

Relationship between Cytologic Results and the Extent of Intraductal Spread in Nonpalpable Breast Cancers with Nipple Discharge

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ABSTRACT

Cytologic results of smears and ductal washings for 51 consecutive cases of nonpalpable breast cancers with nipple discharge were studied. Noninvasive cancer was confirmed in 40 cases and microinvasive in 11 cases. The cytologic results were compared with the extent of cancerous lesions which was measured as the angle of cancerous spread (Q) on a map made from histological preparations. Although the sensitivity of cytologic examinations was quite low (9.8% and 33.3%), the cytologic results correlated with the extent of cancerous spread in the breast ($P < 0.01$) and with the distance from the nipple to the lesion ($P < 0.01$). The results in this study suggest that cytologic results can be affected by the extent of cancerous spread.

The results of cytologic examination should be made use of in the process of assessing the presence of extensive cancerous lesions which cause nipple discharge with no palpable mass.

Key words: Nipple discharge, Nonpalpable breast cancer, Smear cytology, Ductal washing cytology, Breast conserving surgery

INTRODUCTION

Although nipple discharge with no palpable mass is an initial symptom of early breast cancers, it is not easy to diagnose those cancers. Smear cytology has been the main diagnostic method for nipple discharge cases (1-4) but some reports disclosed that smear cytology was not accurate (5, 6) and had little diagnostic value (7). Therefore, a repeated cytology (1) and surgical biopsy have been recommended in the cases where a bloody discharge is present (3, 8, 9).

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On the other hand, it is well known that most nonpalpable breast cancers presenting nipple discharge show extensive intraductal spread in the breast. However, such cancers sometimes present only a localized extent and the authors had an interest in the possibility that the extent of intraductal spread of cancerous lesions may affect the results of cytologic examination.

In this study, ductal washing cytology was tried in cases of nipple discharge with no palpable mass for the improvement of diagnostic accuracy. The object of this study is to clarify the relationship between cytological results and extent of intraductal spread of cancerous lesions.

PATIENTS AND METHODS

During the period between January in 1981 and August in 1995, 583 breasts of 489 cases presented nipple discharge with no palpable mass in Sapporo Medical University Hospital. All of these patients showed no tumor density by mammogram. Histological diagnosis was confirmed in 159 ducts of 154 breasts of 152 cases. Surgical specimens were fixed in formalin and embedded in paraffin after sequential slicing into five mm sections. The histological examination showed cancer in 58 ducts of 58 cases and benign lesions in 101 ducts of 96 breasts of 94 cases. Of the 58 cancer cases, 41 cases were noninvasive and 11 cases in which the size of invasive component was smaller than five mm in histological sections, were microinvasive. Ductal washing cytology was not carried out in one case of noninvasive cancer. Both smear cytology and ductal washing cytology were performed in the 51 cases of cancer which this study included (Table 1). The age of cancer cases varied between 23 and 84 and the mean age was 45 years old. In benign cases, both smear and ductal washing cytology were carried out in 87 ducts of 82 breasts of 80 cases.

Smear cytology was initially performed before other examinations and cytologic specimens were stained using the Papanicolaou and the May-Grünwald-Giemsa techniques. Ductal washing cytology was performed after smear cytology. The procedure for ductal washing cytology was as follows:

- 1) Two kinds of Bowman's lacrimal dilators (Inami Co.Ltd., Tokyo, Japan),

Table 1 *Histological Diagnosis*

Histological diagnosis	No. of Patients
Noninvasive ductal carcinoma	39
Noninvasive lobular carcinoma	1
Microinvasive ductal carcinoma	11
Total	51

whose outer diameters were 0.35 and 0.40 mm, were inserted into the lactiferous duct developing nipple discharge in order to extend the duct orifice on the nipple.

- 2) A thin washing tube (Nakamura type, Inami Co.Ltd., Tokyo, Japan), whose outer diameter was 0.40 mm, was inserted into the duct and 0.2-0.5 ml of saline was slowly injected.
- 3) The injected fluid was collected at the opening of the lactiferous duct of the nipple with a thick washing tube whose outer diameter was 0.60 mm. This procedure was repeated two to three times. As a result, the collected washing was diluted to about 5-7 ml.
- 4) The collected washing was smeared with Autosmear (1500 r/min., one min.) and fixed on a slide glass coated by poly-L-lysine.

The cancerous spread was shown on a map made from histological sections. The extent of cancerous spread was expressed in the form of a Japanese fan in which the nipple was the center. The angle of the fan (Q) was measured as the extent of cancerous spread in a breast. Angles were classified into two groups ($Q < 90^\circ$ in A and $Q \geq 90^\circ$ in B), considering quadrantectomy in breast conserving therapy. Similarly, the distance between the lesion and the nipple (D) was mea-

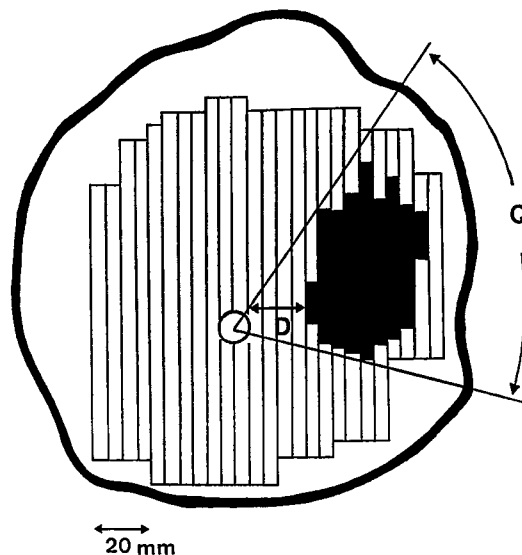


Fig. 1 Map of cancerous spread.

A solid area represents the extent of cancerous spread.

Q : Angle of cancerous spread.

D : Distance between the lesion and the nipple.

sured. When the cancerous lesion extended into a section which contains the nipple areolar complex, the distance was measured on that section (Fig. 1).

RESULTS

1. The extent of cancerous spread in the breast

Of the 51 cases of cancer, 23 (45.1%) were classified into group A and 28 (54.9%) into group B. Age, menopausal status, and the presence of a microinvasive component were not significantly correlated with the extent of cancerous spread. However, the extent of cancer was significantly correlated with the distance between the lesion and the nipple (Table 2).

2. Results of smear cytology and ductal washing cytology

Diagnostic results of smear cytology and ductal washing cytology are shown in Table 3. Smear cytology could not detect malignant or marked atypical cells in 46 cases of cancer of which twelve were diagnosed as malignant or suspicious for cancer with ductal washing cytology. There were significant differences between the results of smear cytology and ductal washing cytology (Table 4).

Table 2 *Relationship between Angle of Cancerous Spread in the Breast and Distance from the Nipple to the Lesion*

Angle of cancerous spread in the breast (Q)	Group A (Q < 90°)	Group B (Q ≥ 90°)
No. of patients	23	28
Age (mean) ^{a)}	44 (23-69)	45 (31-84)
Menopausal status ^{b)}		
premenopausal	18	21
postmenopausal	5	7
Presence of invasive component ^{c)}		
noninvasive	20	20
microinvasive	3	8
Distance from the nipple to the lesion (mm) ^{d)}		
0-20	8	19
25-	15	9

a) Not significant: T-test.

b) Not significant: chi-squared test.

c) Not significant: Fisher's exact test (Yates' correction).

d) Significant: chi-squared test, P < 0.02.

Table 3 *Results of cytologic examinations*

Smear cytology	Ductal washing cytology			Total
	Benign	Suspicious	Malignant	
Benign	34	6	6	46
Suspicious	0	2	0	2
Malignant	0	0	3	3
Total	34	8	9	51

Table 4 *Cases diagnosed as suspicious or malignant in cytologic examinations*

Smear cytology	Ductal washing cytology		Total
	Benign	Suspicious or Malignant	
Benign	34	12	46
Suspicious or Malignant	0	5	5
Total	34	17	51

Significant : Fisher's exact test (Yates' correction) : $P_c < 0.01$.

Table 5 *Diagnostic Rates of Smear Cytology and Ductal Washing Cytology (%)*

	Smear cytology	Ductal washing cytology
Sensitivity	5/ 51 (9.8)	17/ 51 (33.3)
Specificity	87/ 87 (100.0)	85/ 87 (97.7)
Accuracy	92/138 (66.7)	102/138 (73.9)
Positive Predictive Value	5/ 5 (100.0)	17/ 19 (89.5)

On the other hand, all of 87 ducts were diagnosed as benign with smear cytology in consecutive benign cases of which two cases were diagnosed as suspicious with ductal washing cytology. The diagnostic rates of the two cytological methods are shown in Table 5.

3. Relationship between cytological results and the angle of cancerous spread (Q)

Neither age, menopausal status or the presence of a microinvasive component were correlated with the results of the cytologic examinations. Nevertheless, the angle of cancerous spread and the distance from the nipple to the lesion were significantly correlated with the cytologic results (Table 6).

Table 6 *Relationship between results of cytologic examinations and the extent of cancerous spread*

	Cytologic examination	
	Benign	Malignant or suspicious
No. of patients	34	17
Age(mean) ^{a)}	46	43
	(23-84)	(31-63)
Menopausal status ^{b)}		
premenopausal	25	14
postmenopausal	9	3
Presence of		
invasive component ^{c)}		
noninvasive	27	13
microinvasive	7	4
Distance from the nipple		
to the lesion: D (mm) ^{d)}		
0-20	12	15
25-	22	2
Angle of cancerous		
spread: Q ^{e)}		
Group A (Q < 90°)	20	3
Group B (Q ≥ 90°)	14	14

a) Not significant : T-test.

b) Not significant : Fisher's exact test.

c) Not significant : Fisher's exact test.

d) Significant : chi-squared test, $P < 0.01$.

e) Significant : chi-squared test, $P < 0.01$.

DISCUSSION

When nipple discharge cases have no palpable mass, it is difficult to demonstrate the cause of nipple discharge. Although smear cytology has limitations in the diagnosis of early breast cancer, it has been one of the prerequisite methods for nipple discharge cases with no palpable mass (3, 4, 10). When smear cytology played an important role in the assessment of surgically significant discharges, its diagnostic rate (sensitivity) was reported as 41.0 (4), 45.2 (3), 45.5 (5), 60.0 (2) and 66.7 (6, 11) %. The sensitivity of smear cytology in this study was quite low. Surgical biopsies in this study were carried out not only on the basis of cytologic results, but also on the basis of ductographic findings and the

presence of hemorrhage in the discharging fluid. The criterion used to select surgically significant cases may affect the sensitivity in smear cytology.

With the object of obtaining good cellular samples from the discharge, a nipple aspiration device was developed in 1973 (12) and cytologic examination for contrast media on ductography was described (12,13). The ductal washing method was tried in this study to obtain many cellular samples from the discharges. This attempt brought a remarkable improvement in cytologic diagnosis. However, its sensitivity is not satisfactory, yet. Regarding this problem, cellular cohesiveness and histological subtypes of cancerous lesions should be investigated. Endoscopic observation of intraductal space is performed in our hospital to assess the growth appearance of intraductal lesions of the breast, using a silica-fiber-scope of 0.45 mm in outer diameter (14).

This study revealed a close correlation between the extent of cancerous spread and the distance from the nipple to the lesion. This result suggests that cancerous spread near the nipple is associated with an extensive spread of intraductal cancer. The results provided here show that the results of cytologic examination for the discharge are associated with the extent of cancerous spread in the breast. Breast cancers detected by cytologic examination of the discharge may have intraductal spread near the nipple or extensive intraductal growth. In view of the assessment of the extent of cancerous spread, it is important that a practical classification of the histological subtypes of intraductal cancer be made and its relationship to the cancerous spread be studied.

In breast conserving surgery, the presence of an extensive intraductal component and a positive surgical margin are unfavorable factors. Vicini, *et al.* (15) reported the importance of assessing the presence or absence of an extensive intraductal component in determining the optimal extent of breast resection. Recent reports (16-19) stressed that breast conserving surgery is a reasonable alternative to mastectomy for selected women with intraductal carcinoma. Regarding positive margins however, re-excision is recommended because of improved local control (20).

Most nonpalpable breast cancer with nipple discharge is early breast cancer, predominantly with an intraductal component (6, 8). In conclusion, although the results of cytologic examination of the discharge can not reveal the precise extent of cancerous spread, those findings should be made use of in the assessment of the presence of extensive cancerous lesions with no palpable mass which cause nipple discharge.

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