Evaluation of Diagnostic Accuracy of Fine Needle Aspiration Cytology in Palpable Breast Lesions

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SUMMARY

Fine needle aspiration cytology can be viewed as a procedure for the pathologist to provide diagnostic services at the patient bed-side. A total of 497 patients were included in this study, all presenting with palpable breast lumps and then undergoing fine needle aspiration in our established outpatient FNA clinic. Smears were stained with Giemsa and Papanicolaou stains in routine and where deemed necessary a Ziehl-Neelsen stain for acid fast bacilli were also included. Clots prepared from the residual aspirated material were stained with conventional Haematoxylin and Eosin staining technique. Out of the total 497 patients, 171 (34.41%) were malignant which included 165 (33.20%) ductal carcinomas, 5 (1.01%) lobular carcinomas and 1 (0.20%) malignant phylloides tumour. Two hundred and sixty six (53.52%) benign lesions were diagnosed, mainly comprising of 118 (23.74%) fibroadenomas, 46 (9.26%) fibrocystic disease and 21 (4.23%) abscesses. In 31 (6.24%) cases the diagnoses were equivocal (Gray Zone), while 29 (5.84%) aspirates were considered inadequate for assessment. The practice adopted by the cytopathologist who in addition to interpretation of spread smears, also does the clinical assessment followed by aspiration of the same lesion, was found very useful in reaching a correct final diagnosis. No false positive diagnosis was made and only 6 (1.21%) false negative diagnoses were recorded. An absolute sensitivity of 100% and complete sensitivity of 96.80% was achieved. In view of this high accuracy rate, fine needle aspiration cytology of breast lesions is strongly recommended for the proper clinical management of these patients.

INTRODUCTION

Fine needle aspiration cytology (FNAC) is the closest procedure to point of care diagnosis that is currently available in anatomic pathology. In a sense, fine needle aspiration cytology can be viewed as a vehicle for the pathologist to provide diagnostic services at the bed side. In breast lesions, a number of studies have shown the utility of FNAC for the diagnosis of palpable breast abnormalities and in subsequently deciding on an appropriate management protocol for a woman of any age, without the need for a confirmatory excisional biopsy. The technique being simple, accurate and painless is now an accepted part of the pre-operative assessment of palpable breast lesions. False positive diagnoses are rare and the test is regarded as sufficiently reliable to allow mastectomy after an unequivocal diagnosis of malignancy. Also, in view of many new treatment protocols, a diagnosis made on FNAC permits definitive discussion about treatment options with the patients. Cytodiagnosis of breast lesions can replace frozen section diagnosis in centres with sufficient experience. The technique is particularly suitable for use in countries where medical resources are limited.

In view of these considerations we reviewed our experience with the FNAC evaluation of breast lesions at Shaikh Zayed Hospital, Lahore. In addition, the importance of the procedure being performed by the pathologist himself/herself is highlighted for obtaining optimum results.
PATIENTS AND METHODS

Four hundred and ninety seven (497) patients, from January 1991 to December 1994, are included in this study. All these patients were symptomatic, presenting with palpable breast lumps.

Initial assessment was made by the surgeon, who then referred the cases to our FNA clinic in the out patients department, along with relevant clinical information. After studying the clinical notes and re-examining the lumps, the fine needle aspirations were performed by the cytopathologist. Similarly, in patients having breast lumps who were admitted in different wards of our hospital, FNAs were done by the cytopathologist in the respective wards.

All patients were injected local anaesthetic (2% Lignocaine) prior to the procedure, after cleaning the skin (with surgical spirit) overlying the breast lump. The FNA was performed with either a 21 or 23 gauge needle using a 20 ml disposable syringe. While constantly feeling and gripping the lump in left hand, the right hand was used to insert the needle into the lump through the anesthetized focus. Maintaining a constant negative pressure on the plunger, the needle was pushed in and out several times to traumatize the tissue. The detached cells and tissue fragments, mixed with blood, gradually accumulated in the needle and syringe.

After aspirating sufficient material, the negative pressure on the syringe plunger was gradually released and then the needle was taken out. Spread smears on glass slides were immediately prepared, some of the smears were air-dried for subsequent Giemsa staining while few slides were immediately fixed in 95% ethanol for the Papanicolaou staining. On average, a total of 4-6 slides were prepared from each patient.

Wherever possible, and whenever sufficient material was left over after making the smears, it was allowed to clot in the syringe, then fixed in 10% formalin and routinely processed and embedded in paraffin wax. Standard Haematoxylin and eosin (H&E) staining was done on 4 to 5 μm sections from these clots. These sections were evaluated alongside the spread smears while making a final diagnosis.

Cysts were aspirated completely. Then using another syringe a second pass was made in the collapsed cyst to obtain cells from the cyst wall. Smears were made from this aspirate, as well as from the centrifuged deposit of cyst fluid.

In cases of suppurative lesions and suspected tuberculous lesions a separate small sample was always sent for bacteriological culture. In addition to the above mentioned stains, a Ziehl-Neelsen (Z.N.) stain for acid fast bacilli (AFB) was routinely performed on these aspirates. In cases where the inflammatory/granulomatous nature of the lesion was noticed after examining the stained smears, a ZN stain for AFB was then performed on either any remaining unstained slide or on a suitable destained slide.

Evaluation of adequacy of sample

Once aspirated, the unstained spread smears were evaluated on naked eye examination by the operator for the presence of tiny grey white tissue fragments. Where deemed necessary, a second pass or rarely a third pass was made to obtain optimum aspirate.

While evaluating the stained smears, inadequate specimens were identified as those which were either so scanty or so morphologically distorted as to preclude analysis by light microscopy.

Statistical analysis

When available, the cytodiagnosis was compared with the histodiagnosis performed on the subsequently carried out lumpectomy or mastectomy.

Absolute sensitivity: This was calculated as the proportion of malignant lesions correctly diagnosed by FNA.

Complete sensitivity: This was calculated as the proportion of malignant lesions either correctly diagnosed as malignant or diagnosed as suspicious of malignancy by FNA.

RESULTS

A total of 497 patients with palpable breast lesions had fine needle aspiration samples taken between January, 1991 and December, 1994 (Table-1). Out of these, 171 (34.41%) were reported as malignant while benign diagnoses were made in 266 (53.52%) patients. Although a suspicion of malignancy was raised, a definite cytodiagnosis could not be offered in 31 (6.24%) cases. This group is labelled as "Gray Zone" in breast FNAC. In all these "gray zone" patients a biopsy was recommended to confirm the presence or otherwise of malignancy.
Table 1: Year-wise distribution of the total number of breast aspirates included in this study (n=449).

<table>
<thead>
<tr>
<th>Year</th>
<th>Total aspirates</th>
<th>Benign lesions</th>
<th>Malignant lesions</th>
<th>Gray zone (suspicious)</th>
<th>Inadequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>87</td>
<td>29</td>
<td>38</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>1992</td>
<td>117</td>
<td>78</td>
<td>52</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>1993</td>
<td>116</td>
<td>63</td>
<td>12</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1994</td>
<td>117</td>
<td>86</td>
<td>39</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>497</td>
<td>266</td>
<td>171</td>
<td>31</td>
<td>29</td>
</tr>
</tbody>
</table>

Out of 171 malignant lesions, the main bulk was ductal carcinomas (Table-2) which comprised 165 (33.20%) cases of the total aspirates (Fig. 1). Two (1.21%) of these were male patients and 13 (7.88%) ductal carcinomas were reported in young patients aged 18 to 30 years. Only 5 (1.01%) lobular carcinomas (Fig. 2) were reported.

Table 2: Cytological diagnosis of the breast aspirates included in this study (n=497).

<table>
<thead>
<tr>
<th>Cytodiagnosis</th>
<th>Cases</th>
<th>Age range (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td></td>
</tr>
<tr>
<td>Carcinoma*</td>
<td>170</td>
<td>18-80</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>118</td>
<td>10-47</td>
</tr>
<tr>
<td>Fibrocystic disease</td>
<td>16</td>
<td>22-63</td>
</tr>
<tr>
<td>Non-specific (Benign)</td>
<td>52</td>
<td>12-70</td>
</tr>
<tr>
<td>Gray zone (suspicious)</td>
<td>31</td>
<td>10-72</td>
</tr>
<tr>
<td>Inadequate</td>
<td>29</td>
<td>18-68</td>
</tr>
<tr>
<td>Abscess</td>
<td>21</td>
<td>23-50</td>
</tr>
<tr>
<td>Fat, necrosis</td>
<td>9</td>
<td>21-60</td>
</tr>
<tr>
<td>Granulomatous mastitis</td>
<td>7</td>
<td>23-35</td>
</tr>
<tr>
<td>Benign cyst</td>
<td>4</td>
<td>20-45</td>
</tr>
<tr>
<td>Gynaecomastia</td>
<td>1</td>
<td>22-72</td>
</tr>
<tr>
<td>Duct ectasia</td>
<td>3</td>
<td>34-45</td>
</tr>
<tr>
<td>Phyllodes tumour***</td>
<td>3</td>
<td>13-70</td>
</tr>
<tr>
<td>Miscellaneous**</td>
<td>10</td>
<td>20-60</td>
</tr>
<tr>
<td>**Total</td>
<td>497</td>
<td>100.00</td>
</tr>
</tbody>
</table>

This includes 162 ductal carcinomas NST, 2 colloid carcinoma, 1 medullary carcinoma and 5 lobular carcinoma.

No attempt was made to subtype the ductal carcinoma, although in 3 cases, one medullary and 2 colloid carcinomas, the cytological features were sufficiently distinctive that the respective diagnoses were offered (Figs. 3 and 4). Two of these 3 cytodiagnoses could not be confirmed on histology because the patients were lost in subsequent clinical follow-up.

Fig. 1: Sheet of malignant cells from ductal carcinoma breast. X400 (Giemsa stain).

Fig. 2: Sheet of malignant cells from lobular carcinoma breast. X400 (Giemsa stain).

A diversity of benign lesions were diagnosed on FNAC (Table-2). From the total aspirates in this
study, 266 (52.5%) benign conditions were reported. In which 118 (23.74%) fibroadenomas (Fig. 5) and 46 (9.26%) fibrocystic disease were the main lesions. Other lesions diagnosed on FNAC were fat necrosis (9 cases) benign cyst (4 cases) and benign phylloides tumour 2 cases (Fig. 6).

Fig. 3: Colloid carcinoma breast, intra and extracellular mucin. X400 (Giemsa stain)

Fig. 4: Sheet of malignant cells from medullary carcinoma breast. X400 (Giemsa stain)

Fig. 5: Benign ductal cells and bare nuclei from fibroadenoma breast. X200 (Giemsa stain)

Fig. 6: Cells from phylloides tumour of breast. X400 (Giemsa stain)

Out of the 21 (4.23%) "abscesses", in 4 cases Staph. aureus was successfully grown on routine bacteriological culture examination of the aspirated sample, while one case revealed AFB on ZN staining. In 7 (1.41%) cases a diagnosis of granulomatous
FNA of Palpable Breast Lesions

mastitis was offered. All these cases were negative for AFB.

Non-specific but benign diagnoses were made in 42 (8.45%) cases. These cases, although, showed benign ductal cells, however, could not be successfully placed in a specific disease entity. Other benign lesions diagnosed on FNAC, as shown in Table-2, were Gynaecomastia (4 cases) and Ductectasia (3 cases). The miscellaneous group comprised of 2 cases of Galactocele and 1 case each of Neurofibroma, Epidermoid cyst, Hematoma and duct adenoma. One aspirate revealed foreign body type of giant cells only. One case was suspected as phyllodes tumour on FNA and another diagnosed as fibrocystic disease, both were fibroadenomas on histology. The last of miscellaneous group was a case of sampling error, misdiagnosed as fibrocystic disease on FNAC which was in fact infiltrating ductal carcinoma as disclosed on subsequent histology.

Of the total 497 aspirates, 29 (5.84%) were labelled as inadequate based on criteria mentioned above.

Because of lack of proper clinical follow-up many patients were lost subsequently and thus histological correlation could not be made with our cytodiagnosis in those cases. However in 157 (31.59%) of these patients histology was available in the form of subsequently performed lumpectomy or mastectomy. Out of these, 101 (64.33%) were malignant. This comprised of 95 ductal carcinomas, 5 lobular carcinomas and 1 malignant phyllodes tumour. The remaining 56 (33.67%) cases were benign including fibroadenomas, fibrocystic disease and inflammatory lesions.

In cases where histology was available and a definite malignant diagnosis were made on FNAC, the absolute sensitivity of cytodiagnosis was found 100%. When cases of "gray zone" (equivocal diagnosis of malignancy) were also included, the complete sensitivity of the technique in our study was 96.8% (This does not include the gray zone cytodiagnosis where histological confirmation or otherwise is not available).

No false positive diagnosis was made. Six (1.21%) false negative diagnoses were made mainly due to inadequate aspirates.

DISCUSSION

Until a few years ago it was believed that the nature of the mammary lesions could only be established by histological examination following excision. The introduction of new diagnostic techniques, in particular fine needle aspiration cytology (FNAC), and their progressive improvement has modified this belief. These new techniques have now made it possible, in the case of benign lesions, to avoid surgery and therefore, eliminate two major drawbacks connected with it: psychological stress in patients and structural alteration of the breast often creating aesthetic problems11. In fact a policy of performing an open biopsy amounts to unnecessary intervention for a number of patients with benign diseases of the breast2.

The technique is particularly suitable for use in countries where medical resources are limited, as FNAC of breast has proved to be an extremely useful and cost-effective technique16, 17.

FNAC of the breast is an effective method of diagnosing carcinoma of the breast2. One hundred and seventy (170) cases of carcinomas were diagnosed out of a total of 497 aspirations. As also described by various other authors13, 18, the features found most useful in our study to diagnose ductal carcinoma were single cells or sheets of pleomorphic malignant epithelial cells with high N/C ratio, hyperchromatic nuclei with nucleoli.

As the aspirates were performed on palpable breast lumps most of the carcinomas were fairly advanced and moderate to poorly differentiated thus posing little problem in cytodiagnosis. The real mastery of aspiration cytology is the ability to translate cytologic patterns into tissue patterns that have diagnostic meaning18. This principle was regularly applied while evaluating smears in this study. So that in addition to other features of malignancy, the loss of cellular cohesion with single malignant cells and infiltration of stromal fragments were found very important and useful indication of malignancy.

The cytological features of colloid and medullary carcinomas are very well described in the literature2. So that although two of our 3 cases could not be confirmed on histology, we have no doubts about our diagnosis.

The greatest difficulties were experienced in correctly diagnosing lobular carcinoma. One aspirate was inadequate for assessment. In the remaining four, although a diagnosis of carcinoma was made in all cases, only one was correctly labelled as lobular
carcinoma in the first place. In one case, cytodiagnosed as ductal carcinoma, subsequent histology revealed *in situ* ductal carcinoma associated with invasive lobular carcinoma. This case reflects the phenomenon of sampling error, the aspiration needle hitting the *in situ* ductal component of the lesion rather than the invasive lobular carcinoma area. Lobular carcinomas often lead to a low percentage of positive diagnosis on FNA because these carcinomas are usually of low cellularity or secondly because these lesions have a bland monomorphic population of small cells.

Thirdly it is a very rare type of carcinoma in symptomatic breast lumps as compared to mammographically detected carcinomas. It was found to be a rare type in our study accounting for only 1.01% of carcinomas. An experienced cytopathologist is definitely a major factor in making a correct diagnosis. Active and continuous familiarity with FNAC in this area of breast pathology will be of great help in improving our experience and abilities of correctly cytodiagnosing lobular carcinoma in the coming years.

A Gray Zone, defined as cases in which unequivocal diagnosis of benignity or malignancy cannot be reached based on FNAC, does exist in breast cytology. Different reasons are cited including inexperience of the interpreter, overlapping cytologic features of benign and malignant breast lesions and technical reasons e.g. blood stained smears or poorly fixed/stained smears. As compared to other studies, where the incidence of doubtful/suspicious diagnoses ranged from 2% to 17%, our figure is 6.24%. The major factors contributing to this comparatively low figure were the clinical evaluation and performance of the aspirates by the cytopathologist him/herself, multiple passes to obtain adequate material and the practice of making a clot of aspirated material for routine formalin fixation, paraffin-wax embedding and H&E staining in the majority of cases.

When clinical examination of the lump, fine needle aspiration and the final interpretation of the smears are done by the same person, maximum sensitivity and specificity is achieved. This was reflected in our study as well where low figures for inadequate aspirates, Gray Zone and non-specific benign lesions were achieved. The validity of clinical examination of the lumps were also confirmed in fibrocystic disease of the breast, where the cytological findings of benign ductal cells, apocrine cells and macrophages, when combined with the clinical impression of a difficult-to-feel, irregularly outlined and diffuse mass, lend correct diagnosis in most of our cases.

Clots in FNA form an integral part of the procedure. Not only can the pathologist examine the cytological details in spread smears, but can also evaluate the architectural features of the lesions in clots. When both these features of a lesion are seen together, the diagnostic accuracy is greatly enhanced.

The inadequate aspirates were cases where either no cells were seen or the aspirate comprised of fibrofatty stroma or few cells only, insufficient for proper evaluation and diagnosis. Six (20.70%) of the total 29 inadequate aspirates were from malignant lesions as confirmed on subsequent histology. This difficulty in obtaining adequate aspirates in malignant lesions were also observed by others and mainly attributed to the excessively fibrosed and scirrhous nature of infiltrating carcinomas.

Inflammatory conditions of the breast may be confused with carcinoma and thus pose a clinical diagnostic problem. Also the importance of inflammatory lesions of the breast as a cause of morbidity is often over-shadowed by the magnitude of the problem of breast cancer. In the present study FNAC not only provided a diagnosis of an inflammatory lesion but a portion of the aspirate was used for bacteriological culture. Four aspirates from abscesses yielded the growth of staph. aureus, thus lending a specific diagnosis. The remaining culture-negative patients were probably already taking antibiotics at the time of aspirations. Our routine search for acid fast bacilli is fully justified in a community where tuberculosis is so widespread. This special stain for AFB enabled us to categorically separate the AFB positive tuberculous mastitis from the well defined category of granulomatous mastitis. Thus FNAC, besides offering a diagnosis in inflammatory lesions of the breast, can be used in subtyping the lesions into non-specific and specific inflammations and part of the sample can be used for bacteriological studies.

Fibroadenoma can be occasionally misinterpreted as carcinoma. One of our cases was placed in the 'gray zone' due to the presence of some atypical ductal cells, while the second case was suspected as phylloides tumour on cytology. Both lesions were subsequently diagnosed as fibroadenomas. In addition to the cytological
features, the patient's age, size of the lesion and cellularity of the smear can present erroneous diagnosis.27,28

Although no false positive diagnosis was made in the present study, in 6 cases (1.21%) the diagnosis of malignancy was missed. Although a simple procedure, FNA of the breast has limitations that are largely related to the sampling and preparation of the aspirated material as well as skills of the aspirator. In addition to inadequate aspirates, sampling error was the other major factor in our false negative diagnosis, the lesion being missed while aspirating. False negative reports of breast diagnoses our study demonstrated 100% absolute diagnosis. Our experience with FNAC of palpable breast lumps highlights the advantages of this procedure. The importance of FNA clinic as an organizational unit where cytopathologist performs the clinical examination of the patient as well as aspirates the lump is also stressed. This will greatly reduce the rate of inadequate specimens and will increase the number of correct diagnosis. The excellent results obtained by this procedure demands that this simple, painless, rapid and cost-effective method should be routinely employed in all symptomatic palpable breast lesions. The preoperative assessment of breast lumps by FNAC is strongly recommended.

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