Skin diseases of the breast and nipple

Benign and malignant tumors

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The evaluation and management of dermatologic diseases of the breast and nipple requires an understanding of the unique anatomy of the breast and nipple and an awareness of the significant emotional, cultural, and sexual considerations that may come into play when treating this anatomic area. The first article in this continuing medical education series reviews breast anatomy, congenital breast anomalies, and benign and malignant breast tumors. An emphasis is placed on inflammatory breast cancer and breast cancer with noninflammatory skin involvement and on cutaneous metastases to the breast and from breast cancer. Familiarity of the dermatologist with the cutaneous manifestations of breast cancer will facilitate the diagnosis of breast malignancy and assist with staging, prognostication, and evaluation for recurrence. This article also discusses genodermatoses that predispose to breast pathology and provides imaging recommendations for evaluating a palpable breast mass. (J Am Acad Dermatol 2019;80:1467-81.)

Key words: breast; breast cancer; continuing medical education; genodermatoses; nipple; Paget disease.

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The breast and nipple comprise a unique functional unit of the skin with significant emotional and sexual overtones. The evaluation and management of dermatologic diseases in this area requires appropriate sensitivity. Certain dermatologic conditions are unique to the breast and nipple, while other conditions may simply require a specialized approach to diagnosis or treatment.

The first article in this continuing medical education series discusses breast masses. Dermatologists may be the first physician to identify these masses because they frequently examine the skin of the breast and nipple, and dermatologists should initiate an appropriate workup in a timely manner. Relevant genodermatoses that may predispose patients to breast cancer will also be reviewed.

The second article in this series discusses the diagnosis and management of inflammatory and infectious skin processes affecting the breast and nipples.

BREAST ANATOMY

The breast is a modified sweat gland with unique anatomic features. The anatomy of the breast and nipple can be divided into 3 segments: 1) anatomic layers of breast tissue, 2) glandular breast tissue, and 3) the nipple—areolar complex (NAC).[1,2]

The 6 anatomic layers of the breast are 1) the skin; 2) the premammary layer; 3) the mammary layer; 4) the retromammary layer; 5) the muscle layer; and 6) the chest wall (Table I).[3] The premammary layer, composed of subcutaneous fat and connective tissue,[3] is where the Cooper ligaments anchor the glandular breast tissue anteriorly. It forms the anatomic plane through which the surgeon dissects in skin-sparing mastectomy and is the most frequent location of breast cancer recurrence after this procedure.[1,4] Deep to the premammary layer is the mammary layer, which houses glandular breast tissue.[5] The retromammary layer is composed of

Table I. The 6 anatomic layers of the breast

Skin
Premammary layer
Mammary layer
Retromammary layer
Muscle layer
Chest wall

Fig 1. Breast anatomy diagram. (Courtesy Creative Commons, available at https://commons.wikimedia.org/wiki/File:Breast_Anatomy_Sagittal_Cut_Unlabeled.jpg#file [Patrick Lynch, illustrator; adapted by Andrew Meyerson].)

loose connective tissue and adipose tissue allowing for movement of breast tissue over the chest wall.[1] This layer is becoming increasingly popular for breast implant placement. Deep to the retromammary layer are the muscle layer and the chest wall. Most of the breast overlies the pectoralis muscle, with parts of the serratus anterior and rectus abdominis sheath also running deep to breast tissue (Fig 1).[1-3]

The mammary layer is responsible for milk production during lactation. Maturation of this glandular tissue begins in females during puberty and is completed during the pregnancy lactation cycle.[5] Milk is produced by acinar cells within the terminal ductal lobular unit and subsequently flows through a series of ducts that drain to the nipple (Fig 2).[5]

The NAC overlies the T4 dermatome and is of significant functional, cosmetic, and sexual importance.[6,7] The NAC forms from mesenchyme and comprises smooth muscle.[6] The melanin content of the areola is 2.1 times higher than surrounding breast skin, making the areola darker in color (Fig 3).[8] The areola further darkens during pregnancy. The areola houses protrusions known as Montgomery tubercles, which are apocrine glands that produce lubricating secretions that help protect the NAC during lactation (Fig 3).[9] Innervation of the NAC predominately arises from the anterior and lateral branches of the fourth intercostal nerve.[7] The anterior and lateral branches of the third and fifth intercostal nerves also contribute.[7]
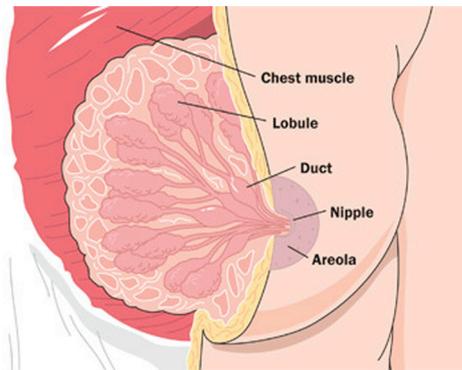
Fig 2. Diagram of breast ducts. (Courtesy Creative Commons, available at https://commons.wikimedia.org/wiki/File:Breast-Diagram.gif [National Cancer Institute, National Institutes of Health].)

Fig 3. Nipple−areola complex with Montgomery tubercles. (Photograph courtesy of Justin Finch, MD.)

BREAST EMBRYOLOGY

During weeks 5 to 6 of embryologic development, the mammary ridge, also known as the mammary lines, begin to arise as ectodermal bands running from the axillae to the groin.[1,5] Mammary buds subsequently develop through the invagination of portions of these ectodermal bands into the underlying mesenchyme.[1,5] These mammary buds regress everywhere except the pectoral area where the primary mammary bud persists.[1,5] The primary mammary bud is responsible for the development of each breast and gives rise to secondary buds that eventually produce the ductal system.[1,5]

Congenital and developmental breast and nipple abnormalities

Congenital and developmental breast and nipple abnormalities occur relatively frequently and can confer significant emotional morbidity to patients.

Polythelia. Polythelia is the presence of a supernumerary nipple (Fig 4).[10-12] Often seen as an

Fig 4. A and **B**, Supernumerary nipple. (Photograph courtesy of Justin Finch, MD.)

inherited trait, it occurs in ≤5.6% of the population with no gender predilection.[11-13] Supernumerary nipples can occur anywhere along the embryologic milk line (Fig 5).[10-13]

Polymastia. Polymastia is the presence of supernumerary breast tissue. Similar to polythelia, supernumerary breast tissue can occur anywhere along the embryologic milk line; however, it occurs most frequently in the axilla.[14,15] Accessory breast tissue is hormonally responsive and will grow during puberty and pregnancy.[14,16] This tissue can be functional, can develop benign breast disease, and can undergo malignant transformation.[14-18] Surgical
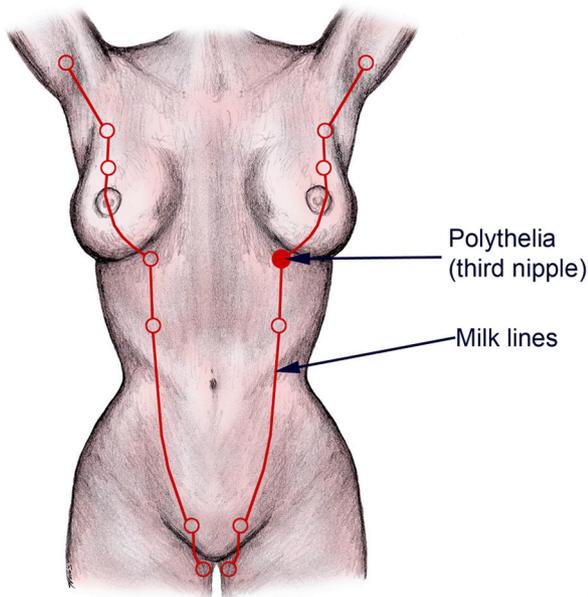
Fig 5. Diagram of milk lines. (Courtesy Creative Commons, available at https://commons.wikimedia.org/wiki/File:Milk_lines.jpg [The Geneva Foundation for Medical Education and Research].)

Fig 6. Nipple inversion. (Photograph courtesy of Janelle Ricketts, MD.)

excision after the completion of breast development is often necessary because it can be painful and carries significant cosmetic morbidity.[14,19,20]

Athelia. Athelia is the absence of the NAC. It typically occurs in conjunction with amastia but may also occur in isolation.[21] All types of athelia are rare and usually arise in the setting of other congenital anomalies.[21] Certain forms of ectodermal dysplasia and scalp-ear-nipple syndrome cause athelia.[21-23] There are also documented familial cases.[21,24]

Amastia. Amastia is the absence of breast glandular tissue. It most commonly occurs unilaterally as part of a syndrome.[10,14,25] The most common cause of amastia, especially in males, is Poland syndrome, an inherited syndrome characterized by ichthyosis, amastia, absence of the pectoralis muscles, other chest wall defects, and ipsilateral upper extremity defects.[10,26] Amastia is also associated with Meyer-Rokitansky-Kuster-Hauser syndrome and certain types of ectodermal dysplasia.[27,28]

Nipple inversion/retraction. Nipple inversion occurs as a normal finding in approximately 3% of women (Fig 6).[29,30] It is often congenital, although it can be acquired in cases of trauma, scarring mastitis, breast cancer, and breast surgeries.[29-32] In addition, some cases of congenital nipple inversion occur with other congenital abnormalities.[33,34] In most congenital cases, the nipple will protract during stimulation, allowing for normal breastfeeding.[29,30] Nipple piercing and other procedures may be

attempted to protract the nipple, although the results are mixed and complications are common depending on procedure type.[31]

Breast asymmetry/tuberous breast. Mild breast asymmetry is normal; a difference in interbreast size of >30% is difficult to conceal with clothing and can be distressing to a patient.[14,35] Although usually idiopathic, breast asymmetry can also occur as a result of trauma.[36] One common cause of trauma-induced breast asymmetry is obtaining a core needle biopsy specimen of prepubescent breast tissue, and therefore obtaining these biopsy specimens should always be avoided in children unless absolutely necessary.[37] Breast asymmetry can also occur because of breast hypoplasia, which is often associated with other developmental abnormalities.[38] For example, Becker nevus syndrome often presents with unilateral breast hypoplasia, polythelia, and pectoralis major aplasia.[38] Tuberous breast deformity is a specific subtype of breast asymmetry where a constricting ring prevents normal breast growth horizontally and vertically. Early consultation with a plastic surgeon is recommended for patients with breast asymmetry and tuberous breast because of the potential for significant emotional morbidity.[35]

Pigmentary demarcation lines. Pigmentary demarcation, also known as Futcher or Voigt lines, are lines of abrupt transition between areas of darker and lighter pigmentation. They are a normal physiologic occurrence in Fitzpatrick skin phototypes IV to VI, most commonly seen on the arms or posterior legs and occasionally on the chest (Fig 7).

BENIGN BREAST MASSES

Benign breast disease is a term describing a broad range of nonmalignant breast conditions affecting

Fig 7. Pigmentary demarcation line. (Photograph courtesy of Justin Finch, MD.)

>1 million American women annually.[39] These diseases may present with palpable breast changes or create an observable breast deformity. Table II reviews common benign breast masses and describes clinical features that are relevant to the dermatologist.

MALIGNANT TUMORS

Proliferative breast lesions that predispose to breast adenocarcinoma frequently are identified incidentally on imaging and less frequently identified on examination as a lump in the breast. While these lesions rarely present to the dermatologist, a brief review of the significance of these lesions is important because they may be identified while a biopsy specimen is obtained or during imaging performed for other reasons (Table III).[40-80]

Invasive breast cancer (adenocarcinoma)

Invasive breast cancer is a type of adenocarcinoma arising from the terminal ductal lobular unit.[81,82] It occurs primarily in females with a lifetime risk of roughly 1 in 8, with increasing incidence with

increasing age.[83] Risk factors for invasive breast cancer are listed in Table IV and include the proliferative breast lesions previously reviewed.[83,84] *BRCA1* and *BRCA2* mutations are the most common heritable cause of invasive breast cancer and they are of additional importance to the dermatologist because they predispose affected individuals to melanoma.[85]

Invasive breast cancer can arise anywhere within the breast, although approximately half of all cases occur in the upper outer quadrant.[86] There are many types of invasive breast cancer, with ductal and lobular types being the most and second most common, respectively.[82,87] Table V lists common types of invasive breast cancer.[82,87] Different types of breast cancer are classified based on histologic findings that better predict tumor behavior and treatment response.[82]

Breast cancer is identified either clinically or based on worrisome findings on mammography. Clinical signs of breast cancer include a palpable breast mass and skin involvement.

Skin involvement in breast cancer

Six percent to 10% of patients with breast cancer present with skin involvement.[88-90] This involvement is divided into 2 major subtypes for the purposes of breast cancer staging: inflammatory breast cancer (IBC) and breast cancer with noninflammatory skin involvement (SI).[88-90] IBC is a distinct subtype of breast cancer; breast cancer with noninflammatory SI can occur secondary to all types of breast cancer.[88-90] These 2 subtypes present with roughly equal frequency. SI in these cases may be the initial clue to a diagnosis of breast cancer; however, these subtypes have radically different prognostic and management implications. Paget disease of the breast is distinct from IBC and breast cancer with noninflammatory SI and will be discussed below.

IBC. IBC is distinct subtype of breast adenocarcinoma that is characterized by the abrupt development of painful, erythematous, and indurated breast skin (ie, peau d'orange) and that is associated with a grave prognosis.[90] These findings occur because of tumor invasion of dermal and inframammary lymphatics that can be identified histologically on a punch biopsy specimen obtained from involved skin.[90] IBC is nearly impossible to clinically distinguish from a benign inflammatory process. Therefore, dermatologists should maintain a low threshold to obtain a biopsy specimen from any suspected breast dermatitis. Topical steroids are unlikely to improve the skin changes associated with IBC because the skin changes are mediated by lymphatic flow disruption rather than from true inflammatory changes. Cases in which skin changes

Table II. Clinical features of benign breast masses

Disease name	Clinical features	Recommended workup	Recommended treatment
Fibrocystic breast changes	Prevalence >50% of women; classically presents as "lumpy breasts" with bilateral area of textural irregularity in the absence of distinct mass formation; hormonally mediated changes that evolve throughout the menstrual cycle	Observe for evolution through the menstrual cycle; if resolution does not occur after monitoring through menstrual cycle, age-appropriate breast mass imaging is required	Reassurance that no underlying mass is present and that this is normal variation of breast tissue
Simple breast cyst	Painless, palpable, freely mobile mass; develops from fluid accumulation in the TDLU	Diagnosed by ultrasound demonstrating nonloculated cyst	Fine needle aspiration for palpable or painful cysts; further workup for malignancy is required if: 1) aspirate is bloody or 2) cyst reaccumulates after aspiration
Fibroadenoma	Typically present as 3- to 5-cm, rubbery, mobile breast masses; most common breast mass in women <40 years of age; 10% present with multiple fibroadenomas; proliferate from TDLU epithelium and stroma	Diagnosis can be suggested by age-appropriate imaging for solid breast masses, and if mass remains clinically stable then no histologic evaluation is necessary; however, if there is a clinical change then histologic evaluation is required; biopsy specimens should be obtained from suspected fibroadenomas >6 cm in size to definitively differentiate from phyllodes tumor	Reassurance of benign nature; excision if symptomatic
Phyllodes tumor	Presents similarly to fibroadenomas; characterized by rapid growth and can grow to sizes >30 cm; tend to recur and have metastatic potential	Indistinguishable from fibroadenomas on clinical examination, ultrasound, mammography, and magnetic resonance imaging; high suspicion for phyllodes tumor should occur when previously diagnosed "fibroadenoma" is growing rapidly; histologic examination is required in these cases; biopsy specimens must be obtained from all lesions >6 cm in size	Surgical excision with wide margins
Hamartoma	Present similarly to fibroadenomas and phyllodes tumors; average age at diagnosis is 45 years; occur in the breast parenchyma and can be fibrous, fibrocystic, or adipose in nature	Diagnosed on ultrasound or mammography; obtaining a biopsy specimen is not necessary unless diagnosis on imaging is not clear	Reassurance of benign nature; excision if bothersome

Continued

Table II. Cont'd

Disease name	Clinical features	Recommended workup	Recommended treatment
Fibromatosis	Typically present as palpable masses that impinge upon Cooper ligaments, causing skin dimpling and retraction; examination is often indistinguishable from and concerning for malignancy; locally aggressive and commonly recur	Ultrasound demonstrates solid, spiculated masses that are often not visible on mammography; biopsy specimens may be obtained to distinguish from malignancy	Excision with wide margins
Lactating adenoma	Painless, freely mobile breast mass in a pregnant or lactating woman; represent nearly 75% of all breast masses in pregnant women; result of hormonally mediated breast gland hypertrophy during pregnancy	Diagnosed by ultrasound examination; some authorities recommend core needle biopsy because 3% of all breast malignancy presents during pregnancy	Watchful waiting as the mass is likely to resolve with termination of lactation; if the lactating adenoma persists or continues to grow after the cessation of lactation, surgical excision is required

TDLU, Terminal ductal lobular unit.

are preceded by a longstanding, neglected breast tumor are not classified as IBC because they behave differently than true IBC.[90,91]

Breast cancer with noninflammatory SI. Approximately 4.7% of patients with breast cancer without IBC present with skin involvement that is termed breast cancer with noninflammatory SI.[89] Noninflammatory SI is subdivided into 3 distinct entities: 1) "classical" SI, 2) "subtle" SI, and 3) "histologic" SI.[88,89] Nearly 70% of patients with noninflammatory SI have classical SI.[89] Classical noninflammatory SI is characterized by the presence of readily evident localized inflammation, ulceration, edema, peau d'orange, or satellite skin nodules that occur directly from the breast adenocarcinoma.[88,89] These changes are of prognostic importance because the presence of classical SI automatically upstages the cancer to locally advanced breast cancer (stage T4b) regardless of tumor size because this type of involvement is predictive of disease with extensive lymph node involvement and distant metastases.[92] Extensive SI also has an impact on whether a patient is a surgical candidate or not.[88,89,93] In contradistinction, patients with subtle SI—characterized by skin dimpling, nipple retraction, or other skin changes not explicitly outlined above—are not considered to have locally advanced breast cancer on the basis of this skin involvement alone because these types of changes reflect impingement on Cooper ligaments rather than true invasion of the skin, which can occur with any breast cancer stage.[92] This type of skin involvement does not have prognostic implications.[89] Finally, some patients are found to have SI on histologic examination in the absence of clinical findings.[88,89] This type of involvement is termed histologic SI, and many recent studies show that it does not have the same prognostic implications as classical SI despite appearing similarly under the microscope.[88,89,94] Nonetheless, some authorities treat this like classical SI.[95]

Paget disease of the breast. Paget disease of the breast comprises approximately 1% of all breast cancers, and patients with Paget disease presents with eczematous changes to the nipple, areola, and surrounding skin (Fig 8).[96,97] Affected skin is typically thickened and may display pigmentary changes and an overlying crust. Pain, itching, or burning of the affected area may either precede or coincide with skin changes and is often confused with a more benign process. A topical steroid challenge is not sufficient to rule out Paget disease because some patients will have symptomatic improvement with topical steroid use.[98] Therefore, biopsy specimens should be obtained from all suspicious cases. The histologic hallmark of Paget disease of the breast is the presence of Paget cells on a biopsy specimen of the affected skin.[99] Approximately 85% of cases of Paget disease are associated with an underlying invasive ductal carcinoma or ductal carcinoma in situ.[97] Underlying cancers do not have to abut the affected skin and can be multifocal.

Table III. Clinical features of proliferative breast lesions that predispose to breast adenocarcinoma[40-80]

Lesion type	Features	Workup and management
Intraductal proliferating lesions		
UDH	Clinically silent benign, polyclonal hyperplasia of duct cells that are normal appearing; increases breast cancer risk by 1.5 to 2 times	No further workup or management
ADH	Clinically silent benign, polyclonal hyperplasia of duct cells that are abnormal appearing but that do not meet the criteria for DCIS; increases breast cancer risk ~4.4 times	If identified on core needle biopsy, excisional biopsy specimen must be obtained to rule out concomitant malignancy in surrounding tissue; if identified on excisional biopsy procedure, no further workup is necessary
DCIS	Usually clinically silent, precancerous proliferation of atypical ductal cells with intact basement membrane; may less frequently present with overlying Paget disease, as a palpable mass, or with nipple discharge; nonobligate precursor of invasive breast cancer (stage 0 adenocarcinoma)	Breast conserving lumpectomy with or without radiotherapy and with or without obtaining a sentinel lymph node biopsy specimen for small lesions; simple mastectomy may need to be performed for larger lesions; hormonally responsive lesions are treated with hormone therapy postoperatively
Lobular neoplasia		
Atypical lobular hyperplasia	Abnormal proliferation of cells within a breast lobule that do not quantitatively or qualitatively meet the diagnostic criteria for LCIS histologically; almost always clinically silent; radiographically silent in >50% of cases; increases risk of breast cancer in ipsilateral and contralateral breast ~5 times	Excisional biopsy specimen must be obtained to rule out concomitant malignancy in surrounding tissue if identified on core needle biopsy; if identified on excisional biopsy specimen, no further workup is necessary; hormonally responsive lesions are treated with hormone therapy postoperatively
LCIS	Usually clinically silent, proliferation of atypical lobular cells; increases risk of breast cancer in ipsilateral and contralateral breast ~11 times	Treated with antiestrogen hormone therapy for chemoprevention for development of breast cancer; bilateral simple mastectomy no longer performed given the efficacy of hormonal therapy at preventing the development of invasive breast cancer
Intraductal papillary neoplasms		
Intraductal papilloma	Solitary, benign lesions of often the larger, central breast ducts that present either as a palpable breast mass, with pathologic discharge, or as an abnormality identified on imaging; not generally associated with increased breast cancer risk unless: 1) histologic examination reveals ADH-like changes, in which case it is termed an atypical papilloma and is associated with increased cancer risk or 2) histologic examination reveals DCIS-like changes, in which case it is termed intraductal papillary carcinoma (stage 0 adenocarcinoma)	Surgical excision may or may not be required to rule out the presence of a higher order lesion
Papillomatosis	Multiple, peripherally located papillomas that typically present with pathologic discharge, only rarely presenting as a breast mass	Surgical excision may or may not be required

ADH, Atypical ductal hyperplasia; *DCIS,* ductal carcinoma in situ; *LCIS,* lobular carcinoma in situ; *UDH,* usual ductal hyperplasia.

Table IV. Major risk factors for breast cancer

Age >50 years
Early menstruation
Late or no pregnancy
Late menopause
Overweight
Known genetic predisposition
Family history of breast cancer
Personal history of cancer
Intraductal proliferating lesions (eg, UDH and ADH)
Lobular neoplasia (eg, ALH and LCIS)
Intraductal papillary neoplasms

ADH, Atypical ductal hyperplasia; *ALH*, atypical lobular hyperplasia; *LCIS*, lobular carcinoma in situ; *UDH*, usual ductal hyperplasia.

Table V. Histologic types of invasive breast cancer

Invasive ductal carcinoma
Invasive lobular carcinoma
Tubular carcinoma
Medullary carcinoma
Mucinous carcinoma
Paget disease of the breast

Table VI. Types of nonadenocarcinoma primary cancer of the breast

Hodgkin and non-Hodgkin lymphoma
Sarcoma
Schwannoma
Cutaneous basal cell carcinoma
Cutaneous squamous cell carcinoma
Cutaneous melanoma
Mycosis fungoides

Fig 9. Mycosis fungoides of the bilateral breasts. (Photograph courtesy of Justin Finch, MD.)

Fig 10. Breast adenocarcinoma metastatic to the breast skin. (Photograph courtesy of Justin Finch, MD.)

Fig 8. Paget disease of the breast resulting in total nipple destruction. (Photograph courtesy of Justin Finch, MD.)

Other primary cancers in the breast (nonadenocarcinoma)

While most primary cancers of the breast are adenocarcinomas, other primary cancers occasionally arise (Table VI).[100-102]

Mycosis fungoides. Mycosis fungoides (MF) commonly affects the breasts and nipples. In fact, the breasts are the most common site of unilesional MF.[103] This is likely related to the lack of sun exposure this area receives.[104] Another theory is that silicone implants predispose to the development of breast MF; however, this is only supported by a singular case series and is unlikely given the lack of direct exposure between the epidermis and the implant.[105]

Breast MF tends to appear clinically similar to MF occurring elsewhere, and may be hypopigmented.[106] Nipple, areolar, and breast ulceration

Table VII. Genodermatoses associated with breast pathology

Genetic condition	Associated breast pathology
Ataxia telangiectasia (heterozygote carriers)	Breast cancer is the second most common solid malignancy in affected individuals (homozygotes) with the lifetime risk of developing breast cancer increased by ~37 times[143,144]; unaffected carriers (heterozygotes) have 5.1 times the risk of developing breast cancer compared with noncarriers[145]
Cowden syndrome	Affected females have a lifetime breast cancer risk approaching 50%[144]; the average age at breast cancer diagnosis is 10 years earlier[146]; affected males are also predisposed to developing breast cancer[147]; fibrocystic breast changes are a minor criterion for diagnosis[148]; the most common breast pathology is fibroadenoma[149]; reported association with gynecomastia in males[150]
Bloom syndrome	Breast cancer occurs in ~12% of cases[151]; the average age at diagnosis of breast cancer is 35.8 years[151]; no increased risk of breast cancer development in heterozygotes[152]
Peutz—Jeghers syndrome	Lifetime breast cancer risk >50% in affected females[153]
Basal cell nevus syndrome	An increased risk of breast cancer in females has been reported[154]
Down syndrome	Breast cancer occurs less frequently in females with Down syndrome, with a decreased risk of ≤25 times[155]
Klinefelter syndrome	Klinefelter syndrome increases the risk of breast cancer ~15 times[156]; almost all patients with Klinefelter syndrome have gynecomastia[157]
Scalp-ear-nipples syndrome	Characterized by a broad range of breast abnormalities, including amastia, athelia, and hypothelia[158]
McCune—Albright syndrome	The risk of breast cancer is increased in affected individuals[159]; precocious puberty characterized by early breast development in affected girls is part of the diagnostic triad for this condition[159]
Poland syndrome	Poland syndrome is characterized by amastia or breast hypoplasia with associated pectoralis muscle absence[29]
Fanconi anemia	Three of the 14 mutations implicated in Fanconi anemia increase the risk of breast cancer in nonaffected carriers[135]
Muir—Torre syndrome	Breast cancer occurs at an increased rate in Muir—Torre syndrome and is the third most common cancer affecting these individuals[136]

have also been reported as the presenting sign of breast and nipple MF. Importantly, nevoid hyperkeratosis of the nipple and areola may mimic MF histologically, so some patients with nevoid hyperkeratosis of the nipple and areola are initially thought to have early MF; however, these conditions can be distinguished by T-cell immunohistochemistry.[107] Treatment of MF affecting the breast and nipple is similar to treatment of MF occurring elsewhere except that irritating topical medications, such as topical retinoids and topical nitrogen mustard, should be used sparingly on the NAC as this area is sensitive to irritation. In addition, patients with unilesional MF of the breast may benefit from consultation with plastic surgery for lesional excision and postoperative reconstruction in cases where excision is otherwise indicated.[108]

Metastatic cancer to the breast. Metastases to the breast from extramammary primaries are exceptionally rare, comprising <2% of all breast malignancy (Fig 9).[109-111] The most common sources of metastases to the breast in women are contralateral breast adenocarcinoma (Fig 10), melanoma, leukemias/lymphomas, carcinomas (ovarian, gastric, etc), and sarcomas (primarily uterine in women).[109-111] In men, prostate cancer is the most common source of metastases to the breast.[112] Metastatic disease typically involves the subcutaneous fat rather than glandular breast tissue and presents as a rapidly growing, palpable subcutaneous mass.[113] Several unique cutaneous presentations also have been reported.

Carcinoma erysipeloides. Carcinoma erysipeloides mimics IBC clinically and pathologically, results from superficial lymphatic tumor invasion, and has been reported secondary to metastases from a variety of primary cancers, including ovarian, gastric, and lung adenocarcinomas.[114-117]

Carcinoma en cuirasse. Carcinoma en cuirasse is related to metastatic disease in the superficial lymphatic vessels and is characterized by dramatic skin thickening with woody induration and breast contraction with volume loss.[117] Less dramatic keloid-like presentations have been described.[118] Although this most frequently
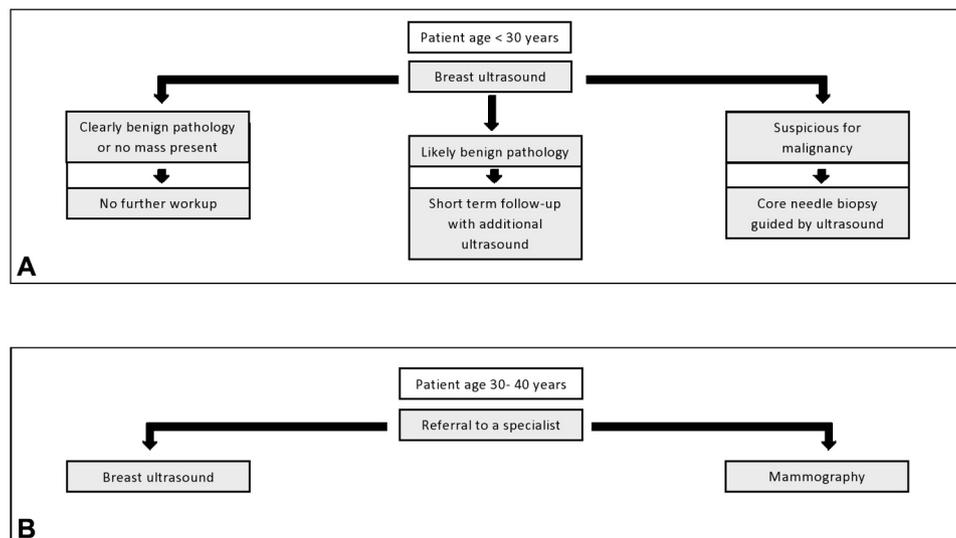
Fig 11. Age-based imaging algorithm for breast mass evaluation.

occurs from breast cancer metastases after mastectomy, it has also been reported in patients with metastases from gastric, lung, and kidney primary cancers.[118,119]

Carcinoma telangiectoides. Carcinoma telangiectoides occurs because of a combination of tumor invasion of both superficial lymphatic vessels and superficial capillaries resulting in violaceous papules and purpura.[120] It is most commonly secondary to breast metastases; however, uterine and parotid tumors have also been reported.[121-123]

Zosteriform. Zosteriform has a dermatomal distribution, mimics herpes zoster, is exceedingly rare, occurs from a breast primary cancer, and has an unknown pathogenesis.[124]

Breast cancer cutaneous metastases

Breast cancer is the most common cause of cutaneous metastases in women, with ≤24% of patients with breast cancer developing them.[125] When breast cancer metastasizes to the skin, it most commonly metastasizes to the trunk and abdomen; however, metastases may occur anywhere.[126] While breast cancer cutaneous metastases can present in a number of ways—including all of those described in the section "Metastatic cancer to the breast" section—the most common clinical presentation is that of a dermal or subcutaneous nodule.[127] When multiple nodules are present, they are usually all located in the same anatomic region. As they progress, these nodules may ulcerate or become infected-appearing. Other reported clinical manifestations of breast cancer cutaneous metastases include alopecia neoplastica, erythema annulare centrifugum—like

metastases, pyogenic granuloma—like metastases, vasculitis-like metastases, Sister Mary Joseph nodule, and targetoid cutaneous metastases.[128-133]

Another important feature of breast cancer cutaneous metastases is that they commonly affect mastectomy scars.[134] Breast cancer cutaneous metastases affecting mastectomy scars often have delayed diagnosis because they are confused for a surgical site infection or other benign process. The high rate of in-scar metastases may reflect tumor seeding during surgery because there are reports of cutaneous metastases seeding from a core needle biopsy procedure.[134]

In patients in whom breast cancer cutaneous metastases are suspected, obtaining a biopsy specimen is necessary to confirm the diagnosis. Histologic assessment of the specimen will reveal a proliferation of cells that are similar appearing to the primary tumor although the configuration of these cells varies depending on what cutaneous manifestation is present.[126] In cases where the histologic diagnosis is unclear, staining for cathepsin D and other antigens that commonly are present in breast cancer metastases can be useful for confirming the diagnosis.[135]

Any patient with a personal history of breast cancer requires thorough skin examinations even when the cancer is thought to be in remission because cutaneous metastases can present over a decade after initial breast cancer surgery and chemotherapy.[136] Furthermore, evaluation for cutaneous metastases is important even in cases of known metastatic disease where the presence of cutaneous metastases will not upstage the cancer because cutaneous metastases may be refractory to

systemic chemotherapy yet respond to topical therapies.[137] Topical therapies for breast cancer cutaneous metastases may also be used in symptomatic patients who no longer wish to undergo systemic chemotherapy.

Genodermatoses that predispose to breast pathology

Many genodermatoses predispose patients to developing breast cancer and other breast tumors (Table VII).[138-159]

Palpable breast mass workup

Dermatologists may be the first physician to identify a palpable breast mass. Imaging guidelines are provided by the American College of Radiology (Fig 11).[158]

In conclusion, dermatologists are in a unique position to identify a wide range of diseases of the breast and may be the first clinician to identify a breast mass. We have discussed gross breast abnormalities, developmental breast abnormalities, and palpable breast masses with a special emphasis on familiarizing dermatologists with current terminology used to describe both benign and malignant breast changes and how to best differentiate and manage these abnormalities.

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