Benign Breast Disease

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INTRODUCTION

Benign breast diseases includes all nonmalignant conditions of the breast and typically do not convey an increased risk of malignancy. Patients with benign breast conditions are often first seen by their primary care physician or their gynecologist. Benign breast diseases are often misdiagnosed and misunderstood because of their variety in presentation and anxiety about the possibility of malignancy. Physicians that interface with patients with benign breast disease must have a complete understanding of the conditions discussed in this article to competently evaluate these disorders and calm concerns regarding the possibility of breast cancer.

In recent years, breast care has become an established specialty throughout our health care system as evidenced by the existence of breast surgical fellowships and dedicated breast care centers. The care of women who have concerns about their

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breast health or breast abnormalities is a complex process that is best addressed by an interdisciplinary, collaborative model of care. These models of breast care often include surgeons with a practice focused on breast diseases, a dedicated team of imaging specialists, and nurse practitioners. Nurse practitioners can play an important role in helping women with breast concerns by incorporating clinical expertise with teaching and counseling skills. Nurse practitioners with specialized training are well qualified to assess, diagnose, and manage all aspects of benign breast diseases, including breast cysts, masses, nipple discharge, mastitis, abscess, breast pain, and abnormal mammograms. The value of incorporating nurse practitioners in a breast care setting has been well documented to include reduced wait times to consultation, expedited diagnosis, and decreased anxiety for patients. At the Medical College of Wisconsin, 2 of the authors’ nurse practitioners (authors A.C.P and J.L.M.) have independent practices that manage most patients who come to their facility with benign breast disorders and serve as a triage for patients with abnormal mammograms.

The following information is organized to allow for easy reference. Diagnoses are grouped by whether or not patients are lactating women, presence or absence of infection/inflammation, and nonproliferative or proliferative disorders.

BREAST INFECTIONS IN LACTATING WOMEN

Mastitis and Abscess

Mastitis is a complication often encountered in primiparous women and develops in 1% to 24% of breastfeeding women. A breast abscess develops as a complication of mastitis in 5% to 11% of cases. The most common bacteria is Staphylococcus aureus. Bacteria enter the skin by a small laceration or proliferate in a stagnant lactiferous duct. Common clinical symptoms of breast infection include pain, redness, and heat. Differentiating between mastitis and abscess can be difficult; when there is suspicion for abscess, the woman should be referred for ultrasound evaluation. Mastitis on ultrasound will appear as an ill-defined area of altered echotexture with increased echogenicity in the infiltrated and inflamed fat lobules. The diagnosis of abscess requires identification of a hypoechoic collection, often with a thick echogenic periphery. Ultrasound is the first-line investigation because it is relatively painless and provides guidance for percutaneous drainage. Antibiotics should always be offered in addition to percutaneous drainage for lesions with well-defined fluid collections. A drain may be placed as needed for full evacuation of the cavity. Aspirates should be sent for culture and sensitivity testing with antibiotic therapy directed accordingly. Oral cephalosporins or clindamycin hydrochloride (Cleocin) are excellent choices to cover the most common organisms.

Women should be encouraged to continue to breastfeed throughout the treatment to keep the ducts from becoming engorged. The only reason to cease breastfeeding would be when treatment with an antibiotic is contraindicated for the newborn or after surgical drainage.

Open surgical drainage may be necessary for patients with loculated collections or for those who have failed conservative management with antibiotic therapy and percutaneous drainage. In general, open surgical drainage should be reserved as a last resort in lactating patients to avoid the potential for milk fistula development.

BREAST INFECTIONS IN NONLACTATING INDIVIDUALS

Mastitis and Abscess

Breast abscess not associated with lactation, termed nonpuerperal, can be a challenging clinical problem that often recurs despite surgical treatment. They are classified...
according to location, either central (periareolar) or peripheral. Tobacco smoking is significantly associated with the development of primary abscesses, and smokers are 15 times more likely to develop recurrence than nonsmokers. Nipple piercing also seems to be associated with an increased risk and may be as high as 10% to 20% after the procedure. Other risk factors include diabetes, black race, and obesity.

Abscesses in nonlactating women form as a complication of periductal mastitis. The first step is squamous metaplasia of the cuboidal epithelium leading to keratin plug formation. Cellular debris distends and obstructs the lactiferous ducts, leading to ductal dilation. Secondary infection occurs with stagnation of bacterial laden debris. Central nonpuerperal abscesses are the most difficult to treat and recur in 25% to 40% of women. Cutaneous fistulae occur in one-third of patients. These abscesses are often caused by mixed flora (Staphylococcus and Streptococcus) and include anaerobes. Antibiotic therapy should be instituted with a broad-spectrum drug that the most common organisms and may require an extended period of treatment (2 weeks or longer) to clear the infection.

Up until the early 1990s, surgical incision and drainage was the recommended treatment of almost all breast abscesses. With the common use of ultrasound, treatment is now typically percutaneous drainage with repeated aspirations as needed and may include saline lavage of the cavity. In up to 54% to 100% of patients, an abscess can be adequately managed using this process. Occasionally, an indwelling catheter may be left in place for collections larger than 3 cm, but even this is seldom necessary. Patients should be encouraged to stop smoking. Mammography is recommended in women older than 35 years to rule out malignancy once the symptoms have calmed sufficiently to allow for compression of the breast. If there is any doubt, a tissue sample should be sent for cytology.

Peripheral nonpuerperal abscesses are less common and can occur with underlying chronic medical conditions, such as diabetes or rheumatoid arthritis. The most common pathogen is Staphylococcus aureus, but mixed flora can also be encountered. These abscesses respond well to drainage and antibiotics and recurrences are rare.

INFLAMMATORY CONDITIONS OF THE BREAST

Mondor Disease

Mondor disease is a rare benign condition defined as superficial thrombophlebitis of the anterolateral thoracoabdominal wall, most commonly the thoracoepigastric, lateral thoracic, or superior epigastric veins. The exact cause is unclear. The clinical presentation is a painful palpable cordlike structure that can last several weeks. This condition is usually self-limiting and responds to application of heat, systemic antiinflammatory medications, and physical support with a brassiere.

Lymphedema After Breast Radiation

For many women with breast cancer, the breast can be conserved with a partial mastectomy (lumpectomy). However, lumpectomy alone is associated with a high incidence of local recurrence. The introduction of adjuvant radiation therapy has improved local control rates that are similar to those of a mastectomy. Despite the high rate of local control, some women are left with breast edema after radiation therapy that causes discomfort and reduced satisfaction with the cosmetic appearance of the breast. Risk factors associated with the development of breast edema after postlumpectomy radiation include the extent of axillary dissection, large breast size, and a shorter time between surgery and the start of radiotherapy. The type of
nodal dissection, the need to treat the axilla with radiotherapy, and/or the presence of a wound infection postoperatively significantly impact the time course of breast edema. Patients who undergo no nodal sampling and those with uncomplicated sentinel lymph node biopsy experience similar rates of breast edema after radiation. The addition of a wound infection or axillary dissection results in significantly more edema that peaks around 4 months after radiation but returns to baseline around 12 months after treatment.9

Postradiation breast edema following may present with erythema, warmth, heaviness, and peau d’orange. It may mimic mastitis or inflammatory breast cancer. If there is any question of infection, a course of antibiotics should be prescribed and imaging performed. If there is a concern for the possibility of inflammatory carcinoma, then a skin biopsy looking for a dermal lymphatic tumor should be performed. Otherwise, breast edema can be treated with lymphatic massage, also known as decongestive therapy, by a physical therapist or lymphedema specialist.10 Wearing a supportive brassiere may improve the physical symptoms.

**Fat Necrosis**

Fat necrosis is associated with some form of injury to the breast, such as trauma or surgery. It typically presents as an irregular mass which is not tender to palpation. Imaging studies are usually insufficient to distinguish fat necrosis from malignant lesions, as fat necrosis typically appears as an undefined, spiculated, dense mass. Biopsy is recommended for definitive diagnosis to rule out malignancy. Fat necrosis does not increase the risk of developing a subsequent breast cancer.4

**NONPROLIFERATIVE DISORDERS OF THE BREAST**

**Cystic Disease**

Cystic disease of the breast is the most frequent female benign breast disease. Up to one-third of women aged 30 to 50 years have cysts in their breasts.4,11 It most commonly presents in the third decade, peaks in the fourth decade when hormonal function is at its peak, and sharply diminishes after menopause. Cystic disease is caused by dilation of ducts and acini to form cysts, proliferation and metaplasia of their epithelial lining, and multiplication of ducts and acini (adenosis) resulting in obstruction of the terminal ductal lobular unit.11

Cysts greater than 3 mm can be visualized by ultrasound and are potentially palpable on breast examination. Ultrasound findings of a simple cyst include round or oval shape, anechoic with posterior enhancement, sharp demarcation, and relative mobility in the surrounding tissue. Cysts with these findings can be classified as benign breast imaging-reporting and data system (BI-RADS 2). Ultrasound has 98% accuracy for diagnosing simple cysts.4 Complicated cysts often have septations within the cyst, homogeneous low-level internal echoes, and brightly echogenic foci. Cysts that have thickened walls, thick internal septations, and are a mixture of cystic and solid components are at a high risk for cancer and should undergo biopsy. Patients are often asymptomatic. If patients are symptomatic with pain or have a very large cyst, aspiration can be performed electively with ultrasound guidance. Aspirated cyst fluid that is clear, yellow, or green may be discarded. Aspirated cyst fluid that is bloody or has floating debris should be sent for cytology. Complex cysts that have been aspirated and have negative cytology can be managed with 6-month follow-up imaging studies instead of intervention, if asymptomatic.11 However, cysts that do not completely collapse after aspiration or that have asymmetric wall thickening should undergo an image-guided biopsy of the cyst wall to exclude the possibility
of malignancy. Any lesion that has atypical cellularity noted in the aspirate should also be excised.

**Duct Ectasia**

Most nipples contain 5 to 9 ductal orifices. Duct ectasia predominantly affects the ducts in the retroareolar region and is defined as a nonspecific dilation of one or more ducts, typically larger than 2 mm in diameter. This finding may be palpable and may be associated with nipple discharge. The cause of the duct dilatation is not well understood but is often seen in conjunction with periductal inflammation. On imaging with mammography, duct ectasia appears as radiodense serpentine tubular structures converging on the nipple-areolar complex. On ultrasound, the duct is an anechoic smooth-walled branching structure that tapers peripherally. The duct is usually filled with fluid or cellular debris but can occasionally contain calcifications. These findings centrally located favor a benign process, but duct ectasia can also be seen in a spectrum of malignant diseases. When located more peripherally with irregular duct margin and focal thickening of the duct wall, malignancy should be considered and appropriate sampling performed.

**Metaplasia, Squamous, and Apocrine**

Apocrine metaplasia is dilated ducts and adjacent cysts that contain inspissated secretions, which can calcify and manifest as heterogeneous calcifications. It is thought that this entity arises from the lobular cells of the terminal duct-lobular unit of the breast. Apocrine metaplasia is present in the epithelial lining of the cysts. Clinically, women may have breast tenderness or irregular nodularity, which may vary during the menstrual cycle. The presence of apocrine metaplasia is not thought to elevate the risk for breast carcinoma.

**PROLIFERATIVE DISORDERS OF THE BREAST**

**Mild Hyperplasia (Usual Hyperplasia)**

Hyperplasia is abnormally increased cell proliferation and can be present with or without atypia. Hyperplasia with atypia is also known as atypical hyperplasia and can be present as atypical ductal or lobular hyperplasia. These entities are covered elsewhere in this monograph.

The ducts in the breast normally contain 2 layers of epithelial cells. When the number of layers increases, this is known as ductal hyperplasia. Mild ductal hyperplasia has 3 or 4 epithelial layers. It is typically noted as an incidental finding after tissue sampling and does not require any further intervention.

**Fibroadenoma**

Fibroadenoma is the most common benign tumor of the breast and typically occurs in women younger than 30 years. It originates in the breast lobules and can be comprised of stromal and epithelial cells. Fibroadenomas are firm, rubbery masses with a well-circumscribed border. Usually fibroadenomas form as a single tumor. However, in up to 15% of patients, multiple tumors are present, and 10% will be bilateral. Fibroadenomas may grow rapidly during pregnancy or whenever there is an increase in hormonal influence. Those larger than 5 cm are termed giant fibroadenomas. Ultrasound can be used to differentiate a fibroadenoma from a cyst. Fibroadenomas are well-defined, usually oval masses with weak, uniformly distributed internal echoes. If imaging cannot conclusively confirm the diagnosis, the mass should be biopsied.

Fibroadenomas carry little to no increased risk of breast cancer. However, on rare occasions, intraductal or invasive cancer can develop in a fibroadenoma, just as it can
in any other part of the breast. In addition, multiple fibroadenomas are associated with some rare cancer syndromes, such as Maffucci syndrome, Cowden syndrome, and Carney complex. Fibroadenomas that develop in these kindred should be excised.13

In many instances, fibroadenoma may be observed and managed conservatively. Criteria for excision include a size greater than 2 to 3 cm, symptomatic tumors, or when the diagnosis is in question such as with imaging findings of vascularity or irregular borders on ultrasound. Additionally, an increase in size documented by ultrasound measurements or clinical examination raises the potential for an alternative diagnosis and warrants removal of the lesion.13 When performed, excision is focused on removing the tumor without additional surrounding breast tissue. Because these lesions are not infiltrative, they usually do not cause deformities of the breast after removal.

Recently an alternative to excision has been developed. Lesions that have undergone the triple test of clinical examination, ultrasound imaging, and tissue sampling with benign findings are candidates for cryoablation. Cryoablation is performed percutaneously and destroys the lesion by freezing. Excellent long-term cosmetic results are possible with the use of cryoablation, but its use requires specialized training and equipment to perform.14 Patients nearing menopause with fibroadenoma should be educated as to the likely involution of these lesions with aging and a changing hormonal environment, which would argue against consideration of either excision or ablation for most patients.

**Papillomas and Nipple Discharge**

Papillomas occur in major ducts and consist of epithelial proliferation on a fibrovascular stalk. They are typically located within a few centimeters of the nipple and grow within the duct, occasionally resulting in obstruction. Clinically, they may be asymptomatic or manifest as serous or serosanguinous nipple discharge. The classic presentation is one of spontaneous nipple discharge noted by patients on their undergarments. Discharge may also be identified during a clinical breast examination or during mammography. Papillomas may also present as an asymmetric density on mammography or found incidentally during ultrasonography for other reasons. A papilloma can be visualized on galactography as a focal filling defect and may completely obstruct further filling beyond the level of obstruction. On ultrasound, a papilloma typically appears as an ovoid solid mass associated with ductal dilation. These imaging abnormalities will often trigger a need for tissue sampling.

When papillomas are diagnosed via a core needle biopsy, whether or not to excise the entire lesion remains controversial. Some investigators have reported large series with a low risk of malignancy (3%) associated with benign papillomas, and those institutions advocate observation for these lesions, reserving excision for lesions with atypia.15,16 Other series have noted a much higher false-negative biopsy rate of benign papillomas, with upstaging up to 19% of the time and rates of malignancy in the range of 14%.17,18 At the Medical College of Wisconsin, the authors have observed a malignancy rate of up to 7.4%, with some variability among racial groups. (Amanda L. Kong, MD, Milwaukee, Wisconsin, personal communication, September 2012) Thus, the authors, like most institutions, recommend excising papillomas diagnosed on core needle biopsy. Higher-risk lesions include a papilloma greater than 1 cm and those located more than 3 cm from the nipple in patients older than 50 years.12 All investigators agree that lesions demonstrating atypia should be excised for a definitive diagnosis.15,17,18

Papillomatosis, or multiple papillomas, may occur in the distal ducts of the terminal duct-lobular unit. This entity is more often associated with hyperplasia, atypia, ductal
carcinoma in situ, invasive cancer, sclerosing adenosis, and radial scars. Patients with papillomatosis are at an increased lifetime risk of breast cancer, although the reason for this is unclear. Most patients with papillomatosis are asymptomatic, although some may present with spontaneous nipple discharge. Nipple discharge is the third most common presenting symptom to a breast clinic, after palpable masses and pain. It can be a source of considerable anxiety but is rarely the presenting symptom of a breast cancer. Discharge that is more suspicious is unilateral, from a single duct, spontaneous, persistent, and clear, serous, serosanguinous, or bloodstained in character. Approximately 55% of patients presenting with nipple discharge have an associated mass, 19% of which are malignant. Milky discharge (galactorrhea) can be caused by benign breast conditions or by some medications, including oral contraceptives, serotonin reuptake inhibitors, tricyclic antidepressants, methyldopa, and morphine. Galactorrhea can also result from increased production of prolactin from a tumor in the pituitary gland or hypothyroidism. Patients who present with bilateral breast discharge warrant an endocrine evaluation. Modalities to investigate nipple discharge include discharge cytology, fluorescent in situ hybridization (FISH) analysis of discharge, ductography, and ductoscopy. Cytology has a low sensitivity for detection of breast cancer and is unlikely to alter the management of patients with nipple discharge. There is a small pilot study using FISH that demonstrates 100% specificity in making a definitive diagnosis of malignancy in patients with indeterminate cytology, and may serve as a good adjunct to cytology, but is not routinely used in clinical practice at this time. Ductography has a high-positive predictive value for the diagnosis of intraductal lesions, papillomas, and carcinoma; but it has a low sensitivity and is painful for patients. Ductoscopy is a promising tool that can be used to localize the lesion to one duct, sparing the others in young women, allowing them to retain the ability to lactate. Duct excision is the only modality that provides a definitive histologic diagnosis and remains the gold standard. When excision is required, a selective excision of the draining duct versus complete excision of the retroareolar major ducts should be discussed. Complete major duct excision has the advantage or reducing the risk of recurrence of discharge while eliminating the potential for future breastfeeding. Patients’ likelihood of future child bearing should be the deciding factor because when performed through a small areolar edge incision, complete excision has no impact on breast sensation or appearance.

**Sclerosing Adenosis**

Adenosis is a fibrocystic change in the breast resulting from an increase in the number of acini in the lobules. Sclerosing adenosis is a proliferative disease whereby the number of acini more than double and the acini lose their normal appearance. The cause is unknown, but the theory is that it is caused by an abnormality in the involution process. It may present as a mass or architectural distortion. On mammogram, calcifications may be present. Biopsy is necessary to diagnose this benign condition.

**Radial Scar/Complex Sclerosing Lesions**

Radial scars and complex sclerosing lesions are benign clinical entities that are rare findings most often identified during screening mammography as an asymmetric density or a distortion with spiculation emanating from a central lucency. Both lesions have a characteristic microscopic appearance of slender, radially arranged bands around a fibroelastic core with entrapped ducts and lobules. Complex sclerosing lesion is the term used for lesions greater than 1 cm in diameter and radial scar is used for lesions less than 1 cm in diameter.
Radial scars and complex sclerosing lesions are associated with malignancy or another high-risk lesion up to 28% of the time. Thus, most institutions have recommended complete excision of these lesions for diagnosis. However, some institutions have taken a more conservative approach and only excise lesions that demonstrate atypia. Long-term follow-up of patients with a history of a radial scar that has been excised has not demonstrated any greater risk of developing cancer, regardless of the size of the lesion, unless other high-risk lesions were identified.

**BREAST PAIN/MASTALGIA**

Mastalgia or breast pain is a common symptom among patients seeking treatment in a breast clinic. About 90% of conditions that cause breast pain are benign. The key to management of breast pain lies in a determination of the cause and whether or not it is cyclic or noncyclic in nature. Cyclic breast pain usually starts within 2 weeks before menses and resolves or diminishes with the onset of menses. It recurs at roughly the same time each month during a woman’s cycle. Although commonly thought to be related to a variety of factors, caffeine intake, iodine deficiency, and dietary fat intake have not been definitively established as causal factors in cyclic breast pain. In most instances, cyclic breast pain can be managed by watchful waiting without treatment once it is established that there is no associated malignant process present. Other modifying factors to try include improving support for pendulous breasts, ensuring proper fit of a brassiere, and a trial of nonsteroidal antiinflammatory agents.

Noncyclic breast pain usually occurs in postmenopausal women and can be caused by certain medications, such as antidepressants, digoxin, thiazide-class diuretics, and methyldopa. However, it is frequently associated with underlying musculoskeletal issues with the chest wall, such as arthritis and costochondritis. Breast pain resulting from musculoskeletal conditions is best appreciated on physical examination and patients’ pain reproduced with palpation of the pectoralis major muscle separated from the breast with patients in the sitting position or palpation of the intercostal muscles through the axilla. The pain is often burning or sharp in nature and may localize to a specific area.

Several agents have been tried for the treatment of cyclical and noncyclical breast pain, including hormonal manipulation, nonsteroidal antiinflammatory agents, and plant derivatives like evening primrose oil (EPO). Srivastava and colleagues published a meta-analysis of the randomized trials using different treatments for mastalgia and assessing their effectiveness on breast pain. The most common treatments included bromocriptine mesylate (Cycloset, Parlodel), danazol (Danocrine), tamoxifen citrate (Nolvadex, Soltamox) and EPO. They found women received significant pain relief using bromocriptine mesylate, danazol, and tamoxifen citrate; but there was no significant difference in pain scores in women treated with EPO. There is a lack of strong data comparing the 3 drugs. However, tamoxifen citrate was associated with the fewest side effects and should be the first drug of choice. The natural history of mastalgia seems to be that in some women that achieve good control of pain, they will remain in remission for a long time regardless of whether they receive any medication or not.

**SUMMARY**

Benign breast disorders are a group of conditions that are commonly managed by surgeons. Benign breast pathologic conditions rarely increases the risk of malignancy. As knowledge of benign breast pathologic conditions improves, many conditions can be managed without the need for open surgery. Collaborative care models including nurse practitioners can improve patient experience and education about their breast health.
REFERENCES


