Cytological Correlates of Axillary Nodal Involvement in Invasive Ductal Carcinoma of Breast

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Abstract

Context: Fine needle aspiration cytology (FNAC) plays an important role in the diagnosis of breast carcinoma. However, its role as a prognostic tool needs to be explored. This can be achieved by studying its correlation with an established prognostic marker such as axillary nodal metastasis. Aims: This study was undertaken to correlate the cytological features of invasive ductal carcinoma (IDC) of breast with axillary lymph node status. Settings and Design: Tertiary care hospital, retrospective analytical study. Materials and Methods: The study group included 150 cases of IDC of breast diagnosed on FNAC, who had subsequently undergone modified radical mastectomy. Cytologic grades were assigned as per Robinson’s grading system. Histopathological sections of axillary lymph nodes were assessed for metastasis. Statistical Analysis Used: The cytologic grade and each feature of the cytologic grade were correlated with the lymph node metastasis using \( \chi^2 \) test. Values of \( P < 0.05 \) were considered significant. Result: A statistically significant correlation was noted between cytologic grade of tumor and axillary lymph node metastasis \( (P < 0.05) \). In addition, a positive correlation was found between two of the individual features of cytologic grade, namely, nuclear size and cell uniformity with axillary lymph node metastasis \( (P < 0.05) \). Conclusion: Robinson’s cytologic grade of breast carcinoma correlates well with the presence of axillary lymph node metastasis and hence can be used as a prognostic tool. As there is an increasing trend toward conservative approach to management of breast carcinoma, patients receive preoperative neoadjuvant therapy which may alter the nodal status on the resected specimen. Hence, a high cytological grade of primary tumor, as assessed on FNAC before initiation of therapy, should alert the treating team of the possibility of axillary lymph nodal metastasis.

Keywords: Axillary nodal metastasis, fine needle aspiration cytology, invasive duct carcinoma, Robinson’s grading system

INTRODUCTION

Breast carcinoma is the most common malignancy among women worldwide and is also the leading cause of carcinoma death among women.[1] Prognosis of invasive ductal carcinoma (IDC) of breast is determined by anatomic extent of the disease as assessed by tumor size, nodal status and metastasis, and biologic markers such as histological grade, hormone receptor expression, HER2 overexpression, and/or amplification and genomic panels.[2]

Although the biologic factors are important predictors of survival, anatomic extent of the disease based on the TNM staging classification is still relevant worldwide, especially in those regions of the world where biological markers are not routinely available.[2] The TNM staging of disease continues to provide quantitative classification categories for the primary tumor (T), regional lymph nodes (N), and distant metastases (M), which are combined to determine overall stage groups which are associated with overall survival and disease-free survival.[2,3] Lymph node metastasis, therefore, is an important prognostic factor of the disease. The presence of metastatic cancer in axillary lymph nodes confirms the capacity of a cancer to metastasize. It represents the single most prognostically potent element of clinical stage in potentially curable cases.[4] Clinical evaluation of the axilla is inaccurate. Hence, axillary lymph node dissection and histological evaluation has a continuing place in the staging and management of patients with breast cancer.

Fine needle aspiration cytology (FNAC) is an established diagnostic modality in clinical practice. At many centers, it is
the only diagnostic procedure performed for invasive breast carcinoma before definitive surgery. The use of FNAC is restricted to ascertaining the benign or malignant nature of a tumor. However, various studies have demonstrated that cytological grade as assessed on FNAC correlates well with the histological grade. Still others have shown that cytological grade correlates well with the axillary lymph nodal metastasis and also prognosis. Robinson’s grading system is one such grading system, based on six cytological parameters. In addition, Robles-Frias et al. have also found that three of the cytological features evaluated in the Robinson’s grading system, namely, cell dissociation, cell uniformity, and nuclear margin, independently correlated positively with the presence of nodal metastasis. This study seeks to evaluate the prognostic value of FNAC in IDC of breast by correlating it with lymph node status which is an established prognostic marker.

**Materials and Methods**

A total of 150 cases of IDC of breast diagnosed on FNAC, who underwent modified radical mastectomy, comprised the study group. FNAC slides of the primary tumor and formalin-fixed, paraffin-embedded blocks of regional lymph nodes were retrieved from case files of the Department of Pathology of a large, referral teaching hospital.

Cytological evaluation of all primary tumors was done using Robinson’s system [Table 1]. The scores of each of the six features were added to arrive at a total score. Grade 1 was assigned to total scores ranging from 6 to 11, grade 2 to a total score ranging from 12 to 14, and grade 3 to a total score ranging from 15 to 18. Assessment of the nuclear size of tumor cells was done by comparing with adjacent red blood cells on the smear.

**Table 1: Robinson’s cytological grading system**

| Criterion          | Score 1 | Score 2 | Score 3 |
|--------------------|---------|---------|---------|
| Cell dissociation  | Cells in clusters | Single, with cell clusters | Mostly single cells |
| Nuclear size       | One to two times size of RBC | Three to four times size of RBC | ≥5 times size of RBC |
| Cell uniformity    | Monomorphic | Mildly pleomorphic | Highly pleomorphic |
| Nucleoli           | Indistinct/small | Noticeable | Prominent/abnormal |
| Nuclear margin     | Smooth | Folds | Clefts, buds |
| Chromatin pattern  | Vesicular | Granular | Clumped and cleared |

RBC: red blood cell

Hematoxylin-and-eosin-stained slides of axillary lymph nodes were analyzed for the presence of metastasis. Statistical analysis was done by SPSS statistical software package, version 14.0. The overall cytological grade and each feature of cytological grade were correlated with axillary lymph node status using χ² test; P < 0.05 was considered significant.

**Results**

The study group had adequate number of cases in each cytological grade, with cases having positive and negative axillary lymph nodal metastases within each grade. Of the 150 cases, 57 were assigned cytological grade 1, 54 were assigned cytological grade 2, and 39 cytological grade 3 [Figure 1]. Of these, 108 had axillary lymph nodal metastasis [Figure 2], whereas 42 did not have axillary lymph nodal metastasis. Whereas of the 57 grade 1 cases, 33 (57%) had and 24 (42%) did not have nodal metastases, among the 54 grade 2 cases, 45 (83%) had and 9 (16%) did not have nodal metastasis; and among the 39 grade 3 cases, 30 (76%) had and 9 (23%) did not have nodal metastasis. The cytological grade was correlated with the presence of axillary lymph nodal metastasis, and a statistically significant correlation (P < 0.05) was found [Table 2].

The score of each feature of the cytological grade was correlated with the presence and absence of axillary lymph nodal metastasis [Table 3]. For cell uniformity cytological
Scores 1, 2, and 3, 15 (13.9%), 45 (41.7%), and 48 (44.4%), respectively, showed lymph node positivity, whereas 15 (35.7%), 15 (35.7%), and 12 (28.6%) showed lymph node negativity. As the score increased from 1 to 3, there was an increase in the proportion of lymph node–positive cases and a decrease in the proportion of lymph node–negative cases. This feature showed a significant correlation with the overall lymph node status ($P < 0.05$). Also, for nuclear size cytological scores 1, 2, and 3, 9 (8.3%), 30 (27.8%), and 69 (63.9%), respectively, showed lymph node positivity, whereas 3 (7.1%), 27 (64.3%), and 12 (28.6%) showed lymph node negativity. As the score increased from 1 to 3, although there was an increase in the proportion of lymph node–positive cases, there was no reciprocal fall in the proportion of lymph node–negative cases. Notwithstanding this, nuclear size was found to correlate significantly with the overall lymph node status ($P < 0.05$). The other four cytological features did not show any correlation with the lymph node status.

**Conclusion**

Robbins’ cytologic grade of breast carcinoma correlates well with the presence of axillary lymph node metastasis and hence can be used as a prognostic tool. As there is an increasing trend toward conservative approach to management of breast carcinoma, patients receive preoperative neoadjuvant therapy which may alter the nodal status on the resected specimen. Hence, a high cytological grade of primary tumor, as assessed on FNAC before initiation of therapy, should alert the treating team of the possibility of axillary lymph nodal metastasis.

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**Conflicts of interest**

There are no conflicts of interest.
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