

Review Article

Breast Pain, Nipple Pain and Nipple Discharge – An Overview

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Abstract

Breast pain (Mastalgia) is the 2nd most common presenting symptom at Breast Clinics all across the world [1]. Nipple Discharge and pain are the next in order. Patients are usually worried about a potential underlying diagnosis of cancer, however, the incidence of malignancy is actually fairly low among the patients presenting with these symptoms. Aetiology of mastalgia is poorly understood, making appropriate treatment methods more difficult to identify. Reassurance, breast support brassiere and topical non-steroidal creams are commonly used in the management of breast pain. Nipple pain, on the other hand, occurs in a particular set of patients – breastfeeding women – and usually has a more clear-cut underlying diagnosis, i.e. infection, cracked nipple, vasospasm or poor breastfeeding technique. The underlying cause should be identified and treated in a timely manner while continuing with breastfeeding, if at all possible. Nipple discharge is the most worrying of the symptoms among these three, in terms of detecting the malignancy, especially, if the discharge is haemorrhagic. Investigations and treatment of nipple discharge largely differs, depending upon whether or not intraductal pathology is identified. Other systemic causes should be considered, especially in patients with bilateral nipple discharge. Novel diagnostic methods are also on the rise and can help practitioners investigate patients with nipple pain and discharge in a less invasive manner, with Magnetic Resonance Imaging, or special biomarkers. All in all, mastalgia, nipple pain and nipple discharge are frequent complaints and each needs to be investigated thoroughly in order to tailor the treatment best suited to the individual patient.

Keywords

- Mastalgia
- Nipple pain
- Nipple discharge
- Breast pain

INTRODUCTION

Breast pain, nipple pain and nipple discharge are symptoms that are not only bothersome to patients, but can also be a source of great anxiety. Patients tend to worry about the diagnosis of breast cancer whenever they experience any of these symptoms. Although breast cancer in these instances is rare, especially in the case of breast pain, these symptoms, unfortunately, can at times, signify and reveal an underlying malignancy.

In addition to the above, patients may also be embarrassed socially and in their relationship with their partner too, particularly in the case of nipple discharge. These symptoms can affect the quality of life, as described later in this article. In light of all of the above, investigating and managing the symptoms appropriately, in consideration of the whole picture and each patient's individual situation, is of paramount importance. Patient education is also crucial, especially in primary care, to ensure that patients feel comfortable reporting the symptoms, as help and advice is readily available. Patients should be encouraged not to suffer in silence.

We will consider each of the symptoms in turn, comparing and contrasting prevalence, aetiology, classifications, investigation techniques and management methods. We will also consider novel diagnostic and treatment methods that have become increasingly more common in day-to-day medical practice over the last few years.

Mastalgia

Mastalgia, or breast pain, is the 2nd most common cause of referral to Breast clinics [1]. It can be an irritating symptom that, in some cases, prevents patients from doing activities they normally engage in and at the same time it also affects the patients' relationships and quality of life [2]. Public understanding of mastalgia is poor and women primarily tend to worry about breast cancer when they experience breast pain. Mastalgia can be difficult to manage, due to uncertainties in aetiology and effective management methods. This can be disappointing, both for the clinician and the patient.

Up to 80% of women may experience mastalgia in their lifetime [3,4]. For instance, a survey of female marathon runners

in the London Olympics in 2012 showed that 32% of all female runners experienced mastalgia. Interestingly, however, many of the runners did not seek any medical help and did not use any medication or other simple preventative measures i.e. wearing support bra and analgesia etc to reduce or manage their pain at all, despite describing it as 'discomforting' [5]. This clearly highlights the lack of public awareness of mastalgia and patients may simply get on with mastalgia without seeking further help or advice.

Interestingly, not only does mastalgia affect sleep and sexual life negatively, but it also tends to persist for many years. According to one study the average span was 7.5 years [2]. In the same study, the patients that were older, had a larger breast cup size and lower activity level, experienced higher level of mastalgia [2].

Mastalgia in men is rare and often occurs in patients who have gynaecomastia, whether primary or secondary to medications, tumours, liver disease or hormonal factors, such as using anabolic steroids, drug abuse and alcoholism. Management of the underlying cause in this case would be the primary aim.

Mastalgia basically falls into two categories: cyclical and non-cyclical breast pain. Cyclical mastalgia begins one or two weeks prior to menstruation and is described as diffuse, bilateral pain, relieved with the onset of menstruation. Patients are usually younger in comparison. Cyclical mastalgia is uncommon after menopause. Non-cyclical mastalgia is mostly unilateral and experienced by older, peri or post-menopausal patients. Other pathological condition may be involved, such as cysts, fat necrosis, periductal mastitis and occasionally neoplasia and hence a thorough work up with appropriate investigations, i.e. Mammogram, Ultrasound imaging and FNAC (Fine Needle Aspiration Cytology) is recommended in United Kingdom by the NICE (National Institute of Clinical Excellence) and SIGN (Scottish Intercollegiate Guidelines Network) guidelines, if the mastalgia persists for over 6 months.

In addition to taking a thorough history, keeping record of the pain by patients, i.e. diaries and charts, might be useful in ascertaining which type of breast pain – cyclical or non-cyclical – patient is experiencing. Patients can be asked to chart their breast pain on a calendar and also mark the days when they had their menstrual periods [6]. This be a useful diagnostic tool and at the same time it also provides an individually tailored way of managing the pain, as patients get involved in the diagnosis and treatment planning. It also helps the patients predict days when the pain may be worse (especially in the case of cyclical mastalgia). This allows patient to feel more in control and could potentially reduce the anxiety about the pain and possible cause.

There is an exhaustive list of possible differential diagnoses when approaching mastalgia; some of the pathologies include Costochondritis, Tietze's disease, Herpes Zoster, Trauma, Fibromyalgia, Thoracic outlet syndrome, Pulmonary embolism, Sickle cell anaemia etc. Vertebral pathologies may also at times present as mastalgia (especially when other underlying causes have been excluded), and in these cases magnetic resonance imaging (MRI) may be a useful diagnostic modality [7].

A recent systematic review has attempted to summarise our current knowledge and understanding of the aetiology of

mastalgia [4]. Endocrine disturbances, water retention, neuroses, caffeine and many other factors have been implicated as the causative factors in breast pain [4]. None of these possible causes seem likely in every case, as hormonal levels were found to be similar in patients and controls in study by Malarkey et al., [8], and water retention was similar between patients and controls in a study by Kumar et al., [9], and Peters et al., [8]. Cardiff Mastalgia clinic studies did, however, show higher prolactin levels in patients with breast pain [9,10].

Imaging may not be necessary, especially in cases where the patient presents with breast pain alone of less than 6 months and no other abnormalities are found on history or examination. In cases where a lump is present or any other pathological abnormalities are detected, Mammography, Ultrasonography and Fine Needle Aspiration Cytology or Core biopsy may be required to establish the exact nature of pathology. Balleyguier et al., produced a helpful diagram that suggests possible investigation routes in breast pain, depending on history and examination findings [11] (Figure 1).

Management of Mastalgia: A recent systematic review on mastalgia and its management has shown that effective methods include reassurance, breast support brassiere and application of topical non-steroidal anti-inflammatory gel, i.e. Ibuprofen and Diclofenac [4]. Although Gamma-linolenic acid (GLA), in the form of Evening Primrose or Starflower oil, is often prescribed, they were deemed ineffective by a systematic review [4]. It is still, however, widely used, and, in fact, is advocated in our Breast Unit and works well with nearly 50% patients (anecdotal evidence) with mastalgia. We have future plan to investigate the use of GLA in Mastalgia carrying out a Randomised prospective study. Many other treatment methods have also been trialled when managing mastalgia, including dietary modifications, vitamin and herbal supplements e.g. vitamin E, soy protein, fish or flax seed oil, but no robust evidence to support use of these dietary supplements is available. Oral contraceptives and HRT have shown varying results [12].

Danazol or Bromocriptine can be used if first-line methods are ineffective, but the side effect profile of both these medication are quite severe and most of our patients have discontinued it after a few months, as they have to trade the breast pain with post-menopausal symptoms, i.e. dryness of vagina and hot flushes, which could be worse than mastalgia itself.

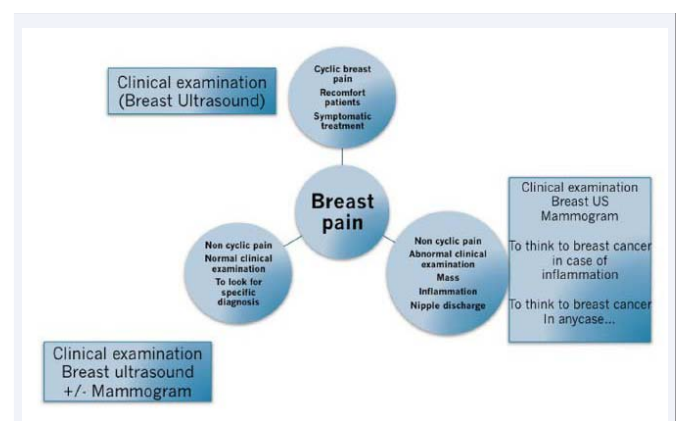


Figure 1 Investigative route for Mastalgia (curtesy of Balleyguier et al. [11]).

Yoga therapy has been considered in management of mastalgia and would relate to suggested anxiety models of causative factor in breast pain. Some evidence to support this exists, albeit it is fairly weak [13]. Psychotherapy and exercise have also been advocated in management of mastalgia [14,15] – but stronger evidence for this form of management is very sketchy.

Tamoxifen has also been used by some Breast Surgeons and it does work reasonably well with controlling the severity of breast pain. Patient must be counselled well before prescribing the Tamoxifen as it increases the risk of uterine cancer after prolonged use and can also precipitate the menopausal symptoms. The authors very rarely prescribe this due to above mentioned reasons and also the fact that the use of an anticancer drug for a benign condition cannot be justified sufficiently.

Novel treatment methods have been investigated by researchers. Centchroman (ormeloxifene, a non-steroidal selective oestrogen receptor modulator) has been shown to significantly reduce breast pain, with minimal side effects; it alleviated pain in both cyclical and noncyclical mastalgia [16]. The researchers also reported that the only side-effect of Centchroman was prolonged menstrual cycle, and that it did not cause nausea, vomiting, dizziness or breakthrough bleeding, as is common with other medical therapies for mastalgia [16]. Nigella Sativa seed oil has also been tried for cyclical mastalgia and has shown effectiveness similar to topical Diclofenac, with no witnessed side effects, and with pain scores significantly lower in the Nigella Sativa group than in the placebo group [17]. Women, whose breast pain is not as severe, may be much more inclined to try complementary therapies first, before resorting to medication. As such, complementary therapies are, in general, on the rise and both Flaxseed and Vitex Agnus have been investigated as potential therapies for treatment of mastalgia. Both Flaxseed and Vitex Agnus were effective in decreasing the severity of cyclical mastalgia, as compared to placebo [18].

A study by Joyce et al. suggested that breast pain could potentially be managed in primary care, as incidence of malignancy, especially in younger patients, in this cohort is considerably low. Reassurance and follow-up by the primary care physician may be more than sufficient for most females who experience mastalgia [19]. This may be a way forward when considering the management of a condition that is common and contributes significantly high volume of patients to secondary care breast clinic workload.

Nipple pain

Nipple pain is a much rarer symptom than mastalgia and is generally experienced by lactating women. Minimal literature exists on this subject. Although it is not quite common, nipple pain can be an extremely irritating symptom that usually lead to cessation of breastfeeding. It is, thus, essential to diagnose and manage nipple pain in a timely and compassionate manner, to ensure that breastfeeding continues – as benefits of breast milk are widely known and encouraged nowadays [20]. Nipple pain is often a problem in the immediate postpartum period, but can persist for weeks after starting breastfeeding [21]. The more persistent the pain is, the more likely it is for women to develop mental health problems, including depression and anxiety; hence impacting on the patient's quality of life [22].

Nipple pain may be caused by a variety of factors, including problems with the positioning or latching-on of the infant, blocked ducts, cracked nipple, dermatitis, eczema, psoriasis, Candida infections, Raynaud phenomenon of the nipple, etc. [23]. Interestingly, the latter seems to be under-diagnosed and appropriate treatment with Nifedipine is usually delayed due to lack of awareness on the part of physicians. This yet again highlights the importance of appropriate investigations and management, as cessation of breastfeeding could be avoided in many of these cases and deal with anxiety and depression in these subjects [24].

Management of Nipple Pain: With little research available on nipple pain, more needs to be done to address this important problem, in order to allow for quick and accurate diagnosis of the underlying cause and development of appropriate and successful treatments. However, prevention seems to be key, with anticipatory guidance, education on breastfeeding techniques and general reassurance playing a significant role in stopping the patients from developing nipple pain in the first place [22,25].

Management depends on the cause of the nipple pain, but as mentioned earlier, diagnosis may be difficult and errors may be made when establishing the appropriate management. Hence, thorough history and examination should be undertaken by the breast physician in order to tailor the treatment for the appropriate condition for each individual. Use of lanolin is encouraged by some practitioners, but evidence behind its use seems controversial, with a recent randomised controlled trial showing no significant differences in pain scores between patients who used lanolin and those who did not [26]. Nipple shield can be used earlier on, if the pain is due to cracked nipple and that is usually quite successful in our experience. If an infective cause is identified in a patient with nipple pain, appropriate antifungal or antibacterial treatment should be started [22]. Antibiotics do not play major role in this condition and their use is not encouraged unless there is clear cut evidence of infection on culture and sensitivity of the discharge. Raynaud phenomenon of the nipple should be treated with Nifedipine [23].

A systematic review done in 2004 showed that no topical treatment has superior benefit in the treatment of nipple pain and that the most helpful management involves education on breastfeeding techniques and guidance regarding high incidence of nipple pain in breastfeeding [25]. If the baby has ankyloglossia and this is presumed to be the underlying cause for the nipple pain, frenotomy may be considered for the infant [27,28].

Novel methods of nipple pain management have also been investigated. Low-level laser therapy has been used successfully in lactating women, and has provided very definitive pain relief, with prolonged exclusive breastfeeding in a triple-blinded randomised controlled trial [29]. Low-level laser therapy seems to ease the pain and promote wound healing, hence addressing nipple pain in lactating women, in particular with cracked nipple [29,30].

Nipple discharge

Nipple discharge can be a bothersome and an embarrassing symptom that affects women of all ages. Around 2 to 5% of women experience nipple discharge [31]. Among the three

symptoms discussed in this review, nipple discharge may be the most worrisome symptom for the patient and the physician seeing the patient, as in a small number of cases this can signify an underlying malignancy. Nipple discharge can be spontaneous or provoked – therefore a thorough history is still most important yet simple step to correct diagnosis when assessing the patient. Nipple discharge is defined as pathological when it is unprovoked, unilateral and blood-stained, serous, watery, creamish or greenish blue. Malignancy rates in this category differ and have been reported to be anywhere from 3% (newer studies) to 23.9% (older studies) [32]. Mammography, Targeted Ultrasonography and Cytology are the main stay of diagnosis depending upon the age of the patient and frequency of discharge. Ductoscopy can be used to evaluate pathological nipple discharge and can detect up to 94 per cent of all lesions. Specificity, however, is low, and histological diagnosis is still essential [32]. Colour alone is insufficient when determining the underlying cause, although malignancy is much more likely in patients presenting with haemorrhagic discharge [33]. Nipple discharge cytology and marker study may aid in diagnosis, as recent studies suggest that certain tumour markers (CA15-3, CA125, CEA, TSGF) can serve as biomarkers in diagnosis and prognosis of breast cancer [34]. Other potential biomarkers have been identified by recent studies, and include proteins of carbonic anhydrase 2, catalase and peroxiredoxin-2 [35]. Levels of these proteins differed significantly between nipple discharge from patients with and without breast malignancy [35]. The use of such biomarkers could facilitate and accelerate diagnostic pathways in breast clinics, making it easier to triage high-risk patients.

A useful table on Salisbury NHS Trust website highlights the differences between innocent and potentially pathological discharge. This diagram can be used as an educational tool when reassuring anxious patients [29] (Table 1).

Nipple discharge may be caused by a multitude of diseases and is not necessarily limited to breast pathology. Systemic illnesses must be considered, including pathological conditions that cause an increase in prolactin. This could be secondary to intracranial pathologies, certain drugs, or diseases of the endocrine system. In general, the three main causative mechanisms of nipple discharge could be divided into benign breast disorders, cancer and hyperprolactinaemia. Benign breast disorders that can cause nipple discharge include intraductal papilloma, duct ectasia, fibrocystic changes and abscess or infection [36,37]. Malignancies causing nipple discharge are usually either invasive ductal carcinomas or intraductal papillary carcinomas [36,37]. Finally, hyperprolactinaemia, which causes galactorrhoea, can be secondary to multiple disorders. It is therefore important to consider that nipple discharge may be caused by a range of diseases and is not necessarily limited to breast pathology. After physiological states related to nipple discharge, such as pregnancy, puberty or early neonatal period, are excluded, the following pathological conditions may need to be considered: prolactinomas, Addison's disease, Cushing's syndrome, Acromegaly, Chronic Renal Disease, Chronic Liver Disease, Hypothyroidism, and Pituitary Stalk Infiltration. Medications can also alter prolactin levels and cause galactorrhoea.

Bilateral nipple discharge is much more likely to be

secondary to systemic diseases and hence an endocrinological profile must be considered. Unilateral nipple discharge should warrant mammography, ultrasound and/or FNAC or Imaging guided biopsy. When conventional imaging tools, such as mammography and sonography, do not yield useful results, other modalities may be considered, for example, magnetic resonance imaging (MRI) or surgical duct exploration [38]. Conventional ductography can be an extremely useful diagnostic procedure, but, in some cases, it is difficult and takes longer to perform. It is quite uncomfortable procedure as well for the patient. Instead, the use of magnetic resonance (MR) ductography is now on the rise and can be particularly useful in cases where ultrasound and radiographs did not show conclusive results. This technique also allows for images to be presented in a three-dimensional fashion, increasing diagnostic accuracy [39]. More sophisticated sonography techniques have also been used in pathological nipple discharge – shear wave elastography has been shown to be a useful triage tool, with high sensitivity and high predictive value, before proceeding with Ductoscopy [40]. It is true that novel techniques may take time to become tools of common usage in daily practice; however as patients nowadays are more informed through the use of media especially, easily available information on Internet (which may not be evidence based), expect (and demand) a prompt diagnosis and effective treatment, such techniques need to be employed in order to increase patient expectation and satisfaction with the service provided.

Management of Nipple Discharge: According to Morrogh et al., the gold standard approach to treating patients with pathological nipple discharge is surgical duct excision; however it is a significant surgical intervention and distinguishing between a patient with pathological and a patient with physiological nipple discharge is essential in this case [41]. A treatment algorithm has been previously suggested by Gray et al., [42]. It is a useful algorithm, which concisely summarises management methods depending on the examination and investigation findings. It suggests that only patients with high risk of carcinoma or those who are unwilling to accept regular follow-ups should be considered for duct excision [42]. This prevents unnecessary radical treatment and formulates a clear plan for patients who are at lower risk and do not need significant surgical intervention (Figure 2) [33].

If a mass can be palpated, a biopsy should be taken. If no mass can be identified, sub-areolar exploration may be considered [43], although practices differ across different health boards. Authors prefer to do Micro-dochotomy in case of persistent haemorrhagic or profuse discharge from single duct and Major Duct Excision (Hatfield's operation) when multiple ducts are involved. If a duct papilloma is identified then a wire guided excision biopsy is recommended by the Association of Breast Surgeons (ABS) in the UK. Both of these procedure are intermediate grade operation and the patient can be treated as day case. The advantage of the operation, whether single duct Microdochotomy or Major Duct excision, are relief of symptoms and the definitive histological diagnosis of the cause of nipple discharge.

CONCLUSION

Mastalgia, nipple pain and nipple discharge are all common symptoms that every breast surgeons encounters in his or her

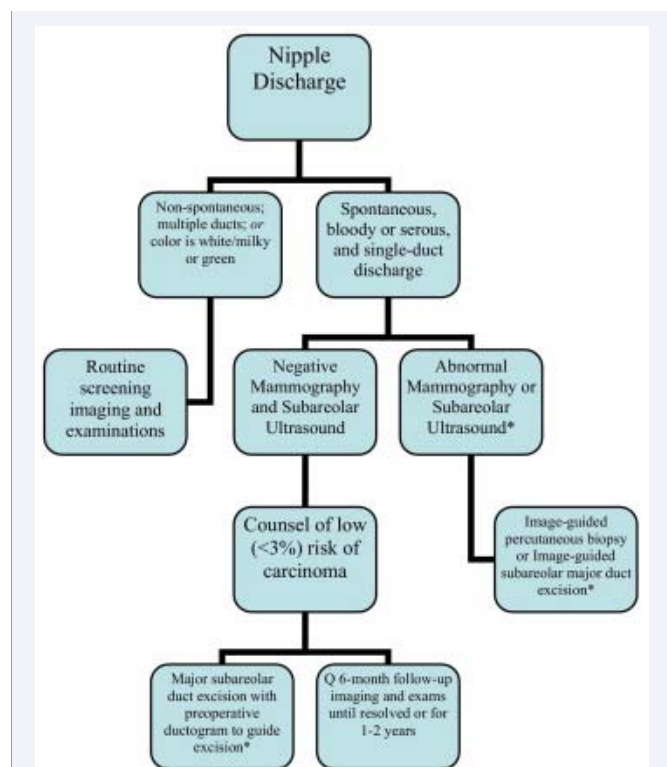


Figure 2 A treatment algorithm for nipple discharge (Gray et al. [42]).

daily practice. Further research is necessary, especially into mastalgia, to clearly define aetiology and help create more effective treatments. Nipple pain is common in breastfeeding women and usually involves treatment of the underlying cause, including adjustment of breastfeeding techniques, if necessary. Finally, nipple discharge has to be always evaluated carefully, as it can be a red flag for an underlying malignancy. Useful algorithms have been established to aid investigations and treatment, but will usually involve invasive testing (e.g. biopsies or duct excision), especially in the case of bloody, spontaneous, single-duct discharge. Novel techniques in diagnosis and treatment of mastalgia, nipple pain and discharge are on the rise and can allow for a more prompt and accurate way of identifying and managing high-risk patients.

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