Cytological Grading of Fine Needle Aspirates from Breast Carcinoma

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Abstract:

Background: Breast carcinoma is the most common malignant tumor in females at the age group (15-74) years. Because neoadjuvant therapy including preoperative chemotherapy and tamoxifen is becoming increasingly common for treating early breast carcinoma, itѕ s desirable to grade the tumor before surgery to select the appropriate treatment

Aim of the study:
1-Grading the cytological material obtained by FNA performed on malignant breast lesions.
2-Assess the reliability of FNA by comparison with histopathology.

Material & Method: One hundred and three malignant cases of breast lesions diagnosed by FNA were reviewed in Al-Kadhmiah Teaching Hospital from 1994-1998. Their histopathological confirmation was present in 91 cases only. Those aspirates were stained by H&E stain & were graded according to the Robinson grading system using six cytological parameters; cell dissociation, cell size, cell uniformity, nucleoli, nuclear margin & chromatin pattern and then grade them into three grades according to the total scores.

Results: We were able to correctly correlate 74 cases (81.3%) of FNA cytological material graded according to the mentioned criteria with their histological grading for ductal carcinoma. For lobular carcinoma only histopathological confirmation was done. Performing Chi-square testX^2=67.4 (p≤0.001).

Conclusions: Cytological grade does not correspond exactly to histological grade but it is equally good if the variability in histological grade is considered due to tumor heterogeneity. Also the value of Robinson´s grading system in cytological grading since it is simple, take little time & the information obtained is of clinical use & may be of prognostic value especially when combined with mammographic findings.

Key words: Breast carcinoma, FNA, grading.

Introduction:

Breast carcinoma is the most common malignant tumor in females. It is responsible for the death of more than other cancers at the age (40-44) years. [1]

Fine needle aspiration is the study of cells obtained by fine needle under vacuum .It can be applied to any mass in the body, with or without the help of ultrasound guide [2]. It is coast-efficient, safe, simple, accurate and reliable technique for the diagnosis of benign and malignant breast nodules with relatively high specificity and sensitivity [3, 4, 5, and 6].

A study of scoring system to grade the cytological specimen is done by Mouriquand. J et al in 1986 [7], Thomas and his co-worker in 1989[8], and Robinson et al. in 1994, [9]. All these systems focused on the following:
1-cell dissociation
2-nuclear size
3-nuclear changes
4-presence and absence of mitosis

In this study, Robinson's grading system was applied to score the fine needle breast aspirates.

Materials & methods:

One hundred and three malignant cases of breast lesions diagnosed by FNA were reviewed. Histopathological confirmation of the grade was available in 91(ninety one) cases only. The cytological smears were stained by hematoxylin and eosin and were assessed for:
1-cell dissociation
2-cell size
3-cell uniformity
4-nucleoli
5-nuclear margin
6-chromatin pattern

Then the score given for each of the six features are added to give the final score between (6-18) for each sample, as shown in table 1.

For histopathological grading of lobular carcinoma, no histopathological grading system was available, so only histopathological confirmation was taken into consideration. Ductal carcinoma graded by the Scarff Bloom Richardson (SBR) system as shown in table 2. (10)

Table (1) The Robinson's cytological scoring scheme

Cytological parameters	Score 1	Score 2	Score 3
Dissociation of cells	Cells mostly in clusters	Mixture of single and cell clusters	Cells mostly singles
Cell size	1-2 x RBC size	3-4 x RBC size	5 x RBC size
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent or pleomorphic
Nuclear margin	Smooth	Folds	Buds or clefts
Chromatin	Vesicular	Granular	Clumped & cleared

6-11 points for GI
12-14 points for GII
15-18 points for GIII

Table (2) The Scarff-Bloom-Richardson histological grading system

Histopathological feature	Score 1	Score 2	Score 3
Degree of differentiation	Tubules, glandular papillary	Intermediate	Not present
Pleomorphism	Regular nucleus similar to benign epithelium	Intermediate	Irregular, distorted in size (giant, bizarre)
Mitotic index (10 fields at the periphery of the tumor is examined, then at x 400, the maximum number of all mitosis / HPF is counted	1 mitosis / HPF x 400	2 mitosis	> 2 mitosis

To obtain the over all SBR grade; the score for each category were added together & the grade was determined on the following basis:
3-5 points for GI (well differentiated).
6-7 points for GII (moderately differentiated).
8-9 points for GIII (poorly differentiated).

Results:

Of the 103(one hundred and three) cases only 91(ninety one) cases were diagnosed by histopathological examination as invasive ductal and invasive lobular carcinoma.

We reviewed those 91(ninety one) cases and graded them according to the cytological criteria which include, (cell clustering, nuclear size, nuclear pleomorphism, nucleoli, nuclear margin, chromatin pattern) as shown in table 1.

Of the 91 cases, 19 (21%) were lobular carcinoma &72 (79%) were ductal carcinoma (table 3).

Performing cytological grading on ductal carcinoma cases, the results are those in table 3.

Based on histolopathological grading of ductal carcinoma the following results were established (table 4).

Table (3) Comparison of cytological grading of both ductal & lobular carcinoma cases.

Type	GI	GII	GIII	Total
Ductal	28 (31%)	39 (42%)	5 (6%)	72 (79%)
Lobular	14 (15%)	5 (6%)	0	19 (21%)
Total	42 (46%)	44 (48%)	5 (6%)	91 (100%)

Table (4) Comparison of histological & cytological grades of ductal carcinoma cases.

Cytological grade	Histological grade			Total
	Well differentiated	**Moderately differentiated**	**Poorly differentiated**	
GI	14 (20%)	11 (15%)	3 (4%)	28 (39%)
GII	0	37 (51%)	2 (3%)	39 (54%)
GIII	0	0	5 (7%)	5 (7%)
Total	14 (20%)	48 (66%)	10 (14%)	72 (100%)

An important finding is 5 (100%) of the cases graded cytologically as III were poorly differentiated ductal carcinoma by histopathological confirmation (table 5). And 3 (4%) of cases graded as I by cytological examination were poorly differentiated ductal carcinoma by histopathological examination (table 6).

Table (5) the histological grade distribution in cases of cytological grade III

Histological grade	No. of patients	Percent of patients
WD (ductal)	**0**	**0**
MD (ductal)	**0**	**0**
PD (ductal)	**5**	**100%**
Total	**5**	**100%**

Table (6) the histological grade distribution in cases of cytological grade I

Histological grade	No. of patients	Percent of patients
WD (ductal)	14	33%
MD (ductal)	11	26%
PD (ductal)	3	7%
Lobular	14	33%
Total	42	100%

(p≤0.001) .This concludes that cytological grade does not correspond exactly to the histopathological grade, but it is equally good.

Discussion:

FNA cytology of the breast has been used long time ago and it's value in the diagnosis of breast cancer has been well established. [4, 11]. The material obtained by FNA can be subjected for detection of estrogen receptors and for flowcytometric and morphometric analysis which are helpful in the evaluation of tumor grade [12,13,14]. Regarding the use of FNA material for cytological grading of breast carcinoma, there was only few retrospective studies performed on this subject with conflicting conclusions; Two studies showed that cell clustering is a useful cytological change but one found it difficult to assess [7,15,16]. Nuclear size was established as a prognostic indicator but it is variable even within the same preparation because of the degree of unavoidable air drying. In this study this problem was overcame by comparing nuclear size with adjacent RBC. Cellular pleomorphism is another important cytological criterion and is easily compared with histological pleomorphism [7, 8].

We assessed three components of cellular pleomorphism separately;(cell uniformity, nuclear outline and chromatin pattern), in addition to the other three parameters that includes the cell clustering ,cell size and the presence or absence of nucleoli which has been used in other grading systems [7,8].

Since a new method of using systemic adjuvant chemotherapy before surgery has been introduced and due to the fact that the response rate with the tumors rapidly growing (grade III) ,was much faster and more likely to respond to chemotherapy than low grade slowly growing lesions. So it is

Statistical analysis done using chi square test X^2: beneficial if we could assess the biological aggressiveness of cancer before removing it.

FNA cytological grading allows such assessment, followed by serial estimates to see how pre-treatment modulates tumor growth.

In this study we were able to correctly correlate74(81.3%) cases of FNA cytological material graded according to the criteria mentioned with their histopathological grading using the Nottingham modification of the Scarff bloom-Richardson system for grading ductal carcinoma [9,10], and only histopathological confirmation for lobular carcinoma. We noticed that all cases graded cytologically as III were poorly differentiated ductal carcinoma by histopathological grading (table 5). This might be due to the fact that cytologically aggressive cells were aspirated from the poorly differentiated areas of the tumor.

The finding regarding the cases of cytological (grade I) that were poorly differentiated ductal carcinoma by histopathological grading; explained by the fact that during performance of FNA, the aspirates were taken from the well differentiated area of the tumor. This is because many tumors show variable areas of differentiation ranging from well differentiated area to poorly differentiated and this is called tumor heterogeneity.

Statistically speaking, performing a chi square test x^2 has yielded a result of x^2=67.4 (p≤0.001) which conclude that cytological grade does not correspond exactly to histological grade but its equal good especially when the variability in histological grade is considered, due to tumor heterogeneity.

The system we have used is simple and takes little time and the information obtained is of clinical use and may be of prognostic value especially if it was combined with a mammographic finding.

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