Clinical Science

Lessons learned from 416 cases of nipple discharge of the breast

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Abstract

BACKGROUND: For patients with nipple discharge (ND), surgical duct excision is often required to exclude underlying malignancy. Our objective was to define clinical predictors of malignancy and examine the utility of common preoperative studies.

STUDY DESIGN: We retrospectively identified 475 patients presenting with a chief complaint of ND from 1995 to 2005; 416 (88%) were eligible for review.

RESULTS: Following standard evaluation (clinical breast examiation/mammogram/ultrasound), 129 of 416 (31%) were considered to have physiological ND and were managed expectantly, whereas 287 of 416 (69%) underwent further evaluation (cytology/ductography/magnetic resonance imaging) followed by biopsy ± surgery. Clinical features associated with pathological ND included bloody ND (adjusted odds ratio 3.7) and spontaneous ND (adjusted OR 3.2). Biopsy/surgery identified a causative lesion in 259 of 287 (90%), of which 37% were either malignant (n = 65) or high-risk (n = 30) lesions. The sole clinical predictor of malignant/high-risk lesion was a palpable mass (adjusted odds ratio 4.3). Preoperative evaluation identified 76 of 95 (80%) malignant/high-risk lesions, whereas 19 of 95 (20%) were identified by duct excision alone.

CONCLUSIONS: Although clinical stratification alone reliably identified patients with pathological ND, neither the clinical characteristics nor preoperative studies can reliably distinguish between benign and malignant pathology. Surgical duct excision remains the gold standard to exclude underlying malignancy.

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Nipple discharge (ND) of the breast is a common complaint. Between 5% and 10% of women presenting for routine examination will report spontaneous ND, and as many as 80% of women will experience at least 1 episode of ND during their reproductive years.[1] Although most NDs are caused by benign conditions such as papillomas and duct ectasia, up to 15% of patients with ND may have an underlying malignancy.[2–5] Although clinical presentation alone may help distinguish between benign/physiological and suspicious/pathological ND, further evaluation is often needed to help rule out an underlying malignancy.[6–8]

Standard evaluation of patients presenting with ND includes a thorough history and physical examination; radiographic studies such as mammography and ultrasonography may be performed depending on the age of the patient and findings on physical examination.[9] In the setting of an actively discharging duct, ductography (DG) may provide a means of localizing the underlying causative lesion, but it has not been shown to reliably exclude an underlying malignancy

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or accurately differentiate between benign and malignant pathology.[10,11] Evaluation of the intraductal system using ductoscopy with or without ductal lavage may be performed; however, there is little evidence to suggest that they facilitate the detection of underlying pathology, and the utility of these approaches remains investigational.[12,13] Preliminary research suggests that magnetic resonance imaging (MRI) may have a role in the evaluation of patients with ND because of its ability to identify otherwise occult disease; however, available data are limited.[14] Therefore, the gold standard diagnostic and therapeutic approach for patients with pathological ND is surgical duct excision.[15] The challenge for the breast surgeon is to identify patients with pathological ND in the clinical setting and to avoid unnecessary surgical intervention in patients with physiological ND.

We reviewed our institutional experience with patients presenting for the evaluation of ND over a 10-year period. The aim of the study was to define clinical predictors of underlying pathology and to examine the utility of common preoperative studies in identifying an underlying malignancy.

Methods

Using the *International Classification of Diseases–9th Revision* code for "breast symptoms" (611.79), we identified 2,319 patients without a current cancer diagnosis who presented to our institution for evaluation between January 1995 and October 2005. Retrospective chart review revealed that of these, 475 (20%) presented with a chief complaint of ND. Male patients (n = 24) and those with no clinical follow-up (n = 35) were excluded from this analysis; the remaining 416 patients comprised our study group.

Data were collected by a retrospective chart review with the approval of our institutional review board. Standard clinical parameters were reviewed, including age at presentation, previous history of breast disease, medical history, family history, and smoking history, as well as salient features regarding the nature of the discharge (duration, laterality, amount, color, spontaneity, and number of involved ducts). Discharge was classified as "bloody" based on color and/or hemoccult testing if performed by the treating surgeon.

Patients received a standard evaluation (ie, clinical breast examination [CBE], mammography, and/or sonography) at the discretion of the treating surgeon. All imaging studies performed at an outside facility were reviewed by a dedicated breast radiologist at Memorial Sloan-Kettering Cancer Center and repeated as needed. All mammograms (MMGs) greater than 6 months old were updated. Further management (clinical observation, ND cytology, DG, MRI, biopsy, and/or surgery) was undertaken at the discretion of the treating surgeon. For those patients proceeding to further evaluation with DG or MRI, investigations were performed

and interpreted at our institution by an experienced radiologist according to previously described protocols.[12,16] For the purposes of this analysis, investigations were interpreted as follows: MMGs and MRIs were interpreted based on the Breast Imaging Reporting and Data System (BIRADS), and thus a BIRADS score of ≥4 was considered suspicious and a BIRADS score of 1 to 3 was considered negative. Sonography reports were interpreted as positive based on the finding of either a mass and/or dilated ducts. Cytology was considered positive based on the presence of either "papillary," "atypical," or "suspicious" cells, whereas "benign" or "inflammatory" cells on cytology were considered negative. DG was considered suspicious for an underlying lesion based on the presence of either a "filling defect" or "duct ectasia."

Pathology reports for those patients proceeding to biopsy and/or surgery were reviewed. A patient was considered to have a false-positive preoperative study if the excised lesion identified by the investigation did not reveal a carcinoma or a high-risk lesion (HRL) (lobular carcinoma in situ or atypical ductal hyperplasia). Conversely, a patient was considered to have a false-negative study if there was no suspicious finding on imaging but the pathological specimen revealed either a cancer or a HRL. HRL were included in this analysis because of their clinical importance in determining a patient's risk of underlying breast cancer. For those patients who did not proceed to biopsy or surgery, clinical status at the last follow-up was obtained from the medical records.

Unadjusted associations among patient characteristics, clinical characteristics, test results, and the presence of malignant or HRL were evaluated using the Pearson chi-square test, Student's *t* test, and logistic regression analysis as appropriate. Multivariable logistic regression analysis was used to assess the relationship between (1) clinical characteristics and the odds of having pathological ND, and (2) clinical characteristics, test results, and the odds of having a malignant or HRL. In all statistical tests, a *P* value less than .05 was considered statistically significant. All analyses were performed in SPSS (version 11, Chicago, IL) or SAS software (version 9.1, Cary, NC).

Results

Initial clinical assessment: physiological or pathological ND?

All patients underwent standard evaluation, including CBE (n = 416, 100%) followed by mammography (n = 380, 91%) and sonography (n = 132, 32%) as indicated. Based on the initial clinical evaluation, 129 (31%) patients were considered to have physiological ND and were managed expectantly (Fig. 1). Although unadjusted analysis reported a trend for patients managed expectantly to be younger (45.5 vs 53.4 years) and premenopausal (47% vs