Ultrasound-guided wire localization of focal ductal dilatation in the evaluation and treatment of pathologic nipple discharge

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Abstract
Patients presenting with pathologic nipple discharge (PND) often pose a diagnostic and therapeutic challenge. We used ultrasound to identify focal ductal dilatation—hypothesized to be a radiographic manifestation of the causative lesion—in patients with PND and no relevant clinical or radiographic findings. Twenty-two excisions guided by ultrasound wire localization of focal duct dilatation were performed. Surgical pathology revealed papilloma in 20 cases (91%); atypia or carcinoma was detected in 7 cases (32%). The ultrasound finding of focal duct dilatation enables excision of otherwise occult though clinically significant lesions and is worthy of further study.

KEYWORDS
breast cancer, breast ultrasound, focal ductal dilatation, papilloma, pathologic nipple discharge

1 INTRODUCTION

Patients presenting with pathologic nipple discharge (PND) often pose a diagnostic and therapeutic challenge. While the clinical presentation of PND—spontaneous discharge of clear or bloody fluid from a single duct orifice—is readily apparent, the underlying causative lesion is often occult on physical and routine radiographic exam.1-9 In 4 studies reporting on a total of 692 patients with PND, clinical exam was normal in 81-86% of patients, mammogram was negative in 67-80%, and ultrasound showed no findings in 52-60%.1,3-5 Ductography, probe-guided surgical excision, and ductoscopy are often used to evaluate PND; however, these techniques are limited by the difficulty of accessing and visualizing the delicate, branching ductal system from within. The default procedure of blind central duct excision is disconcerting in that large volumes of tissue are often removed with no certainty of excising the causative lesion.3,5,9,10

The challenge of identifying and excising the causative lesion has led to a lack of consensus on the management of PND. Some authors have accepted nonoperative surveillance unless PND presents with findings that suggest malignancy.1,5,7 Others stress the importance of surgical treatment with precise localization to ensure certain excision of the lesion causing PND.3,9,10 Their paramount concern is leaving atypia or carcinoma behind, particularly as surgical disruption of central ducts eliminates further PND and offers a false sense of security for patient and surgeon. The results of surgery for PND are often disappointing. Studies report high rates of fibrocystic change and duct ectasia,1,5,7,9,11 both of which have been questioned as legitimate causes of PND.3,9,10

These considerations led us to develop a new technique using ultrasonography for the diagnosis and treatment of PND. Our preferred method of evaluating PND has been through ultrasonographic detection, localization, and excision of an intraductal mass.3,5,9,10 When ultrasound fails to identify this finding, presumably because of the small size or echogenicity of the lesion, we have often detected focal ductal dilatation (FDD) in the axis correlating with the site of PND. We hypothesized that FDD is a radiographic manifestation of the lesion itself and that ultrasound-guided wire localization of this finding would enable identification and excision of the causative lesion. We describe our experience to date with this technique.
MATERIALS AND METHODS

An Institutional Review Board approved retrospective study was conducted of all patients with PND who presented to a single breast surgeon (CW) from 2003 to 2015. PND was defined as spontaneous discharge of clear or bloody fluid from a single duct orifice. Patients with physiologic nipple discharge were not included. Furthermore, patients with any clinical or radiographic finding diagnostic or even suggestive of a causative lesion were excluded from the study.

On presentation, patients underwent history, physical examination and review of imaging studies performed to date. Nipple discharge was sent for cytology, and the axis of the involved orifice was noted. Patients were referred to a dedicated breast radiologist (JM) who was informed of the site of nipple discharge. Ultrasound was performed with either an ATL HDI 5000 or Philips HD 11XE unit (Bothell, WA) and a high-frequency linear array (12.5 MHz) transducer. If the dedicated study ultrasound identified an intraductal lesion or other entity that explained PND, the patient was excluded from the study.

Focal ductal dilatation was defined as the ultrasonographic finding of a discrete dilatation of a duct, typically reaching a diameter of at least 2 mm, and manifesting as a distinct contour change relative to the normal ductal caliber. Patients with this finding underwent ultrasound-guided wire localization of FDD on the day of surgery. This was performed using local anesthesia with a Kopans needle (Cook Medical, Bloomington, IN). Localization was not performed for patients with no finding of FDD on study ultrasound.

Intraoperatively, the breast was manipulated to reproduce PND and the discharging duct was cannulated with a lacrimal duct probe which was advanced until it met resistance. In patients who had undergone ultrasound-guided wire localization, the targeted tissue was excised. We noted whether the localizing wire and duct probe came into contact, and if they were not, excision included the tissue at the distal end of the probe. Patients with no findings on study ultrasound underwent central duct excision targeting the tissue around the probe. All tissue specimens were processed for permanent section analysis and were read by dedicated breast pathologists.

RESULTS

Twenty-four female patients with PND and no potential causative lesion identified on physical examination or conventional imaging were evaluated by targeted ultrasound. In 3 cases, the study ultrasound failed to reveal FDD. These patients underwent excision guided by lacrimal duct probe placement as described above and resultant pathology revealed papilloma in each case. These patients were excluded from the study.

Ultrasound identified FDD in the remaining 21 patients (1 with bilateral PND) and details are summarized in Table 1. Preoperative ultrasound-guided wire localization of the site of FDD was successfully performed in all cases. Of the 22 cases taken to the operating room following wire localization, 19 underwent successful cannulation through the discharging nipple orifice with a lacrimal duct probe. In 3/22 cases, cannulation failed because discharge could not be

### Table 1: Demographic and clinical data for patients presenting with pathologic nipple discharge

| Variable                  | Patients n = 21 |
|---------------------------|-----------------|
| Age, mean (range)         | 52 (23-79)      |
| Presenting symptom        |                 |
| Bloody nipple discharge    | 18 (82)         |
| Clear nipple discharge     | 4 (18)          |
| Mammogram discharge       |                 |
| None                      | 19 (86)         |
| Unrelated to PND          | 3 (14)          |
| Ultrasound findings       |                 |
| None                      | 16 (73)         |
| Unrelated to PND          | 6 (27)          |
| Cytology                  |                 |
| Benign                    | 14 (64)         |
| Atypical                  | 7 (32)          |
| Not obtained              | 1 (5)           |

Values in parentheses are percentages.

### Table 2: Study ultrasound findings and results of surgical excision in patients with pathologic nipple discharge

| Findings                             | Affected breasts (n = 22) |
|--------------------------------------|---------------------------|
| Duct dilation on study ultrasound in mm, mean (range) | 2.3 (1.7-3.5) |
| Gross size of surgical specimen in cm³, mean (range) |                 |
| All cases                            | 18.7 (1.25-63.3)         |
| First 7 cases                        | 22.8 (12-63.3)           |
| Second 7 cases                       | 18.76 (6-43.7)           |
| Final 8 cases                        | 15.35 (1.25-30.4)        |
| Intraoperative ductal cannulation, n (%) |                 |
| Yes                                  | 19 (86)                   |
| No                                   | 3 (14)                    |
| Did ultrasound wire and ductal probe meet, n (%) |                 |
| Yes                                  | 16 (73)                   |
| No                                   | 2 (9)                     |
| N/A (no cannulation)                 | 3 (14)                    |
| Not known                            | 1 (5)                     |
| Pathology, n (%)                     |                           |
| Papilloma alone                      | 14 (64)                   |
| Papilloma + ADH                       | 2 (9)                     |
| Papilloma + DCIS                      | 2 (9)                     |
| Papilloma + invasive ductal carcinoma | 2 (9)                     |
| DCIS + LCIS                           | 1 (5)                     |
| No lesion (duct ectasia)              | 1 (5)                     |
reproduced (2 cases) or because the duct orifice was too small to access (1 case). These patients underwent excision guided solely by the ultrasound-localized wire.

Pathology revealed papilloma in all but 2 cases. Fourteen cases had papilloma alone. Two cases had papilloma with atypical duct hyperplasia. In 5 patients, final pathology revealed cancer: 2 papilloma with invasive ductal carcinoma, 2 papilloma with ductal carcinoma in situ (DCIS), and 1 DCIS alone. In 1 case, only duct ectasia was identified. Ultrasound and surgical findings are summarized in Table 2.

4 | DISCUSSION

Until now, the role of ultrasound in the diagnosis and treatment of PND has been limited to targeting an actual intraductal lesion for biopsy or excision Authors have, however, noted the significance of more subtle ultrasonographic findings, including ductal prominence and contour change. In 2003, Cabioglu5 observed that the ultrasonographic finding of duct ectasia was linked to a pathology finding of papilloma or malignancy, and therefore that "patients with nipple discharge with imaging findings of duct ectasia, but no other discrete abnormalities, might require further evaluation to ensure that no pathologic lesion is missed." In 2007, Rissanen12 reported that in 3 of 5 patients with PND in whom malignancy was ultimately detected, the only ultrasonographic finding was a dilated duct without an actual mass. He stated that ductal dilatation "might be an important abnormality in patients with nipple discharge," but ultimately described this finding as "negative... not considered sufficiently reliable for accurate preoperative wire localization." These authors were describing the conceptual basis of our study, but did not recognize duct dilatation as a legitimate target for localization and excision in and of itself.

**FIGURE 1** (A) Ultrasound of a 39 year-old patient with 18-month history left breast of pathologic nipple discharge. Arrow marks focal duct dilatation (FDD), which was targeted for localization and excision. FDD contrasts with normal caliber duct to the right. (B) Pathology of same patient showing longitudinal view of duct. Arrow marks intraductal papilloma with associated FDD which contrasts with normal caliber duct to the right (hematoxylin and eosin—magnification 40x)

**FIGURE 2** (A) Ultrasound of a 36 year-old female with 2-year history of left breast PND. Arrow marks focal duct dilatation (FDD), which was targeted for localization and excision. To the left of this is a dilated ductal branch point and to further left is a normal caliber duct. (B) Pathology of same patient showing longitudinal view of duct. Arrow marks papilloma with associated FDD. To the left of this is a dilated ductal branch point and to further left is a normal caliber duct (hematoxylin and eosin—magnification 40x)
The premise of our study is that the ultrasonographic finding of FDD is a manifestation of an otherwise radiographically occult lesion and is reliable for preoperative wire localization. This was noted in the operating room as the probe introduced through the discharging orifice came into contact with the localizing wire (Table 2). It was reinforced by the identical configuration of the duct seen longitu-
dinally on ultrasound and in cross-sectional histology (Figures 1 and 2). Most importantly, the validity of this approach is reflected in the pathology findings. While specimen sizes reflected the targeted nature of the excision and became increasingly small with experience (Table 2), in 21/22 (95%) cases, a lesion was found which explained the patient’s PND.

The pathology findings of atypia and cancer detected in this study were not anticipated. The 9% incidence of atypia, 14% incidence of in situ carcinoma and 9% incidence of invasive carcinoma are high, particularly as this study excluded patients with any clinical or radiographic findings indicative of an underlying lesion—a population well known to have a higher incidence of malignancy.2,5,8,10,13 These pathology findings underscore the clinical significance of PND and papillomas in general and challenge those who advocate nonop-
erative management of PND.1,7 These findings also contrast with pathology findings of duct ectasia, fibrocystic change, normal breast tissue, and even uninterpretable cauterized tissue that are commonly reported in the literature.1,6,8,10,13,14

While some authors accept fibrocystic change and duct ectasia as legitimate causes of PND,1,3,9,10 we agree with others that they are not.5,14 We argue that such pathology findings indicate cases where physiologic nipple discharge was mistaken for PND or more worrisome cases in which the true causative lesion was left behind. One patient in our study had undergone probe-guided excision for treatment of PND 9 years earlier and presented with recurrent PND in the same axis, indicating a retained lesion. While her pathology in our study proved to be a benign, albeit large papilloma, others have reported cancer in this context.10,13 Chaudary10 wrote that “failure to demonstrate a specific cause for the discharge is a cause of concern, and it would seem prudent to recommend indefinite follow-up for those whose discharge contained hemoglobin.” In only one of our study cases was there no pathology finding that explained PND—rather only duct ectasia (Table 2). This patient’s follow-up has included MRI and close clinical and radiographic surveillance for 5 years with no findings to date. We recommend similar surveillance in these cases. Most importantly, we advocate careful evaluation of PND, precise localization, and targeted excision of the true underly-
ing pathology.

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