Fine-needle Aspiration (FNA) Cytologic Diagnosis of Breast Lesions

Ali Hassan Al-Timimi          Haythem Ali Al-Sayigh
Medical Collage, Babylon University, Babylon, Iraq

Abstracts

Background: Surgical excision breast biopsy procedures have proved to be costly, cosmetically disfiguring to the breast, and psychologically traumatic to patients. Only 15%-30% of the lesions subjected to biopsy are malignant; the rest are benign or atypical. It is desirable to decrease the number of surgical biopsies, particularly in cases of benign breast disease, provided the detection rate of cancer remains unaffected.

Aims: To study the accuracy of fine-needle aspiration (FNA) cytological diagnosis of breast lesions

Patients and Methods: FNA cytological examination was performed in 96 breast lesions. The centre area of the lesions was located and accurate placement of the fine-needle, followed by aspiration. A successful aspirates yielded sufficient cytological materials adequate for diagnosis.

Results: The cytological examination was considered unsatisfactory in 6 cases (6.25%) of the 96 specimens due to insufficient material. The cytological diagnosis was benign in 55 cases (57.29%), atypical in 9 cases (9.3%), suspicious for malignancy in 6 cases (6.25%), and malignant in 20 cases (20.8%). All cases diagnosed as suspicious or malignant and 3 of 55 cases diagnosed as benign at cytological examination proved to be malignant at histological examination.

Conclusions: It is concluded that fine-needle aspiration cytology of the breast lesions is safe, inexpensive, minimally invasive, and highly accurate in the diagnosis of breast disease. The procedure has a central role in the management of breast lesions and should be used as the initial diagnostic test. However, false negative do occur mainly through sampling error, and invasive cancer cannot distinguish from in situ disease.

Introduction

Surgical excision breast biopsy procedures have proved to be costly, cosmetically disfiguring to the breast, and psychologically traumatic to patients. Only 15%-30% of the lesions subjected to biopsy are malignant

(Hann et al 1989 and Boerner et al 1999) the rest are benign or atypical, it is desirable to decrease the number of surgical biopsies, particularly in cases of benign breast disease, provided the detection rate of cancer remains unaffected.

Fine-needle aspiration (FNA) cytologic examination of palpable breast lesions has shown encouraging results in differentiating benign from malignant diseases (Hann et al 1989, Boerner et al 1999 and Zardawi et al 1999). It may not only help avert surgery in many patients (Sneige et al 2000, Wang et al 1989 and Verkooijen et al 2002) but will substantially reduce the cost of diagnosing breast cancer (Ariga et al 2002 and Putwain et al 2009). This is contingent on accurate placement of the biopsy needle, adequate sampling of the lesion, and a low false-negative rate of cytological results.

Using various localizing methods and equipment, some investigators have reported a false-negative rate of 3%-6.7% for the diagnosis of carcinoma (Evans et al 1992 and Liberman et al 2008). Insufficient material has been reported in 8.1%-26% of cases (Liberman et al 2008 and Eloubeidi et al 2003). The reasons for obtaining insufficient material are believed to be related to the accuracy of needle placement and type of breast tissue sampled (Dundas et al 1988 and Farshid et al 2005). We have attempted to assess the accuracy and limitations of the FNA cytological procedure. Faulty needle placement as a source of sampling error was eliminated by accurately aspirating the area of abnormality.

The glandular portion of the breast develops from the ectoderm. It arises from the local thickening of the epidermis. From this thickening, 16 to 24 buds of ectodermal cells grow into the underlying mesoderm (dermis) during the twelfth week. These buds, at first solid, will become canalized near term to form the lactiferous ducts. The tips of the buds will give rise to the secretory acini during lactation. The epidermal surface of the future nipple is at first a shallow pit. Near term it becomes everted. The areola is
suggested to be visible from the fifth month onward. Note that an inverted nipple may be a developmental arrest rather than a true pathological condition (C.S Sinnatamby, et al 2006).

The adult female breast is located within the superficial fascia of the anterior chest wall. The base of the breast extends from the second rib above to the sixth or seventh rib below, and from the sternal border medially to the midaxillary line laterally. Two-thirds of the base of the breast lies anterior to the pectoralis major muscle; the remainder lies anterior to the serratus anterior muscle. A small part may lie over the aponeurosis of the external oblique muscle. (Moor et al 2000 and Snell et al 2004).

Both men and women have breasts (C.S Sinnatamby, et al 2006) normally they are well developed only in women. The mammary glands in the breasts are accessory to reproduction in women but are rudimentary and functionless in men, consisting of only a few small ducts or epithelial cords. Usually, the fat present in the male breast and the glandular system does not normally develop. The breasts are the most prominent superficial structures in the anterior thoracic wall, especially in women. The mammary glands are in the subcutaneous tissue overlying the pectoralis major and minor muscles. The amount of fat surrounding the glandular tissue determines the size of non-lactating breasts. At the greatest prominence of the breast is the nipple, surrounded by a circular pigmented area of skin, the areola (Moor et al 2000 and C.S Sinnatamby, et al 2006).

Materials and Methods

Fine-needle aspiration biopsy, an office procedure, is relatively simple and is described in detail elsewhere (Zardawi et al 1999 and Verkooijen et al 2002). In brief, after careful breast palpation, the lesion to undergo biopsy is identified. The skin is cleaned with alcohol; usually, no local anesthesia is necessary. A 21- or 23G gauge butterfly needle attached to a 10-mL disposable syringe were used. (Norman et al 2008)

With one hand holding the pistol-grip holder and the other hand palpating the lump, the aspirator places the needle into the lump, applies suction, and moves the needle within the nodule and negative pressure applied. Suction is then released and the needle is withdrawn; aspirated material is expelled on glass slides and prepared in a manner similar to that for blood smears. Slides are either air-dried and stained using the May-Grunwald-Giemsa technique or immediately wet-fixed in 95% ethyl alcohol and stained using a modified Papanicolaou method (Kanhoush et al 2004). We prefer Papanicolaou staining because it is more similar to other cytological preparations.

Two to 3 aspirations were done, as the number of aspirations increased, false-negative results decreased. After the procedure is completed, the patient is observed for a few minutes and then allowed to depart. Serious complications have not been reported; minor pain was transient and tolerable the results of the cytologic and histologic examinations of the resected specimen were later compared. The results of cytologic examinations were classified into five groups:

1. Unsatisfactory (ie, specimen showing four or fewer groups of epithelial cells and/or fewer than 100 epithelial cells);
2. Benign (ie, including benign epithelial groups without atypia, sclerosing adenosis, hyalinized fibroadenoma, fibrous mastopathy, fat necrosis, and intramammary lymph node);
3. Atypical (ie, atypical duct-cell hyperplasia with or without intraductal papillomatosis);
4. Suspicious for malignancy (ie, abnormal cells that are almost certainly malignant but either are too scanty or show incomplete criteria for an unequivocal diagnosis of malignancy).
5. Malignant.
Results

Table 1, shows the results and correlation of FNA cytological findings with histological diagnoses in 96 surgically resected breast lesions studied. The cytological examination was considered unsatisfactory in 6 (6.25%) of the 96 specimens due to insufficient material. The histological diagnoses of the surgically resected specimens were compared with that cytological results. The cytological examination was diagnosed as benign in 55 cases, three proven to be malignant at histological examination, one an infiltrating ductal carcinoma (Figure 1,2); the second, a DCIS; and the third, a single focus of LCIS. A correlation of FNA cytologic and findings with histologic diagnoses in these 3 surgically resected breast lesions may be considered as false-negative. 9 cases were diagnosed as showing atypia with fibrous mastopathy by both at cytologic and histologic examination. The cytologic interpretation was suspicious for carcinoma in 6 cases, and malignant in 20 of these 90 aspirates. Histologically, all these 20 cases proved to be malignant, with 7 infiltrating (Figure 3) and 13 in situ carcinomas. There were no false-positive diagnoses in this group.

Discussion

Fine needle aspiration cytology is the least invasive technique of obtaining a cell diagnosis and is rapid and very accurate if both operator and cytologist are experienced (Krishnamurthy et al 2003 and Norman et al 2008). Fine-needle aspiration has two major limitations: non diagnostic results and suspicious or indeterminate results. Inadequate or non diagnostic, smears often occur in the setting of cystic or vascular lesions (White RR et al 2001 and Liao et al 2004). Examination of cystic fluid, biopsy of the cyst capsule, or repeat biopsy may produce satisfactory results. Clearly, the success of fine-needle aspiration depends on careful aspiration and smear preparation as well as on cytologic evaluation. Hall and colleagues (Bauer et al 2003 and Choi et al 2004), reviewing the experience at the University of California at Los Angeles (UCLA), found that the frequency of inadequate smears was 15% for hospital-based physicians and 32% for community-based clinicians.

On the other hand, the number of years of experience with the procedure did not influence results. These findings imply that the acquisition and maintenance of aspiration skills are more important than the total number of years of experience in influencing the rate of non diagnostic results.

The second limitation of fine-needle aspiration is the "indeterminate" or "suspicious" result, this problem was previously reviewed and found that in most series, between 10% and 15% of aspirates show a "suspicious" result because of the cytopathologic difficulty in differentiating cellular benign from their malignant counterparts sometime. Approximately 5-15% of nodules with indeterminate cytologic findings are found to be malignant at surgery. Different ways to minimize suspicious cytologic findings have been suggested such as, the use of large-needle biopsies (Tonegutti et al 2004 and Meracado et al 2006) or the quantitative analysis of nuclear size and shape so the sampling error decreases as the biopsy volume increase and using 8G-11G needle allows more extensive biopsy to be taken. This is useful in management of microcalcifications or in the complete excision of benign lesion such fibroadenomas (Norman et al 2008 and Sivakumar et al 2009). High-resolution real-time US can depict focal lesions of the breast less than 1 cm in diameter (Sneige et al 1994). Because of limitations of tissue characterization on US, noncystic breast masses must often undergo biopsy for definitive diagnosis. Furthermore, carcinomas sometimes appear as well-defined smooth nodules on either x-ray mammograms or sonograms.

As the number of breast lesions being found at mammography or sonograms
increases, clinicians are becoming more reliant on the opinion of the radiologist for the management of these lesions. The low specificity of mammography, however, which in the ranges of 25% for the diagnosis of carcinoma (Shah et al 2003 and Choi et al 2004), has led to an increasing number of surgical biopsies being performed for diagnostic purposes. FNA biopsy may be helpful to increase the specificity of diagnosis of breast lesion and to reduce the number of unnecessary biopsies (Green et al 2001 and Medina et al 2004). The major difficulties of FNA biopsy are accurate needle placement and obtaining of sufficient cytologic material from breast lesions that have abundant reactive fibrosis. Many reports of the usefulness of FNA biopsy have appeared in the recent literature, but different equipment and techniques have been used by various authors.

(Farshid et al 2003, Tez et al 2008 and Vuolo et al 2009), which may account in part for the variation in their results. The rates of obtaining insufficient cytologic material ranged from 8.1% to 26%. The size of the needle used ranged from 21- to 23-gauge and did not seem to be an important factor. Therefore, we have attempted to evaluate FNA cytologic examination after having eliminated or minimized needle placement as a source of error for adequate sampling of the lesion. Concern has also been expressed as to whether a neoplasm in the vicinity of the lesion might be missed with FNA biopsy. These difficulties were addressed in our study by accurately placing the biopsy needle for FNA in the centre area of the lesion in all cases, then submitting the entire surgical specimen for histologic examination after having inked the area that was aspirated, to allow the histopathologist to include it in the area and to study it separately from the rest of the specimen.

Despite the accuracy of needle placement, I of the lesions yielded unsatisfactory cytologic samples, in 6.25%, this was attributed to technical difficulties because the lesion was located at the periphery of the specimen, thus not allowing adequate aspiration. The remaining unsatisfactory samples were attributed to the type of breast tissue aspirated. Abundant fibrosis, scarring, and lesions with low cellularity or a small number of ductless reduced the chances of obtaining representative material (Schawrtz et al 1988, Sauer et al 2006 and Simon et al 2009). Similar lesions were successfully aspirated in the rest of our material, however, and therefore, other undetermined technical factors may have played a role. This rate of unsatisfactory samples would have decreased further had we aspirated the specimen more than once whenever insufficient material that could be seen with the naked eye was expelled from the needle. It has been shown that three or four aspirations of a breast lesion produce a better yield than does one (Fajardo et al 2004 and Khurana et al 2009). Moreover, having a cytopathologist present at the time of needle aspiration to confirm the adequacy of the sample is helpful but not always possible. Although it is difficult to eliminate insufficient cytologic material as a sampling error, it can perhaps be reduced to 4% or less if the needle is accurately placed and if multiple needle passes are performed.

Lesions that yield insufficient material should be restudied, either with repeated aspiration or with surgical excision. In our study, cases involving insufficient material were considered neither benign nor malignant and were not included in the statistical analysis of the results because they did not provide cytologic information.

A specific diagnosis of benign breast disease was made cytologically in 55 cases and was confirmed histologically in 55. In three of the 55 cases— the only 3 in the entire series in which malignancy was found unrelated to the radiologic abnormality— single foci of carcinoma in situ were found in the specimen outside the area. These two cases were not considered to give false-negative re-suits because they did not lie in the cytologically sampled area. Moreover, one of the two cases showed a single focus of LCIS. Foci of LCIS are incidental findings not uncommonly found in tissue adjacent to,
but not in the area of, the mammographic abnormality for which the biopsy was performed (Mitnick et al. 1996 and Sneige et al. 2006). Of the 55 cases diagnosed cytologically as benign, three showed carcinoma in the S area at histologic examination. These results were considered false-negative. A low false-negative rate of 3%-6.7% has been reported in vivo studies (Masood et al. 1990, Lies et al. 1996 and Mitnick et al. 1996). A review of the mammographic findings in cases reported as cytologically benign can play an important role in further evaluating such lesions. Those lesions appearing suspicious mammographically should be restudied with either a repeated FNA or surgical excision of the nine specimens that were diagnosed cytologically as showing atypia, two showed carcinoma at histologic examination. A cytologic diagnosis of atypia is an indication for surgical biopsy (Liao et al. 2004 and Jayaram et al. 2005). Therefore, carcinomas in this group should not be missed because all patients with atypia will undergo surgical resection. Investigators of in vivo studies have treated atypia similarly (Krishnamurthy et al. 2003, Choi et al. 2004, Snell et al. 2004 and Putwain et al. 2009). All 20 specimens diagnosed cytologically as malignant or suspicious for malignancy were found at histologic examination to be cancerous. Similar results have been reported in in vivo studies in which no false-positive results were found in those cases diagnosed cytologically as malignant or highly suspicious of malignancy (Chaiwun et al. 2005, Medina-Francisco et al. 2004 and Kerlikowaskie et al. 2004). The infiltrating cancers in this group, appeared mammographically as a mass or parenchymal distortion, cases involving DCIS showed multifocal or extensive disease. Multifocality cannot be determined cytologically and may play an important role in determining the therapeutic management. Therefore, FNA cytologic assessment may not provide sufficient information to pursue breast conservation treatment, in interested patients. If the cases diagnosed as atypical at cytologic examination are considered neither benign nor malignant and are excluded from the statistical analysis, the sensitivity of FNA cytologic assessment in this series is 91%, overall accuracy is the specificity is 100%. If the cases of cytologic atypia are not excluded, however, the sensitivity is 91%, the specificity is 92%, and the accuracy is 91%. Fine-needle aspiration biopsy is safe, simple, and accurate. It is done in an outpatient setting, and repeated aspirations may be done. The procedure should be done by pathologist or clinicians with a special interest in breast diseases. Cytologic interpretation should be done by a pathologist with a special interest and expertise in cytdiagnosis (Sneige et al. 2000, Kanhoush et al. 2004 and Lacoste et al. 2009). The procedure has no serious disadvantages.

Conclusions
Fine-needle aspiration biopsy is safe, accurate, and cost-effective. The procedure has a central role in the management of breast lesions and should be used as the initial diagnostic test. However, false negative do occur mainly through sampling erro, and invasive cancer cannot distinguish from in situ disease (Schawrtz et al. 1988, Sauer et al. 2002 and Norman et al. 2008.).
Figure 1. Specimen from fine-needle aspiration biopsy of breast showing cytologic features of carcinoma and followed by the performance of a mastectomy, which confirmed the cytologic interpretation (pap stain, *40, cytology).

Figure 2. Fine-needle aspiration biopsy of breast showing cytologic features of invasive ductal carcinoma. (Pap stain, *40, cytology)
Figure 3. Invasive ductal carcinoma showing small glands infiltrating stroma (H&E, *25, histological section).

Table 1. Correlation of FNA Cytologic Findings with Histologic Diagnoses in 96 Surgically Resected Breast Lesions

<table>
<thead>
<tr>
<th>Type</th>
<th>FNA</th>
<th>Histological</th>
<th>different</th>
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<tbody>
<tr>
<td>Unsatisfaction</td>
<td>6 (6.25%)</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>Benign</td>
<td>55(52)</td>
<td>52</td>
<td>3</td>
</tr>
<tr>
<td>Atypical</td>
<td>9(9.3%)</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Suspicious</td>
<td>6(6.25%)</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>Malignant</td>
<td>20(20.8)</td>
<td>-all</td>
<td>Malignant</td>
</tr>
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Abbreviations: DOS = ductal carcinoma in situ, FNA = fine-needle aspiration, LCIS = lobular carcinoma in situ
References


