



Nipple discharge: a sign of breast cancer?

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ABSTRACT

INTRODUCTION Nipple discharge is regarded a sign of breast cancer. Type of discharge and cytology are unreliable for diagnosis. Most malignant cases have a detectable breast mass. The aim of this study was to assess the association between nipple discharge and breast cancer.

PATIENTS AND METHODS Patients who underwent operation for nipple discharge at a district general hospital (population 460,000) over a 3-year period were included. All had normal clinical, radiological and cytological examination. Operation and histopathology reports were reviewed.

RESULTS Eighty-six patients underwent operation for nipple discharge. Median age was 54 years (range, 32–84 years). Analysis of nipple discharge revealed red blood cells (RBCs) in 35 patients (40%). At operation, 81 patients underwent radical sub-areola duct excision (Hadfield's procedure) and five microdochectomy. Histopathology reported duct ectasia in 59 patients and benign ductal papilloma in 25. Two patients had occult malignancy – DCIS (1) and LCIS (1). No invasive cancer was found.

CONCLUSIONS Nipple discharge alone is not usually a sign of breast cancer. Occult malignancy is rare. A period of 'watchful waiting' may prevent patients undergoing unnecessary surgery.

KEYWORDS

Breast – Cancer – Nipple – Discharge

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Nipple discharge is the presenting symptom for 3–9% of patients seen in breast cancer clinic.^{1,2} The majority of patients are referred under the cancer guidelines because nipple discharge is traditionally regarded a sign of breast cancer,³ the incidence reported at 5–12%.⁴ However, although nipple discharge may be the presenting symptom, many cases may also have an underlying breast mass or abnormal mammography.^{4,5} The aim of this study is to assess the incidence of breast cancer in patients presenting with nipple discharge alone, who had normal clinical and radiological examinations.

Patients and Methods

The study was carried out in a district general hospital where three consultant breast surgeons serve a population of approximately 460,000. All patients who underwent operation for pathological nipple discharge over a 3-year period (1997–2000) were reviewed. Patient demographics were recorded.

This is a retrospective study that looked at the pathological outcome following the operation of this policy on a consecutive

series of patients who presented with significant nipple discharge in isolation with no suspicious imaging or clinical mass.

Nipple discharge was regarded as pathological if blood stained, serosanguinous, serous or clear. White/green discharge was regarded as physiological and benign. All patients with nipple discharge underwent triple assessment (clinical examination of the breast, mammography or ultrasound imaging and cytology). Patients were included for analysis if they had pathological nipple discharge and normal triple assessment. Patients with a palpable breast lump or radiologically suspicious area were excluded, the investigation and treatment of the lump according to standard protocol took precedence. Patients with benign discharge, with normal triple assessment were reassured and discharged from breast clinic. These patients with benign discharge were not included.

All patients with pathological nipple discharge were offered operation. Patients with surgically significant nipple discharge only of 40 years and above are recommended to undergo Hadfield's procedure (radical subareolar duct excision). Patients below 40 years of age, particularly if intending to

breast feed, with persisting discharge are given the option of microdocheotomy. All histopathology results were reviewed. Patients were divided into two groups – those with red blood cells (RBCs) present in the nipple discharge and those without. In cases of incidental malignant disease, details of further treatment and follow-up were recorded.

Results

Eighty-six consecutive patients underwent operation for isolated nipple discharge during the study period. Median age was 54 years (range, 32–79 years). Analysis of nipple discharge revealed RBCs in 35 patients (40%). The remainder, 51 (60%), had no RBCs on analysis of nipple discharge. Eighty-one patients (93%) underwent Hadfield's procedure and five (7%) microdocheotomy. Histopathology revealed all patients with RBC-positive nipple discharge had benign disease – 16 (47%) had an intraductal papilloma and 19 (53%) had duct ectasia. Most patients with RBC-negative nipple discharge had benign disease – 9 (17%) had intraductal papilloma and 40 (80%) duct ectasia. Two patients (3%) with RBC-negative nipple discharge had occult *in situ* breast cancer. No patient had invasive cancer. No patient with occult malignancy had RBC-positive discharge. There was no significant difference in age between those who had RBC-positive (median, 53 years) or negative (median, 55 years) discharge. Both patients with *in situ* disease were older (64 and 67 years). Overall incidence of benign disease was 97.7%. Overall incidence of occult *in situ* disease was 2.3%.

Two patients had incidental *in situ* disease, one had lobular carcinoma *in situ* (LCIS) and one ductal carcinoma *in situ* (DCIS). Both patients underwent Hadfield's procedure at initial operation. The patient with LCIS had a benign intraductal papilloma with a small focus of non-invasive squamous metaplasia and a small focus of LCIS. No further management or surgery was performed, Follow-up at 47 months remains disease-free. The patient with DCIS (low grade) underwent total mastectomy, as the disease was centrally located. No residual DCIS was present on subsequent histology. Follow-up at 18 months remains disease-free. Independent review of radiological investigations performed prior to operation in these cases revealed no abnormality (Andrea Brown).

Discussion

Nipple discharge is a common reason for referral to breast cancer clinic.²⁻⁴ However, the incidence of breast cancer in patients with nipple discharge may not reflect an association with the nipple discharge alone but with secondary findings on assessment. Indeed, many patients presenting with the

symptom of nipple discharge may also have a palpable breast mass or abnormal mammogram. In these cases, investigation of abnormal clinical or radiological examination should take preference.

Investigation of the nipple discharge includes triple assessment. Clinical examination may reveal an underlying mass or deformity of the nipple-areolar complex. Radiological imaging is inaccurate in establishing the cause of nipple discharge. In our series, all imaging was reported as normal. Ductal imaging by ductography is helpful but non-specific.⁶ Filling defects seen may be due to inspissated secretion rather than a significant duct lesion and cases of duct ectasia, small intraduct lesions may be missed entirely. The investigation is uncomfortable to the patient and not commonly utilised in our practise. Furthermore, in this study, patients with pathological nipple discharge were not segregated on the basis of numbers of discharging ducts. Only those patients under 40 years of age, particularly if intending to breast feed, with pathological nipple discharge were offered microdocheotomy. Most were recommended to undergo Hadfield's procedure.

Nipple discharge cytology is specific in cases of malignancy but often inadequate for routine assessment.⁷ Similarly, presence of red blood cells in nipple discharge is not a reliable marker for breast cancer^{8,9} as was seen from our data. Advances in combination procedures of ductoscopy and lavage cytology may lead to increased diagnostic accuracy and possibly enable curative ablation of intraductal lesions.¹⁰ However, these techniques of ductoscopy, lavage cytology and intraductal biopsy are evolving and not available in many centres.

Most commonly performed operations for nipple discharge are microdocheotomy with isolation and removal of the affected duct or radical subareolar duct excision otherwise known as Hadfield's procedure.^{11,12} These operations are both diagnostic and therapeutic. Histopathology of excised tissue is often benign.⁵ In this series, the most common benign histopathological findings were duct ectasia (53%) and duct papilloma (47%). Duct ectasia is a benign involutional change not associated with malignancy.¹⁵ It may be associated with nipple discharge, a palpable lump or slit-like retraction of the nipple. Intraductal papilloma are commonly symptomatic when they develop in larger ducts where they can cause duct obstruction with proximal dilatation. Papilloma are more likely to present with bloody discharge.⁹ In this series, the majority with underlying intraduct papilloma had RBC-positive discharge.

Incidence of malignancy associated with nipple discharge in this series was low, both cases had *in situ* disease. Neither had RBC discharge. Data from pathological series suggest incidence of undetected DCIS may be 5–10% depending on age.¹⁴ LCIS is uncommon and not regarded as an obligate precursor of malignancy.¹⁵ It is possible that the

two cases of incidental DCIS/LCIS in this series may reflect the normal incidence in an asymptomatic general population and not reflect a higher incidence of disease in patients with nipple discharge.

Age has been implicated as a risk factor when associated with nipple discharge.⁵ Our findings corroborated this, although small numbers prevent significant statistical comparison. Hadfield's procedure and microdochectomy are the most common techniques for the surgical treatment of patients with nipple discharge. Both techniques enable histopathological diagnosis and treatment of symptoms. Recognised side effects of these procedures include nipple deformity, necrosis, and peri-areolar anaesthesia in some cases (20%).¹⁶

Our findings suggest that the incidence of malignant disease in isolated nipple discharge is low. Surgical intervention can be associated with significant morbidity. Following triple assessment, a period of watchful waiting may be justified in a significant proportion of patients.

Conclusions

Isolated nipple discharge is not usually a sign of breast cancer. The majority of patients have benign disease. A period of watchful waiting may prevent patients undergoing unnecessary surgery.

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References

- Vargas HI, Romero L Chlebowski RT. *Management of bloody nipple discharge. Curr Treat Options Oncol* 2002; **3**: 157–61.
- Seltzer MH. Breast complaints, biopsies, and cancer correlated with age in 10,000 consecutive new surgical referrals. *Breast J* 2004; **10**: 111–7.
- Leis Jr HP. Management of nipple discharge. *World J Surg* 1989; **13**: 736–42.
- Carpenter A, Adamson A, Royle GT. A prospective study of nipple discharge. *Br J Clin Pract Suppl* 1989; **68**: 54–7, discussion 67–72.
- Lau S, Küchenmeister I, Stachs A, Gerber B, Krause A, Reimer T. Pathologic nipple discharge: surgery is imperative in postmenopausal women. *Ann Surg Oncol* 2005; **12**: 546–51.
- Hou MF, Tsai KB, Ou-Yang F, Lin HJ, Liu CS, Chai CY *et al*. Is a one-step operation for breast cancer patients presenting nipple discharge without palpable mass feasible? *Breast* 2002; **11**: 402–7.
- Gupta RK, Gaskell D, Dowle CS, Simpson JS, King BR, Naran S *et al*. The role of nipple discharge cytology in the diagnosis of breast disease: a study of 1948 nipple discharge smears from 1530 patients. *Cytopathology* 2004; **15**: 326–30.
- Sauter ER, Schlatter L, Lininger J, Hewett JE. The association of bloody nipple discharge with breast pathology. *Surgery* 2004; **136**: 780–5.
- Devitt JE. Management of nipple discharge by clinical findings. *Am J Surg* 1985; **149**: 789–92.
- Mokbel K, Escobar PF, Matsunaga T. Mammary ductoscopy: current status and future prospects. *Eur J Surg Oncol* 2005; **31**: 3–8.
- Hadfield GJ. Excision of the major duct system for benign disease of the breast. *Br J Surg* 1960; **47**: 472–7.
- Hadfield GJ. Further experience of the operation for excision of the major duct system of the breast. *Br J Surg* 1968; **55**: 530–5.
- Dixon JM, Anderson TJ, Lumsden AB, Elton RA, Roberts MM, Forest APY. Mammary duct ectasia. *Br J Surg* 1983; **70**: 601–3.
- Alpers C, Wellings S. The prevalence of carcinoma *in situ* in normal and cancer associated breast. *Hum Pathol* 1985; **16**: 796.
- van Dongen JA, Fentiman IS, Harris JR, Holland R, Peterse JL, Salvadori B *et al*. *In situ* breast cancer: the EORTC Consensus Meeting. *Lancet* 1989; **2**: 25–7.
- Dixon JM. ABC of breast diseases. *BMJ* 1994; **309**: 946–9.