

นิพนธ์ต้นฉบับ

Original Article

Fine Needle Aspiration of the Breast

การใช้เข็มขนาดเล็กเจาะดูดก้อนเต้านม

ผดาดาวรรณ ธรรมประดิษฐ์ พ.บ.

กลุ่มงานพยาธิวิทยากายวิภาค

โรงพยาบาลสระบุรี

Chadawan Dhampradit M.D.

Department of Anatomical Pathology

Saraburi Hospital

ABSTRACT

Objective : To evaluate the efficiency of breast FNA by correlation between cytologic and histologic diagnoses.

Materials and methods : The author reviewed the records of patients who had undergone breast fine needle aspiration and subsequent histopathologic diagnoses during January 2001 to December 2003 at the Department of Anatomical Pathology, Saraburi hospital. Sensitivity, specificity, positive and negative predictive values were calculated with the assumption that the "suspicious" group was classified as positivity for malignancy and cases with a diagnosis of unsatisfactory were not included in further analysis.

Results : There were 55 matching cases. Eliminating unsatisfactory results, statistical analysis of the remaining 46 cases yielded the following results : sensitivity 85%, specificity 96.1%, positive predictive value 94.4% and negative predictive value 89.2%.

Conclusion : The results compared favorably with those in the literature. An understanding of the performance and limitations of FNA can enhance its value as diagnostic method in the management of breast disease.

บทคัดย่อ

วัตถุประสงค์ : เพื่อประเมินความแม่นยำของการวินิจฉัยผลเซลล์วิทยาของก้อนเต้านมที่ได้จากการเจาะดูดด้วยเข็มขนาดเล็ก

วัสดุและวิธีการ : โดยการรวบรวมผลการวินิจฉัยเซลล์วิทยาของก้อนเต้านมที่ได้จากการเจาะดูดด้วยเข็มขนาดเล็กในผู้ป่วยที่มาตรวจรักษาตั้งแต่เดือนมกราคม 2544 ถึงเดือนธันวาคม 2546 โดยเปรียบเทียบกับผลการตรวจชิ้นเนื้อในผู้ป่วยรายเดียวกัน และคำนวณค่าความไว ความจำเพาะ และความแม่นยำของการทำนายค่าผลบวกและผลลบ

ผลการศึกษา : เมื่อเปรียบเทียบผลการวินิจฉัยเซลล์วิทยากับผลการตรวจชิ้นเนื้อแล้ว พบว่า ผลการวินิจฉัยเซลล์วิทยามีความไวร้อยละ 85 ความจำเพาะร้อยละ 96.1 ความแม่นยำของการทำนายค่าผลบวกและผลลบร้อยละ 94.4 และ 89.2 ตามลำดับ ผลลบลงร้อยละ 6.5 และผลลบบวกร้อยละ 2.1

สรุป : การวินิจฉัยเซลล์วิทยาของก้อนเต้านมที่ได้จากการเจาะดูดด้วยเข็มขนาดเล็กของโรงพยาบาลสระบุรีมีความแม่นยำใกล้เคียงกับรายงานอื่น

Introduction

Fine needle aspiration (FNA) cytology is well established as diagnostic procedure for detecting benign and malignant breast lesions.¹⁻³ This technique has a number of advantages over the open biopsy. It is minimally invasive since very thin gauge needles are typically used. Thus fine needle aspiration is well tolerated by patient and side effects are usually limited.⁴ It is also a fast, cost-effective and reliable method.^{1-3,5,6} However, FNA alone is subject to inaccuracy and does not definitively diagnose all breast lesions. It is most commonly used in combination with clinical examination and mammography in the so-called "triple test". When all components of the triple test are in agreement, the diagnosis is over 99% reliability, according to several studies.^{1,3,5,7}

The aim of this retrospective study was to evaluate the efficiency of breast FNA by correlation between cytologic and histologic diagnoses and as an internal quality assurance exercise for cytologic diagnosis in the Department of Anatomical Pathology, Saraburi Hospital.

Materials and methods

A retrospective review of the records of patients who had undergone breast fine needle aspiration and subsequent histopathologic diagnoses during January 2001 to December 2003, were included. Histopathologic confirmation consisted of either incisional biopsy, excisional biopsy or mastectomy specimen. All FNAs were performed by clinicians and were submitted to the Department of Anatomical Pathology, Saraburi Hospital for interpretation. Samples were usually smeared onto glass

slides. They were immediately fixed in 95% alcohol and stained by Papanicolaou method. The number of smears submitted varied from two to eight smears per patient ; the average number was about four smears per patient. All the smears were interpreted by either one or two pathologists at Saraburi Hospital. The FNA reports were classified in four groups ; unsatisfactory, benign/negative, suspicious and malignant. Unsatisfactory aspirates were those not representative in regarding to sampling, cellularity, quality of smear and/or the staining. Benign smears usually contained only normal-appearing cells. Suspicious smears were those in which the cells had morphologic features of malignancy but there was an inadequate number of cells to evaluate and also if the cells were atypical but with insufficient cytologic abnormalities to allow a final diagnosis. Malignant smears were those containing abnormal cells- an unequivocal feature of malignancy.

Corresponding cases of FNA and histology were compared and slides of the cases of major discrepancy including unsatisfactory smears were reviewed. Sensitivity, specificity, positive and negative predictive values were calculated with the assumption that the ç suspiciousé group was classified as positivity for malignancy and cases with a diagnosis of unsatisfactory were not included in further analysis.

Results

During the study period, 155 breast FNAs were reported. There were 55 matching cases. Ten specimens were classified as positive, twenty-eight as negative, nine as unsatisfactory and eight as

Table 1 Cytohistological correlation of fine needle aspiration of the breast

FNA	Histology				Total
	FC	Fibroadenoma	Carcinoma	Inflammation	
Unsatisfactory	1	-	8	-	9
Benign / Negative					
Benign	12	3	2	-	17
Cyst	2	-	-	-	2
Fibroadenoma	-	2	1	-	3
Inflammation	3	-	-	3	6
Suspicious	1	-	7	-	8
Malignant / Positive	-	-	10	-	10
Total	19	5	28	3	55

FC = Fibrocystic disease

Table 2 Summary of statistical analysis

Cytology	Histology	
	Benign	Malignant
Benign	25 (TN)	3 (FN)
Malignant/Suspicious	1 (FP)	17 (TP)
Sensitivity		85.0%
Specificity		96.1%
Positive predictive value		94.4%
Negative predictive value		89.2%
Accuracy		91.3%

Of the 28 masses diagnosed on FNA as negative, 25 were confirmed as benign and 3 as malignant on excisional biopsy. Seven of the 8 suspicious specimens taken at FNA proved to be malignant.

Eliminating unsatisfactory results and assuming that suspicious and positive cytologic findings represented carcinoma of the breast, FNA detected cancer with a sensitivity of 85%, specificity of 96.1%, positive predictive value of 94.4% and negative predictive value of 89.2%. Table II showed aggregated results.

Discussion

The value of any diagnostic method usually lies in its ability to detect the presence of disease when it is present (sensitivity) and verify the absence of disease when it is not present (specificity). The

suspicious. The cytohistological correlation of the 55 cases is shown in Table I. All positive cytologic diagnoses were confirmed to be carcinoma on biopsy.

high rates of sensitivity and specificity indicate the high reliability of the test. FNA of the breast in the literature showed a wide range of sensitivity from 65% to 100%, with a specificity of 32% to 100%. The positive and negative predictive values ranged from 68% to 100% and 70% to 100%, respectively.^{2,5,8-13} The results of the present study allow a reliable evaluation of the accuracy of FNA in the diagnosis of breast masses. The accuracy rate of FNA improves when the well-trained pathologist performs the FNA and makes immediate feedback about the specimen adequacy.^{1,9}

The overall rate of unsatisfactory specimens in this study was 16.3%. The incidence of unsatisfactory aspirates in the literature ranged from 0% - 57.2%.^{4,6,10} The poor quality of unsatisfactory aspirates mainly results from acellularity or not being representative of an aspirated lesion. The lack of cellular material is explained in most case by histological properties of the tumor i.e. fibrosis, hemorrhagic necrosis, vascularity, cell type and tumor size.^{3,6,9,10} Other contributing factors are failure in the technique of FNA (number of needle passes and aspirator's experience), missing the tumor by puncture at more advanced stages and improper specimen preparation.^{8,9}

Sufficient sampling of the breast lesion is essential to provide satisfactory cell yield in order to avoid false negative or unsatisfactory aspirates. Definitions of adequacy are variable. Scopa et al defined a minimum of 10 clusters composed of at least 10 epithelial cells on more than one slide and the background should be non-inflammatory and/or non-necrotic as satisfactory specimen. Sneige et al

reported that unsatisfactory specimen were "those containing less than four to six well-visualized cell groups and / or specimen distorted or obscured by blood".^{3,9,14}

The acceptable rate for inadequate specimen is $\leq 25\%$. In this study, the rate of unsatisfactory specimen was 16.3%. The subsequent histologic diagnosis revealed seven invasive ductal carcinomas, one medullary carcinoma and one fibrocystic disease. The review of FNA of all these cases demonstrated acellularity in 8 cases and scanty cellularity in 1 case.

The false negative rate varied considerably in the published documents, from 1% - 35%.^{1,2,5,6} The major causes of false negative discussed in the literature were lack of experience in either aspiration or interpretation of smears, small tumor size, deep location, well-differentiated carcinomas, fibrosis and associated with fluid or benign specimen.^{4,6,14} Malignant tumor adjacent to a fibroadenoma, desmoplasia and severe edema are some factors that contributed to a false negative report.¹⁰

In this report, 6.5% (3/46) of cases were diagnosed as false negative. They were as follow : one case was reported as fibroadenoma and the two cases were negative. Review of the 2 negative cases revealed a few small clusters of degenerated atypical cells against a background of lysed blood. The abnormal cells had a high nuclear to cytoplasm ratio and hyperchromatic nuclei. Histologic examination showed a well-differentiated invasive ductal carcinoma in one case and intraductal carcinoma with focal areas of invasion in another case. The false negative case that was reported as fibroadenoma

showed hypercellularity, loss of cellular cohesion and hyper-chromatic nuclei. Pathologist's interpretation error was contributed to this false negative case. Apart from aspiration sampling and interpretative errors, tumor-size paucicellularity, special histologic types such as tumor showing extensive fibrosis, those with cell having bland cytologic features like lobular carcinoma, can also contribute to an increase the false negative rate.^{1,14} Awareness of these potential pitfalls can be helpful in avoiding a false negative report in the future.

True false positive diagnoses are rare in breast fine needle aspiration and are mainly due to interpretative errors.^{1,5,6} The error may be either misinterpretation of clearly benign cells as malignant or misinterpretation of cytologic abnormalities induced by a benign process as reflecting cancer.⁴ False positive rate in the previous documents ranges from 0.3% to 5.8%.^{2,5,6,11,13} Proliferative fibrocystic disease and fibroadenomas with atypia are the most common causes of false positive diagnoses.^{1,5,6} In this study, there was 2.1% (1/46) false positive rate. This case was histologically diagnosed as fibrocystic disease. Review of the cytologic smears revealed hypercellularity with cohesive ductal epithelial groupings. Neither significant nuclear atypia nor pleomorphism of the ductal cell population is observed.

According to some inevitable limitations of breast fine needle aspiration, this procedure should not be used as the sole criterion for evaluating of breast masses.^{9,10} The best avoidable practice with subsequent inappropriate clinical decision is the usage of the so called triple diagnostic procedure of clinical examination, mammography and FNA cyto-

logy which increase the accuracy for the diagnosis of breast cancer. The triple test has been shown to be highly sensitive and specific in the diagnosis of breast.^{1,3,5,7,14}

In conclusion, this study described the experience with FNA breast diagnosis in a general hospital in a three-year period. The results compared favorably with those in the literature. An understanding of the performance and limitations of FNA can point to ways of enhancing skills in sampling and interpretation FNA specimens and can contribute to making FNA a more widely used diagnostic method.

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