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ROBINSON CYTOLOGICAL GRADING OF BREAST CARCINOMA ON FINE NEEDLE ASPIRATION CYTOLOGY- AN OVERVIEW

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ABSTRACT

Aim: *To find out utility of grading breast carcinoma on fine needle aspiration (FNA) as per the criteria proposed by Robinson and Colleagues and compare it with histological grading proposed by Elston and Ellis based on method by Nottingham's modification of Bloom and Richardson system.* ***Methods:*** *Cytological smears of 58 cases of breast carcinoma diagnosed on fine needle aspiration cytology (FNAC) were graded according to the Robinson grading system. The corresponding histological sections were classified as per the classification proposed by World Health Organization (WHO) in 2003 and histological grading was done by Elston and Ellis's modification of Bloom-Richardson method.* ***Results:*** *Cytological grading showed an absolute correlation with the histological grade in 82.76% cases.* ***Conclusion:*** *Cytology grading proposed by Robinson and colleagues could be a useful parameter for selection of neoadjuvant therapy and for predicting the prognosis of the patient on fine needle aspiration cytology alone.*

KEY WORDS

Fine needle aspiration, breast carcinoma, cytological grading, histological grading.

INTRODUCTION

Breast carcinoma is the most common malignant tumor and the leading cause of death in women with more than 1,000,000 cases occurring worldwide annually. The value of histological typing and grading of breast carcinoma is well established. Histological grading of breast carcinoma using Nottingham method described by Elston and Ellis [1] (Modified Bloom-Richardson system) is a widely accepted tumor grading system and has been found to have good prognostic correlation. Neoadjuvant therapy is becoming increasingly popular as primary medical treatment for breast cancer. There is much to be gained by grading a tumor on FNAC. Of the different cytological grading methods corresponding to Elston and Ellis's histological grading, method described by Robinson IA et al. was found to be useful in grading breast carcinoma in fine needle aspirates. [2]

The purpose of the present study is to find utility of grading breast carcinoma on FNAC as per the criteria proposed by Robinson and colleagues in 1994 and compare it with histological grading based on method proposed by Nottingham's modification of Bloom and Richardson system by Elston and Ellis.

MATERIALS AND METHODS

The work represents the retrospective and prospective study of breast carcinomas diagnosed on FNAC in the Department of Pathology from January 2008 to July2012. **Inclusion criteria**: 58 cases of breast carcinoma diagnosed on FNAC and confirmed on histology were included in the study. **Exclusion criteria:** Breast carcinoma diagnosed on FNAC but not confirmed on histology. Out of these 58 cases, 48 were infiltrating duct carcinoma (NOS), four invasive papillary carcinomas and two each, mucinous

carcinomas, medullary carcinomas and sarcomatoid carcinomas. FNAC was done by using 10 ml syringe with 22-23 gauge needle using aseptic standard technique. Smears were air dried and stained with Leishman's stain. Cytological features were carefully evaluated and breast carcinomas were graded using Robinson's grading system. Six parameters viz. Cell dissociation, Cell size, Cell uniformity, Nucleoli, Nuclear margin and Chromatin pattern were carefully evaluated. [**Table 1**]

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

Surgical specimens received for histopathological examination were fixed in 10% formalin. Three to four sections were taken from tumor and paraffin processed. Three to five thick micron sections were cut and stained with Hematoxylin and Eosin stain [H&E]. Histological typing of tumors was done according to world health organization (WHO) 2003. [3] Histological grading was done according to Elston's and Ellis's modification of Bloom-Richardson method [1]. Criteria such as tubule formation, nuclear formation, and mitotic count was evaluated. [**Table 2**] Cytological and histological grades were correlated to find the concordance between the two grading systems.

Table 1: Cytological grading according to Robinson's Grading 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)

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

Table 3 to 8 show score of six features on FNAC in 58 cases. Maximum number of cases of carcinomas were moderately differentiated (n=44), followed by poorly differentiated (n=8) and well differentiated (n=6). [**Table 9**] **Table 10 to 12** show score of three features on histopathology. On the basis of histological grading, maximum number of carcinomas (n=38) were moderately differentiated, followed by poorly differentiated (n=14) and well differentiated (n=6). [**Table 13**] Out of 58 cases 82.76% cases (n=48) showed an absolute cytohistological correlation [**Table 14**]. The correlation of cytological and histological grades of 8 special varieties of carcinoma

viz. four invasive papillary, two mucinous, medullary and sarcomatoid carcinoma each was found to be 100%.

Table3: Score of cell dissociation in 58 cases.

Score	No. of cases	Percentage of cases(%)
1	14	24.14
2	40	68.96
3	4	6.90

Table 4: Score of cell size in 58 cases

Score	No of cases	Percentage of cases (%)
1	2	3.45
2	8	13.79
3	48	82.76

Table 5: Score of cell uniformity in 58 cases

Score	No of cases	Percentage of cases (%)
1	2	3.45
2	8	13.79
3	48	82.76

Table 6: Score of nucleoli in 58 cases

Score	No of cases	Percentage of cases (%)
1	6	10.35
2	44	75.86
3	8	13.79

Table 7: Score of nuclear margins in 58 cases

Score	No of cases	Percentage of cases (%)
1	4	6.90
2	52	89.65
3	2	3.45

Table 8: Score of chromatin pattern in 58 cases

Score	No of cases	Percentage of cases (%)
1	8	13.79
2	48	82.76
3	2	3.45

Table9: Cytological grading with respect to their degree of differentiation in 58 cases

Total Score	Grade	Degree of Differentiation	No of cases	Percentage of cases (%)
6-11	I	Well differentiated	6	10.35
12-14	II	Moderately differentiated	44	75.86
15-18	III	Poorly differentiated	8	13.79

Table10: Scores of tubule formation in 58 cases.

Score	Tumor area showing tubule formation	No of cases	Percentage of cases (%)
1	>75 %	2	3.45
2	10- 75%	36	62.07
3	<10%	20	34.48

Table11: Scores of nuclear features in 58 cases.

Score	Nuclear pleomorphism	No of cases	Percentage of cases (%)
1	Mild	6	10.35
2	Moderate with visible nucleoli	42	72.41
3	Marked with prominent nucleoli	10	17.24

Table12: Scores of mitotic count in 58 cases.

Score	Mitotic count per10 high power field.	No of cases	Percentage of cases (%)
1	0-5	2	3.45
2	6-10	22	37.93
3	>11	34	58.62

Table 13: Histological grading in 58 cases with respect to their degree of differentiation

Total Score	Grade	Degree of Differentiation	No of cases	Percentage of cases (%)
3-5	I	Well Differentiated	6	10.35
6-7	II	Moderately Differentiated	38	65.51
8-9	III	Poorly Differentiated	14	24.14

Table13: Comparison of cytological and histological grades of carcinoma in 58 cases.

Cytological Grade	Histological Grade			
	I	II	III	
I	6	0	0	6 (10.35%)
II	0	36	8	44 (75.86%)
III	0	2	6	8 (13.79%)
Total	6 (10.35%)	38 (65.51%)	14 (24.14%)	58

Table 14: Comparison of absolute concordance of histological and cytological grade by various workers

Study	Year	Correlation (%)
Kapila K et al.	1986	77.44
Das A K et al.	2003	71.2
Robles-Frias A et al.	2005	97
Meena SP et al.	2005	83.10
Present study	2008	82.76

DISCUSSION

The advantages of FNAC in the diagnosis breast carcinoma have been known since a long time but grading of the breast carcinoma on FNAC has been underestimated. In our study, we have attempted grading of carcinoma breast on FNAC as per the criteria proposed by Robinson and colleagues in 1994. (**Table 1**) Besides infiltrating duct carcinoma (NOS), a cytological grading of special varieties of breast carcinoma viz. Invasive papillary carcinoma, Mucinous carcinoma, Medullary carcinoma and Sarcomatoid carcinoma was also done. As proposed by Robinson IA et al. [2], we used six criteria to facilitate grading. These were cell dissociation, cell size, cell uniformity, character of nucleoli, nuclear margin and chromatin pattern. Each criterion was given one to three score. Sum of total score of all criteria was calculated. 58 cases were diagnosed as breast carcinoma by FNAC.

After scanning the slide comment was made on cell dissociation. 68.96% (n=40) cases were given score 2 followed by 24.14% (n=14) cases of score 1 and 6.90% (n=4) cases of score 3. Cell size was assessed by comparing the size of tumor cell with adjacent red blood cell present in the aspirate. 82.76% (n=48) of cases were given score 3 followed by 13.79% (n=8) of score 2 and 3.45 %(n=2) cases of score 1. 82.76 % (n=48) were given score 3 for cell uniformity followed by 3.79 %(n=8) cases of score 2 and 3.45 %(n=2) of score 1. In nucleoli, 75.86% (n=44) of cases got score 2, 13.79% (n=8) of cases got score 3 and 10.35% (n=6) got score 1. After assessing nuclear margin, 89.65 %(n=52) of cases were given of score 2 followed by score 1in 6.90 %(n=4) cases and score 3 in 3.45 %(n=2) cases. In nuclear margins, 89.65% (n=52) were given score 2, 6.90% (n=4) were given score 1and 3.45% (n=2) cases were given score 3. Morphology of chromatin in 82.76% (n=48) got score of 2, 13.79% (n=8) got score 1and 3.45(n=2) cases got score 3. After observing morphology of these six criteria, a sum of the scores of each criteria contributed to cytological grade of breast carcinoma. On the basis of cytological grading, 75.86% (n=44) cases were moderately differentiated followed by 13.79 %(n=8) cases of poorly differentiated and 10.35 %(n=6) were well differentiated. Mucinous carcinoma (n=1) and medullary carcinoma (n=1) were put into well and moderately differentiated category respectively. Histopathological grading was done using Elston and Ellis Nottingham modification of Bloom and Richardson method. Out 58 breast carcinoma, 48(82.76%) were infiltrating duct carcinoma (NOS), two cases each of medullary, mucinous and sarcomatoid carcinomas and four cases of invasive papillary carcinoma. Three histological features viz. tubule formation, nuclear pleomorphism and mitotic count were evaluated. Each of which were given 1 to 3 score.

1) Tubule formation – After scanning all parts of tumor, assessment of percent of tubule formation in particular tumor was made. Tubules which showed lumen were counted. Care was taken not to mistake clefts induced by shrinkage artifacts for tubules. 62.07 %(n=36) cases were given score of 2, followed by 34.48 %(n=20) cases of score 3and only 2 (3.45%) cases score of 1.

2) Nuclear pleomorphism- Tumor areas having cells with greatest atypia were evaluated. 72.41 %(n=42) cases were given score of 2, followed by 17.24 %(n=10) cases of score 3. Score 1 was given to10.35 %(n=6) cases.

3) Mitotic count- Peripheral areas of tumor were selected for mitotic counting, as it was the most active part of the tumor. Mitotic figures per 10 high power fields were calculated and scored accordingly. 58.62 %(n=34) were given score 3 followed by 37.93 %(n=22) cases of score 2. Only 3.45% (n=2) cases were given score 1.Total score was given after adding score of all 3 criteria and the tumors were graded as Grade I,II and III viz. well, moderarately and poorly differentiated carcinoma respectively. On the basis of histological features, 65.51 %(n=38) were moderately differentiated, 24. 14 %(n=14) were poorly differentiated and 10.35 %(n=6) were well differentiated.

Cytology grading was correlated with histological grading. Robinson IA et al[2] reported equal importance to all these mentioned criteria. However, we found that the features on FNAC which showed the closest correlation with histological grade were cell dissociation, character of nucleoli, nuclear margin and chromatin.

In the present study, the criteria of cell dissociation for grading could be easily assessed. Wallgren et al. first evaluated this feature and found it to be useful

for cytological grading.[4] This was used by other workers in further studies for cytological grading of breast carcinoma.[2,5-9]

The presence or absence of nucleoli was found to be a useful feature in cytological grading and correlated well with the histological grade of the tumor. The observations by Black M et al. [10](1956), Moriquand J et al. [6](1986), Hunt CM et al. [11] (1990), Dabbs D[12](1993) and Zoppi JA et al. [13](1997) are in agreement with the importance of this criteria for grading purpose.

The present study also included features of nuclear margins and character of chromatin in deciding the cytological grade. Our observations were in correlation with findings of other workers. [2, 4, 6, 7, 10-13]

In the present study, cytology grading showed an absolute correlation with the histological grade in 82.76% (n=48) cases. [**Table 15**] Various workers have correlated the cytological and histological grading to see whether the agreement was good enough for cytological grading to substitute for histological grading.[7-9,14] They found cytology grading was feasible and reproducible for assessing biological aggressiveness of the cancer without surgical intervention.

Lack of good correlation between cytological and histological grading reported by earlier workers could be due to their using the relatively subjective grading system of Bloom and Richardson in 1957.[7] Robinson IA et al further improved correlation with histological grading by defining 6 criteria assessed by a scoring system [2]. They reported that every cytological feature had a significant relation to the histological score and each was related to the others. Other workers graded the tumors on cytology by Robinson grading system and on histology by Elston and Ellis's modified Bloom and Richardson system with better correlation comparable to that in the present study. [8, 9, 14]

CONCLUSION

Cytological grading of infiltrating duct carcinoma (NOS) as well as special varieties of breast carcinoma correlates well with histological grading. Evaluation of cytology grade using FNAC permits determination of the aggressiveness of breast carcinoma. It is a useful parameter to take into consideration when selecting neoadjuvant therapy for breast carcinoma.

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