

Fine needle aspiration cytology of the breast: an analysis of 1,094 aspirates

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Abstract

Our experience with 1,094 consecutive fine needle aspirations (FNAs) of the breast in 918 cases is presented. Correlation between the FNA cytology and subsequent histology of the lesions was available in 211 cases. FNA had a sensitivity rate of 87.3%, a specificity rate of 99.3% and a positive predictive value of 98.2%. A false negative diagnosis rate of 5.1% occurred. The overall diagnostic accuracy rate was 95.7%.

Key words: Fine needle aspiration cytology, breast, aspirates.

INTRODUCTION

Fine needle aspiration (FNA) cytology is now a well established technique used in the diagnosis of a variety of neoplasms. Since its introduction in the early 1930's by Martin and Ellis,¹ the technique has undergone much refinement with the use of very fine needles and fluoroscopic equipment for deep seated lesions. However, it was not until the 1970's that FNA became broadly accepted. In Universiti Kebangsaan Malaysia (UKM), FNA of palpable masses has been performed on a regular basis since 1988. Presently, approximately 1400 FNAs are performed every year, of which approximately 26% are of breast masses. This paper presents our experience with FNA of palpable breast lesions referred to the FNA clinic. Our main aim is to assess the value of FNA in the diagnosis of breast lesions.

MATERIALS AND METHODS

From January 1988 to December 1991, a total of 1,094 aspirations were carried out by the Cytopathology Unit, UKM. The FNAs were performed on 918 patients (915 females, 3 males), some of whom presented with multiple breast lesions. FNAs performed on both breasts or on different anatomical sites in the same breast were analysed as separate samples. Multiple lesions were all needled and labelled separately.

The FNAs were performed in the FNA clinic UKM on an appointment basis, unless the requests were urgent. The majority of patients were referred through the Department of Surgery UKM or the General Hospital Kuala Lumpur as outpatients. A few were ward cases of the

General Hospital Kuala Lumpur and some were referred from other hospitals in the country.

The majority of FNAs were performed by one pathologist. All smears were prepared by a trained cytotechnologist attending the clinic and all samples were evaluated for adequacy and quality of material. The whole procedure would be repeated if insufficient cellularity was obtained.

The breast was palpated and the lesion localised and held in position with one hand. The skin was cleansed with 70% alcohol soaked in cotton. A 20 ml disposable plastic syringe attached to a syringe holder and a 25 gauge disposable needle was used for the aspiration. The skin was punctured and the needle advanced towards the mass. Once the mass was entered into, full suction was applied. The needle was moved back and forth within the lesion along the same track with the negative pressure maintained. When aspiration was completed, the negative pressure was released with the needle still in the lesion. The needle was then withdrawn and immediate pressure applied to the punctured site with a sterile gauze pad.

Following the FNA, the aspirated material was expressed onto glass slides which were labelled with the patient's name. Smears were prepared by placing a second glass slide onto the first and pulling across gently. At least two smears were prepared, one fixed in 95% ethyl alcohol and the other air-dried. Lesions were aspirated a maximum of three times if samples were inadequate.

After the smears were prepared, the syringe and needles were rinsed in saline medium (cytospin, Shandon). The fluid was centrifuged

and the cell button retrieved for preparation of cell blocks. Alcohol fixed smears were stained by the routine Papanicolaou technique and air-dried smears stained with May Grunwald Giemsa (MGG).

All smears were interpreted by a single pathologist. A short descriptive report would be issued with a definitive diagnosis given wherever possible. All smears which fulfilled definite morphological criteria of malignancy² were reported as malignant. An example of a typical malignant smear is shown in Fig. 1. A "suspicious" diagnosis was issued for those cases in which cytological findings were suggestive of a tumour, but lacked sufficient diagnostic features to establish the presence of malignancy. All smears displaying the basic benign pattern³ (Fig. 2) were classified as benign. An "unsatisfactory" category was utilised for those cases in which the material obtained did not contain adequate cellular fragments or when cytopreparation was not optimal. The corresponding histopathology reports were retrieved from the Department of Pathology files and compared with the cytology reports. The results from patients who had both cytological and histopathological diagnoses were utilised to assess the sensitivity, accuracy and

predictive values⁴ of a positive FNA result in the diagnosis of breast masses.

RESULTS

In the 4-year period between 1988 and 1991, a total of 1,094 fine needle aspirations were carried out. Of these, 865 (79%) aspirates were reported on cytology as benign, 111 (10%) as malignant and 43% (4%) as suspicious. 75 (7%) were cytologically inconclusive. These findings are summarised in Table 1.

Histological correlation was available for 211 cases. Comparisons of the FNA and histological findings are summarised in Table 2.

The cytological terminology used to designate the various subtypes of benign lesions included fibroadenoma, fibroadenosis, fibrocystic disease, simple cyst, breast abscess, duct papilloma, epithelial hyperplasia, gynaecomastia and changes due to lactation. Smears which were adequate and showed cytological features of benignancy but which were difficult to subtype were simply reported as benign.

Of the 155 aspirates reported as benign on cytology, 147 were histologically benign. The histological diagnoses comprised 83 fibroadenomas, 19 fibroadenosis, 21 fibrocystic

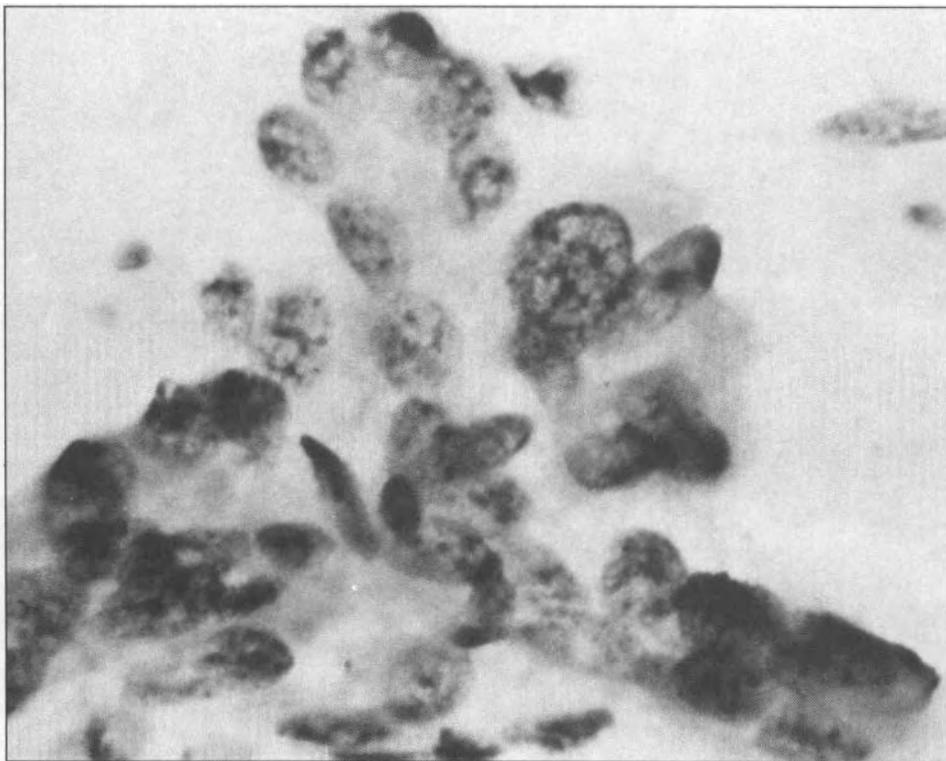


FIG. 1: Loosely arranged malignant epithelial cells displaying coarse granular chromatin from a ductal carcinoma. Papanicolaou stain x400

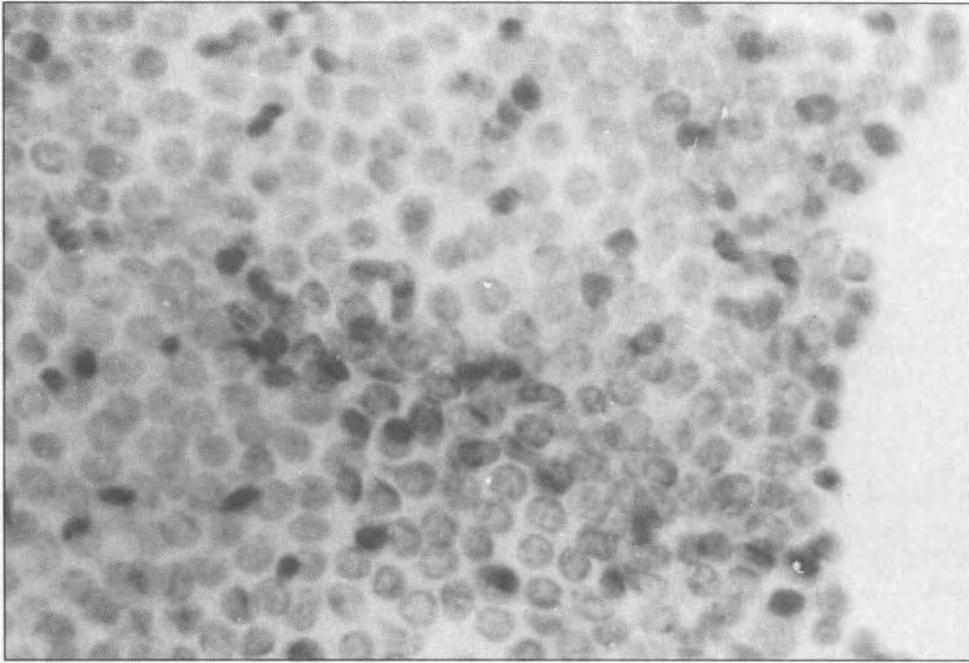


FIG. 2: Uniform benign epithelial cells in a cohesive sheet from a fibroadenoma x200

disease of the breast, 9 breast abscesses, **3** duct ectasias, 3 duct papillomas, 3 **apocrine** cysts, 1 **sclerosing** adenosis, 1 epithelial hyperplasia and 1 lactation changes. 3 biopsies from post mastectomy patients on follow-up who presented with suspicious breast masses over the mastectomy scars were reported as negative for recurrent tumour, consistent with the cytology reports.

8 cases were reported as malignant on histology. Of these, 2 were cystic carcinomas, 1 an infiltrating lobular carcinoma and 5 were infiltrating ductal carcinomas. The cystic carcinomas yielded about 10 mls and 5 mls of fluid on aspiration. Review of the smears did not show diagnostic carcinoma cells. The 5 cases of infiltrating ductal carcinomas reported as benign on cytology were reviewed. In 2 cases the smears showed neoplastic cells which were

generally bland looking. No marked **pleomorphic** features were noted on the cytology smears. Review of the histology slides showed areas of infiltrating as well as intraductal carcinoma of the breast. Both cases were reported on cytology as benign with fibroadenomas as the likely diagnoses. In the third case reported on histology as infiltrating ductal carcinoma, no malignant cells were present in the FNA smears. The sample obtained showed mainly degenerative changes, benign epithelial cells and **macrophages** and was reported as benign with fibrocystic disease as the possible **subtype**. Review of smears from the fourth case showed a blood-stained smear with a few tightly cohesive **epithelial** cells which were very heavily stained. The poor cytopreparation made interpretation very difficult. The fifth case showed very few small clusters of epithelial cells which were interpreted

TABLE 1: Diagnoses based on FNA of the breast: 1988-1991

FNA diagnosis	No.	%
Benign	865	79
Malignant	111	10
Suspicious	43	4
Inconclusive	75	7
Total	1094	100

TABLE 2: Correlation of breast FNA cytology with histopathology

FNA diagnosis	Histopathological diagnosis		
	Benign	Malignant	Total
Benign	147	8	155
Malignant	0	48	48
Suspicious	1	7	8
	148	63	211

as benign on cytology. The lesion was aspirated three times with similar results. Subsequent histopathology sections showed an infiltrating ductal carcinoma with marked desmoplastic reaction.

Review of the case of infiltrating lobular carcinoma showed very few small cells which were generally distributed singly and thought to be lymphocytes. Also present were several benign and necrotic fat cells, macrophages and some inflammatory cells. The smears were reported as most probably fat necrosis but an excision biopsy was strongly advised based on clinical findings.

All 48 cases reported on cytology as malignant concurred with the histological diagnoses. There were 44 infiltrating ductal carcinomas, 2 mucinous carcinomas, 1 malignant lymphoma (non-Hodgkin's, poorly differentiated) and 1 metastatic sarcoma.

In the "suspicious" category, 7 (87.5%) of the aspirates turned out to be malignant on follow-up tru-cut biopsy. Review of these smears showed a spectrum of morphological changes. There was a marked inflammatory component in 2 cases, cystic degeneration in 2 cases and mainly necrotic changes in 2 cases, even after repeated aspiration of the latter. In 1 case in which the patient was lactating, cytology smears showed atypical changes thought to be due to lactation. Suboptimal cytopreparation also contributed to the difficulty in interpreting some of the cyto-

logical changes.

75 aspirates were reported on cytology as "unsatisfactory" (Table 1). The majority were due to the lack of sufficient material from patients referred with very small or vaguely palpable breast lesions most of which were less than 1 cm in diameter. These patients responded to conservative treatment. No tissue biopsies were performed.

Results of both cytological and histological correlations are shown in Table 2. For statistical purposes, the cases reported as "suspicious" for malignancy were combined with the malignant cases. This gave a total of 211 cases for histopathologic correlation (Table 3).

Of the 155 cases reported as benign on cytology, 8 turned out to be malignant on histological examination, giving a false negative rate of 5.1%. Of the 56 cases in the malignant category, 55 correlated with the histology report. One case reported on cytology as "suspicious" turned out to be benign. This was a case of a chronic breast abscess. The positive predictive value was 98.2%. Fine needle aspiration cytology was able to correctly identify 55 malignant cases out of the 63 histologically malignant cases, giving a sensitivity rate of 87.3%. The diagnostic accuracy was 95.7%.

DISCUSSION

The management of recently discovered breast masses represents a significant clinical chal-

TABLE 3: Specificity and sensitivity of breast FNA

FNA diagnosis	Histopathological diagnosis		
	Malignant	Benign	Total
Malignant	55	1	56
Benign	8	147	155
Total	63	148	211

Sensitivity* : 87.3%
 Specificity : 99.3%
 Positive predictive value : 98.2%
 Diagnostic accuracy** : 95.7%
 False negative rate# : 5.1%
 False positive rate### : 1.8%

* Sensitivity: includes suspicious cases.
 ** Diagnostic accuracy (efficiency of the test) calculated as:
 (Total negative + Total positives)/TP+FP+TN+FN
 # False negative rate is calculated as the ratio of false negative diagnoses to all negative cytological diagnoses.
 ## False Positive Rate is calculated as the ratio of false positive diagnoses to the total number of positive cytological diagnoses.

lenge. Standard clinical practice dictates an open biopsy, 80% of which prove to be benign on histopathological examination.⁵ FNA cytology as a diagnostic modality has many advantages for the patient as well as for the physician. For the patient, the technique is rapid and inexpensive compared to open biopsy, is relatively painless and does not leave a scar. When a positive cytological diagnosis of malignancy is made, the patient has time to prepare herself emotionally and review and discuss therapeutic options. When a negative diagnosis is made, a choice to follow-up the patient or perform an open biopsy can be decided upon based on the individual clinical presentation. Hence, not all patients who have had an FNA of the breast need undergo subsequent biopsy. For the physician, FNA is an expeditious, time saving and cost effective diagnostic method. In a large and busy hospital set-up like the General Hospital Kuala Lumpur, this technique has proven to be very helpful as the results can help decide which patients should be given priority for mastectomy or excision biopsy. A confident report of malignancy in the presence of a consistent clinical presentation may obviate the need for biopsy altogether.

In patients with metastatic or recurrent breast carcinomas, FNA may avoid an operative procedure. Also, oestrogen⁶ and progesterone⁷ receptor studies can be performed on FNA material.

The use of stereotaxic technique to aid in FNA of mammographically identified non-palpable breast lesions is now improving results. This technique allows a wider application of FNA cytology.

Our results are comparable with those of other large series^{8,9,10}. Our sensitivity rate was 87.3% and diagnostic accuracy 95.7%. The false negative rate was 5.1%. Diagnostic inaccuracies in our series were caused by technical problems as well as interpretative errors. Review of the 8 false negative reports showed 2 to be due to purely interpretative errors which occurred early in our FNA experience, and 6 to be related to technical difficulties. Technical difficulties generally arose due to the small size of lesions, most of which were less than 1 cm in diameter and vaguely palpable, poor cellular composition of aspirates due to tumour desmoplasia, degenerative changes especially if the tumour is cystic, necrosis and haemorrhage. Marked desmoplasia was seen in two carcinomas on histological review. The tight fibrotic stroma is believed to inhibit the release of neoplastic cells. Predominantly cystic lesions encountered in intracystic carcinomas have also been reported by others to

contribute to false negative diagnoses." They usually yield partially degenerated material. Other types of tumours e.g. comedo carcinomas with extensive necrosis, may yield mainly necrotic material with few recognisable tumour cells.

Aspirator experience plays a significant role in achieving an acceptable frequency of false negative breast FNA specimens. Dixon *et al*¹² and Lee *et al*¹³ documented a technical failure of about 10% for a single experienced aspirator compared to a 49.5% failure rate for a group of less experienced clinicians. Barrows *et al*¹⁴ demonstrated that the person performing the aspiration was the most important variable determining success in obtaining adequate material in their study of 689 women with primary breast carcinoma.

Interpretative errors appeared to be less responsible for false negative results than technical mistakes. Interpretative skills improved with experience. Certain histological types of carcinomas appeared to be associated with more false negative results than other histological types. These difficulties have been reported with infiltrating and *in-situ* lobular carcinoma, intraductal carcinoma and tubular carcinoma. Their small cell size and often bland appearance result in their being underdiagnosed.

False positive diagnoses are rare in breast FNA cytology if the interpretations are made by experienced cytopathologists.⁸ A false positive FNA diagnosis can lead to inappropriate radical surgery if cytology is used as the sole criterion for therapy. Some workers believe that FNA diagnosis of carcinoma must be confirmed by open biopsy or intraoperative frozen section, while others suggest that mastectomy may be performed on the basis of a cytological diagnosis of carcinoma in the appropriate clinical setting.

Optimal cytopreparation is very important in the final interpretation of fine needle aspirates. Poor fixation and inadequate staining can contribute to a false impression of malignancy. Slow fixation with air-drying of alcohol-fixed smears may result in apparent nuclear enlargement and hyperchromasia creating a suspicion of a malignant tumour for the unwary.

Suboptimal cytopreparation can make interpretation difficult. This problem contributed our aspirates in the "suspicious" category. We preferred to report a lesion as "suspicious" if there is the slightest uncertainty and request an urgent biopsy to exclude malignancy. This explains the high percentage (87.5%) of malignant cases in our suspicious category. Only one case reported

as "suspicious" was benign. This was considered a false positive report for statistical purposes. All smears reported as malignant were histologically malignant. Based on the correct clinical findings and an FNA report of malignancy, it is a common practice to proceed with mastectomy in our institution.

Unsatisfactory cases comprised 4% of our aspirates. The majority were from cases referred for vaguely palpable tender lesions in the breast. Most of these lesions were less than 1 cm in diameter and generally yielded hypocellular or acellular material even after repeated attempts. These cases were followed up and responded to conservative management.

We attribute our high diagnostic accuracy rate of 95.7% to a combination of experience with FNA, awareness of the importance of proper smearing and cytopreparation, familiarity with the variable cytological appearances of the different entities of breast lesions on cytology, the correct attitude and approach when interpreting reports and, last but not least, a good working relationship and rapport with our clinicians.

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