Original article

Fine-needle aspiration of palpable breast lesions with histopathologic correlation

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Abstract: Fine-needle aspiration biopsy of the breast has been used as a diagnostic step in the investigation of palpable breast lumps in the Department of Pathology, Tikur Anbessa Hospital, for more than 10 years. The purpose of this study is to evaluate the accuracy of fine-needle aspiration with histopathologic confirmation. A retrospective study was performed using records of fine-needle aspiration and biopsy results and request forms over four and half years. All women and men who had had fine-needle aspiration breast biopsy with histopathologic confirmation of the diagnosis were included. Fine-needle aspirations were interpreted as malignant, suspicious, or benign. Histopathologic diagnosis included incisional, excisional, and mastectomy specimen. A total of 244 patients fulfilled the criteria. Only eight (3.3%) of the specimens were inadequate for study. There were 52 total malignant fine-needle aspiration diagnoses, with only two falsepositive specimens. One was flbroadenoma and the other benign phylloides. There were 20 suspicious readings; 14 of these were malignant and six were false-suspicious specimens. Fibroadenoma, fibrocystic change, and papilloma were two each for the the six false suspicious specimens. Of the 164 lesions interpreted as benign, there were 10 false negative specimens. The test had 86% sensitivity, 95% specificity, 89% positive predictive value, and 94% negative predicitive value. Fine-needle aspiration is a sensitive and highly specific test that can be useful as an adjunct in the diagnosis of breast cancer. "Malignant" and "benign" interpretations are highly predictive but must be used only in the context of other diagnostic modalities. "Suspicious" "atypical" or "papillary" lesions require further investigation. [*Ethiop. J. Health Dev.* 1999;13(3):181-186]

Introduction

Various diagnostic methods have been developed to evaluate palpable and non- palpable breast lesions with the goal of identifying a sensitive, specific, efficient, and economical approach to diagnose breast cancer. Physical examination, mammography, ultrasonography, core needle biopsy, open excisional biopsy, thermography, and Fine- Needle Aspiration (FNA) are all used to a greater or lesser extent in the diagnostic workup of a palpable breast mass (1). Various combinations of these approaches have been studied and have been found to increase sensitivity and specificity over that of any one test alone (2).

FNA has been used as the first diagnostic step in the investigation of palpable breast lumps in the Department of Pathology of the Tikur Anbessa Hospital for more than ten years. FNA of palpable breast masses has become increasingly popular as a diagnostic technique as it provides a sensitive, expedient, and economical method of obtaining cytologic material for examination. Its distinct advantages include accurate diagnosis, low cost, excellent patient acceptance, and minimal or no morbidity. In recent times in the best center, it has largely replaced excisional biopsy.

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FNA alone, however, is subject to inaccuracies and does not definitively diagnose all breast cancers with the reliability of an

open biopsy. It is most commonly used in combination with physical examination and mammography in the so called "triple test" diagnostic triad, which is a highly accurate method of evaluating breast masses.

The purpose of this study was to evaluate the experience with FNA biopsy in a series of patients and compare the findings on FNA cytology with that of histopathology.

Methods

A retrospective review of the biopsy requisition forms and reports at the Department of Pathology, Faculty of Medicine, Addis Ababa University (FMAAU) was performed from 1994 to Mid-1998. The records of all female and male patients who had undergone (FNA) and histopathologic diagnoses of palpable breast lesions at the Department of Pathology, FMAAU, were included. Histopathologic confirmation consisted of either incisional biopsy, excisional biopsy or Mastectomy specimen.

FNA was performed by either a pathology resident or a pathologist as follows: a 20-23 gauge needle was attached to a 10 ml syringe, which was mounted on an aspiration cameco gun. One or two separate passes were made into the lesion with the needle. During each pass the needle was moved throughout the lesion multiple times while aspirating. Smears from the aspirates were air dried and stained by the May-Grünwald Giemsa. The FNA specimens were examined and assigned to one of the three different diagnoses: malignant, suspicious (including atypical and papillary neoplasms) or benign. The malignant diagnoses were assigned when 1) there are abundant cellularity, loosely cohesive and individual cells; 2) the cells show variable size, nuclear molding, and loss of polarity; or 3) individual tumour cells demonstrate malignant cytologic features, such as increased nucleocytoplasmic ratios, hyperchromatic and coarsely granular chromatin and small to prominent nucleoli. The benign diagnoses were assigned to the specimens lacking the above mentioned picture, and in the presence of abundant bipolar naked nuclei. A "suspicious" diagnosis is when 1) the cytologic features for malignancy are not completely fulfilled, 2) the presence of cell groupings in the form of three dimensional papillary groups along with scattered, high columnar cells, and a bloody diathesis with haemosiderin laden "macrophages" or foam cell are seen.

A diagnosis of "atypical ductal hyperplasia" is rendered when 1) the aspirate is highly cellular with crowded groups consisting of cells with both benign and atypical features (greater variation in cell size and shape and loss of polarity); 2) hyperchromatic nuclei with readily visible nucleoli are seen and 3) occasional single atypical cells are present. A diagnosis of "atypical Fibroadenoma" is rendered when there are loose cohesions of the cell groupings with some anisonucleasis and prominent nucleoli of the cells.

Sensitivity and specificity, both of which require either a positive or a negative diagnosis, were calculated for the entire group with the assumption that the "suspicious" group was positive for malignancy. The atypical and papillary neoplasm groups were included in the "suspicious" category. This was done to ensure that the most conservative approach was taken to achieve the greatest sensitivity. The positive and negative predictive values were calculated for the malignant and benign diagnoses alone (excluding the suspicious category) and for the entire set of the specimens (including the suspicious category).

Results

A total of 244 cases that fulfilled the study criteria were identified. Only eight FNA specimens (3.3%) were deemed inadequate for the study (Figure). All histopathologic specimens were adequate to make final pathologic diagnoses. A diagnosis of "malignant" was made for 52(21.3%) of the 244 FNA specimens. Only two (3.8%) were false-positive results when read as malignant;

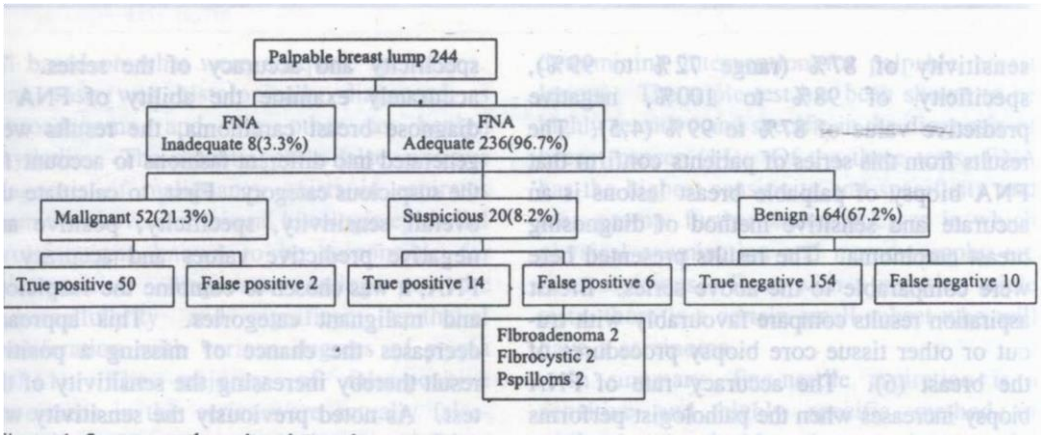

Figure 1: **Summary of results of FNA for entire series.**

in these two the histopathologic diagnosis were fibroadenoma and benign phylloides.

The positive predictive value of an FNA reading of "malignant" was 96%. A diagnosis of "suspicious" was made for 20(8.2%) of the 244 specimens. Of these 14(70%) were malignant and 6(30%) were benign or "false suspicious", fibroadenoma, fibrocystic change and papilloma accounted for two cases each of the benign cases (false suspicious).

A total of 164(67.2%) of the 244 FNA specimens were read as benign and, of these, 154(94%) were true negative benign lesions. Fibroadenoma accounted for 81(52.6%), fibrocystic change 40(25.9%), adenosis 10(6.5%) gynaecomastia 5 (3.2%), adenoma 4(2.6), benign phylloides 4(2.6%), fat necrosis 3(1.9%), chronic non-specific inflammation 3(1.9%), tuberculosis 2(1.3%) and, granuloma 2(1.3%) of the true benign lesions.

Ten lesions diagnosed as benign were found to be malignant on histopathologic examination. Most of the cases were high grade invasive ductal carcinoma. This represents a false negative rate of 4.2% for the entire series and 6.0% of the 'benign' readings were, infact, malignant. The negative predictive value of a benign reading in this series is 94% when considered alone. For the entire series, the false-positive rate was 3.4% and the false negative rate was 4.2% (Table 1). The sensitivity of FNA for the entire series was 86% assuming, for calculation purposes as described previously, that the "suspicious" lesions are considered to be positive. The specificity was 95%. The overall positive and

Table 1: **Summary of fine-needle aspiration of 244 palpable breast lesions with histopathologic correlation, Department of Pathology, FMAAU, Addis Ababa, 1999.** negative predictive values were 89% and 94%, respectively. The accuracy of FNA in this series is 92%.

No. of Samples (% of Total)	%
Inadequate Sample	3.3
Comparison of True Positives	27.1
Comparison of True Negatives	65.3
Comparison of False Positives	3.4
Comparison of False Negatives	4.2
Sensitivity	86
Specificity	95
Positive Predictive Value	89
Negative Predictive Value	94

Accuracy	92

Discussion

The value of any diagnostic test lies in its ability to detect the presence of disease when it is present (sensitivity) and reliably verify the absence of the disease when it is not present (specificity). To contribute to the diagnostic workup of a palpable breast mass, FNA biopsy sensitivity and specificity should approach that of an open excisional biopsy. FNA biopsy of the breast is reported to have an average sensitivity of 87% (range 72% to 99%), specificity of 98% to 100%, negative predictive value of 87% to 99% (4,5). The results from this series of patients confirm that FNA biopsy of palpable breast lesions is an accurate and sensitive method of diagnosing breast carcinoma. The results presented here were comparable to the above series. Breast aspiration results compare favourably with tru-cut or other tissue core biopsy procedures of the breast (6). The accuracy rate of FNA biopsy increases when the pathologist performs the FNA biopsy and uses immediate assessment to guide specimen adequacy (7).

There were few unsatisfactory specimens in this series. In most series the inadequate specimen rate is up to 10% to 15% (3). This low rate in this series is, in part, because of the aspirator who performed a great number of the aspirations would perform an initial immediate quick staining to assess specimen adequacy and reaspirate if the specimens were unsatisfactory on the first attempt. The pathologist added the category “suspicious” or “atypical” to include the borderline specimens that could not definitely be diagnosed as being malignant or benign. These were specimens that had some characteristics of malignancy but did not fulfil the criteria of being malignant as previously mentioned. The other category included in the “suspicious” category was a papillary neoplasm because differentiating a benign papilloma from a well differentiated papillary carcinoma can be difficult on FNA sample. Surgical excision is advised when a papillary lesion is encountered. At times this group of neoplasia can be confused with fibroadenoma or fibrocystic change as it was seen in six patients in this series.

In general, the suspicious category contained some of both malignant and benign lesions according to final histopathology. So, this category, therefore, contained some of the false positive (benign) lesions. Instead of false-positive they are actually false suspicious. The large number of false positive or false-suspicious readings adversely affect the overall specificity and accuracy of the series. To accurately examine the ability of FNA to diagnose breast carcinoma, the results were generated into different fashions to account for the suspicious category. First, to calculate the overall sensitivity, specificity, positive and negative predictive values and accuracy of FNA, it was chosen to combine the suspicious and malignant categories. This approach decreases the chance of missing a positive result thereby increasing the sensitivity of the test. As noted previously the sensitivity was close to the reported average. Also, by performing the calculations in this manner,the specificity of the test decreases, as there will necessarily be more false-positive specimens-those that are included in the suspicious category but are benign. In fact the overall specificity in this series is slightly low because of the number of false-positive specimens in the suspicious category. The vast majority of false-positive specimens classified as suspicious were benign fibrocystic change and fibroadenoma.

In the second method by which the predictive values were generated, the calculations were performed using only those specimens that were definitely diagnosed malignant or benign. This was done to determine how reliably the definitive diagnoses were themselves, exclusive of the confounding variable included in the suspicious category. This is to determine how predictive the test was when the pathologist was confident in assigning a definitive diagnosis. When considered by themselves, the malignant and benign diseases posses high positive and negative predictive values, respectively. This indicates that, when a definitive diagnosis is made from FNA, it is a highly accurate and predictive tool. Interpretative errors are most often responsible for false-positive diagnosis. False-positive rates in the literature are reported in the range of 0 to 41%(4,8,9). In this

series, there was a low rate of false- positive results in the group read definitely as malignant. The false-positive specimens were all based on what were adequate specimens. One case was histologically diagnosed as fibroadenoma and the other as benign phyilodies. The potential for a false- positive diagnosis of malignancy exists in aspirates from the above and several histologic epithelial proliferations known to be responsible for false-positive diagnoses owing to the hypercellularity and significant epithelial proliferation with various degrees of atypia (10,11). The majority of false-positive specimens in this series were actually false-suspicious. When the pathologist was confident in diagnosis, it was rarely incorrect. The false-negative rate varies from 1% to 31% with a 10% average rate reported in the literature. A false-negative FNA is most often due to sampling problems; interpretation errors are rare (12,13). However, tumour-size paucicellularity, special histologic types such as tumours showing extensive fibrosis (therefore, decreased numbers of malignant cells), those with cells having relatively bland cytologic features like lobular carcinoma, colloid carcinoma, papillary carcinoma, monomorphic pattern of ductal carcinoma that can occur in older individuals, can also contribute to an increase in the false-negative rates. Awareness of these potential pitfalls can be helpful in avoiding a false-negative report in many of these cases. In this study many false- negative cases belong to high grade invasive carcinoma on histopathologic report. These may indicate that the sampling error could be part of the reason.

Diagnostic errors with subsequent inappropriate clinical decisions can be best avoided if clinicians use the so called triple (triplet) diagnostic procedure of clinical examination, mammography, and FNA cytology which increases the accuracy for the diagnosis of breast cancer (14). If FNA were used alone as the sole determinant of further therapy its low false-negative rate would still be too high to be acceptable. However, FNA is never used as the sole diagnostic modality determining intervention for palpable breast lesions. The triple test has been shown to be highly sensitive and specific in the diagnosis of breast cancer (14). Of the three tests, FNA has the highest sensitivity and specificity and may prompt further action in cases in which physical examination and mammography are not suspicious. Even with a negative triple tests, there is a certain small subset who will have a carcinoma.

In summary, fine-needle aspiration is a sensitive and highly specific method of evaluating palpable breast lumps for malignancy. It can be useful in confirming a diagnosis that is suspected by other diagnostic modalities. When a definitive diagnosis is assigned to a specimen, it is highly predictive of that mass being positive or negative for cancer. When suspicious lesions are included

in the analysis, the specificity and sensitivity of the test declines, as there are a considerable number of false-positive and false-negative lesions in the suspicious category. Because of the inherent inaccuracies within the test, it is difficult to recommend definitive treatments based on FNA unless the other diagnostic modalities concur with the FNA diagnosis. Even when FNA is combined with other tests there is a small occurrence of false-negative diagnoses. Suspicious, atypical or papillary lesions should be investigated further with open biopsy.

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