RESEARCH COMMUNICATION

Validity of Different Cytological Grading Systems of Breast Carcinoma - a Hospital-based Study in South India

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Abstract

Introduction: With increase in the incidence of breast carcinoma, fine needle aspiration cytology (FNAC) has began to play a major role in diagnosing and grading. The study was aimed at validating the different cytological grading systems like Hunt's cytological grading (HCG), modified Black grading (MBG), Robinson's cytological grading (RCG) and Masood's cytology index (MCI) in comparison with a modified Bloom-Richardson (MBR) histopathological grading. Methods and Material: Fifty breast carcinoma cases were prospectively studied by comparing various cytological grading methods with histopathological grading over a period of three years. All statistical analyses were carried out with the Epi-info package. Results: The concordance rate of RCG was 82% which is highest of all, while that of MBG was 68%. HCG and MCI were not comparable with MBR due to insufficient grading. Conclusions: RCG for breast carcinoma is validated. A consensus for a standard cytological grading method similar to the gold standard MBR histological grading must be arrived at based on conducted comparative studies and has to be inculcated in routine cytology reports.

Keywords: Cytological grading - breast carcinoma - Hunt's - modified Bblack - Robinson's - Masood's

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Introduction

The incidence of breast carcinoma is gradually increasing and approaching to replace cervical carcinoma as a leading malignancy among women in developing countries including India (Murthy et al., 2009). The reason attributable for this is the shift towards Western life style (Bhatt et al., 2002) and rise in the awareness about signs and symptoms of breast lesions and its early detection by regular self-examination of breast. The breast lesions are easily accessible to FNAC, which is an easy, cost effective and less time consuming procedure. Therefore, the number of breast FNACs are equivalent to that of other common sites like lymph nodes, thyroid etc. FNAC is used to diagnose both palpable and nonpalpable breast lesions, as well as to classify them into different benign and malignant groups.

Amongst all breast carcinomas, the commonest type is invasive ductal carcinoma – not otherwise specified. The cytological features to diagnose them are well defined. Now, diagnosis of other uncommon types of breast carcinomas like lobular carcinoma (Jayaram et al., 2000), secretory carcinoma (Mardi et al., 2007), colloid carcinoma (Krishnamurthy et al, 2010), medullary carcinoma (Akbulut et al., 2009) and signet ring carcinoma (Kelten et al., 2009) based on specific cytological features are also well defined.

The Modified Bloom-Richardson (MBR) histological grading system is the gold standard in grading breast carcinoma. Based on the study of cytological features, various grading methods of breast carcinoma have evolved. Authors have also compared the outcome of these grading methods with the biological behavior, similar to histopathological prognostication. The treating surgeon can plan preoperative therapy to minimize the associated morbidity and enhance the postoperative prognosis. The objectives of the study were:

1) To study the validity of different cytological grading methods, like Hunt's cytological grading (HCG), modified Black grading (MBG), Robinson's cytological grading (RCG) and Masood's cytologic index (MCI) of breast carcinoma; 2) To compare these grading methods with the MBR histological grading system.

Materials and Methods

This was a prospective study of fifty cases of breast carcinoma over a period of three years between the age groups of forty to eighty years. Women diagnosed with breast carcinoma on FNAC and subsequently subjected to surgical excision were selected for the study. FNAC was done using 23G needle, fixed to a 10ml syringe. The aspirate was expressed and thinly spread on 4-5 clean dry glass slides. Haematoxylin-Eosin and Papaniculaou stains were used for the slides which were fixed in 95% ethyl alcohol. Air dried smear was stained with May-Grunwald Giemsa. Papaniculaou stained smears were subjected for grading since the nuclear morphology were better

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Table 1. Comparison of Robinson's Cytological Grading RCG) with Modified Bloom Richardson grade

	Modified Bloom-Richardson grade			
RCG	1	2	3	Total
1	7(100%)	3	0	10(20%)
2	0	22(81.5%)	4	26(52%)
3	0	2	12(75%)	14(28%)
Total	7(14%)	27(54%)	16(32%)	50

Table 2. Comparison of Modified Black Grade (MBG) with Modified Bloom Richardson Grade

	Modified Bloom-Richardson grade			
MBG	1	2	3	Total
1	7(100%)	2	0	9(18%)
2	0	16(59.3%)	5	21(42%)
3	0	9	11(68.8%)	20(40%)
Total	7(14%)	27(54%)	16(32%)	50

preserved. They were graded with HCG, MBG, RCG and MSI cytological grading methods by two independent observers. These patients underwent excision surgery and specimens were histopathologically examined and graded by MBR method. The results obtained by different cytological grading methods were compared with the gold standard MBR histological grading system by estimating concordance rates. All the data were entered into Microsoft excel worksheet and analysed using Epi-info package.

Results

The present study included 40 cases of invasive ductal carcinoma, 5 cases of colloid carcinoma, 2 cases of invasive lobular carcinoma, 2 cases of tubular mixed cell carcinoma and 1 case of medullary carcinoma. The results of grading breast carcinomas by RCG were 10 cases of Grade I, 26 cases of Grade II and 14 cases of Grade III (Table 1). On the application of MBG, 9 cases of Grade I, 21 cases of Grade II and 20 cases of grade III breast carcinomas were detected (Table 2). HCG has only two grades, and divided breast carcinomas into 10 cases of low Grade and 40 cases of high Grade tumors. The MCI criteria can only diagnose breast carcinoma; therefore all the 50 cases belonged to Group IV (carcinoma category). Further grading, however, is not possible by MCI. On MBR histopathological grading there were 7 cases (14%) of Grade I, 27 cases (54%) of Grade II and 16 cases (32%) of Grade III breast carcinomas.

Grade wise concordance was not possible with HCG and MCI methods, due to the lack of sufficient cytological grading and to compare with MBR histopathological grading. However, both these methods confirmed that all the cases belonged to carcinoma category. The overall concordance rate for MBG and RCG were 68% (34/50 cases) and 82% (41/50 cases) respectively.

Discussion

The technique of FNAC was first described in 1847 and was introduced into clinical practice by Ellis and Martin in 1930s (Bowa et al., 2008). FNAC breast is generally considered as a rapid, reliable, safe diagnostic tool to diagnose both non-neoplastic and neoplastic breast lesions. Tham et al. (2009), Zagorianaku et al. (2005) and Koss et al. (2006) have found that in diagnosis of palpable breast lesions in developing countries by FNAC is the initial method of pathological assessment as a component of Triple test.

On diagnosing breast carcinoma by FNAC, they are further subjected to cytological grading. The different cytological features like cellular arrangement, cellular pleomorphism, presence or absence of myoepithelial cells, nuclear size, nuclear pleomorphism, nuclear margin pattern, chromatin pattern and presence of nucleoli were taken into consideration to derive at various methods to grade breast carcinomas.

Hunt's cytological grading (Hunt et al., 1990) includes nuclear diameter, nuclear pleomorphism, and the presence of nucleoli in their cytological grading. A scoring system based on these three parameters enabled the classification of tumors into high and low cytological grades which showed a close correlation with histological grade. In the present study there were 40/50 cases of high grade and 10/50 cases of low grade breast carcinomas. Insufficient categorization of HCG compared to MBR renders comparison difficult.

The modified black grading *(*MBG) includeschromatin pattern and mitosis for cytological grading. Even though the study by Cajulis et al. (1997) concluded that high reproducibility in the cytological grading of FNA of breast carcinoma can be more readily attained among private practice pathologists using the two-tier simplified black than the three-tier MBG grading system, we considered MBG for our study. The results obtained by MBG are comparable with the gold standard MBR histological grading system (Elston et al., 2002). There were 9/50, 21/50 and 20/50 cases of grade I, II and III of breast carcinomas respectively. Out of 9/50 grade I cases, 7 belonged to grade I and 2 belonged to grade II breast carcinomas. Out of 21/50 grade II cases, 16 belonged to grade II and 5 belonged to grade III breast carcinomas. Out of 20/50 grade III cases, 11 belonged to grade III and 9 belonged to grade II breast carcinomas.

The concordance rate of MBG by Ohri et al (2006), Zoppi et al. (1993) and were 54%, 71% and 95% respectively. In our study the concordance rate of MBG (68%) was low due to inclusion of mitoses as one of the criteria, which is difficult to identify on cytological aspirates.

Masood's cytologic index (MCI) (Masood et al., 1991) has included myoepithelial cells and excluded cell size and mitoses for cytological grading. MCI has helped mainly in differentiating between the benign and malignant lesions of breast rather than grading breast carcinomas. MCI helped in only confirming all the 50 cases as malignant and insufficient categorization compared to MBR renders comparison difficult.

Robinson's cytological grading has included cell dissociation and nuclear margin included and excluded mitosis for cytological grading (Robinson et al., 1994). There were 10/50, 26/50 and 14/50 cases of grade I, II and III breast carcinomas respectively. Out of 10/50

grade I cases, 7 belonged to grade I and 3 belonged to grade II breast carcinomas. Out of 26/50 grade II cases, 22 belonged to grade II and 4 belonged to grade III breast carcinomas. Out of 14/50 grade III cases, 12 belonged to grade III and 2 belonged to grade II breast carcinomas.

Sinha et al. (2009) have found that the RCG correlated well with MBR histopathological grading, especially in grade III, where the concordance was nearly perfect. The present study also found similar results. All grade I had stage A, two of grade II had stage B, while all grade III had either stage B or stage C disease. The concordance rate in the present study by RCG was 82%, compared to 57% by Robinson et al, 59% by Meena et al. (2005), 65% by Chabra et al. (2005) and 88% by Khan et al. (2009).

In order to diagnose carcinoma with histopathology, features like cellular arrangement, degree of cellular pleomorphism, degree of nuclear pleomorphism, absence of myoepithelial cells are given importance. The MBR histological grading system is based on extent of tubule formation, number of mitotic figures and degree of nuclear pleomorphism. But several features like nuclear margin, chromatin pattern and nucleoli that are included in cytological grading which are not of much importance in diagnosing or grading by histopathological study.

Howell et al. (1994) have evaluated the applicability of the Scarff-Bloom-Richardson breast carcinoma grading system to cytology aspirates and found a large number of disparities in the cytological and histological grading due to difficulties in detecting mitoses or tubules in the cytology of breast carcinoma. In cytology, the nuclear features alone have contributed more to grading than the others, which is also one of the criteria in histopathological grading.

FNAC is one of the components of Triple tests to diagnose palpable breast lesions in developing countries (Steinberg et al., 1996). In neoadjuvant therapy, tamoxifen is administered to high grade tumors which act mainly on proliferating cells thereby reducing the size of tumor. Low-grade tumors are not benefitted by this therapy and also results in unnecessary morbidity (Taniguchi et al., 2000). Therefore it is essential to not only diagnose breast carcinoma but also to grade them comparable to MBR histopathological grading.

Insufficient categorization of HCG and MCI compared to MBR renders comparison difficult. In MBG inclusion of mitosis renders difficult to indentify on cytological smears. The study indicates that RCG is valid with a high concordance rate of 82%. An ideal cytological grading system should not only help the cytologist to differentiate between benign and malignant lesions of breast but also aid in grading the malignant lesions comparable to gold

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