Case Report

Pathological Nipple Discharge

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Abstract. Introduction: Pathological nipple discharge is usually of benign aetiology but cancer may be the underlying cause in up to 20% of the presentations. The diagnostic value of discharge cytology and significance of presence of blood remains a topic of interest. Our study sets out to review the distribution of histopathology and diagnostic application of blood-staining and cytology in pathological nipple discharge. Methods: We performed a retrospective analysis of those patients that had surgery for pathological nipple discharge. The hospital’s electronic medical records and breast cancer information systems were used to identify our study cohort. Parameters evaluated included patient demographics, radiological assessment, if discharge was blood-stained and histological/cytological analysis. Results: Of 123 patients, intraductal papilloma was the leading diagnosis (n = 62) followed by duct ectasia (n = 34). Carcinoma in-situ and invasive carcinoma occurred in nine cases. Seventy-one patients presented with blood-stained nipple discharge of which 41 had a diagnosis of intraductal papilloma, 17 had duct ectasia, and seven cases were due to carcinoma. Two cases of cancer were negative for blood. Cytology was done only in 23 patients and was not diagnostic of carcinoma and identified intraductal papilloma in only 3 cases. Conclusion: This study supports the generally accepted view that cytology has very poor sensitivity for detecting breast cancer and has therefore very limited diagnostic value. Nipple discharge that is negative for blood is still associated with cancer. It also confirms that intraductal papilloma is the leading cause of pathological nipple discharge.

Keywords: Breast cancer, nipple discharge, cytology, papilloma

1. Introduction

Spontaneous nipple discharge (SND) is a relatively common manifestation of breast disease, accounting for up to 5% of overall breast symptoms [1, 2]. Bilateral nipple discharge involving multiple lactiferous ducts is usually non-pathological and reported by up to 90% of these patients [3–5]. Conversely, pathological nipple discharge (PND) is typically spontaneous, unilateral, uniductal and may be serous or bloody, the latter either overt or occult [1, 3–5]. While the commonest cause of PND is intraductal papilloma (IDP), responsible for nearly 40% of cases [3], an underlying malignancy, usually ductal carcinoma in-situ (DCIS), has a reported incidence of 4-20% [6–9]. The likelihood of malignancy is greater in women over the age of 50 or those presenting concurrently with a palpable mass [4, 5, 8, 10].

Until 2010 the consensus was that all women with PND should have mammography if they were over the age of 35 years in order to identify ipsilateral lesions [11]. However, in the Association of Breast Surgery’s diagnostic guidelines document published in November 2010 the recommended age for mammography was revised to patients over 40 years of age [12]. Ultrasound scan may be helpful in visualising retro-areolar lesions that can potentially be biopsied. Other
Histological diagnosis in 123 cases presenting with pathological nipple discharge

Figure 1: Histological diagnosis in 123 cases presenting with pathological nipple discharge.

Histological diagnosis in 71 cases of Hb +ive pathological nipple discharge

Figure 2: Histological diagnosis in 71 cases of Hb +ve pathological nipple discharge.

2. Methods

A review of Guy’s Hospital electronic medical records system, breast clinic data and the Cancer Information System (CIS) was undertaken in order to identify all patients presenting with unilateral, single or multi-ductal pathological nipple discharge that needed surgery in the form of DMD or TDE between January 2006 and December 2009. For patients presenting with non-pathological discharge (bilateral discharge, discharge only on expression that is not blood stained and is negative on cytology and/or dipstick) and no other radiological or clinical abnormalities, no other investigations or follow up was deemed needed and they were not included in the cohort. On the other hand, patients that presented with nipple discharge and were found to have malignancy on investigations without the need for DMD or TDE were treated accordingly and also not included in the cohort.

In total, 131 female patients were identified between the ages of 19-82 (mean 46.8) who were assessed and treated for PND at Guy’s Hospital. Eight patients were excluded from the study due to incomplete records, leaving 123 patients. The data collected for each patient was: age, haemoglobin (Hb) positive/negative discharge, cytological evaluation (if performed), imaging studies (USS or mammography), diagnostic procedure (DMD or TDE) and the final histological diagnosis in the excised tissue.
Histopathology results in cases where discharge cytology was requested

- N = 14
- N = 6
- N = 2

<table>
<thead>
<tr>
<th>Pathology</th>
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<tbody>
<tr>
<td>IDP</td>
<td>N = 14</td>
</tr>
<tr>
<td>Duct ectasia</td>
<td>N = 6</td>
</tr>
<tr>
<td>DCIS &amp; LCIS</td>
<td>N = 2</td>
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<td>EH</td>
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**Figure 3:** Histopathological results in cases where discharge cytology was requested.

Where NDC evaluation was undertaken, acellular smears were categorized as non-contributory and smears containing epithelial cells and/or blood were considered as abnormal. A fine needle aspiration (FNA) or core biopsy was attempted if an abnormality in was identified and the result of this was collected. Operative procedures were either DMD or TDE.

### 3. Results

Of the total (n = 123), 67 patients had diagnostic DMD and 56 had TDE in order to make a definitive histological diagnosis. The distribution of histological findings is shown in Figure 1. The commonest diagnosis in this cohort was IDP, accounting for 50.4% of the total (n = 62), followed by duct ectasia in 34 patients (27.6%). Ductal carcinoma in situ (DCIS) was diagnosed in 5.7% of cases (n = 7) that presented with PND while invasive carcinoma was diagnosed in 1.6% of patients (n = 2). Eighteen patients out of a total of 123 (14.6%) presenting with PND had a diagnosis of inflammatory or benign changes on histological analysis.

71 (57.7%) presented with blood-stained nipple discharge (Hb positive [+ve]). Figure 2 illustrates the range of histological diagnoses in this group. The majority of patients with Hb +ve discharge had IDP 57.7% (N = 41). The second most common diagnosis in this cohort was duct ectasia, accounting for 23.9% (N = 17). Six cases out of a total of 71 (8.5%) were due to DCIS while only one case (1.4%) was the result of invasive carcinoma. Of note, one case of DCIS and another of invasive carcinoma were Hb-ve.

Of the 123 patients in our cohort, only 23 (19%) had the discharge sent for cytological analysis. The final histopathology results in patients from whom NDC was sent, are shown in Figure 3. Only one of 23 patients had a final diagnosis of DCIS; this was, however, not diagnosed through cytology, which was reported as showing no malignant cells. In 14 out of the 23 specimens sent for NDC, IDP was the underlying pathology. However, cytology was suggestive of papillary lesion in only three, the rest deemed as not showing malignant cells or equivocal.

### 4. Discussion

At present there is no nationally published algorithm regarding the use of diagnostic tests in women presenting with PND. However, it is agreed that patients who are deemed to have PND from the history and examination should have appropriate radiological screening (mammography +/- ultrasonography) with magnetic resonance imaging (MRI) reserved for those requiring further evaluation or following the diagnosis of breast cancer [18]. The key is to identify malignancy, which, according to the literature can be found in up to 20% of women identified as having PND [6–9]. In our series of 123 patients, nine cases (7.3%) were diagnosed with DCIS and/or invasive carcinoma. Most had a diagnosis of IDP (62/123), whilst 34 were found to have duct ectasia. This is in keeping with large studies, which have shown that
IDP is the leading cause of PND (48%), while duct-ectasia is the second most common diagnosis, accounting for 15-20% [4, 19–21]. Interestingly 14.6% of our cohort (n = 18) had only inflammatory and/or benign changes in spite of presenting with symptoms and signs of PND.

The value of nipple discharge characteristics such as cytology and blood-staining in investigating PND has long been a subject of debate. NDC is usually only undertaken if patients are having active discharge at the time of assessment in clinic. Of the 123 patients in our cohort, although all were assessed and deemed to have PND, only 23 had nipple discharge that was sent for evaluation at the time of their assessment. Of those, one contained no cellular material.

A noteworthy point is that although 50.4% of our cohort (62/123) was diagnosed as having IDP, NDC indicated a papillary lesion in only three of these. Specifically, none (62/123) was diagnosed as having IDP, NDC indicated a malignancy. Although few cases had NDC, the study supports the generally accepted view that NDC has very poor sensitivity for detecting breast cancer and is therefore of limited diagnostic value.

**References**


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Although publications covering various aspects of nuclear receptors (NRs) appear every year in high impact journals, these publications are virtually buried among an overwhelming volume of articles that are only peripherally related to NRs. The latter fact prompted a group of prominent scientists active in the field of nuclear receptor research to conclude that gathering publications on this superfamily of receptors under one umbrella would provide an invaluable resource for a broad assemblage of scientists in the field; thus the idea for a new journal, **Nuclear Receptor Research**, was born.

I am pleased to share with you that **Nuclear Receptor Research** is now a reality as an open access peer-reviewed journal devoted to publishing high-quality, original research and review articles covering all aspects of basic and clinical investigations involving members of the nuclear receptor superfamily. **Nuclear Receptor Research** has an editorial board comprised of a group of renowned scientists from around the world. Board members are committed to make **Nuclear Receptor Research** a vibrant forum showcasing global efforts in this ever-expanding area of research.

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Mostafa Badr
Editor-in-Chief
**Nuclear Receptor Research**