Robinson Cytological Grading of Invasive Ductal Carcinoma of Breast And Comparison with Histological grading

Dr. Jigna P. Prakashbhai Patel [1] , Dr. Trupti Rajeshbhai Jansari [1] , Dr, Jasmin Jasani [1]

1 Assistant Professor, Department of Pathology, Smt BK Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth an institution deemed to be UniversityPiparia 391760 Vadodara Gujarat

***Corresponding author**

Dr. Trupti Jansari

Department of Pathology

Smt BK Shah Medical Institute & Research Centre,

SumandeepVidyapeeth an institution deemed to be University

Piparia 391760 Vadodara Gujarat

Email: creativity.art.j@gmail.com

Phone no. : +9727079195

ABSTRACT

Background

Diagnosis of breast carcinoma is still made on fine-needle aspiration cytology (FNAC) in developing countries. Instead of merely reporting as benign or malignant, we should focus on extracting the maximum prognostic information from cytological smears so this will help clinicians to enhanced effects on the survival of patients using new chemotherapeutic agents.

The Robinson et al introduce cytological grading system which is well corresponds to the histological grading method of Elston's modification of Scarff Bloon Richardson. **Aims:** This study was done to grade ductal carcinoma of breast and compares it with histological grading. **Setting and design:** Retrospective. **Material and Methods:** The present study was done over a sample size of 35 patients for over a span of 12 months. 35 Patients who went through FNAC and mastectomy for carcinoma of breast were cytological and histological graded. The results obtained by both grading methods were then compared. **Statistical analysis:** Comparison was done between these two grading systems and concordance rates were calculated between two grading system. Sensitivity and specificity were calculated for each cytological grade. **Results:** In the present study all were female. Oncology comparison of cytological and histological grades, 100% cases were grade III, 81% cases were grade II, 72% were grade I both on cytology and histology. **Conclusion:** The present study proves that, a simple cytological grading helps in evaluating the prognosis of the patient and provides varied treatment options depending on the grade.

Keywords: Robinson, Elston, FNAC, Cytology

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Introduction

Carcinoma of breast is commonest malignancies with heterogeneous prognosis.[1]It is a source of anxiety so that the assessment of prognostic parameters is of growing interest.[2] Histological grade has been an important prognostic indicator that can predict overall and metastasis free survival.[3] Histological grading by Elston and Ellis is a widely accepted grading and prognostically correlate very well.[4] Nowadays grading of breast carcinoma on cytology smears is being focused as primary modality of treatment like Tamoxifen and Neoadjuvant chemotherapy is gaining popularity.[5]Such cytological grading allow us choose most appropriate treatment and morbidity related with overtreatment of low- grade tumors.[6]

Material and methods

In this study 35 cases of infiltrating ductal carcinoma (IDC) breast, diagnosed with FNAC and histology were included. Cytological smears stained with haematoxylin and eosin (H&E), Giemsa, and Papinacolau's stain were evaluated and tumor was graded according to Robinson's grading system.(table1).In the which six different cytological parameters were used. Each of the parameter score of 1-3 and then the tumor was graded by adding up the scores. Scored between 6 to11weregradeI, between 12 to14weregradeIIandbetween 15 to 18 were grade III.

The surgical specimens which were received in our histology department stained with H&E were assessed and graded by the Elston's modification of Bloom- Richardson system (table 2). There were three parameters as describe in table was given a score of either 1, 2 or 3, and the overall score for each case range between 3to9.

Statisticalanalysis

Comparison was done between these two grading systems and concordance rates were calculated between two grading system. Sensitivity and specificity were calculated for each cytological grade.

Results

35 cases were cytologically graded on FNAC smears using Robinson's grading system and then graded on histology using Elston's modification of Bloom-Richardson grading system. Most of cases i.e. 17 (49%) were grade III (Fig 3), 11(31%) cases were grade II(Fig 2) and only 7(20%) cases were grade I on cytology (Fig 1). On histological grading ,19(55%) cases belonged to grade III,11(31%)cases belonged to grade II,and5(14%) cases belonged to histological grad I. From 7 cases cytologically graded I, 5 (71%) cases corresponded to grade I of histopathology: Table 3 show comparison between two grading system which show concordance rate for grade I, II and III about 71%, 82%, 100% respectively. Table 3 shows that concordance rate between cytology and histology for grade I tumors was 71.4% (5cases), in case of grade II tumors was 81.8% (9 cases) and in case of grade III it was 100% (17 cases). The absolute concordance rate between all three corresponding grades was 88.5 %(31/35).

Table 4 shows that in case of cytologically grade I tumors, the sensitivity was 100% that's because of 0number of false negative cases and specificity was 93.3%, in case of cytological grade II tumors the sensitivity was 81.8% as the number of false negative cases were 2 and specificity was 91.6% and for grade III tumors the sensitivity and specificity was 89.4%and 100% respectively.

Discussion

FNAC is a routinely done as investigation procedure for rapid diagnosis in case of breast cancer since a long time but breast carcinoma grading on FNAC has been underestimated which will give us valuable information to the treating oncologist for planning the management without any additional morbidity or expense for the patients.[5] In this study, we have attempted cytological grading of breast carcinoma as per the criteria proposed by Robinson and colleagues.

Before studying various criteria for grading it was ensured that the FNAC was performed excluding the areas of necrosis and excessively schirrous areas, material was adequate, smears were cellular, cell morphology was well preserved excluding ruptured cells and H&E, Papanicolau's and Giemsa stained slides were available.

The cell dissociation means how the cells are arranged in smear means in cluster, separately or both is give knowledge about cell cohesion status and the degree of e-cadherin/ catenin complex expression. Loss of cell cohesion appears to smooth the way for vacular infiltration by tumor cells, which gives rise to an increased incidence of regional LN metastasis. A number of study studies have shown that the neoplasms with greater cell dissociation show a higher incidence of lymph node metastasis.[12,13]

As almost all neoplastic smears are hemorrhagic, RBCs are considered as internal micrometer. Cell size was assessed by comparing the size of tumor cell with nearest red blood cell present in the smear. H&E slides were almost always found better for judging cell size.[12,13]

Pleomorphism is one of the constant features of breast carcinoma. The three cellular components of cell pleomorphism were assessed separetly, they are cell uniformity i.e. the similarity of cell appearance, nuclear outline, and chromatin pattern.[14] Pleomorphism was judged independent of cell dissociation and cell size features, as large cells can be large through (cell size) without varying much among themselves (cell uniformity).[14]

Robinson et al found the presence and the character of nucleoli valuable in grading independently as well in combination with the cytological feature as it give idea about cells growth and synthesis.[6,15]

All the smears were carefully scrutinized for this parameter, and were scored even when few cells showed the nuclear folding or budding. Nuclear folding was better appreciated in H&E slides, while nuclear clefts and budding was seen only in Giemsa stained slides Chromatin pattern of nuclei may help to identified type of breast carcinoma means well or poorly differentiated but because of subjective variability it is not statistically significant. While ascending from lower grade to higher grade, chromatin showed progressive granularity, clumping and clearing. [16, 17]

H&E, Pap and Giemsa stained slides were considered for all cases. H&E stained smears were must for chromatin, while Giemsa stained smears were indispensible for judging Nuclear margins. When two or more slides from same patient revealed different scores, highest score among them was given, while nowhere, average of two was taken into account.

Table 5 shows that grade III tumors were the commonest comprising of 49% followed by grade II tumors (31%). There were only 7 cases of grade I tumor in our study.

Table 6 shows that Robinson et al[7] ,Taniguchi et al[18], Pandit et a1[19] , Das et al[20] , Chhabra et al[21], Meena et al[22],Nazoora Khan et al[23]and Farooq et al[24] found grade II tumors the commonest on cytology while in our study grade III tumors were the commonest comprising of 49% followed by grade II tumors 31%.

Table 7 shows that Among the cases in which both cytology and histology were available, grade III tumors were the commonest comprising 55% followed by grade II tumors (31%) .

Table 8 shows that Shet et al[25], Muddawa[26], Nidal M. Almasri et al[27] found grade III tumors the commonest as in our study, while Dutta et al [28] found grade II tumors more common than grade III.

Table 9 shows that Das et al [20], Chhabra et al [21] , Meena et al[23] and Nazoora khan et al[25] like in our study, found good correlation between Robinson cytologic grade and Elston's modification of Bloom- Richardson system.

FNA allows the judicious use of neoadjuvant therapy by giving information regarding tumor grade, lymph node status which can then be monitored by repeating the fine needle aspirate. So it is good to include grading in FNAC report.

Conclusion

Our study shows that we can do invasive ductal carcinoma grading on FNAC .FNAC should be performed by expert personnel, avoiding the areas of necrosis and excessive schirrous areas, material should be adequate, smear should be cellular and cell morphology should be well preserved. Grading helps to select type of operation and the level of lymph node resection before head.

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Table 1: Robinson cytological Grading System[6,7,8,9]

Sr no.	Criteria	Score 1	Score 2	Score 3
1	Dissociation of cell	Mostly in cluster	Cells in cluster as well as singly scatter	Mostly single cells
2	Size of cell	1 to 2	3 to 4	More than 5
3	Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
4	Nucleoli	Indistinct (Not seen on 40 X)	Noticeable (Seen on 40 X)	Prominent or pleomorphic (Seen on 10 X)
5	Margin of nucleus	Smooth	Folds	Buds/clefts
6	Nuclear chromatin	Vesicular	Granular	Clumped and clear

Table 2 :Bloom Richardson Grading System for carcinoma of breast [10,11]

FEATURE	SCORE
Formation of tubule	
Majority of tumor: more than 75%	1
Moderate degree: between 10 to	2
75% Little or none : less than 10%	3
Nuclear pleomorphism	
Small,uniform	1
Moderate increase in size/variation	2
Marked variation	3
Mitotic counts – per 10 hpf (40x fields)	
0 to 5	1
6 to10	2
More than 11	3

Table 3: Distribution of cases according to cytology and histology grading along with comparison between two grading system

Cytological grades	Histological grades						Total		Concordance rate(%)
	1		2		3				
	No	%	No.	%	No.	%	No.	%	
1	5	71	2	29	0	0	7	20	71.4
2	0	0	9	82	2	18	11	31	81.8
3	0	0	0	0	17	100	17	49	100
Total	5	14	11	31	19	54	35	100	
Absolute Concordance									88.5

Table 4 : Calculation of sensitivity and specificity

Cytology Grade	True positive cases	False positive cases	True negative cases	False negative cases	Sensitivity (%)	Specificity (%)
I	5	2	28	0	100	93.3
II	9	2	22	2	81.8	91.6
III	17	0	16	2	89.4	100

Table 5: Distribution of cases according to Robinson's cytologic grade

Total score	Grade	Number	Percentage of cases (%)
6-11	I	7	20
12-14	II	11	31
15-18	III	17	49
	TOTAL	35	100

Table 6 : Comparative study of cytological grading of breast carcinoma

Cyto grade	Robin son et al[7] (1994)	Taniguchi et al[18] (2000)	Pandit et al[19] (2000)	Das et al[20] (2003)	Chha bra et al[21] (2003)	Meena et al[22] (2006)	Nazoora khan et al[23] (2009)	Farooq at el[24] (2010)	Our study
I	34.07	32.23	34.66	29	30	31	30.23	25.45	20

II	43.77	40	34.66	46	51.66	56.33	41.87	41.82	31
III	22.06	27.77	30.68	25	18.34	12.67	27.90	32.73	49

Table 7: Distribution of cases in which correlation was available according to histopathlogical grades

TOTAL SCORE	GRADE	NUMBER OF CASES	PERCENTAGE OF CASES(%)
3-5	I	5	14
6-7	II	11	31
8-9	III	19	55
	TOTAL	35	100

Table 8: Comparison of histological grade with other studies

GRADE	Shet et al[25]	Muddaw a[26]	Nidalm. almasri et al[27]	Dutta et al[28]	OUR STUDY
I	2	14.6	3.2	10.6	14
II	28	36.4	37	76	31
III	70	49	41	13.4	55

Table 9: Showing comparison of cyto-histo grading correlation with other studies

Histo grade	Das et al[20]			Chhabra etal[21]			Meenaet al[23]			Nazoor a khan et al[25]			Our study		
Cyto grade	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III
I	7	6	2	11	6	1	19	3	0	12	1	0	5	2	0
II	2	20	2	5	21	5	4	32	4	2	15	1	0	9	2
III	0	3	10	1	3	7	0	1	8	0	1	11	0	0	17
TOTAL	9	29	14	17	30	13	23	36	12	14	17	12	5	11	19

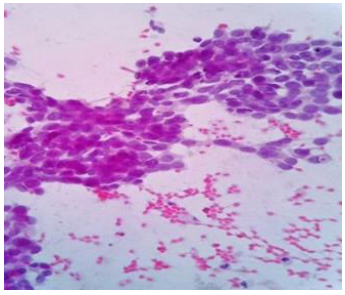

Figure1:CytologicgradeI tumor slide show mild pleomorphic ductal cells arrange in loosely cohesive cluster and smooth nuclear membrane within distinct nucleoli(H&E400x)

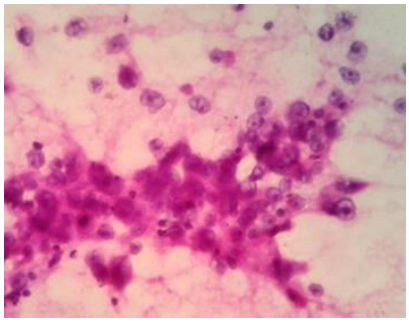

Fig2:Cytologic grade II tumor show loosely cohesive cluster as well as single cells, moderate pleomorphism, irregular nuclear membrane with noticeable nucleoli(H&E400x)

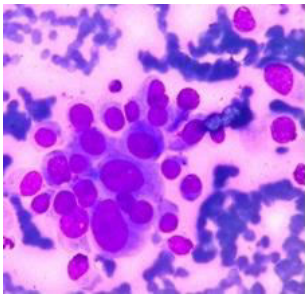

Fig 3: Cytological grade III tumor show cells singly scatter, highly pleomorphic nuclei with prominent nucleoli. **(MGG stain 400x)**