Original Article

Usefulness of Cytological Grading in Predicting Tumor Behavior in Breast Carcinoma-An Institutional Experience

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ABSTRACT

Background: Breast carcinoma is a frequently encountered malignancyand several modifications are under-way in the management of breast malignancies including Neo-adjuvant chemotherapy.In this context to give an idea to the oncologist about the behavior of the tumor through FNAC is becoming increasingly expected.So,in this study an attempt has been made to compare cytological grading with histological grading and the usefulness of cytology alone in predicting tumor behavior has been evaluated.

Methods: 40 cases of breast carcinoma for which both cytological samples andhistological specimens are available are included in the study.Robinson's method is used for cytological grading.Elstonand Ellis modification of Bloom-Richardson grading method is used for histological grading.The exactness of cytological grading is compared by its concordance with histological grading.

Result: 83.6% of overall concordance of cytological grading was obtained.

Conclusion: Based on the fairly good level of concordance between cytological and histological findings in the study,it can be concluded that Robinson's method of cytological grading is a fairly dependable method that can be used to give an exact idea to the oncologist about the tumor behavior

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Introduction

Breast carcinoma is the most common malignant tumor and the leading cause of cancer deaths in women with more than 1,000,000 cases occurring worldwide annually.[1] Accurate diagnosis of breast cancer is made in 99% of cases by the combination of clinical examination, mammography and simple, noninvasive, cost-effective outpatient department procedure, fine-needle aspiration cytology (FNAC). Technique of FNAC has wide applicability and utility for the tumors which are easily palpable on external examination.[2],[3] In developed world, the practice and usefulness of breast FNA have been overshadowed by core needle biopsy. On the contrary, in developing countries like India, even today, the core needle biopsy is still not practiced routinely at most of the medical centers. The treatment of breast carcinoma cases is begun with the first hand diagnosis made on FNAC. Moreover, for resource-poor countries, FNA in comparison to core needle biopsy, is cheaper, less invasive, can sample different areas of the lesion in the same sitting at no added expenses and usually fetch good results the same day.[4],[5] The acceptance of FNA report reliability both by surgeons and pathologists allows for radical surgery on the basis of an FNA diagnosis. Regrettably, instead of signing a more precise "surgical pathology" type diagnosis on FNA, its widest application is limited to just categorizing the breast lesion as benign or malignant. The prognostic markers important for deciding the treatment modality should be conveyed to the surgeon, as recognition of the aggressiveness of the disease is central to the effective medical management of breast cancer and avoid the needless morbidity.[6],[7],[8].With the advent of neo-adjuvant chemotherapy,the need for giving an idea of the aggressiveness of the tumor by FNAC has further more increased.

Of the different cytological grading (CG) methods corresponding to Elston-Ellis modified SBR HG, the method described by Robinson et al,[9]was found to be useful in grading breast carcinoma in fine needle aspiration .The present study not only applies the Robinson grading system but also studies its concordance with histological grading system, Elston and Ellis Nottingham modification of Bloom and Richardson method.

Materials and Methods

The work represents the retrospective andprospective study of breast carcinomas diagnosed onFNAC in the Department of Pathology from January2013 to January 2016. 40 cases of infiltrating duct cellbreast carcinoma diagnosed on FNAC and confirmed on histology were included in the study. FNAC was done by using 10 ml syringewith 22-23 gauge needle using aseptic standardtechnique. Smears were alcohol fixed and stained with H&E,alsoair dried and stained withleishman'sstain. Cytological features were carefullyevaluated and breast carcinomas were graded usingRobinson's grading system[9]. Six parameters viz. Cell dissociation, Cell size, Cell uniformity, Nucleoli,Nuclear margin and Chromatin pattern were carefullyevaluated. [Table 1].

After observing cyto-morphology of these six criteria,each criteria was given one to three score. Sum ofeach score of these criteria was added and based on total score, breast cancers were graded viz. Grade Iwith score of 6 to 11, Grade II with score of 12-14and Grade III with score of 15-18.

Surgical specimens received for histopathological examination were fixed in 10% formalin. Three to foursections were taken from tumor and paraffinprocessed. Three to five thick micron sections werecut and stained with Haematoxylin and Eosin stain[H&E]. Histological typing of tumors was done according to world health organization (WHO) 2003.[10] Histological grading was done according toElston's and Ellis's modification of Bloom-Richardson method.[11]Criteria such as tubule formation, nuclear morphology and mitotic count were evaluated. [Table 2] Cytological and histological grades were correlatedto find the concordance between the two grading systems.

Tabel-1 cytological grading by Robinson's system

score	1	2	3
Cell dissociation	Cells mostly in clusters	Mixture of single cells and clusters	Mostly single cells
Cell size	1-2 times size of RBC	3-4 time size of RBC	>= 5 times size of RBC
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent or Pleomorphic
Nuclear margins	Smooth	Slightly irregular/folds and grooves	Buds and clefts
Chromatin	Vesicular	Granular	Clumped and cleared

Table-2 Histological grading of breast carcinoma.(Elston and Ellis modified Bloom and Richardson grading system) (Nottingham's grading)

score	1	2	3
Tubule formation	Tubular formation in > 75 % of the tumor	Tubular formation in 10 to 75 % of the tumor	Tubular formation in < 10 % of the tumor
Nuclear pleomorphism	Nuclei with minimal variation in size and shape	Nuclei with moderate variation in size and shape	Nuclei with marked variation in size and shape
Mitotic count per 10 high power fields	0-5/hpf	6-10/hpf	>11/hpf

Results

Tables 3,4 show the results of cytological grading of breast cancer clearlyshowing that moderately differentiated tumors constituted the majority followed by poorly differentiated and then well differentiated tumors.

Similar pattern is also observed with histological grading as shown in Tables 5,6.

The cytological pictures of grade 1,grade 2,grade 3 are depicted in Figures1,2,3.

Regarding concordance of CG with HG, out of the 6 cases cytologically graded as grade 1,4 cases were histologically grade 1 and 2 cases were histologically grade 2.Thus the concordance of CG with HG would be 66% for grade 1 tumors.

With respect to grade 2,out of the 27 cases cytologically graded as grade 2,only 23 cases were histologically grade 2.Among the remaining 4 cases,3 cases were histologically grade 1,one was histologically grade 3.Thus the concordance of CG with HG would be 85% for grade 2 tumors.

With respect to grade 3 tumors,all the 7 cases that were cytologically grade 3 were also graded as grade 3 on histology.Thus the concordance rate for grade 3 tumors is 100%.The overall concordance rate between CG and HG would be 83.6%.

Chi-square test was done and a chi-square value of 0.2205,degree of freedom of 2 and pvalue of 0.8956 was obtained

Table 3-scores of all the 6 cytological features

Cytological feature	No of cases with score 1	No of cases with score 2	No of cases with score 3
Cell dissociation	10	21	9
Cell size	6	23	11
Cell uniformity	7	26	7
Nucleoli	6	29	5
Nuclear margins	4	30	6
Chromatin	5	28	7

Table-4 cytological grading based on the total score obtained

Total Score	Grade	Degree of Differentiation	No of cases	Percentage of cases
6-11	I	Well differentiated	6	15%
12-14	II	Moderately differentiated	27	67.5%
15-18	III	Poorly differentiated	7	17.5%

Table-5 showing scores of histological features

Histological feature	Score 1	Score 2	Score 3
Tubule formation	6	27	7
Nuclear features	10	24	6
Mitotic count	7	28	5

Table-6 showing histological grading based on total score obtained

Total score	Grade	Degree of differentiation	No of cases	percentage
3-5	I	Well differentiated	7	17.5%
6-7	II	Moderately differentiated	25	62.5%
8-9	III	Poorly differentiated	8	20%

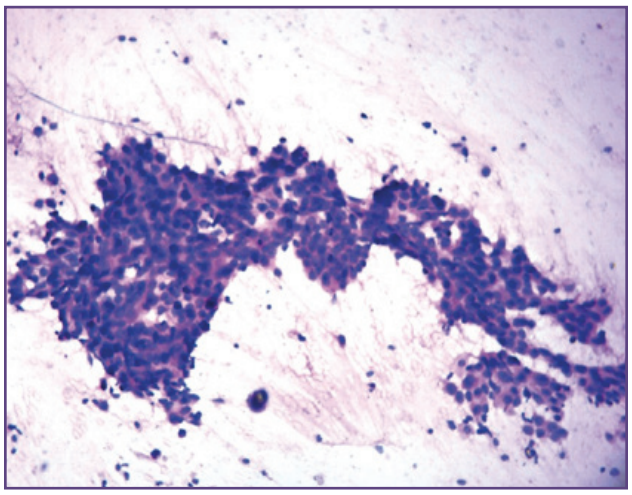

Fig. 1: showing the features of cytological grade1

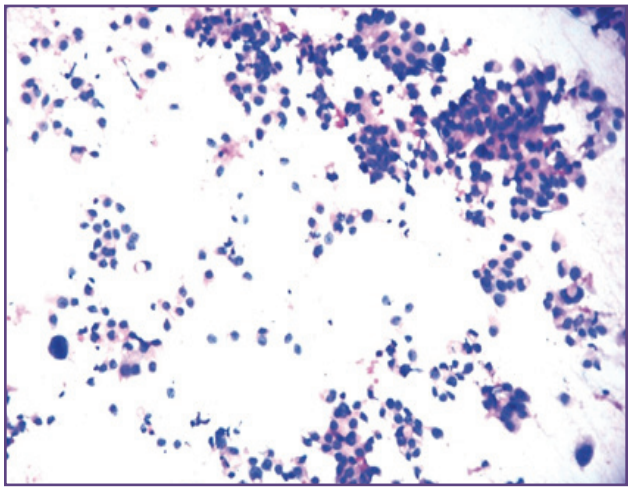

Fig. 2: showing the features of cytological grade 2

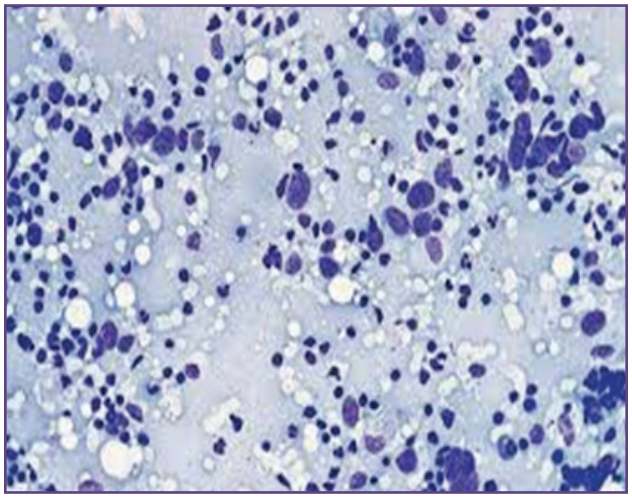

Fig. 3: showing the features of cytological grade 3

Discussion

Breast cancer is one of the most common causes of death in many developed countries in middle-aged women and is becoming frequent in developing countries. In India, breast cancer is the second most prevalent cancer in women after cervical cancer. [12]

The idea of CG is to assess the tumor in situ, so that the most suitable treatment could be selected immediately, and the morbidity associated with overtreatment of low grade tumors could be avoided. According to uniform approach to breast FNAC as recommended by the National Cancer Institute, tumor grading on FNA material should be in reports of FNAC for prognostication. [13]Again simultaneous performance of CG and HG helps in measuring accuracy of CG in breast carcinoma. Histological concordance gives the cytopathologist a feedback and helps in increasing the efficiency of work.

Various CG systems of breast carcinoma are presently in use. Robinson's grading system is found to be better in various studies because of its simplicity, specificity and reproducibility. [14],[15],[16],[17]It uses six different parameters namely; cell dissociation, cell size, cell uniformity, nucleolus, nuclear margin and nuclear chromatin. Robinson's CG had a concordance rate ranging from 56.9% to 89.1% with HG in different previous studies. [18]

In the present study, out of total 40 cases, 06 (15.0%), 27 (67.5%) and 07 (1.57%) cases were graded as grade I, II and grade III respectively. Hence majority of cases were in CG grade II which is comparable with previous studies. Robinson et al. in their study of 608 cases had the distribution of cases as 38.3%, 38.5% and 23.2% in cytological grades I, II and III respectively. [9] Pandit and Parekh et al. graded 75 breast carcinomas by same method and found 34.7% each in grades I and II, and 30.6% in grade III. [19]A similar study was carried out using Robinson's criteria by Das et al. showed that 28.8% cases were grade I, 46.2% as grade II and 25.0% as grade III. [14] The result of the present study showed similar concordance with these studies.

Regarding concordance of CG with HG, the present study showed 66% concordance in grade I, and 85% concordance in grade II and100% concordance in grade III. The overall concordance of CG with HG is 83.6% which is comparable with other published data. The original study by Robinson et al. found only 57% concordance, while Das et al., Sinha and Sinha and Lingegowda et al. found 71.2%, 73.0% and 64.0% concordance between CG and HG respectively. [9],[16],[20],[21]Sood et al. found highest concordance (75%) in grade I tumors and lowest (60%) in grade III tumors with overall concordance of 68.67%.[22] A study carried out by

Saha et al. found absolute concordance of 77.19% between CG and HG using Robinson's grading system involving 57 cases of breast carcinoma. [17]

P value of 0.8956 shows that the discordance between CG and HG is statistically not significant and cytological grading by Robinson's method is a reliable replica of Nottingham's histological grading system.

Majority of discordance between CG and HG was observed in grade I tumors (4/6). Of the 6 cases graded as grade I by CG, only 4 cases were graded as grade I by HG and other 2 cases were graded as grade II. In the majority of cases there is one grade difference. Similar results were obtained by Pandit and Parekh et al. [19] and Das et al. [14]. Among the 40 cases,3 cases were undergraded by one grade and similarly another 3 cases were overgraded by one grade

Histological grading was based on the degree of tubule formation, mitosis and nuclear pleomorphism. As tubule formation and mitotic index were difficult to assess on cytology, it might be the cause of discordance between cytological and HG systems.[23-25]In CG, much importance have been given to nuclear features like nuclear size, nucleoli, nuclear membrane and chromatin pattern in contrast to HG; in which nuclear feature in only one component. This can also lead to cytohistological disparity in grading of breast carcinomas.

Current management of breast carcinoma relies on various clinical and pathological prognostic andpredictive factors for guiding the selection of treatment options.The three main prognostic determinants used in routine practice are lymph node status,tumor size and histological grade. Nottingham grading system used in the present study for comparison of the cytological grading is the grading system recommended by various bodies.[14,26]Higher concordance values of the Robinson's cytological grade with the internationally accepted Nottingham's histological grade would mean that the Robinson's cytological grading system can be universally used for clinical decision making even beforesurgical intervention is contemplated.This would be the dawn of accessibility of morebetter treatment options.

Conclusion

In the present study, a high degree of concordance was seen between cytological and HG system. Preoperative grading using FNAC helps in determining neo adjuvant chemotherapy as well as prognostication. This grading system is relatively a new approach in diagnostic pathology, and its arena is ever increasing. The method is in its infancy. It could be said in confidence that this grading system will be fruitful in prognostication of malignant breast lesions and may become mandatory in the near future

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Competing Interests

None declared

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