Original Article

Correlation between cytological and histological grading of breast cancer and its role in prognosis

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Aims: The present study was undertaken to grade breast carcinoma on cytology by Robinson’s grading system and correlate it with Elston’s modified Bloom Richardson histological grading system. Assigning grade to breast cancer on FNAC provides prognostic information and guides optimal therapy. Materials and Methods: It is a prospective study done on fifty cases of breast cancer reported on cytology. Thirty-four patients who underwent FNAC and mastectomy for breast carcinoma were cytologically and histologically graded. Correlation between cytological and histological grading system was determined. Sensitivity and specificity of Robinson’s cytological grading system was calculated in each grade. Results: Concordance rate between cytological and histological grade was 86%. The coefficient of correlation between cytological grade and histological grade was 0.879 and P value was 0.001 which indicated a strong correlation and significant association between the cytological and histological grade. Sensitivity was maximum in cytological grade I and grade III tumors (100%) and least in cytological grade II tumors (71.42%). Specificity was maximum in cytological grade II tumors (100%) and least in cytological grade I and III tumors (93.75%). Conclusions: Cytological grade strongly predicts histological grade and is useful in selecting neoadjuvant chemotherapy.

1. Introduction

The incidence of breast cancer in recent decades has increased worldwide, mainly due to improvements in screening and diagnosis, as well as to changes in the lifestyle and habits of women[1]. Breast cancer is the most common non skin malignancy in women and it is second only to the lung cancer as a cause of cancer death.[2] Incidence of breast cancer increases with age like that of other epithelial tumors. Patients with breast cancer will have very good prognosis if detected at an early stage.[3] According to GLOBOCAN 2012 project, breast cancer is the second most common cancer in the world with an incidence of 1.67 million cases. Breast cancer is the most common cancer in women in India, way ahead of cervical cancer. In India, 1,44,937 women were newly detected with breast cancer and 70,218 died of breast cancer. Male breast carcinoma accounts for less than 1% of all cases (male and female) of diagnosed breast cancer & less than 1% of all cancers in men.[4] Breast cancer incidence peaks between the ages of 40 and 50 years, with a mean age of occurrence at 47 years. Breast cancer patients in India mostly presents with palpable lump and with the lymph node metastasis at the time of diagnosis.[5]

A method of definitive diagnosis of the breast lesions is therefore needed in order to reassure the patient and to offer best possible treatment.[6] Grading of breast carcinoma has both therapeutic and prognostic significance. Cytological grading is done by Robinson grading system based on 6 parameters: cell dissociation, nuclear size, cell uniformity, nucleoli, nuclear margins, and nuclear chromatin, and is correlated by Elston & Ellis modification based on tubule formation, nuclear pleomorphism and mitoses. Each parameter is given a score of 1, 2 or 3. The scores are added up to get the total scores for grading the carcinomas.[7] FNAC has superseded the use of frozen section examination in the diagnosis and management of patients with breast cancer, and plays a major role as an important preoperative assessment along with clinical correlation and mammography which are referred to as the ‘Triple test’. [8]

This study aims to estimate the benefits of using Robinson grading system in fine needle aspiration for breast cancer and to estimate the correlation of Robinon grading system in fine needle aspiration and histological grading system of modified Bloom Richardson in breast cancer.

Materials and Methods

Thirty four cases of infiltrating duct carcinoma (IDC) breast, diagnosed on cytology, and undergoing surgery were included in the study. May-Grünewald-Giemsa (MGG) stained smears were evaluated and the tumor was graded based on the grading system described by Robinson et al. In the Robinson’s grading system, six...
different cytological parameters, namely cell dissociation, cell size, cell uniformity, nucleolus, nuclear margin, and nuclear chromatin were used to grade the tumors. A score of 1-3 was given to each of these parameters, and the tumor was graded by adding up the scores.

| Parameter          | Score 1  | Score 2  | Score 3  |
|--------------------|----------|----------|----------|
| Cell dissociation   | Mostly single cells, single cells/cluster | Mostly single cells, single cells/cluster | Mostly single cells, single cells/cluster |
| Nuclear size       | < 2 times the size of RBC | 2-4 times the size of RBC | > 5 times the size of RBC |
| Cell uniformity     | Monomorphic | Moderately pleomorphic | Pleomorphic |
| Nucleolus          | Indistinct/small, Not visible | Noticeable, Prominent | Abnormal |
| Nuclear margin     | Smooth | Slightly irregular/folds | Bulky, clumps |
| Chromatin pattern  | Vascular | Granular | Clumping |

Grade 1- Score of 3 to 5
Grade 2- Score of 6 to 7
Grade 3- Score of 8 to 9

Histopathological correlation was done wherever surgical biopsy specimen was received. All cases of Infiltrating Duct Carcinoma-Not Otherwise Specified type were graded as per modified Scarff Bloom Richardson’s criteria based on 3 parameters - amount of tubule formation, nuclear pleomorphism and mitoses. Each parameter was given a score of 1, 2 or 3 and the scores were added up to give the final grade as shown below:

| Parameter          | Score 1  | Score 2  | Score 3  |
|--------------------|----------|----------|----------|
| Tubule formation   | >75%     | 10 to 75% | < 10%   |
| Nuclear pleomorphism | Mild | Moderate | Marked |
| Mitotic count      | 0-5/10hpf | 6-10/10hpf | >11/10hpf |

The overall score for each case ranged from 3 to 9. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) statistical software package. P value <0.05 was considered statistically significant.

RESULTS

Of these 28 cases, 20 underwent a surgical procedure with the excision of the neoplasm. The cytological diagnosis of carcinoma was confirmed in all these cases. The breast aspirates were graded using the Robinson’s criteria and the results showed a Grade 1 category in 6 cases, Grade 2 category in 12 cases, and Grade 3 category in 10 cases. 20 cases were subsequently graded on histology using Elston’s modification of Bloom-Richardson grading system.

| Cytological grade | Histological grade | Total no of cases |
|-------------------|--------------------|-------------------|
|                   | I      | II     | III    |        |
| I                 | 4      | 10    | 0      | 5      |
| II                | 0      | 10    | 0      | 10     |
| III               | 0      | 1     | 4      | 5      |
| Total no of cases | 4      | 12    | 4      | 20     |

Table 1: Cytohistopathological grading of infiltrating duct carcinoma-NOS type

Table 2: Comparison of case distribution between the cytological and histological grades

| Grade | No of concordant cases between each cytological grade and histological grade | No of cases in each cytological case | Concordance rate (%) | Kendall’s tau-b Correlation coefficient(r) |
|-------|-------------------------------------------------------------------------|------------------------------------|----------------------|-------------------------------------------|
| I     | 4                                                                       | 5                                  | 80                   | r: 0.879**** p: 0.001                      |
| II    | 10                                                                      | 10                                 | 100                  |                                           |
| III   | 4                                                                       | 5                                  | 80                   |                                           |
| Total | Total 18                                                                | Total 20                           | 96                   |                                           |

Table 3: Comparison of concordance rates between the cytological and histological grade

| CYTOLICAL GRADE | NUMBER OF POSITIVE CASES | NUMBER OF NEGATIVE CASES | SENSITIVITY(%) | SPECIFICITY(%) |
|-----------------|--------------------------|----------------------------|----------------|---------------|
|                 | TRUE         | FALSE | TRUE | FALSE |               |               |
| I               | 4            | 1     | 15   | 0     | 100            | 93.75          |
| II              | 10           | 0     | 6    | 4     | 71.42          | 100            |
| III             | 4            | 1     | 15   | 0     | 100            | 93.75          |

Table 4: Sensitivity and specificity of Robinson cytological grading system

Table 5: Comparison of concordance rates in different studies with the present study employing Robinson’s cytological grading system

| Studies                        | Concordance rate(%) |
|--------------------------------|---------------------|
| Das et al[14]                  | 71.2                |
| Chhabra et al[13]              | 65                  |
| Sultana and rehman[15]         | 86.3                |
Figure 1: (a) Cytological grade I tumor showing cohesive clusters of cells with smooth nuclear membranes, vesicular chromatin, and inconspicuous nucleoli (MGG stain, x1000). (b) Cytological grade II tumor showing cells having visible nucleoli, granular chromatin, and moderate pleomorphism (MGG stain, x1000). (c) Cytological grade III tumor showing cells with highly pleomorphic nuclei, prominent nucleoli, and budding of nuclear membrane (MGG stain, x1000)

Discussion

FNAC is a routinely used investigation for rapid diagnosis of breast cancer. The ability to predict the accurate grade on cytology smears would add to the diagnostic value of FNAC, without any additional morbidity or expense for the patients. The purpose of prognostic grading on cytology is to identify high-grade tumors that are more likely to respond to chemotherapy than the low-grade tumors, which may be better suited to pretreatment with tamoxifen[9]. Of the various cytological grading methods described for breast cancer, the method proposed by Robinson et al[10] has been widely accepted. The concordance rate between the cytological grade (using Robinson’s method) and histological grade, obtained in our study, was 78% that was found to be fairly comparable to that reported by previous studies [Table 5][11,12,13-21].

The lack of correlation between cytological and histological grading in 14% of our cases may be the presence of varying degrees of atypia within the same tumor and interobserver subjectivity when assigning a cytological nuclear grade [21]. Another possible reason for the discordance may be the difficulty in identifying features such as nuclear margins (smooth/buds/folds), chromatin clumping, and granularity on cytology smears[13]. We found a statistically significant correlation between the cytological and histological grade with a “r” = 0.879 and P value of <0.001 [Table 3].

In the present study, we found sensitivities of 100%, 71.4%, and 100% for cytological grade I, II, and III tumors, respectively. Sultana and Rehman[15] reported lowest sensitivity of cytological grade III tumors (37.50%) as compared to 96.96% for cytological grade I and 87.18% for cytological grade II tumors. We found that Robinson’s cytological grading system was highly specific for cytological grade II tumors (100%), while it is moderately specific for grade I tumors (93.75%) and grade III tumors. This low specificity could also be due to the variation in cytological features in different areas of tumor on histology, which cannot be appreciated in cytology because of limited area of approach (93.75%).

Although many studies have been conducted on cytological grading of breast cancer, only a few of them have calculated the sensitivity and specificity of cytological grading system in each grade. In this study, we have separately calculated the sensitivity and specificity of Robinson’s cytological grading system in each grade that conveys how accurately this system has diagnosed the grade I, II, and III cases on cytology. Cytological grading on FNAC smears provides information about the aggressiveness of the tumor, which is a crucial parameter for selecting neoadjuvant chemotherapy/hormonal therapy. FNAC is especially useful in low-resource settings, where core biopsy is not routinely performed for diagnosis, and the treatment is often based on the cytology report itself. The National Cancer Institute (NCI), Bethesda, sponsored conference has recommended that tumor grading on FNAC material should be incorporated in cytology reports for prognosis [22].

Conclusion

Our study shows that it is possible to grade breast cancer on fine-needle aspirates and that the cytological grade corresponds well with the histological grade. The cytological grade also provides relevant prognostic information regarding the aggressiveness of the tumor. Thus, it is suggested that a conscious effort should be made to include the cytological grade in all the FNAC reports of breast cancer so as to guide the surgeon regarding the judicious use of neoadjuvant therapy and hence avoiding overtreatment of low-grade cancers.

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