

## How often is cytologically unsuspected nipple discharge a symptom of underlying breast cancer?

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*Background.* Nipple discharge is a common health problem. It can be caused by benign diseases of the breast, but it also may be a symptom of underlying breast cancer. In our center the main issue motivating patients and their physicians to treat this disorder surgically was fear that nipple discharge might be a symptom of underlying cancer. We decided to assess whether such fear was justified.

*Objective.* To assess whether the incidence of underlying cancer in patients with cytologically unsuspected nipple discharge justifies surgical treatment of such patients.

*Material and methods.* From January 1977 to September 2002, 414 women were operated for nipple discharge in our Clinic. In 234 of these women, no palpable tumor was identified on palpation, no cancer or suspected cells were identified on cytologic examination of the nipple discharge. They constitute the study group. In 177 of women discharge was unilateral and in 57 was bilateral. Altogether 291 cases were analysed. We evaluated the incidence of cancer diagnosed on pathological examination of the excised breast tissue in these patients.

*Results.* Breast cancer was diagnosed in 4 cases (4/291; 1.4%). In all these cases the character of nipple discharge was described as bloody.

*Conclusions.* (1) The incidence of breast cancer in patients in whom cytologically unsuspected nipple discharge is a sole symptom of breast pathology, does not justify surgical treatment in each case. (2) There is a necessity of further diagnostic workup of patients with nipple discharge, to identify the women in whom the risk of breast cancer is increased (patients with intraductal papilloma and papillomatosis), and to treat them surgically. Women who are not qualified for surgical treatment should undergo regular follow-up.

### Jak często niepodejrzany cytologicznie wyciek z brodawki sutkowej jest objawem raka piersi?

*Wprowadzenie.* Wyciek z brodawki sutkowej jest dolegliwością częstą. Może być spowodowany łagodnymi chorobami piersi, ale również może być objawem raka tego narządu. W naszym ośrodku, główną przyczyną motywującą chore oraz lekarzy do podejmowania leczenia chirurgicznego tej dolegliwości był strach, że wyciek może być objawem raka piersi. Postanowiliśmy ocenić, czy obawy te były uzasadnione.

*Cel.* Ocena, czy częstość występowania raka piersi u chorych z niepodejrzanym cytologicznie wyciekaniem z brodawki sutkowej uzasadnia podjęcie leczenia chirurgicznego.

*Materiał i metody.* Od stycznia 1977 r. do września 2002 r., w Klinice operowano 414 kobiet z powodu wycieku z brodawek sutkowych. U 234 spośród nich nie stwierdzono palpacyjnie guza w piersi, a przeprowadzone badanie cytologiczne wydzieliły nie ujawniło obecności komórek nowotworowych ani podejrzanych. Kobiety te weszły w skład grupy badanej. U 177 kobiet wyciek występował jednostronnie, a u 57 obustronnie. Łącznie analizowano 291 przypadków wycieku z piersi. Oceniano odsetek przypadków, w jakim rozpoznano raka w trakcie badania histopatologicznego po zabiegu.

*Wyniki.* Raka piersi rozpoznano w 4 przypadkach (4/291; 1,4%). We wszystkich tych przypadkach charakter wycieku określono jako „krwisty”.

*Wnioski.* 1. Częstość występowania raka piersi u chorych, u których niepodejrzany cytologicznie wyciek z brodawki sutkowej jest jedynym objawem chorobowym, nie uzasadnia leczenia chirurgicznego w każdym przypadku. 2. Istnieje potrzeba przeprowadzenia dalszej diagnostyki w celu wyłonienia tych chorych, u których ryzyko występowania raka piersi jest podwyższone (chore z brodawczakiem lub brodawczakowatością wewnątrzprzewodową), a następnie leczenie ich chirurgicznie. Kobiety nie zakwalifikowane do leczenia operacyjnego powinny być poddane regularnym badaniom kontrolnym.

**Key words:** nipple discharge, breast cancer, pathology, treatment

**Słowa kluczowe:** wyciek z brodawki sutkowej, rak piersi, patologia, leczenie

## Introduction

Nipple discharge is a common health problem, accounting for up to 7% of all breast symptoms [1]. Spontaneous nipple discharge is recognized in up to 10% of women undergoing routine health examinations [2]. It can be caused by many benign diseases of the breast, but may also be a symptom of underlying breast cancer [3-9]. The discharge may appear with, or without, an associated lump and with, or without, suspicious mammographic findings. When an associated lump or suspicious mammographic findings are present, surgical treatment is mandatory [4, 6, 10, 11]. Surgical treatment is justified only in a small number of patients in whom nipple discharge is the only symptom of breast pathology [2, 4, 12-16]. Identification of patients in whom surgical treatment would be necessary is a diagnostic challenge. The main step of diagnostic workup is cytologic examination of the discharge [17]. In a majority of patients no cells are found on cytologic examination. If cells are identified in the discharge, the pathologists evaluate their features and describe them as normal or atypical. The presence of atypical cells is an indication for surgical treatment. In the remaining patients the decision is more complex, as for example patients in reproductive age fear that surgical procedure may impair their breast feeding ability. In our center the main issue motivating patients and their physicians to treat the pathology surgically was fear that cytologically unsuspected nipple discharge (not containing atypical cells) might be a symptom of underlying cancer. Therefore, we decided to assess whether such fears are justified.

## Objective

To assess whether the incidence of underlying cancer in patients in whom nipple discharge does not contain atypical cells, justifies surgical treatment.

## Material and methods

From January 1977 to September 2002 in the Clinical Department of Surgical Oncology, Medical University of Lodz, 414 women were operated due to nipple discharge. These women were operated on if nipple discharge was: unilateral, arose from a single duct, was serous, clear or bloody. Nipple discharge causing serious discomfort or unacceptable fear of cancer was also an indication for surgical treatment.

In 234 of these women, no tumor was identified on palpation, no cancerous or atypical cells were identified on

cytologic examination of the nipple discharge, and they were not previously treated surgically for nipple discharge. These patients constituted the study group. Retrospective review of the files provided clinical and pathological data for these patients. In 177 women (75.6%) nipple discharge was unilateral, and in 57 (24.4%) it was bilateral. Total number of occurrences was 291.

We evaluated the incidence of cancer diagnosed on pathological examination of the excised breast tissue.

## Patients

Mean age in the studied group was 43.7 years (range: 22-81 years; median: 40 years). The pathology was almost equally distributed between the left (145/291; 49.8%) and the right side (146/291; 50.2%). Distribution of types of nipple discharge in the studied group is presented in Table I.

**Table I. Nipple discharge characteristics**

| Type of nipple discharge | Number of patients | Rate   |
|--------------------------|--------------------|--------|
| Bloody                   | 101                | 34.7%  |
| Serous                   | 67                 | 23.0%  |
| Green                    | 47                 | 16.2%  |
| Brown                    | 36                 | 12.4%  |
| Milky                    | 15                 | 5.1%   |
| No data                  | 25                 | 8.6%   |
| Total                    | 291                | 100.0% |

In 9 cases (9/291; 3.1%) non-surgical treatment was unsuccessfully introduced before surgery: in 7 cases – hormonal, in 2 cases – anti-inflammatory.

## Surgical treatment

Surgery began with injection of a blue dye into the discharging nipple duct by a needle inserted into the duct orifice. Then, the stained tissues were carefully excised and the specimen delivered to the pathology laboratory.

## Results

Breast cancer was diagnosed in 4 cases (4/291; 1.4%). Clinical features of patients in whom the cancers were diagnosed, as well as pathologic characteristics of the cancers, are presented in Table II. In all these patients modified radical mastectomy was performed. The results of pathologic examination of the remaining 287 cases are presented in Table III.

**Table II. Clinical and pathological characteristic of four patients in whom breast cancer was diagnosed**

| Patient nr | Age | Type of nipple discharge | Type of cancer        | Number of cancer – positive axillary lymph nodes |
|------------|-----|--------------------------|-----------------------|--|
| 1          | 28  | bloody; unilateral       | ductal invasive G2    | 2  |
| 2          | 25  | bloody; unilateral       | intraductal papillary | 0  |
| 3          | 67  | bloody; unilateral       | ductal invasive G2    | 4  |
| 4          | 50  | bloody; unilateral       | ductal invasive G1    | 0  |

**Table III. Results of pathologic examination of surgically treated 287 cases, in whom cancer was not diagnosed**

| Diagnosis                           | Number of cases |
|-------------------------------------|-----------------|
| <i>Dysplasia benigna</i>            | 243             |
| <i>Papillomatosis intraductalis</i> | 19              |
| <i>Fibrosclerosis</i>               | 13              |
| <i>Inflamatio chronica</i>          | 7               |
| <i>Ductectases</i>                  | 4               |
| <i>Hyperplasia intraductalis</i>    | 3               |
| <i>Cystes</i>                       | 2               |
| <i>Atrophia lipomatosa</i>          | 2               |
| <i>Fibroadenoma intraductalis</i>   | 1               |
| <i>Adenosis sclerosans</i>          | 1               |

## Discussion

Breast cancer was diagnosed in 1.4% of the operated cases. In all these cases nipple discharge did not contain atypical cells, and was the sole symptom. It should be remembered that calculated incidence of breast cancer refers to a selected group of patients. Our patients with nipple discharge who did not undergo surgical treatment, but were followed-up in an out-patient clinic, were not included in the study. Therefore, the real incidence of breast cancer in patients with unsuspected nipple discharge is much lower. We did not have an opportunity to analyse the results of mammography in all patients, as the study period began in 1977, when mammography was not performed routinely. It is possible that cancers found in pathologic examination might have been depicted on mammography if such an examination had been performed.

The incidence of breast cancer reported by other authors in cases of nipple discharge ranged up to 10% [5,11,18,19]. The reported incidence of breast cancer depended mostly on the enrolment criteria to the study group, used by different authors. This is the reason for such a big divergence of results. In our studied group, in some patients the main indications for surgical treatment were: fear of underlying cancer and/or strenuousness of discharge even if the symptom was classified by a physician as clinically insignificant. Therefore the incidence of cancers in our material is so small.

Our results and literature data suggest that the risk of underlying cancer in patients with cytologically unsuspected nipple discharge is too small to justify surgical treatment in all patients. Nipple discharge may be caused by infections, eczematous lesions, hormones and may appear secondary to drug intake. There is no need to treat such discharges surgically [15].

On the other hand, in many women, nipple discharge is caused by the presence of intraductal papilloma or papillomatosis [8, 9, 13-15]. As the presence of such conditions is associated with an elevated risk of breast cancer, these women should be treated surgically [2, 17,

20, 21]. However, identification of such patients is difficult.

It is generally acknowledged that patients with heme-negative, bilateral, unilateral but from multiple ducts, green or milky discharge do not require surgical treatment. In such cases, the discharge should be examined cytologically and the patients followed-up regularly. In patients with unilateral, single-duct, heme-positive, clear, serous or bloody discharge further diagnostic workup should be introduced [16]. When the presence of papilloma or papillomatosis is found, surgical treatment should be undertaken [2, 17, 20, 21]. It seems that modern diagnostic tools such as fiberoptic ductoscopy and intraductal aspiration cytology allow for the precise identification of patients in whom surgical treatment is necessary [11, 15, 16, 22].

In all patients, the essential step in diagnostic workup is cytological examination [17]. However, the sensitivity of conventional cytological examination is low, ranging from 40% to 80% [7, 23, 24]. This implies the necessity of repeating cytological examination. In our patients cytologic examination was performed only once. It is therefore possible that if we had performed cytologic examination three times or more we would have identified cellular atypia in patients in whom cancer was found on pathologic examination. Therefore, patients not qualified for surgical treatment should be followed-up. Follow-up should consist of physical examination every 3-4 months, and cytological examination of the discharge repeated at last 3 times. In patients over 40 years of age mammography is mandatory once a year.

## Conclusions

1. The incidence of breast cancer in patients in whom cytologically unsuspected nipple discharge is the only symptom of breast pathology does not justify surgical treatment in each case.
2. There is a necessity of further diagnostic workup of patients with nipple discharge, to identify the women in whom the risk of breast cancer is elevated (patients with intraductal papilloma or papillomatosis), and to treat them surgically. Women not qualified for surgical treatment should be regularly followed-up.

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