inside lymph node capsule in a case of IDC (NOS) -(H & E stain x 100)



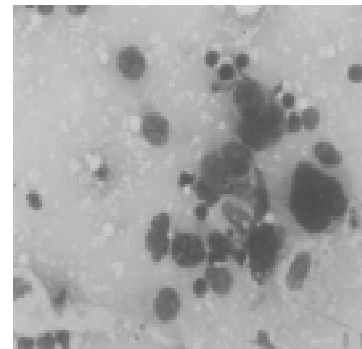
Photomicrograph 2: Histological section of lymph node metastasis in invasive tubulo-lobular carcinoma.



Photomicrograph 3: Imprint smear of lymph node metastasis in invasive tubulo-lobular carcinoma



Photomicrograph 4: Histological section of lymph node metastasis in invasive ductal carcinoma (NOS)



Photomicrograph 5: Imprint smear of lymph node metastasis in invasive ductal carcinoma - NOS

On the basis of the above findings, imprint cytology in this study has the following statistical results:

Sensitivity : 86.7%

Specificity : 100.00%

Discussion

Intraoperative imprint cytology of the sampled sentinel lymph nodes during operation is a well-accepted procedure in developed countries because of its high sensitivity and specificity in detecting metastases in axillary lymph nodes and that information can be used in deciding about axillary lymphadenectomy in individual cases⁴⁻¹⁵. The sensitivity and specificity of imprint cytology varies from as low as 53 percent to 100 percent in different studies^{4,5,6}. There are several factors influencing the results. In many studies the commonest reason for false negative imprint results was the presence of small metastases measuring less than 2mm (micrometastases)^{7,8,9}. Charles Cox et al found sensitivity of detecting micrometastases at 6.4 percent while the sensitivity of detecting macrometastases was 69.3 percent⁷. The value of 25 percent sensitivity for micrometastases is far lower than the figure 73 percent for macrometastases in another study done by Creager G et al⁶. Andrew J et al also found similar picture; 81percent versus 21 percent⁴. In the present study, there were only two cases with micrometastases and both of these were missed by imprint cytology. Two cases of invasive carcinoma (one was invasive ductal carcinoma NOS and another was mixed invasive ductal and lobular carcinoma) that had macrometastases in hematoxylin and eosin stained section were given false negative by imprint cytology. Thus the sensitivity for macrometastases came out to be 86.66 percent. Another variable affecting sensitivity of imprint cytology is 'lobular histology' of the breast carcinoma. We had a false negative diagnosis by imprint cytology in mixed ductal and lobular carcinoma. The metastasis in this case was of macrometastasis type. Another case of lobular carcinoma was of infiltrating tubulo-lobular carcinoma type and in this case the metastases in axillary lymph nodes were demonstrated by imprint cytology. Thus, sensitivity of imprint cytology in the detection of metastasis in lobular carcinoma came out to be 66.67 percent. Charles Cox et al found sensitivity of 38.7 percent in lobular carcinoma⁷. A research by AJ Creager et al also demonstrated similar picture with the sensitivity of 52 percent⁸. Metastatic lobular carcinoma is difficult to identify in imprint cytology because of its low-grade cyto-morphology, its tendency to infiltrate lymph nodes in a single cell pattern and because individual

cells can resemble lymphocytes. In addition, the cell-yield of FNAC in cases of lobular carcinoma is low because of desmoplastic reaction associated with these tumors⁸.

Conclusion

The current study has demonstrated that imprint cytology is highly specific and sensitive method to show presence or absence of metastases in axillary lymph nodes in breast cancer specimens. Although this study was not limited exclusively to sentinel lymph node, the method of preparing imprint cytology smears and microscopic analysis is the same once it is excised after its localization. Therefore imprint cytology can safely be used to know about the status of sentinel lymph node intraoperatively. To achieve the objective, close cooperation between surgical team and pathology unit is very important so that pathology report can be prepared within five minutes while the patient is still in the operation table.

It is the opinion of author that imprint cytology should be introduced in the major hospitals of Nepal where breast cancer surgery is being performed. However, further studies are needed to assess technical and administrative feasibility of imprint cytology in the real set-up of our hospitals¹.

It was also observed that metastatic status of lymph nodes was directly proportional to the size of the primary tumor.

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