The radiologists guide to nipple discharge: Pathology, imaging techniques, and treatment plan.

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Learning objectives

After reviewing this exhibit, the radiologist will be able to:

1. Discuss and illustrate the pathology of nipple discharge including duct ectasia, lactation, papilloma, mastitis, ductal carcinoma in situ and invasive breast malignancy
2. Understand multi duct and single duct nipple discharge and worrisome features
3. Understand imaging techniques used in evaluation of nipple discharge including breast ultrasound, mammography and MRI
4. Understand a treatment algorithm to plan management for nipple discharge, discussing use of interventional techniques including breast core biopsy and vacuum assisted mammotomy
5. Understand radiological and pathological concordance and appropriate follow-up of patients with nipple discharge
6. Review 1 year’s follow-up of patients with nipple discharge at Chelmsford Breast unit who have been managed using our treatment algorithm
Nipple discharge is a common presenting complaint to the breast radiologist and can be caused by a wide range of conditions, most of which are benign or easily treated. However, nipple discharge can signify a potentially serious breast problem including malignancy. Several types of nipple discharge exist including milky, multi-coloured and sticky, purulent, clear (watery), yellow (serous), pink (serosanguineous) and bloody (sanguineous) [1]. Nipple discharge may occur spontaneously or upon manipulation of the breasts, however, to be considered significant it should be spontaneous, persistent and non-lactational [1].

The breast is naturally designed to produce and secrete fluid to provide necessary nutrition for a newborn and production of breast milk occurs secondary to hormonal as well as physical stimulation from suckling. A bilateral, spontaneous, multi duct discharge which is milky in appearance in usually seen in premenopausal patients of childbearing age and is known as galactorrhoea [Fig. 1] [2]. It is due to an increased production of prolactin by the direct action of the pituitary gland or indirectly by inadequate hypothalmic inhibition of the pituitary gland. Prolactin stimulates the glandular tissue in the breast, resulting in breast milk production [2]. Patients should be investigated for the source of hyperprolactinaemia including prolactin levels and thyroid function tests and if persistent, a MRI brain should be obtained to rule out a prolactinoma [3]. Women who have completed breastfeeding can continue to have persistent discharge after weaning and can persist for 1-2 years and sometimes longer [4].

Mammary duct ectasia is a benign breast condition which can mimic invasive carcinoma clinically and most commonly affects middle-aged to elderly parous women [5]. It is characterised by dilation of major ducts in the subareolar region [Fig. 2, Fig. 3] which contain eosinophilic granular secretions and foamy histiocytes [5]. The secretions may undergo calcification and this may be the presenting sign as well as nipple retraction, inversion, pain and nipple discharge which may be bloody, serosanguineous, or multi-coloured (purulent, grey or milky) [3]. The aetiology of this condition is still under debate but smoking has been implicated as a possible aetiological factor. This condition can be managed conservatively and there is no evidence to suggest it is linked to an increased risk of breast cancer [5].

Acute mastitis refers to the inflammation of the breast resulting in a cellulitis of the interlobular connective tissue within the mammary gland [Fig. 4, Fig. 5] which can result in abscess formation and widespread sepsis [4]. It commonly presents with swelling, pain, tenderness and redness during the first 3 months post-partum as a result of breast feeding [4]. Predisposing factors include stasis of milk and cracks in the nipple as a result of poor breast feeding technique and reduced immunity caused by stress and sleep deprivation.
Staphylococcus aureus is implicated as the most common infecting agent and treatment consists of antibiotic therapy which should not be delayed due to the possibility of abscess formation [4].

Intraductal papillomas are localised areas of epithelial proliferation within large mammary or lactiferous ducts [Fig. 6][5]. The lesion may be single or occur as part of the multiple intraductal papillomatosis syndrome [Fig. 7] which is associated with an increased risk of malignancy. Patients usually present with bloody nipple discharge and are largely premenopausal. In a third of cases, a small painful subareolar nodule may also be present. Treatment is by microdectomy which involves surgical excision of the affected segment of breast tissue [4].

The two most common types of non-invasive breast malignancies which may present with pathological bloody nipple discharge include ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) [4]. DCIS is a malignant clonal proliferation of cells growing into breast ducts [Fig. 8], with no evidence of invasion into the surrounding stroma. Very few cases of DCIS present as a palpable mass; most are diagnosed by mammography, usually as clustered microcalcifications [4, 5]. LCIS is a marker for increased risk of developing invasive carcinoma [Fig. 10] with the risk equal for both breasts. Breast carcinoma which occurs subsequently may be lobular or ductal [4, 5].

Invasive breast carcinoma is an infiltrating malignant proliferation of neoplastic cells in breast tissue and may also present with bloody nipple discharge [Fig. 9]. However, more commonly patients will present with a lump, nipple changes, breast pain/mastalgia and skin contour changes. Many different types of invasive cancers exist including ductal (85%), lobular (1%) [Fig. 10], mucinous (5%), papillary (<5%) [Fig. 11, Fig. 12] and medullary (<5%) [6].

The evaluation of nipple discharge is important in determining whether it is benign or physiological in nature or shows worrisome features likely to represent sinister pathology such as breast malignancy. Key features that should be identified during history and physical examination include whether the nipple discharge is spontaneous or provoked. Spontaneous discharge that is noticed on clothes is more worrisome than provoked nipple discharge. Furthermore, if nipple discharge occurs from both breasts it is more likely to be benign than if it occurs from both ducts. Similarly, discharge from a single duct is regarded as more worrisome than discharge from multiple ducts [5]. The appearance of the discharge is also important in determining its likely cause. Nipple discharge that is coloured grey, green, white, yellow or clear is more likely to represent fibrocystic fluid which represents physiological discharge unlike watery or bloody discharge which is more likely to be pathological [5].
Several diagnostic tests are used to establish the cause of nipple discharge including ultrasound, mammograms and cytology. Mammography is the investigation of choice for less dense breasts, found in postmenopausal women and is nearly always done. Ultrasound is very effective in younger women with more dense breasts and can be more diagnostically useful in this cohort. Ultrasound can be used to examine the retroareolar ducts to identify duct ectasia. The use of both ultrasound and mammography in combination can detect more invasive cancers [7]. MRI is sometimes used in more challenging cases, for example in young women with dense breast tissue [Fig. 7], familial breast cancer associated with BRCA mutations, breast implants, positive axillary lymph node status with occult primary carcinoma in the breast or where multiple tumour foci are suspected [8].
Images for this section:

**Fig. 1:** US showing lactational change: arrow shows dilated ducts leading up to the nipple. The breast parenchyma appears of higher echogenicity than would be expected for normal which is in keeping with lactational change

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Fig. 2: US showing well defined duct ectasia with intraductal homogeneous echogenecity

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Fig. 3: US showing mammary duct ectasia with intraductal homogeneous echogenecity

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Fig. 4: US showing a well-defined simple cyst (arrow far left) and an area of interlobular oedema (arrow far right), appearances in keeping with acute mastitis

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Fig. 5: Mammogram showing cystic changes within the breast tissue representative of acute mastitis

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**Fig. 6:** US showing breast papilloma, a hypo echoic mass within a retro areolar duct.

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**Fig. 7:** MRI scan showing multiple gadolinium enhancing bilateral breast masses in keeping with papillomatosis
Fig. 8: US showing ductal carcinoma in situ with calcifications present in a branching and ductal distribution. This condition often presents with single duct bloody discharge
Fig. 9: US showing invasive cancer appearing as an irregular hypo echoic mass responsible for single duct blood stained nipple discharge

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**Fig. 10:** Mammogram showing an invasive lobular carcinoma as an area of increased density and distortion

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Fig. 11: US showing a papillary carcinoma as an intracystic mass

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**Fig. 12:** Mammogram showing a papillary carcinoma as a marge mass in the centre of the left breast.

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Findings and procedure details

Following a thorough history and physical examination, further evaluation with cytology and imaging should be pursued. Two different treatment algorithms have been devised at Chelmsford Breast Unit for investigation of women with single duct discharge [Fig. 18] or multi duct discharge [Fig. 19].

For patients with single duct or any bloody discharge [Fig. 18] and age less than 40 years, USS and cytology are recommended. For patients presenting with similar types of discharge but aged greater than 40 years, a mammogram [Fig. 13] is recommended in addition to these investigations. If cytology is benign, a watch and wait approach is undertaken with repeat cytology 3 months later. If repeat cytology is negative, a repeat triple assessment is advised in one year following which the patient is usually discharged from follow-up if results are all negative or suggestive of benign pathology. Patient choice should be taken into account and if nipple discharge is found to be benign following investigations but the patient is troubled by persistent discharge or it is affecting their confidence or quality of life, surgery should be offered. If cytology findings are suspicious, surgery is recommended. This can be in the form of a micrroductectomy, which involves the removal of a single breast duct, or a major duct excision which involves the removal of the end of all breast ducts.

Patients presenting with multi duct discharge [Fig. 19] who are less than 40 years of age undergo cytology. If greater than 40 years of age, ultrasound and mammogram are performed in addition to cytology. If cytology results are reported as C1 (inadequate sample) and C2 (definitely benign), patients are written to with the results. Patients with C3 cytology (indeterminate) are reviewed in 6 weeks to 3 months' time. If cytology is reported as C4 (suspicious of malignancy) and C5 (definitely malignant), the patient is offered surgery in the form of a major duct excision. If multi duct nipple discharge is most likely to be benign following all investigations but becomes persistent in nature, patient may insist on a major duct excision.

Suspicious findings on a mammogram may require biopsy for a histological diagnosis. Open surgical biopsy is reserved for times when needle biopsy techniques have failed to deliver a concordant result. Core needle biopsy involves using a 14 gauge hollow-core needle directly aimed at the area of a palpable mass, known as freehand biopsy, or under imaging to localise the breast lesion. One or more pieces of breast tissue are removed [4]. Imaging techniques used in core needle biopsies include x-ray stereotactic localisation, ultrasound and MRI. The biopsy specimen is extracted using either vacuum assistance or with an automated gun. Not only is core needle biopsy a minimally invasive biopsy technique compared with open surgical biopsies but has been found to produce more reliable and consistent diagnostic results compared with other techniques such
as fine needle aspiration (FNA) [4, 5]. However, core needle biopsy techniques using the automated gun have shown to produce false negative results when taking biopsies from masses less than 1.5cm in size and in stereotactic biopsies of microcalcifications. Furthermore, it can be time-consuming by requiring many needle insertions only to yield insufficient sample tissue [4,5]. Vacuum assisted techniques [Fig. 14, Fig. 15, Fig. 16] were introduced as a result of the drawbacks of the standard automated core biopsy technique and allow a greater amount of breast tissue to be extracted including adjoining tissue, ensuring the entire biopsied area is sampled [Fig.17]. Vacuum assisted mammotomy is also available for treatment and excision of breast lesions such as papillomas. These procedures are usually performed with ultrasound guidance. Vacuum assisted techniques have provided a small additional increase in sensitivity and have found to be particularly useful in areas of microcalcifications, masses less than 1.5cm in size, complex cysts and ductal lesions and subtle lesions which require biopsy [4,5].

Clinical, radiological and pathological (the breast triple assessment) concordance is vital in management of all breast pathology. This is achieved following discussion of all cases in a multi disciplinary team meeting. If there is non concordance between the different aspects of the triple assessment then further investigations should be performed.

In this single-centre study, retrospective data was collected of every patient that had presented with nipple discharge at the Chelmsford Breast Unit over a one year period from October 2012 to October 2013. Clinical letters for each patient were accessed through the InfoFlex database and used to establish the nature of nipple discharge. Cytology and histopathology reports were obtained using MEHT review. Radiology imaging and reports for ultrasounds and mammograms were obtained via Impax software.

36 patients presented to the Chelmsford Breast Unit with nipple discharge. The ages of the patients ranged from 26 to 83 years (mean of 48.7 years). 21 (58%) patients had multi duct nipple discharge and 15 (42%) patients had single duct nipple discharge [Fig. 20]. Of the 15 patients presenting with single duct nipple discharge, 15 (100%) patients were shown to have followed the treatment algorithm. Of the 21 patients presenting with multi-duct discharge, 18 (86%) were shown to have followed the treatment algorithm and 3 (14%) were shown not to have followed the treatment algorithm. The three patients who were shown not to have followed the treatment algorithm, one did not have an ultrasound, one did not have a mammogram and one did not have either in the management process. However, all patients that had presented with nipple discharge had cytology. The most common condition demonstrated was duct ectasia, however, 2 cases (5.5%) of breast cancer were identified comprising of high-grade DCIS and invasive papillary carcinoma. Other conditions included duct papilloma (11%), benign cysts (5.5%), fibrocystic disease (5.5%) and in 17 cases (47.5%) no abnormality was identified with all investigations being unremarkable [Fig. 21].
These findings demonstrated 91.7% compliance to the nipple discharge treatment algorithm. Possible reasons for non-compliance to the treatment algorithm include normal clinical findings which favour physiological nipple discharge in comparison to pathological nipple discharge and therefore no further investigations are proposed. Furthermore, in some situations, an ultrasound may not appear necessary in the presence of a normal mammogram and normal cytology results and therefore might not be done. In other instances, if the patient wishes to have surgery despite the likelihood of a benign condition causing nipple discharge, some investigations may not be felt necessary.
Fig. 13: A picture showing the upright GE Mammography machine used at Chelmsford Breast Unit

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**Fig. 14:** A picture showing the vacuum mammotomy device used at Chelmsford Breast Unit

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**Fig. 15:** A picture showing the vacuum mammotomy needle used at the Chelmsford Breast Unit

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**Fig. 16:** A picture showing the display screen of the vacuum mammotony device used at Chelmsford Breast Unit

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Fig. 17: A picture showing the biopsy obtained used the vacuum mammotony device at the Chelmsford Breast Unit

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Fig. 18: Treatment algorithm for single duct nipple discharge
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Fig. 19: Treatment algorithm for multi duct nipple discharge
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Fig. 20: A graph showing the percentage of patients presenting with single duct and multi duct nipple discharge

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**Fig. 21:** A graph to show the breast pathology identified at Chelmsford Breast Unit from October 2012-2013

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Conclusion

Nipple discharge is a common complaint with radiologists as the first contact point. It can signify a potential breast problem including cancer. The challenge in evaluating nipple discharge is determining whether it is physiological or pathological. Following a thorough history and physical examination, cytology and imaging are helpful in further evaluation. Our review of one year of cases managed using our treatment algorithm demonstrates that the most common condition is duct ectasia followed by duct papilloma and the least likely was breast malignancy. Furthermore, nearly half of all patients presenting with nipple discharge were found to have no abnormality on investigation.
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