Diagnosis of Breast Lesions by Aspiration Biopsy Cytology

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ABSTRACT: From November 1981 to the end of August 1984, 456 patients with breast lesions underwent aspiration biopsy cytology (A.B.C.). This study includes 109 for whom the diagnosis was histologically confirmed at surgical biopsy. Seventy-five lesions were histologically proven to be malignant and 34 were benign. The accuracy of diagnoses with A.B.C. was; true positive 86.7 per cent (65/75) of the time, true negative 82.6 per cent (28/34) of the time, false negative 5.3 per cent (4/75) of the time and false positive 5.7 per cent (2/34) of the time. Unsatisfactory or inadequate aspirated tissue made A.B.C. diagnosis difficult in 5.5 per cent (6/109) of the cases. Three out of 7 with malignant tumors, who were wrongly diagnosed as benign by A.B.C., had tumors with a diameter of 1.0 cm or less. Two benign cases which were falsely diagnosed as malignant also had small tumors about 1.0 cm in diameter. Although A.B.C. is more reliable than other conventional supplementary diagnostic techniques (mammography, ultrasonography, etc.), it is important to carefully follow clinically questionable cases which appear negative, using A.B.C..

KEY WORDS: aspiration biopsy cytology, breast cancer

INTRODUCTION

Supplementary diagnostic techniques for breast cancer include mammography, ultrasonography, thermography and various tumor markers. The combined use of such techniques results in a considerably high rate of accurate diagnoses.[1-3] Aspiration biopsy cytology (A.B.C.) is useful as a diagnostic technique only for areas which the aspiration needle can reach. Negative or non-diagnosable cases should be carefully followed.[3-7] This study was conducted to elucidate the causes of erroneous A.B.C. diagnoses with the ultimate aim of obtaining an accurate diagnosis.

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MATERIALS AND METHODS

Technique of aspiration biopsy cytology

A detailed description of the materials and methods used was reported by Linsk and Franzén.[8] Briefly, a 10 ml disposable Cathelin syringe with a small gauge needle (usually 23 gauge) was attached to a pistol typed syringe holder (Cameco, Sweden). An aspiration biopsy was taken and a smear was made of the sample. The smear was stained utilizing the May-Grünwald-Giemsa (MGG).

Clinical materials

We studied patients whose chief complaint was either breast tumor or induration at the first visit to our clinic, during the period from

November 1981 to the end of August 1984. In addition, several patients with non-palpable tumors but who had needle biopsies of microcalcification sites that had been revealed by xeromammography were included in the study. Those who had undergone smear cytology of nipple discharge were excluded. Those for whom the diagnosis was made at the time of re-examination through A.B.C. (Re-A.B.C.) were included in the re-A.B.C. group.

The General Rules for Clinical and Pathological Records of Mammary Cancer, determined by the Japan Mammary Cancer Society were used for the classification of histological type and location of the tumor.[9] Those with malignant tumors in which the cytological diagnoses were consistent with the histological findings were classified as true positives. True negatives were those confirmed as having benign tumors. Cases in which the cytologic and histologic diagnoses were inconsistent were divided into false negative (when falsely diagnosed cytologically as benign tumors) and false positive (when erroneously diagnosed as malignant tumors) groups. A.B.C. was performed 525 times in 456 patients including re-A.B.C. examination. Among them, 109 cases were histologically proven by open biopsy. The subjects included 75 with breast cancer, all of whom presented either solid tumor or induration. Of these, 3 also had bloody or serous nipple discharge. Tumor diameters did not exceed 1.0 cm in 7, 1.1-2.0 cm in 16, 2.1-3.0 cm in 19, 3.1-4.0 cm in 14, 4.1-5.0 cm in 7 and 5.1 cm or more in 12. In terms of histological type, 6 were classified as having non-infiltrating carcinoma, 11 as papillotubular carcinoma, 32 as medullary tubular carcinoma, 19 as scirrhous carcinoma, 2 as mucinous carcinoma, 2 as medullary carcinoma with lymphoid infiltration, 1 as lobular carcinoma, 1 as signet-ring cell carcinoma and 1 as Paget's disease.

There were 34 with benign disease of which 2 were cystic and 32 were solid tumors. Tumor diameter did not exceed 1.0 cm in 9, 1.1-2.0 cm in 12, 2.1-3.0 cm in 10 and 3.1 cm or more in 3. Classification by histological type resulted in 1 duct-papillomatosis, 10 fibroadenomas, 15 fibrocystic diseases, 2 duct ectasias, 2 sclerosing adenoses, 1 mastitis, 1 accessory mammary gland and 2 normal glands.

Table 1. Accuracy of Aspiration Biopsy Cytology in 109 Histologically Proven Cases

Histological Diagnosis	Total No. of Cases	Accuracy of A.B.C.	No. of Cases
Malignant	75	True positive[a)]	65 (86.7%)
		Suspicious[b)]	3 (4.0%)
		False negative[c)]	4 (5.3%)
		Unsatisfactory[d)]	3 (4.0%)
Benign	34	True negative[e)]	28 (82.6%)
		False positive[f)]	2 (5.7%)
		Unsatisfactory[d)]	3 (8.8%)
		Suspicious[b)]	1 (2.9%)

a) True positive: malignant cases in which cytological diagnoses were consistent with histological findings
b) Suspicious: malignant or benign cases which were diagnosed as suspicious malignant or benign diseases
c) False negative: malignant cases which were falsely diagnosed as benign diseases
d) Unsatisfactory: undiagnosable cases because of insufficient aspirant materials
e) True negative: benign cases in which cytological diagnoses were consistent with histological findings
f) False positive: benign cases which were erroneously diagnosed as malignant diseases

Results

As shown in Table 1, A.B.C. resulted in true positives 86.7 per cent of the time, false negatives 5.3 per cent of the time, false positives 5.7 per cent of the time and true negatives 82.6 per cent of the time. Falsely diagnosed cases at the first A.B.C. are shown in Table 2. Particularly, one case of duct-papillomatosis and 2 cases of sclerosing adenosis were all falsely diagnosed. The total false diagnostic rate was as high as 22.9 per cent (25/109), which emphasizes the importance of re-A.B.C. examination. The true diagnostic rate of A.B.C. was calculated in 75 breast

Table 2. Rate of Incorrectly Diagnosed Aspiration Biopsy Cytology

Histological Diagnosis	Total No. of Cases	No. of Incorrectly Diagnosed Cases	Error Rate (%)
Cancer	75	7	9.3
Duct-papillomatosis	1	1	100
Fibroadenoma	10	4	40
Fibrocystic disease	15	8	53.3
Duct ectasia	2	1	50
Sclerosing adenosis	2	2	100
Mastitis	1	0	0
Accessory mammary gland	1	0	0
Normal mammary gland	2	2	100

Total error rate=22.9% (25/109)

Table 3. Accuracy of Aspiration Biopsy Cytology Histologically Proven Breast Cancers

Histological Type	Total No. of Cases	Size of Tumor (cm)					
		-1.0	1.1-2.0	2.1-3.0	3.1-4.0	4.1-5.0	5.1-
Non-infiltrating ca.[a]	6	2/3[b]		2/2			1/1
Papillo-tubular ca.	11		3/3	2/2	0/1	1/1	4/4
Medullary tubular ca.	32	1/3	5/5	8/9	8/8	1/1	6/6
Scirrhous ca.	19		6/6	6/6	1/2	1/1	3/4
Others	7		4/4	1/1	1/1	1/1	

a) ca.=carcinoma
b) ratio=correctly diagnosed number by A.B.C./total number of A.B.C.

Table 4. False Negative Cases

Name	Age	Sex[a]	Menopause	Size of Tumor Diameter (mm)	Location of Tumor[c]	Cytology	Histology[c]
A.K.	37	F	Pre.[b]	6×10	Lt.[d]—C	Benign	Non-infilt. ca[f] (I—a)
Y.U.	33	F	Pre.	70×70	Lt.—CDABE	F.c.d.[e]	Infilt. ca. (II—a—3)
Y.S.	66	M	—	10×10	Lt.—E	Duct-papillomatosis	Infilt. ca. (II—a—2)
S.K.	25	F	Pre.	40×40	Lt.—C	F.c.d.	Infilt. ca. (II—a—1)

a) F=female, M=male b) Pre.=premenopause c) Location of Tumor and Histology were classified according to the General Rules for Clinical and Pathological Records of Mammary Cancer[9] d) Lt.=left breast e) F.c.d.=fibrocystic disease f) Non-infilt. ca.=non-infiltrating carcinoma

Table 5. False Positive Cases

Name	Age	Sex	Menopause	Size of Tumor Diameter (mm)	Location of Tumor	Cytology	Histology
F.S.	39	F	Pre.	6×10	Rt.—C	Cancer	Sclerosing-adenosis
F.K.	41	F	Pre.	10×10	Rt.—ECD	Cancer	Duct-papillomatosis

Abbreviations are as described in Table 4.

Table 6. Cancer not Diagnosed at the First Aspiration Biopsy Cytology

Name	Age	Sex	Menopause	Size of Tumor Diameter (mm)	Location of Tumor	First A.B.C.	Second A.B.C.	Histology
M.T.	51	F	Pre.	less than 10	Lt.—C	Cell (−)[a]	—	Infilt. ca. (II—a—2)
K.W.	43	F	Pre.	35×30	Lt.—BD	Cell (−)	Cancer	Infilt. ca. (II—a—3)
Y.N.	48	F	Pre.	20×30	Lt.—D	Cell (−)	Cancer	Infilt. ca. (II—a—2)

a) Cell (−)=inadequate sample aspirated
Abbreviations are as described in table 4.

cancer cases according to histological type and tumor size (Table 3). Seven cases falsely diagnosed included 3 out of 32 (9.3 per cent) medullary tubular carcinoma, 2 of 19 (10.5 per cent) scirrhous, 1 of 11 (9.1 per cent) papillotubular and 1 of 6 (16.7 per cent) non-infiltrating. In 7 cases of other types of cancer, cytological diagnoses were consistent with the histological diagnoses. The tumor sizes of these 7 falsely diagnosed cases were as follows: no more than 1.0 cm in 3, 2.1-3.0 cm in 1, 3.1-4.0 cm in 2 and 5.1 cm or more in 1.

Table 4 lists the 4 false negative cases. Three women were premenopausal. Two had tumors of no more than 1.0 cm in diameter. Cytological diagnoses included fibrocystic disease in 2, duct-papillomatosis in 1 and a benign lesion in 1. Table 5 shows the 2 false positive cases. Both were premenopausal with breast tumors no more than 1.0 cm in diameter. Histologically they proved to be sclerosing adenosis and duct-papillomatosis, respectively. In 3, the first A.B.C. did not yield sufficient material to allow for diagnoses of the disease (Table 6). Two were diagnosed as having cancer after re-A.B.C. examination. Histologically, two were proved to be

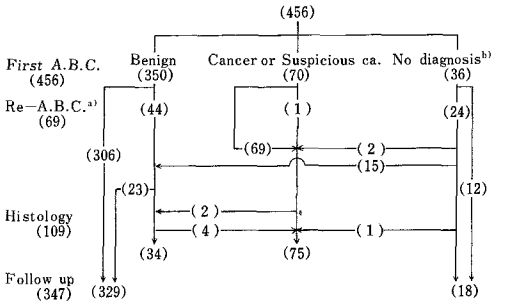

Fig. 1. Flow-chart of total patients diagnosed by aspiration biopsy cytology. a) Re-A.B.C.=re-aspiration biopsy cytology examination, b) No diagnosis=unsatisfactory or inadequately aspirated cases.

medullary tubular carcinoma and 1 scirrhous carcinoma.

Figure 1 shows a flow chart of A.B.C. cases. Re-A.B.C. examinations were conducted in 69, including 2 diagnosed as having cancer after the 2nd examination. Three hundred and twenty-nine A.B.C. benign cases and 18 A.B.C. non-diagnosed cases are being followed.

Discussion

Martin and Ellis[10] were the first in 1930, to describe aspiration biopsy cytology as a diagnostic technique for breast cancer. We compared the diagnostic rates in cancer and benign disease of the breast reported in various papers (Tables 7 and 8).[5,7,11-15] Our data on the true positive, false negative and true negative rates approximate the reported mean values, while our false positive and unsatisfactory rates are slightly above average. False positive cases may be attributable to careless microscopic examination of preparations. Retrospectively, it is apparent that incorrect diagnoses in 2 false positive cases were attributable to errors in diagnosis. If we had spent more time to carry out a careful microscopic examination with gradually increasing magnification rate, we could have ruled out cancer. Since 1 of the 3 non-diagnosable A.B.C. cases had a minimal breast cancer, the aspiration site might deviate from the center of the tumor. The other 2 cases in whom unsatisfactory A.B.C. resulted from technical error were diagnosed as cancer at the re-A.B.C. examination.

Several workers[8,13,15-17] described the criteria for classifying malignant tumors after

Table 7. Accuracy in Diagnosis of Breast Cancer by Aspiration Biopsy Cytology

Authors	Total No. of Cases	True Positive (%)	Suspicious (%)	False Negative (%)	Unsatisfactory (%)
Kern[5]	93	74 (79.0)		19 (21.0)	—
Zajdela et al[7]	1745	1539 (88.2)	54 (3.1)	63 (3.6)	80 (4.6)
Duguid et al[11]	60	56 (93.4)		2 (3.3)	2 (3.3)
Franzén and Zajicek[12]	873	662 (75.8)	117 (13.4)	94 (10.8)	—
Kline[13]	432	290 (67.1)	98 (22.7)	40 (9.3)	4 (0.9)
Nishizawa et al[14]	162	125 (77.2)	—	24 (14.8)	—
Takeda et al[15]	71	56 (78.9)	3 (4.2)	7 (9.9)	5 (7.0)
Present series	75	65 (86.7)	3 (4.0)	4 (5.3)	3 (4.0)

Table 8. Accuracy in Diagnosis of Benign Diseases by Aspiration Biopsy Cytology

Authors	Total No. of Cases	True Negative (%)	Suspicious (%)	False Positive (%)	Unsatisfactory (%)
Kern[5]	68	60 (88.2)	8 (11.8)	—	—
Zadjela et al[7]	1027	916 (89.2)	42 (4.0)	3 (0.3)	66 (6.4)
Franzén and Zajicek[12]	807	783 (97.0)	23 (2.9)	1 (0.1)	—
Kline[13]	3809	3681 (96.6)	68 (1.8)	—	60 (1.6)
Nishizawa et al[14]	212	172 (81.1)	—	10 (4.7)	—
Takeda et al[15]	75	68 (90.7)	1 (1.3)	2 (2.7)	4 (5.3)
Present series	34	28 (82.6)	1 (2.9)	2 (5.7)	3 (8.8)

Table 9. Cytological Patterns of Malignant Breast Lesions

1)	Biopsy smear contains numerous cells
2)	Multilayered cell clusters are present
3)	Lipid droplets are present in epithelial cells
4)	Glove- and papilla-like structure
5)	Cells tend to scatter
6)	Volume of cytoplasm is abundant and viscous
7)	Smear contains necrotic material
8)	Naked bipolar cells do not appear around the cell clusters

A.B.C.. Our criteria attaches importance to the patterns listed in Table 9. The absence of naked bipolar cells is particularly useful for making a diagnosis of cancer. Even with such criteria, incorrectly diagnosed cases occasionally appear. Kline et al.[18] demonstrated that half of the false negative cases, particularly microphyma tumors less than 0.8 cm in diameter and lobular carcinoma, were attributable to technical errors such as false puncture and malaspiration.

Takeda et al.[15] reported that, compared to other cancers, more negative cases have occurred in papillo-tubular or scirrhous carcinomas. Zajdela et al.[7] pointed out an increase of negative cases of scirrhous and well-differentiated carcinomas due to poor aspiration.

The 7 incorrectly diagnosed cases in this study had common types of cancers, including 6 infiltrating carcinoma cases. There was no significant difference in the erroneous diagnostic rate by histologic types. However, there was a high correlation between tumor size and the erroneous diagnostic rate for tumors less than 1.0 cm in diameter.

Only a few reports have described benign lesions in detail. Duguid et al.[11] indicated that it was sometimes difficult to differentially diagnose fibroadenoma, sclerosing adenosis and duct ectasia, because most benign lesions were part of a complex of several lesions and not easily aspirated. While efforts are being made to identify lesions, including malignant diseases, cytologically,[19] it is difficult at present.[8,11,13] Generally, it is difficult to obtain a sufficient number of cells from benign lesions, and only a part of the lesioned area is biopsied. Also, most benign lesions are difficult to aspirate correctly because they do not form clear phyma.

Cases with either false negative or unsatisfactory A.B.C. results need careful follow-up. Bauermeister[4] and Kern[5] reported that findings such as negative and normal smears were not satisfactory grounds for eliminating malignancy. Zajdela et al.[7] also suggested that it was risky to make a diagnosis merely because of the absence of malignant cells. Vorherr[3] noted that in 20-30 per cent of epithelial atypia carcinoma occurred and he pointed out the necessity of a careful follow-up.

Patient benefit with little risk of danger by A.B.C. is well demonstrated.[17,20,21] A.B.C. is a useful diagnostic examination, particularly since it is a simple preoperative diagnostic technique.[22,23] It is an important adjunct to other diagnostic procedures such as mammography and sonography and provides the attending physician with valuable information necessary to develop a course of treatment. Ultimately, the patient is spared unnecessary anguish and anxiety.

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