

Surgical management of nipple discharge

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Summary

Purpose: Nipple discharge is reported in 2.5-3% of women with breast carcinoma. Breast carcinoma is found in approximately 8% of surgically treated patients presenting with bloody nipple discharge (ND).

Methods: In the present study 110 women with ND as a presenting symptom were examined. The discharge was spontaneous in 76 and elicited in 11 patients.

Results: After surgical intervention benign breast disease was found in 85% of patients. Thirteen women (15%) were found to have malignancy and underwent additional surgery. Cytology of the discharge was positive or suspicious for malignancy in only seven out of 13 patients found to have *in situ* or invasive carcinoma.

Conclusion: Women with spontaneous, single duct ND, especially when it is darkish or bloody, should have cytological examination of the fluid and mammography according to their age or additional clinical findings. Most of them will require a microdochectomy, as the possibility of finding a carcinoma among those women is between 10-15%. However, single duct papilloma is the most common cause of bloody discharge.

Key words: Nipple discharge; Papilloma; Ductal carcinoma in situ.

Introduction

The term discharge means the fluid that escapes spontaneously from the nipple, while secretion is the fluid present in the duct that must be collected by nipple aspiration or by other means. Non-spontaneous secretions display cellular patterns related to a variety of disease processes in the breast.

Nipple discharge (ND) is an important symptom ranking second only to a lump as the most common complaint among the largest series of patients undergoing breast surgery [1, 2] and is often the first indication of an underlying breast pathology. As a presenting symptom, it is reported in 10% to 15% of women with benign breast diseases and 2.5% to 3% of those with breast carcinoma [3, 4]. Spontaneous or expressible ND may occur in palpable and nonpalpable breast lesions.

ND is often classified according to its appearance as physiological (discharge with evidence of secretory products), and abnormal or pathological. The majority of fluids with secretory components are associated with fibrocystic changes [3, 5]. Abnormal ND may be bloody, blood tinged, sticky or clear.

The significance of bloody discharge is its frequent association with intraductal papilloma and other papillary lesions. Breast carcinoma is found in approximately 8% of surgically treated patients presenting with bloody fluid [3]. However, the latter is also frequently found in the absence of such lesions since duct ectasia, infection and other benign breast lesions are common causes of gross or occult blood in ND [3].

The single most important point in the patient history is whether the discharge is spontaneous or elicited. Spontaneous nipple discharge in the nonlactating breast is considered as an abnormal discharge that needs further evaluation even in the absence of a palpable mass. Several reports in the literature have pointed out that spontaneous ND is considered pathological and more frequently related to cancer [1, 6].

The number of ducts producing discharge is almost as useful a guide as spontaneous discharge. ND from multiple ducts is rarely malignant, whereas single duct discharge can represent a genuine risk of malignancy [1, 6].

The clinical significance of ND and appropriate management choices become most important when there is no palpable mass. Kilgore *et al.* [7] found 35% of carcinomas associated with ND that had no palpable tumour whereas this percentage varied significantly from 12% to 82% in other studies [1, 6].

All patients with single-duct nipple discharge and no palpable mass should have mammograms. Others advocate galactography and routine cytological studies. Woods *et al.* have combined galactography with wire localization to find duct papillomas [8]. Since a single procedure is always more desirable and histological confirmation will be needed, galactography may be omitted [5].

Exfoliative cytology is useful when positive [9-11], but because of a high, usually unacceptable, false-negative rate [12], many experts do not agree that the decision for surgical treatment should be based on cytological findings [3, 5, 13].

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In the present study we reviewed all surgically treated cases referred for ND in our Breast Clinic over a period of six years and correlated histological diagnoses with clinical features of the discharge.

Materials and Methods

Selection of patients

From 1993 to 2003, 110 women with nipple discharge as a presenting symptom were examined in our Breast Clinic. The mean age of the patients was 49.6 years (SD \pm 13.1, range 18-78). In this study, only women with persistent single duct nipple discharge were included. If a discrete lump was found, it was investigated as the priority but the patient was not excluded from the study. Patients were selected for surgery by a triple assessment: clinical examination, discharge cytology and breast imaging. Mammography was performed in 88 out of 110 cases.

Statistical analysis

Statistical analysis was based on the t-test and chi-square test with Yates' correction. Fisher's exact test was applied in certain correlations. All computations were carried out using statistical programme SPSS version 9.0 (SPSS Inc., Chicago, IL).

Results

Of the 110 women with single duct nipple discharge, 14 were followed-up after clinical, mammographic and cytologic evaluation. Surgery was advised in 96 patients but nine refused any surgical intervention. The 87 operated women had a mean age of 49.6 years (SD \pm 13.1, range: 18-78 years). The discharge was spontaneous in 76, and elicited in 11 patients. The consistency of discharge was evaluated. In 38 of the 87 patients the discharge was either black or bloody. Of these, 31 had benign breast disease as compared with seven that had cancer. In the remainder, it varied from colourless to grey to green to brown. In patients with unilateral nipple discharge, the left and right sides were affected with statistically equal frequency (left 46, right 57). Only seven women presented with bilateral nipple discharge. In 13 of 87 women an associated mass was revealed on examination, and three of them were found to have invasive carcinoma.

Mammogram was normal in 73 out of 88 (83%) patients, demonstrating benign breast disease in three, densities in six, and microcalcifications in six patients. Surgical intervention was required in 87 patients and the initial operation they underwent was duct exploration and biopsy for pathologic discharge. The histologic diagnosis of all 87 cases is summarised in Table 1. Benign breast disease was found in 74 (85.1%) patients with the most frequent being intraductal papilloma (66.7%). Thirteen women (15%) were found to have malignancy and underwent additional operations. The mean age of the patients in all five diagnostic groups is also shown in Table 1. Papillomatosis and ductal carcinoma in situ (DCIS) was observed in older patients ($p = 0.0001$ and $p = 0.06$, respectively). Bloody discharge was noticed more fre-

Table 1. — *Histologic diagnosis in relation to age of patients with nipple discharge undergoing surgery.*

Histological diagnosis	Frequency N (%)	Mean age	p value (t-test)
Intraductal papilloma	58 (66.7)	48.6	0.1
Papillomatosis	7 (8.1)	64.5	< 0.0001
Duct ectasia	9 (10.3)	39	0.6
LCIS	2 (2.3)	33	—
DCIS	8 (9.2)	57.5	0.06
Invasive ca	3 (3.4)	55.3	—
Total	87 (100)	49.6	

quently in carcinoma than benign breast lesions (7/10 or 70% vs 31/74 or 41.9%, $p = 0.1$, two-tailed Fisher's exact test) but this finding did not reach statistical significance. Histologic diagnosis was not statistically related to other characteristics of ND.

The clinical and histologic features of in situ carcinoma cases in our series are shown in Table 2. The majority of DCIS (6/8 or 75%) and the two lobular carcinomas in situ (LCIS) presented with spontaneous ND. The cytology was positive or suspicious for malignancy in four tumours while the other five were suspicious for papilloma. The remaining case was reported as benign breast disease.

The ten patients with DCIS and LCIS are under review and have remained well. Of the remaining patients none has gone on to develop breast cancer.

Discussion

Unilateral non-milky ND coming from a single duct orifice is surgically significant and warrants special attention [14]. However, not all discharges require duct exploration or biopsy for diagnosis. Patients who need surgery can be detected by consideration of the characteristics of the discharge, physical examination and radiological investigation. Fluid cytology is most important for those cases with pathologic discharge and suspicious clinical findings.

In this series, surgery was required in 87 patients, which in 74 (85.1%) provided both definitive therapy and diagnosis. The remaining 13 (15%) were found to have DCIS, LCIS or invasive cancer and underwent further surgery for treatment. Leis *et al.* [1] reported similar findings in a large series, where 13% of the patients operated on for ND had cancer.

In the management of a patient complaining of nipple discharge, the first requirement is to determine whether the discharge comes from one or multiple ducts. In this series of 87 surgically treated women, all discharges were from one duct and 76 (87.4%) were spontaneous. The ratio of spontaneous ND to elicited ND compares favourably with that reported by Gulay *et al.* [15]. Bloody or black fluid was observed in 43.7% of cases in this series and found to be more frequent in benign breast lesions (81.9%) than in carcinoma (55%) but this differ-

Table 2. — Clinical and histological features of ten *in situ* carcinoma cases presenting with nipple discharge.

Age	Clinical features of nipple discharge		Mammography	Cytology	Histologic type	LN (+)	ER/PR	Treatment
48	+	Sp	—	+	DCIS	0/17	ND	Mastectomy
78	+	E	—	Suspicious (Ca)	DCIS+ MINV	0/18	ND	Mastectomy
29	+	Sp	Density	Suspicious (papilloma)	LCIS + papilloma	—	ND	Cutaneous mastectomy
45	+	Sp	MCF	Suspicious (papilloma)	DCIS + papilloma	—	+/+	Wide local excision +Tamoxifen
48	—	Sp	—	Suspicious (papilloma)	DCIS+MINV	0/12	+/+	Right Mastectomy +Tamoxifen
65	—	Sp	MCF	—	DCIS	—	+/+	Wide local excision +Tamoxifen+Radiotherapy
61	+	Sp	MCF	Suspicious (Ca)	DCIS	—	ND	Wide local excision +Tamoxifen+Radiotherapy
78	+	Sp	—	Suspicious (Ca)	DCIS	0/10	ND	Mastectomy
61	+	E	MCF	Suspicious (papilloma)	DCIS+ MINV	0/14	+/+	Mastectomy
37	—	Sp	Density	Suspicious (papilloma)	LCIS + papilloma	—	ND	Cutaneous mastectomy

M: multiple, S: single, Sp: spontaneous, E: elicited, MCF: microcalcifications, DCIS: ductal carcinoma in situ, LCIS: lobular carcinoma in situ, MINV: microinvasion, LN: lymph nodes, ER: estrogen receptors, PR: progesterone receptors, ND: not done.

ence did not reach high statistical significance ($p = 0.1$). Similar findings have been noticed by other authors [3, 4, 12] who reported that 50-70% of the carcinoma cases and approximately 30-80% of benign disease cases presented with bloody ND. When the discharge is serous, bloody or black it is desirable to explore the duct system. An occult blood positive discharge does not necessarily indicate cancer but suggests intraductal disease, whereas a clear discharge does not rule out cancer [3, 4].

The majority of our patients presented with unilateral ND, and in these both sides were affected equally, a finding which is in agreement with other reports [13]. Bilateral ND was found in only 8.1% of the patients in this series.

Histology of the excised mammary lesion revealed intraductal papilloma in the majority of our cases (66.7%) (Table 1). This is in accordance with previous reports where papillary lesions were found in a high percentage of surgically treated women with ND and, more specifically, in those with spontaneous and/or bloody fluid [3, 5, 6, 15]. Interestingly, papillomatosis was more frequently detected in older women in this series (Table 1, $p < 0.0001$). Comparable with published data [6, 15] was also the frequency of duct ectasia, which was diagnosed in 10.3% of the breast biopsies in the present study.

Malignancy was observed in 14.9% of women presenting with ND (Table 1) with DCIS being the commonest histology (8 out of 10 *in situ* carcinomas). In the largest published series up to now [1], breast cancer was detected in 13% of surgically treated women who presented with ND while Fung *et al.* [16] evaluated 176 operated patients and found malignant tumour histology in 8.5% of them. More than half of these lesions were DCIS. The latter was the predominant malignancy in a large series of Bauer *et al.* [18] who reported 15.5% of DCIS including a subset of cases (28%) with a microinvasive component. In the present study, microinvasion was found in two DCIS (Table 2). Age was statistically related to DCIS histology which was noticed in older patients ($p = 0.06$, Table 1) as expected by means of cancer epidemiology [2].

The usefulness of mammography in the diagnosis of an underlying carcinoma appears to be controversial. Mammogram has been advocated as being valuable in this setting, with an abnormality being detected in 60% of patients with *in situ* carcinomas (Table 2). Among other authors, Carty, Fung, Tabar and associates [13, 16, 17] reported 13% to 50% of malignancies had a positive or suspicious mammogram. However, Leis *et al.* [10] in the largest of the published series observed only a 9.5% false-negative and a 1.5% false-positive rate, respectively. Mammography should be considered in all cases of single duct discharge, unless a specific lump or lesion has already been identified. Nevertheless, a negative mammogram does not preclude an occult carcinoma. Ductography seems to be more reliable for diagnosis, since it is the only known method for preoperative evaluation of the nature, location and extent of the lesions [17], but yet, could be omitted [4, 5].

Cytology of the fluid from patients with DCIS or LCIS in the present study was useful in four of ten (40%) cases and misleading in 60%. Other authors have shown similar observations [12, 16, 18], whereas higher accuracy rates of cytological diagnosis have been reported as well [9, 10]. An argument can be made for restricting the use of cytology to blood stained discharge [12].

Recently Inaji and colleagues showed that evaluation of c-erbB-2 and CEA levels in ND, by enzyme immunoassays or even molecular biological techniques, can assist in the diagnosis of non palpable breast cancer [20-22] but further investigation is needed to establish reliable markers of malignancy which could be detectable in nipple fluid.

Subsequent mastectomy or wide local excision was chosen as the appropriate surgical treatment for *in situ* carcinoma cases in our series (Table 2). However, in the vast majority of patients who present with pathologic ND, non worrisome breast pathology is found and duct exploration with or without biopsy should be performed for diagnostic and therapeutic purposes, regardless of cytological or radiological findings.

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