



Breast duct microendoscopy in nipple discharge

Microbrush improves cytology

N. Beechey-Newman,¹ D. Kulkarni,¹ A. Kothari,¹ C. D'Arrigo,² G. Culora,³ H. Hamed,¹ I. Fentiman¹

¹ Department of Academic Oncology, Breast Unit, 3rd Floor, Thomas Guy House, Guy's Hospital, London SE1 9RT, United Kingdom

² Department of Pathology, Guy's Hospital, London SE1 9RT, United Kingdom

³ Department of Cytopathology, St Thomas' Hospital, London

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Abstract

Background: Breast duct microendoscopy is a new technique that allows direct visualization of the mammary ductal epithelia and has the potential to provide greater accuracy in the diagnosis of benign and malignant breast conditions. We have already established the feasibility of BDME on mastectomy specimens and in patients both under general and local anesthesia. It was the aim of this study to investigate the use of BDME in patients with pathological nipple discharge and to explore the feasibility of using an endoluminal microbrush to take cytology samples from specific lesions.

Materials and methods: Breast duct microendoscopy was offered to all patients undergoing surgery for nipple discharge. Surgery included microdochectomy (younger women) and total duct excision (especially in postmenopausal women). The microbrush was used to collect samples whenever an endoluminal papilloma was seen on endoscopy. The results of microbrush cytology samples were compared to ductal lavage samples.

Results: Fifty consecutive patients undergoing microdochectomy or total duct excision for nipple discharge had breast microendoscopy (28 general, and 22 under local anesthesia). Thirty-one patients had microdochectomy and nineteen had total duct excision. Visualization of discharging ducts was accomplished in 100% cases. Endoluminal abnormalities were seen in 33 (66%) patients and dilated ducts were seen in 17 patients. Among the 33 patients, 15 had single papilloma, 3 multiple papilloma and 15 inflammation (erythema, fronds, adhesions). Seven out of eight patients with an intraductal papilloma who had microbrush cytology showed papillary cells whereas only 2 out of 11 patients who had ductal lavage were positive for papillary cells. Thus the sensitivity of the brush cytology technique for

the diagnosis of papilloma was 87.5% and the sensitivity of ductal lavage 18% ($p = 0.0055$).

Conclusion: Breast duct microendoscopy is an effective way of establishing the etiology of nipple discharge. The microbrush increases the sensitivity of cytology significantly.

Key words: Breast duct endoscopy — Breast ductoscopy — Nipple discharge

Nipple discharge is found in 5% of the patients presenting to a symptomatic breast clinic. After mastalgia and lumps, nipple discharge is the most frequent condition that brings women to breast clinics [5]. A variety of diseases such as intraductal papillomas, mammary duct ectasia, periductal mastitis, breast cancer, breast abscess and infections, and pituitary adenomas can manifest as nipple discharge.

Breast duct microendoscopy (BDME) is a new technique that allows direct visualization of the mammary duct epithelia and has the potential to provide a more accurate diagnosis of benign and malignant pathology. This technique, first described in 1991, has been taken up widely in the Far East [11]. Although breast microendoscopy has been possible for more than a decade, it is only over the past 3 to 4 years that the technique has started to attract serious interest in the West.

We have already established the feasibility of BDME with mastectomy specimens [7] and for patients under both general and local anesthesia. This study aimed to investigate the use of BDME for patients with pathologic nipple discharge, and to explore the feasibility of using an endoluminal microbrush to take cytology samples from specific lesions. We hoped to ascertain the

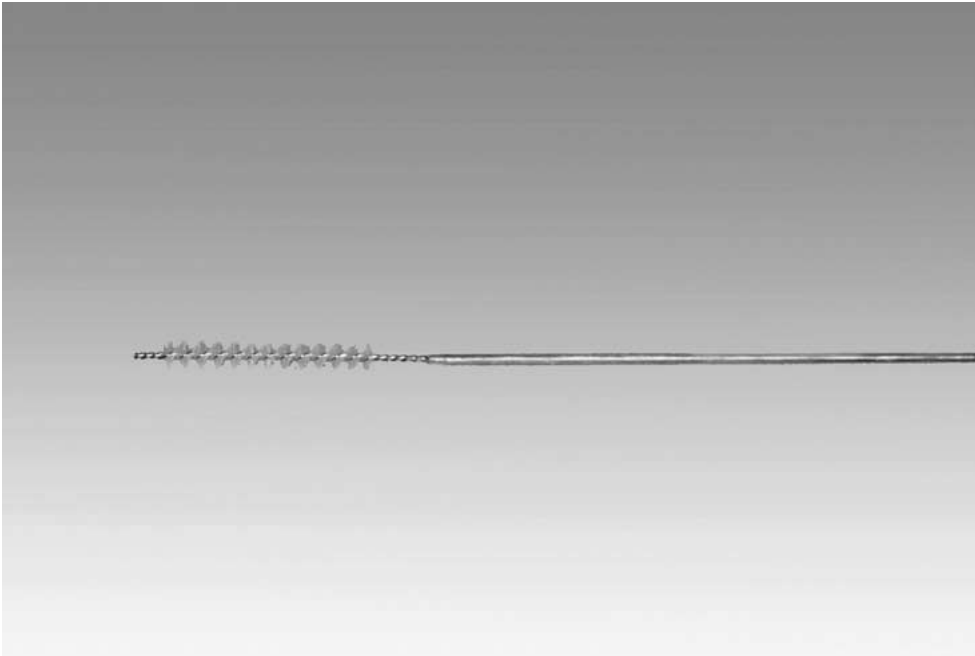


Fig. 1. Microbrush (diameter of 0.55 mm)

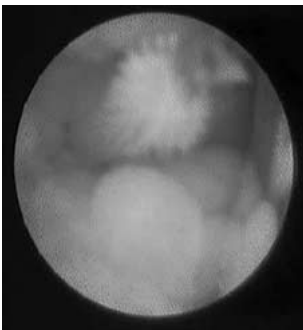


Fig. 2. Microbrush with papilloma as seen on BDME.

incidence of endoluminal pathology that could be recognized endoscopically, and to correlate the observed morphologic abnormalities with the final histology.

The microbrush was designed to allow us, for the first time, to take diagnostic samples from precise areas under direct vision. We aimed to establish the adequacy of the cell sample yield with the microbrush, and to assess the quality of the diagnostic information that it provided. The results of this study may further ability to decide whether BDME might safely replace diagnostic surgery for some patients with nipple discharge.

Materials and methods

Patient selection

Breast duct microendoscopy was offered to all patients referred to our breast unit with nipple discharge who had diagnostic surgery. Surgery included microdochoectomy (for younger women) and total duct excision (especially for postmenopausal women). The criteria for diagnostic surgery in our unit specify patients with unilateral single duct discharge, patients with hemoglobin-positive or clinically blood-stained discharge, and patients who have discharge containing epithelial cells with cytological atypia and a copious nipple discharge that is embarrassing for the patient.

Instruments and procedure

Methyl alcohol was used to clean the nipple before the procedure in an effort to remove the cellular debris and keratin plugs that normally block the duct ostium. Our own dilator with a firm pointed rubber tip (Beechey's dilator) was used to dilate the duct ostium at the nipple skin surface.

Two different breast microendoscopes were used in this study: one with an external diameter of 0.95 mm and another with a diameter of 1.1 mm (PolyDiagnost GmbH, Pfaffenhofen, Germany). These are compact scopes with a 6,000-pixel optic, fiberoptic illumination (illumination depth more than 4 cm), a 0° direct view, and a 70° field of view. Both scopes have an irrigation channel for continuous irrigation with saline. This helps to clear the field of vision, and the irrigation fluid also can be collected afterward and used as a cytology sample. The 1.1-mm scope also has 0.45-mm working channel, which can be used to insert the microbrush. The scopes have a working length of 8 cm.

Endoluminal breast brush cytology has not been described previously. The microbrush wire has a diameter of 380 μm and a 0.55-mm outer diameter with nylon bristles (Fig. 1). The microbrush is inserted through the working channel of the 1.1-mm microendoscope while the lesion to be sampled is viewed (Fig. 2). The handle of the microbrush is rotated and pulled in and out to ensure that the bristles make good contact with the lesion to be sampled. The microbrush then is pulled out of the working channel of the microendoscope, and the bristle tip (Fig. 3) is cut off with a pair of scissors before being sent to the laboratory in saline.

After endoscopic examination of each breast duct, the irrigation fluid was milked out. This fluid was sent for cytologic examination and afterward referred to lavage aspiration cytology, although it is not necessarily equivalent to ductal lavage performed without microendoscopy. Patients undergoing microendoscopy who had single or multiple visible papillomas were divided into two groups: one group that had cytology sampling by combined microbrush and lavage and another group that had lavage alone.

Surgery was performed as a day procedure with the patient under general or local anaesthesia depending on the patient's choice and physical condition. The average time required for the procedure was 15 min.

Cytology samples processing

The tip of the brush was wiped across a glass slide, which then was stained. The brush tip was inspected under a dissecting microscope for



Fig. 3. Tip of microbrush with cluster of cells under microscope.

Table 1. Papillomas: correlation of cytology and endoscopy^a

Cytology sample	Papillary lesions seen on endoscopy	Papillary cells seen on cytology
Brush + lavage	8	7
Ductal lavage only	11	2

^a The sensitivity of the brush cytology technique is 87.5%, and the sensitivity of ductal lavage is 18% ($p = 0.0055$)

any additional material, which then was removed by mechanical blowing through a pipette. Any cells removed by blowing were suspended in saline and gently centrifuged before being spread on a glass slide. The slides were stained using papanicolau (PAP) and May-Grunwald-Giemsa (MGG) stains.

The morphologic findings at endoscopy were correlated with the final histopathology report and the report from the brush and lavage cytology.

Results

A total of 50 consecutive patients undergoing microdochectomy or total duct excision for nipple discharge had breast microendoscopy (28 under general and 22 under local anesthesia). Of these 50 patients, 31 had microdochectomy and 19 had total duct excision. Visualization of discharging ducts was accomplished in all cases (100%). The median depth of the duct visualized was 5.2 cm. The maximum depth of the duct visualized was same as the working length of the scope (i.e., 8 cm). The median number of bifurcations crossed in this study was 3.

Endoluminal abnormalities were seen in 33 patients (66%), whereas dilated ectatic ducts only were seen in the other 17 patients. Among the 33 patients with visible endoluminal pathology, 15 had a single papilloma, 3 had multiple papillomas, and 15 had signs of either acute inflammation (erythema, bleeding, fronds) or previous inflammation with healing (adhesions and blocked ducts). A false passage was created for 10 (20%) of the 50 patients.

The cytology microbrush was used to sample the papillomas seen endoscopically, and the results of the cytology compared with lavage alone appear in Table 1. Papillary cell clusters were evident in only 2 of 11 pa-

tients who had lavage cytology only (sensitivity 18%). In contrast, 7 of the 8 patients with visualized papillomas who had both cytology by microbrush and lavage showed papillary cell clusters (sensitivity, 87.5%; $p = 0.0055$). Thus, microbrush significantly increases the sensitivity of the cytology study.

Complications

All the patients were seen in the outpatient clinic 1 week after surgery. Recovery was uneventful for all the patients, and no adverse events were apparent from either the microendoscopic procedure or the surgery.

Discussion

We have previously shown the clinical feasibility of breast duct microendoscopy [7]. In the current series of patients with nipple discharge, we again found that cannulation of the discharging duct with microendoscopic examination is straightforward and usually achievable. One barrier to successful visualization is the creation of a false passage early in the procedure. The walls of the breast duct are delicate and thin so that undue pressure or force used to pass the scope can easily cause damage. In our series, we created a false passage in 10 of the 50 patients (20%) at some point during the procedure.

Preoperative investigations such as ultrasonography, mammography, hemaocult test, galactography, immunologic studies such as carcinoembryonic antigen study of the nipple discharge, and even magnetic resonance galactography all have been described in the investigation of nipple discharge [10]. These investigations have relatively poor sensitivity for the diagnosis of papilloma and *in situ* malignancy [3, 5, 14, 15], and the clinician frequently ends up with a series of negative results. It usually is a matter of reducing the chance of an underlying malignancy instead of establishing with any scientific certainty the cause of the discharge. This is because none of these tests give direct access to the mammary epithelium, which of course is the site of the pathology in all cases of nipple discharge. In this respect, BDME is a more appropriate method of investigation for patients with nipple discharge. This does not mean that BDME could replace all the traditional investiga-

tions because it is most important to exclude malignancy as accurately as possible. However, it remains to be seen whether BDME is a useful addition to our current management of nipple discharge.

Breast duct microendoscopy gives a direct view of the mammary duct endothelium. The use of the microbrush in this study represents the first time that precise sampling of endoluminal lesions under direct vision has been made possible. Our data show that the microbrush increases the sensitivity of cytology significantly. Various techniques have been used to collect cytology samples from mammary ducts, including intraductal biopsy using a needle [9], ductal lavage [4], and nipple aspirate [6]. These tests are minimally invasive and well tolerated [1]. Although nipple discharge cytology is as specific as guided fine-needle aspiration, it is less sensitive because the sample is not taken from a specific lesion [8].

In this study, we have shown that cytology samples produced with the use of the microbrush are better able to show benign papillomas than ductal lavage. The method used for obtaining the lavage sample cannot be described as strictly equivalent to ductal lavage performed without microendoscopy. However, because the irrigation fluid was aspirated after the papilloma had been disturbed by the endoscope (50% of patients did not have the brush cytology), lavage might be expected to be more informative than usual.

Nonetheless, the sensitivity of lavage in this study was poorer than that reported by other groups using duct lavage alone for the diagnosis of malignancy. In a study of ductoscopy involving 415 women with nipple discharge, ductal lavage after ductoscopy increased the yield of cytologically interpretable ductal epithelial cells 100-fold, as compared with discharge fluid alone [12].

In the current series, the microbrush had a high sensitivity for the diagnosis of papillomata and provided lesion-specific information, which ductal lavage cannot do. In contrast to BDME and the microbrush, all other techniques are either not lesion specific or not site specific. Techniques that sample the entire ductal tree create diagnostic and treatment problems because there is no indication as to the exact site of the lesion. For a similar reason, the results of lavage cytology are much more difficult to correlate with the final histopathology. Further studies are required to establish whether the microbrush has a high sensitivity for other epithelial lesions such as ductal carcinoma *in situ*.

The studies by Shen et al. [13] demonstrated that many intraduct papillomas are located within the proximal duct at a mean depth of 2.7 cm from the nipple orifice. Most are in the main duct, and fewer lesions are in the branches. Despite possible problems with sensitivity caused by its inability to examine every branch of a typical duct system, microendoscopy has the ability to locate many intraduct papillomas specifically. In our experience, intraoperative guidance seems to be helpful when diagnostic surgery is performed for nipple discharge. In particular, lesions deep within the ductal system, likely to be missed by blind duct excision, can be identified and removed through an appropriately small incision [2]. In cases of multiple papillomata, it usually is possible to establish accurately the extent of the duct

resection required, whereas without duct microendoscopy, the surgeon often is unaware that the discharge is caused by multiple lesions, and the resection may be insufficient.

Conclusion

Breast duct microendoscopy is useful for investigation to determine the likely cause of nipple discharge. Additionally, it provides information regarding the site of endoluminal lesions. The microbrush significantly increases the sensitivity of cytology for duct papillomas. Findings have proved BDME to be free of any significant complications. The role of the microbrush in the detection of preinvasive malignancy requires further study.

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