Cyto-Histo Grading Correlation in Breast Malignancies

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ABSTRACT

Background :

A palpable breast lump is a common diagnostic problem. The breast lesions are spectrum of diseases ranging from non-neoplastic to neoplastic lesions. Fine Needle Aspiration Cytology(FNAC) is an important tool in the diagnosis of breast lesions. It is important not only to diagnose breast lesion as benign or malignant, but also to assay the prognosis.

Objectives of study :

The purpose of the present study was to compare cytologic grading of breast carcinoma by Simplified Black grading system with histologic grading by Nottingham modification of Bloom-Richardson grading system.

Methods :

The study included smears from 25 cases of palpable breast lump diagnosed as malignant on FNAC. The cytological grading by Simplified Black system was compared with histopathologic grading by Nottingham modification ofBloom Richardson. The statistical test used was Chi – square test.

Results :

Cytologic grading by Simplified Black system and histologic grading by Nottingham modification ofBloom Richardson done in 25 cases of breast carcinoma had good correlation (p value < 0.05).

Conclusion :

Fine needle aspiration cytology is a safe, rapid and minimally invasive procedure for the diagnosis of breast lesions. It is effective replacement for open biopsy. Cytologic grading by Simplified Black system correlates well with histologic grading by Nottingham modification ofBloom Richardson. Hence it must be included in the cytology report of breast carcinoma whenever possible as it helps in determining the tumour aggressiveness and further treatment plan.

KEYWORDS : Breast lump; Fine Needle Aspiration Cytology; Grading

INTRODUCTION

A palpable breast lump is a common presentation to surgical OPD. Benign breast lesions must be differentiated from malignant lesions. It is important not only to diagnose breast lesion as benign or malignant, but also to assay the prognosis of both. To assay the prognosis, grading of breast malignancies is very important. FNAC is an important diagnostic tool which is cheaper, less traumatic, requires no local anaesthesia, can generate rapid diagnosis. It is the most convenient method of sampling even small palpable and multiple lesions.[1-3]

MATERIALS AND METHODS

This is astudy undertaken in Department of Pathology, Sri DevarajUrs Medical College, Kolar, from 01-12-2008 to 30-11-2009.

Inclusion Criteria

25 cases diagnosed as malignant on FNAC of clinically palpable breast lesions along with its subsequent histopathology.

Exclusion Criteria

Radiologically detected breast lesions but clinically impalpable.

FNAC was performed using 22-23 gauge needle fitted to a 10 millilitre syringe. Smears were promptly fixed in a fixative containing 95% ethyl alcohol, andstained by Papanicolaou stain. Thesubsequent surgically resected specimens were fixed in 10% formalin for 24-48 hours and blocks were prepared by routine processing and 5 microns thick sections were stained with HE.

Malignant lesions on cytology were graded by Simplified Black grading system. histologic sections were graded according to Nottingham modification of Bloom-Richardson grading system. Both grading systems were correlated. Chi- square test was used to compare the results. p value < 0.05 was considered statistically significant.

RESULTS

The diagnosis of malignancy was offered in 25 cases on FNAC. Nottingham modification ofBloom Richardson grading can be applied to ductal carcinoma, special types of ductal carcinoma and lobular carcinoma.[4] One case which was put under suspicious for malignancy category on cytology was diagnosed as ductal carcinoma on histopathology. Hence it was retrospectively included under grading. The cytologic and histologic grading was performed on Ductal carcinoma NOS (21 cases), mixed ductal and lobular carcinoma (1 case), tubular carcinoma (1 case), metaplastic carcinoma (1 case) and medullary carcinoma (1 case).

On cytologic grading 9 cases (36%) were low grade and 16 cases (64%) cases were high grade. Low grade Simplified Black grade when correlated with Nottingham modification ofBloom Richardson grade revealed 6 cases out of 9 cases to be grade 1. 16 cases of high grade Simplified Black grade when compared with Nottingham modification ofBloom Richardson grade revealed only two cases to be grade 1, five cases to be grade 2 and nine cases to be grade 3 9 (figure 1 and 2).

In the present study, by application of Chi – square test, p value was <0.05 which is statistically significant. This indicates that the cytologic grading by Simplified Black method correlated well with Nottingham modification of Bloom Richardson histological grading (table 1).

DISCUSSION

Grading

The evaluation of the possible prognostic parameters in breast carcinoma like tumour histologic grading, cell proliferation index, estrogen receptor status and lymph node status is of growing interest.[5] Grading of breast carcinoma as an independent factor has prognostic value.[6]

Histologic grade has been an important prognostic indicator that can predict overall and metastasis free survival for local and regionalized breast cancer.[7]Apart from establishing the benign and malignant characters of a given lesion FNA can provide additional information about intrinsic features of the tumour as well as its prognosis.[8] There is much attraction in grading a tumour because neoadjuvant chemotherapy is becoming increasingly popular as primary medical treatment for breast cancer.[6]Attention must be focused on grading tumours on FNAC as it would allow assessment of the tumour and the morbidity associated with overtreatment of low grade tumours could be avoided.[9]

Histologic type of tumour and nuclear grade are two of the most important microscopically derived morphologic prognostic factors for breast carcinoma patients.[10] The value of histological grading of breast carcinoma is well established.[6] Hence assignment of a histologic grade has been recommended as a standard in all surgical pathology reports.[7]

Cytologic grading has shown a positive correlation with histologic grade, therefore cytological grading is useful in predicting histological grade preoperatively.[8] Tumour grading based on cytology plays an important role in planning the treatment based on which pre-operative chemotherapy and/or radiation therapy is instituted.[11]

Histologic grading
Several histologic grading systems were proposed, some consider ductoglandular differentiation or tumour secretory state. Some score only nuclear and nucleolar characteristics and others use both duct formation and nuclear abnormalities.[12]There is always subjective element in the assessment of histological differentiation. Lack of strictly defined criteria is one of the fundamental problems with many of the systems used in previous studies.[13]Greenough developed a histologic grading system for breast carcinoma which was simplified by Patey and Scarff. Bloom and Richardson made it more acceptable by introducing a numerical scoring system to the method described by Patey and Scarff.[14]

Nottingham modification ofBloom Richardson grading (table 2) combines measurement of differentiation (tubule formation) with details of cell morphology (nuclear pleomorphism) and an assessment of proliferation (mitotic frequency).[15]

Cytologic grading
The number of breast carcinomas diagnosed is increasing with the advent of FNAC. Cytologic tumour grading correlates well with histological grading and is highly reproducible.[11]For practical purpose one pathologist's cytologic grade must be able to predict another's histologic grade, because in many practice situations the cytologic and histologic specimens will be signed out by different pathologists. [7]

Cytological grading systems of breast carcinoma :
1. Hunt's et al grading system.[16]
2. Mouriquand et al grading system.[16]
3. Modified Black grading system.[6]
4. Simplified Black grading system.[6]
5. Fisher's modification of Black's nuclear grading.[17]
6. Khan's grading system.[17]
7. Robinson grading system.[18]
8. Scarff-Bloom-Richardson grading system.[7]

According to a study done by Ohri A et al[6], cytological grading was done by Hunt's, Simplified Black and Modified Black grading systems. These systems were compared with modified Scarff Bloom-Richardson grading done on histologic sections. They concluded that among the three cytologic grading systems, the two- tier Simplified Black system (table 3) has greater degree of correlation, well defined set of criteria, simple and objective.

Cytologic and histologic correlation
FNAC report whenever possible should include nuclear grade because it has been found that nuclear grading of breast carcinoma is performed with ease, correlates well with tissue nuclear grade.[19]The aim of comparing the cytological grading system with histological grading is to see whether the agreement is good enough for one to

replace another.[6]It is important to correlate because it is of clinical use and of prognostic value as it enables assessment of the biological aggressiveness of the malignancy. Thus cytological grading system which closely reflects the histological grade, biological behaviour of the tumour is assessed and systemic adjuvant treatment is instituted before surgery.[6]

The value of histological grading of breast carcinoma is well established.Since diagnosis of breast carcinoma is often made by FNAC, it is important toperform grading on aspirates which will provide valuable information to the treatingoncologist for further management.[20] In the present study the cytologic and histologic grading showed good correlation (p value <0.05).In the study done by Ohri A et al [6], cytological grading was done by Hunt's, Simplified Black and Modified Black grading systems. These systems were compared with modified Scarff Bloom-Richardson grading done on histologic sections. They concluded that among the three cytological grading systems, the two-tier Simplified Black system is simple, objective, has greater degree of correlation and has well defined set of criteria.

In the study done by Cajulis RS et al[21], they concluded that the Simplified Black nuclear grading (two-tier system) system not only showed high reproducibility and concordance with histopathology but also a high correlation with flow cytometric analysis.Another study done by Cajulis RS et al[22] also concluded similarly.

In the study done by Fisher B et al[23] using the two-tier system, the nuclear grade had an independent influence on outcome of breast cancer.According to a study done by Dantas KAN et al[24] the classifications were divided according to criteria of tumoural grading (nuclear and architectural criteria -Mouriquand and Guilford systems) and nuclear criteria (Black modified by Fisher, simplified Black system and Hunt system). The cytologic grading systems were compared with histological grading using Scarff-Bloom-Richardson modified by Elston (SBR modified). The cytological grading systems that showed best agreement were Black modified by Fisher and simplified Black system based on nuclear criteria (anisonucleosis, size, mitosis, and chromatin).

CONCLUSION
FNAC diagnosis will help the clinician to confirm or exclude the differential diagnosis made by the clinician. The rapid diagnosis made by FNAC relieves the anxiety of patient and helps the clinician to plan the treatment. Histological grade has been shown to be a valuable prognostic parameter in patients with breast cancer. As simplified Black cytological nuclear grading correlates well with Nottingham modification of Bloom-Richardson histopathologicalgrading system it should be included in the cytology report.Along with cytological diagnosis, cytological grading provides important prognostic information. Simplified Black grading system is simple, objective, takes little time and has better reproducibility with lesser degree of observer errors.
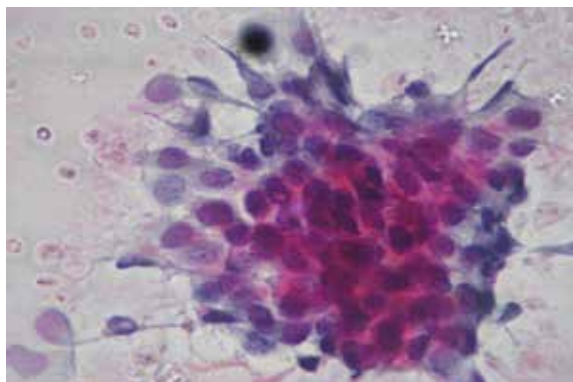

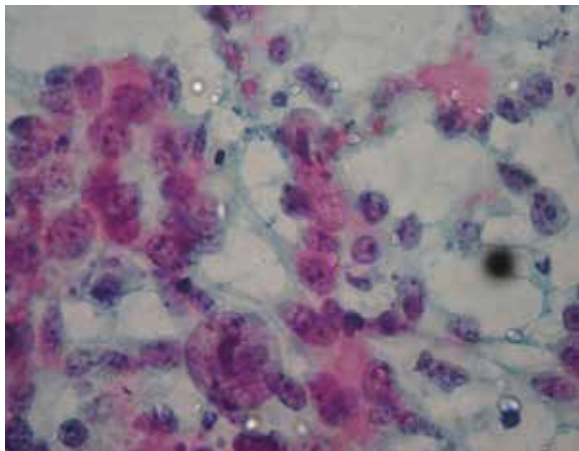**FIG 1 - FNAC of low grade Simplified Black system. PAP X 400.**

FIG 2 - FNAC of high grade Simplified Black system. PAP X 400.

TABLE 1 – CORRELATION OF SIMPLIFIED BLACK CYTOLOGIC GRADING WITH NOTTINGHAM MODIFICATION OF BLOOM RICHARDSON HISTOLOGICAL GRADING.

CYTOLOGICAL GRADE	HISTOPATHOLOGICAL GRADE			
	TOTAL NO OF CASES	GRADE 1	GRADE 2	GRADE 3
LOW GRADE	9	6	3	-
HIGH GRADE	16	2	5	9
TOTAL	25	8	8	9

Chi – square value : 10.35
Degree of freedom : 2
p value < 0.01

TABLE 2 - NOTTINGHAM MODIFICATION OF BLOOM-RICHARDSON GRADING.[4]

FEATURE	SCORE
Tubule formation	
> 75% of the tumour	1 point
10-75% of the tumour	2 points
< 10% of the tumour	3 points
Nuclear pleomorphism	
Nuclei with minimal variation in size and shape	1 point
Nuclei with moderate variation in size and shape	2 points
Nuclei with marked variation in size and shape	3 points
Mitotic counts - per 10 HPF (40 x fields)	
0 – 5	1 point
6 – 10	2 points
> 11	3 points

Grade 1 (well differentiated) : 3 – 5 points
Grade 2 (moderately differentiated) : 6 – 7 points
Grade 3 (poorly differentiated) : 8 – 9 points

TABLE 3 - SIMPLIFIED BLACK GRADING SYSTEM.[7]

LOW GRADE	HIGH GRADE
Nuclear uniformity	Anisonucleosis
Fine chromatin	Chromatin clumping
Absent nucleoli	Nucleoli easily seen at 100x
<3 mitosis per 10 HPF	>3 mitosis per 10 HPF
Small nucleus (<3x size of mature lymphocyte or RBC)	Large nucleus (>3x size of mature lymphocyte or RBC)

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