The most common metastatic tumors in the breast are from mammary primaries, but these are excluded in most series and are not discussed here. Breast metastases from extramammary malignant neoplasms are uncommon and account for approximately 2% of all breast malignancies, although their incidence at autopsy is greater than 6%. More than 500 cases of breast metastases from extramammary sites have been reported in the English-language literature, mainly as small series or case reports. Most metastases to the breast from extramammary malignancies occur in women, whereas only 5% to 8% occur in men.

The most common extramammary solid tumors that metastasize to the breast are hematopoietic neoplasms and malignant melanoma, followed by lung carcinoma, ovarian carcinomas, sarcomas, gastrointestinal carcinomas, and genitourinary carcinomas. Case reports of metastatic involvement from osteosarcoma, thyroid neoplasms, as well as cervical, vaginal, and endometrial carcinoma, have been described in the literature. However, previous studies have reported a variety of metastatic malignancies to the breast, reflecting the specific patient population studied. Gastric carcinoma followed by thyroid carcinoma are the most common metastatic tumors to breast in Korean women, whereas melanoma followed by lung carcinoma are the most common metastatic tumors to breast in the Australian population. In men, the prostate is the most common primary source of metastatic tumors in the male breast, with a 5% incidence, followed by lung carcinoma. However, one-fourth of the men with prostatic carcinoma show microscopic breast involvement at autopsy. In children, rhabdomyosarcoma is the most common malignant tumor metastasizing to the breast.

METASTATIC TUMORS IN THE BREAST

Clinical Presentation

Metastatic breast tumors are especially difficult to diagnose, especially when breast metastasis is the first manifestation of an occult extramammary malignancy. Breast metastasis is the initial presentation of extramammary occult malignant neoplasm in approximately 25% of patients. The most common sites of occult carcinomas presenting with breast metastases include lung, particularly small cell carcinoma, followed by kidney, stomach, intestinal carcinoid, ovarian carcinoma, uterine cervix, and thyroid gland. Moreover, even in patients with a history of malignancy presenting with a single breast mass, a second primary breast lesion is always considered more probable than a metastasis. The majority of cases of extramammary malignancy metastatic to the breast have a history of primary malignancy. Vaughan and coworkers and others have reported an average interval of 50 to 60 months between the initial diagnosis of primary malignancy and the development of a metastasis to the breast.

Breast metastasis shows a female predominance, mostly in the reproductive age group (30 to 45 years). The upper outer quadrant is the one most commonly involved. Some studies have reported that the right breast is more frequently involved than the left. In contrast, others have reported that the left side is more frequently affected than the right. Bilateral involvement is not uncommon. Metastases to the breast can be multiple and bilateral with axillary lymph node involvement, features often seen in primary tumors. Enlarged axillary lymph nodes are encountered in about 40% of cases. The frequency of axillary lymph nodes involvement tends to be higher in series that include malignant lymphomas. Involvement of axillary lymph nodes in metastatic breast carcinoma is a manifestation of systemic spread and signifies a poor prognosis.

Clinically, regardless of the origin, metastatic lesions in the breast present as rapidly growing painless swellings. Rarely, pain and nipple discharge are reported. Metastatic carcinomas to the breast are generally well-circumscribed and freely mobile masses, often misinterpreted as a benign breast lesion such as a fibroadenoma. Unlike primary tumors, the mass...
is superficially located without skin involvement. A preceding history of extramammary carcinoma can be helpful in suspecting a mass being metastatic in origin.

Metastatic carcinoma to the breast may produce clinical signs mimicking inflammatory breast cancer. Patients present with a swollen, erythematous breast with diffuse skin thickening. A punch biopsy demonstrating intralymphatic carcinoma cells is generally regarded as confirmatory for inflammatory breast cancer. This phenomenon has been reported with neoplasms metastatic from ovarian origin, gastric carcinomas, rarely from squamous cell carcinoma of the tonsil, and lung and pancreatic adenocarcinoma.

Clinical Imaging

The most common mammographic appearance is a rounded mass with well-defined or slightly irregular margins that lack microcalcifications and are, therefore, indistinguishable from benign lesions such as a fibroadenoma. Multiple or bilateral tumors are seen in a minority. Ultrasound typically shows a hypoechoic mass, which is sometimes heterogeneous or poorly defined. It has been suggested that lack of tumor-associated acoustic shadowing is a characteristic ultrasonographic feature of metastatic tumors in the breast. Absence of microcalcifications is considered a characteristic feature of metastatic lesions to the breast, with the exception of ovarian cancer. McCrea and colleagues even suggested that the presence of recognizable calcification in a mass on a mammogram virtually excludes metastatic disease to the breast. However, microcalcifications can occasionally be seen in metastatic malignancies such as hepatocellular carcinoma, gastric carcinomas, renal cell carcinoma (RCC), and medullary thyroid carcinoma.

Differential Diagnosis

Recognizing a breast tumor as being metastatic is crucial for appropriate treatment and prognosis. The diagnosis can be particularly challenging for pathologists when fine-needle aspiration (FNA) cytology or core needle biopsy (CNB) is performed owing to the relatively limited amount of tissue available for microscopic examination and additional ancillary studies. To date, there are no reliable or specific clinical or radiologic tests that can predict a tumor being metastatic rather than a primary lesion. However, several features may suggest the presence of metastasis to the breast, such as a well-circumscribed tumor with multiple satellite foci, unusual histologic features, tumors that microscopically surround and displace ducts and lobules with little or no hyperplasia, absence of an in situ carcinoma component, and the presence of many lymphatic emboli. Care must be taken to distinguish true in situ carcinoma from metastatic lesions with confluent necrosis that may mimic comedo necrosis. Immunohistochemical markers such as smooth muscle myosin and p63 that are used to confirm a continuous myoepithelial layer surrounding the ductal structures of ductal carcinoma in situ, which would not be seen in metastatic lesions. The diagnosis of a metastatic tumor should be considered in patients with known extramammary malignancy and whenever the morphology does not correspond to the typical histologic patterns of primary breast tumors. Comparison of previously diagnosed neoplasms and metastatic breast lesions is a very important factor in establishing a correct diagnosis of metastasis.

Immunohistochemistry plays a crucial role in the accurate identification of metastatic lesions. Breast cancer is typically positive for cytokeratin-7 (CK7), negative for CK20, and positive for low-molecular-weight cytokeratin (LMWCK), CAM5.2, and epithelial membrane antigen (EMA). $\alpha$-151 $\alpha$100 is expressed in 50% and carcinoembryonic antigen (CEA) in 30% of breast carcinomas. Convincing expression of estrogen receptor (ER) is largely restricted to carcinomas of the breast, endometrium, and ovary. Occasionally, tumors from other sites may express ER, but usually it is weak and focal. Gross cystic disease fluid protein-15 (GDFP-15) and mamoglobin are often expressed by carcinomas of the breast (50%–70%). GATA3, a transcription factor of the GATA family, is a relatively newly described marker that is positive in breast and urothelial carcinomas. More than 95% of primary breast ductal and lobular carcinomas have shown strong nuclear expression of GATA3, and up to 61% to 67% of triple-negative breast carcinomas are positive for GATA3.

In patients without a history of a prior neoplasm, the work-up of a breast metastasis should generally follow the path of work-up of a tumor of unknown origin. Because of the fact that the most common secondary breast tumors are lymphoma and melanoma, an initial panel of antibodies should be directed to exclude these malignant lesions. Expression of CK7 and CK20 is considered to be most helpful in identifying the origin of an adenocarcinoma. By combining the results of CK7/20, ER/progesterone receptor (PgR), and site-specific antibodies such as thyroid transcription factor-1 (TTF-1), CDX2, PAX-8, and prostate-specific antigen (PSA), most metastatic malignancies to the breast can be properly classified. In practice, a panel of antibodies should be selected on the basis of each patient’s history and gender as well as the frequency of possible primaries.

Microscopic Examination

MELANOMA

Melanoma metastases to the breast account for 1.2% of all malignant melanomas. Patients are usually premenopausal and have primary skin lesions on the upper body. Ravdel and associates reviewed 27 patients with breast metastatic melanoma, and all the patients had a history of primary cutaneous melanoma involving the upper body. Metastatic melanoma presenting as a breast mass may be difficult to recognize if the primary lesion is occult. In addition, malignant melanoma can mimic adenocarcinomas and may overlap with mammary carcinoma on microscopic
Metastatic Tumors in the Breast

examination and clinical presentation. Useful clues to the diagnosis are cytoplasmic pigment, intranuclear inclusions, and spindle cells (Fig. 36.1A). The negativity for cytokeratins and hormonal receptors should provide a clue to the right diagnosis. S100 is the most sensitive immunohistochemical marker of melanoma, but not specific, because it can also be expressed in breast cancers. Homatropine methylbromide-45 (HMB45), Melan-A, and microphthalmia transcription factor are all less sensitive, being present in about 70% of melanomas, but more specific than S100 (see Fig. 36.1). Uncommonly, melanoma may show aberrant expression of LMWCK, CAM5.2, EMA, and CD68. A relatively newly described marker, SOX10 (a transcription factor), is principally expressed in melanocytes and Schwann cells, and hence a very useful marker for melanoma. Up to 95% of metastatic melanoma and 98% of desmoplastic melanoma are positive for SOX10, making it a valuable addition to the panel of immunohistochemical stains for melanocytic differentiation. However, up to 40% of primary breast carcinomas, predominantly triple-negative, basal-like, and metaplastic carcinomas, can also show SOX10 expression.

PULMONARY TUMORS

In 1959, Sandison reported a case of small cell carcinoma of the lung initially presenting as a breast mass. Shortly after the diagnosis, subsequent systemic metastases and progressive fatal course occurred. The possibility of metastasis, particularly from the lung, should be considered if small cell carcinoma is diagnosed in the breast (Fig. 36.2). The route of metastases from the lung is still unclear because axillary lymph node metastases were noted, which rarely occurs in hematogenous spread.

The differential diagnosis includes rarely reported primary small cell carcinoma of the breast (Fig. 36.3) and Merkel cell carcinoma (primary skin tumor with neuroendocrine features). Both primary and metastatic small cell carcinomas are positive for neuroendocrine markers, LMWCK, CAM5.2, CK7, and TTF-1. ER expression favors the diagnosis of primary mammary small cell carcinoma. However, the majority of primary mammary small cell carcinoma show absence of ER, SOX10, with negative staining for hormonal receptors and positive staining for TFF-1, similar to metastatic pulmonary small cell carcinoma, leading
FIG. 36.2  Metastases from pulmonary carcinoma involving the breast parenchyma. A and B, Metastatic small cell carcinoma of the lung. Note the neuroendocrine features of the nuclei with streaming phenomenon. C, Poorly differentiated adenocarcinoma. D, Pulmonary tumors are often diffusely and strongly positive for thyroid transcription factor-1 (breast metastasis of small cell carcinoma is shown in this picture) and negative for estrogen receptors.

FIG. 36.3  Primary breast neuroendocrine carcinoma. A and B, Tumor shows nuclear neuroendocrine features, tumor necrosis, and absence of an in situ component. In addition, these tumors may be positive for estrogen receptor and can be positive for thyroid transcription factor-1. Differentiating this entity from metastatic pulmonary neuroendocrine carcinoma should rely on clinical findings.
Metastatic Tumors in the Breast

The absence of clinical history of pulmonary small cell carcinoma supports the diagnosis of primary small cell carcinoma. Merkel cell carcinoma is positive for CK20 and mostly negative for TTF-1.

Most lung primaries metastasizing to breast are adenocarcinomas (see Fig. 36.2). Carcinoma of the lung has diverse histologic appearances, some of which may resemble mammary carcinoma. Metastatic papillary carcinoma of the lung can mimic primary papillary carcinoma of the breast. TTF-1 is commonly expressed in the majority of pulmonary adenocarcinoma (80%), but is rarely present in breast primary. Conversely, Schnitt and colleagues reported positive TTF-1 in approximately 2% to 3% of breast cancers, which could serve as a potential diagnostic pitfall.

Pulmonary adenocarcinoma can be focally ER+. Squamous cell carcinoma of the lung has rarely been reported to metastasize to breast. With the overlapping morphology and immunophenotype between metastatic and primary squamous cell carcinoma, the clinical history is crucial for making the correct diagnosis. A rare source of metastatic tumor in the breast is epithelioid mesothelioma. Strong positive staining for D2-40 and calretinin favors mesothelioma over carcinoma.

FEMALE GENITAL TRACT TUMORS

Serous carcinoma is the most common type of female genital tract malignancy to metastasize to the breast. Fewer than 50 cases have been reported, of which five were primary peritoneal serous carcinomas. Most of the patients have a known history of serous carcinoma. Metastases to the breast from ovarian primaries generally occur 2 to 3 years after the initial diagnosis, but they can occur as an initial presentation of occult carcinoma or several years later. The presence of psammoma bodies and the papillary architecture favor a metastatic ovarian carcinoma (Fig. 36.4). However, primary micropapillary breast and ovarian carcinoma can share similar morphologic features (Fig. 36.5). Both primary and serous ovarian carcinomas are typically CK7+, CK20−, and often ER+. However, most ovarian carcinomas are strongly positive to Wilms
tumor antigen-1 (WT1) (nuclear staining) and negative for GCDFP-15 and GATA-3. Nuclear WT1 expression is present in a minority of invasive micropapillary and mucinous breast carcinomas, and when present, expression is focal (<10% of cells). CA125 is expressed more frequently in serous carcinoma than in breast carcinoma (see Fig. 36.4) and may be helpful in the differential diagnosis. In addition, the pattern of EMA expression is useful where invasive micropapillary carcinoma has expression of EMA on the outside of the papillary clusters, but not around the central spaces, versus serous papillary carcinoma, which has expression on both surfaces.

In addition, PAX8 and to a lesser extent PAX2 are transcription factors that are highly specific for female genital tract tumors, and their use in the metastatic setting is very helpful. In addition, NY-BR-1 is seen in breast carcinomas with a sensitivity of 60%, but is negative in female genital tract tumors.

Metastatic endometrioid carcinoma to breast has been reported, frequently demonstrating an endometrioid appearance with focal areas of adenosquamous differentiation. The histomorphology of the metastatic endometrial carcinoma depends on the tumor grade, whereas a solid growth pattern can mimic poorly differentiated breast carcinoma. Endometrioid adenocarcinoma is positive for CK7, ER, PAX8, and PgR but usually negative for GCDFP-15. Few cases of metastatic cervical and vulvar squamous cell carcinoma to the breast have been reported. In all cases, breast metastasis usually indicates disseminated metastatic disease and a poor prognosis. An uncommon cause of metastatic tumor in postpartum breast is choriocarcinoma.

**GENITOURINARY TRACT TUMORS**

There are only isolated case reports documenting renal cell carcinoma (RCC) metastasizing to the breast. Metastatic RCC to the breast has been reported 16 times, with eight cases representing the initial presentation of metastatic disease. Although metastases were present in approximately 30% of patients with RCC, the breast was rarely involved. Metastatic RCC in the breast may precede the diagnosis of the occult RCC or metastasis may occur decades later (≤18 years) after initial resection of the tumor. Conventional RCC is the most common renal malignancy that metastasizes to the breast. The abundant clear or granular cytoplasm with a relatively low nuclear-to-cytoplasmic ratios and prominent fine vessels are useful clues to the correct diagnosis (Fig. 36.6).

Although RCC antigen is helpful to identify renal cell carcinoma, up to 33% of breast carcinomas may be positive for RCC. PAX2 is more helpful in this situation because it is positive in more than 75% of clear cell and papillary renal carcinomas. PAX8 shows similar labeling as PAX2 and is expressed in all RCC subtypes, although PAX8 is reported to be more sensitive than PAX2.

Benign breast lesions with foam cells, such as fat necrosis, or benign neoplasms (eg, granular cell tumors), adenomyoepithelial lesions, or lactating adenoma can be confused with this neoplasm. Primary breast carcinomas such as secretory carcinoma, glycogen-rich carcinoma, histiocytoid carcinoma, and lipid-rich carcinoma are also among the main entities considered in the differential diagnosis. An unusual case of metastatic RCC to the breast from an occult renal primary in a woman who had previous lumpectomy owing to mammary carcinoma in the same breast has been reported.

Prostate carcinoma is one of the most common primary sites that metastasizes to the male breast. Prostatic carcinoma may have columnar cells with relatively bland nuclei with nucleoli, with overlapping histology with breast carcinoma (Fig. 36.8). In men, involvement of the breast by metastatic prostatic adenocarcinoma has been a frequent finding at autopsy. Breast involvement was identified in 26% of patients with prostatic adenocarcinoma with microscopic examination. Charache in 1953 reported metastatic prostatic carcinoma...
FIG. 36.6 Metastasis from renal cell carcinoma, clear cell type, involving the breast parenchyma. 

FIG. 36.7 Primary breast carcinoma with clear cytoplasm. A, Primary breast carcinoma, glycogen-rich type, shows clear cytoplasm, mimicking metastatic renal cell carcinoma. B and C, Core biopsy of a breast mass in a patient with a history of renal cell carcinoma. Biopsy shows poorly differentiated carcinoma with occasional clear cytoplasm. D, Tumor cells are strongly and diffusely positive for estrogen receptor (and negative for other renal carcinoma markers), reinforcing the diagnosis of primary breast carcinoma.
initially presenting as a breast mass, and the primary site was not detected until autopsy. Several authors have described patients with bilateral breast metastases from prostatic adenocarcinoma.\textsuperscript{104–106} Although any breast mass in a patient with a history of prostatic carcinoma should raise the question of metastases, rare reports have described independent synchronous or metachronous primary carcinomas of the prostate and breast.\textsuperscript{107} A collision tumor consisting of metastatic prostatic carcinoma in a solid papillary carcinoma of the male breast has also been described.\textsuperscript{108} 'Transitional cell carcinoma of the urinary bladder has also been reported to metastasize to the breast.\textsuperscript{9,109}

Immunohistochemistry is crucial in the differential diagnosis between primary and metastatic carcinoma in the male breast. Conventional RCC is usually positive for the RCC marker (90%), whereas up to 33% of breast cancers are positive.\textsuperscript{100,110} CD10 is present in a high proportion of conventional and papillary RCCs (90%), but it is rarely expressed in breast cancer (5%).\textsuperscript{111} ER, GCDFP-15, and CK7 are rarely expressed in conventional RCC,\textsuperscript{112} although CK7 is usually expressed in the papillary type of RCC.\textsuperscript{112,113} Note that although GATA3 is a highly sensitive marker for primary breast carcinomas, its utility is diminished in male breast carcinomas (as low as only 32%).\textsuperscript{116} PAX8 is the most useful marker to exclude a primary breast carcinoma and establishing a diagnosis of metastatic RCC because it is completely negative in breast, whereas strong nuclear PAX8 staining is seen in all subtypes of RCC with sensitivity of approximately 95%.\textsuperscript{114,115} When considering prostatic carcinoma as the origin, PSA and prostatic acid phosphatase are excellent initial markers because both are sensitive and specific.\textsuperscript{116,117} However, poorly differentiated prostatic adenocarcinoma and those that are treated with androgen deprivation therapy tend to have decreased immunoreactivity for PSA and PSAP. In these situations, P501s (prostein), which has 99% sensitivity in metastases and no decrease after androgen deprivation therapy, can be very useful.\textsuperscript{118} NKX3.1 is another very useful and sensitive marker (94% sensitivity) that has been recently described, but it is also reported to show positivity in ER+ and androgen receptor (AR)+ primary breast invasive lobular carcinomas (21%).\textsuperscript{119} ER, GCDFP-15, and CK7 positivity are uncommon in prostatic carcinoma.

**GASTROINTESTINAL TUMORS**

The intestinal type of gastric carcinoma may resemble invasive ductal carcinoma of the breast, and diffuse gastric carcinoma may resemble invasive lobular carcinoma of the breast (Fig. 36.9). Gastric carcinomas are reported to be the most common metastatic malignancy to the breast in the Korean population.\textsuperscript{2} Metastatic gastrointestinal mucinous carcinoma is histologically indistinguishable from primary mucinous carcinoma of the breast.\textsuperscript{13} In 1936, Dawson\textsuperscript{120} described a woman with diffuse lymphatic invasion of both breasts from signet-ring cell gastric adenocarcinoma. Later, Yeh and coworkers\textsuperscript{2} reported additional cases with a similar presentation.

ER and GCDFP-15 are rarely expressed by gastric carcinoma, whereas CK20 and CDX2 are occasionally positive in gastric carcinoma (see Fig. 36.9).

Despite being the most common gastrointestinal tract tumor among adults, colorectal carcinomas are rarely reported to metastasize to the breast (Fig. 36.10). Only a few cases have been reported in the literature, three of which were seen in men, including one case of rectal small cell carcinoma.\textsuperscript{2,121–125} Metastatic breast colorectal carcinoma and the primary tumor can present as synchronous lesions, or breast metastases may follow the primary by months to years. Immunohistochemistry shows that most colorectal carcinomas are negative for CK7 and positive for CK20 and CDX2.\textsuperscript{126} In contrast, primary breast carcinomas are positive for CK7 and negative for CK20 and CDX2. Metastases to the breast are usually associated with disseminated metastases and a poor prognosis. Yeh and coworkers reported seven cases of hepatocellular carcinomas metastatic to the breast.\textsuperscript{2} Gallbladder carcinoma and esophageal squamous cell carcinoma have also been reported to
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metastasize to the breast, progressing from asymptomatic lesion to death within 3 weeks.127–129

NEUROENDOCRINE TUMORS (CARCINOID TUMORS)

Well-differentiated neuroendocrine neoplasms (carcinoid tumors) are slow growing with a tendency for late metastases (<19 years).130 Upalakalin and colleagues estimated that 41% of all carcinoid tumors in the breast were metastases from extramammary sites.130 Patients with metastases to the breast present an average 10 years younger than patients with primary breast carcinoids and have a worse prognosis.131

In carcinoid syndrome, an enlarged liver and multiple metastatic nodules in both breasts are possible presenting manifestations.19,131 Although the presence of carcinoid syndrome is highly suggestive of metastases from a gastrointestinal origin, its absence does not rule out the possibility of an extramammary origin.19,131 A breast mass may be the first indication of an occult carcinoid tumor.19,109,130,132,133 Most primary occult carcinoid tumors are located in the lung and ileum/ileocecum, followed by the appendix and ovary.19,109,130,132 Fishman and associates have reported breast metastases from an occult ovarian carcinoid tumor.134 The lesion was diagnosed and treated as a lobular carcinoma for 1 year before the ovarian primary was identified.

A carcinoid tumor of the breast may be misdiagnosed as an epithelial malignancy even when the patient has a known history of a carcinoid tumor elsewhere. Immunohistochemical analysis can provide some clues to the primary site of carcinoid tumors. Expression of CDX2 and CK20 favors gastrointestinal origin, whereas TTF-1 and CK7 expression favors pulmonary origin.133 ER, PgR, and GCDFP-15 are often expressed by mammary neuroendocrine carcinomas. However, PgR can be expressed in some pancreatic endocrine tumors.136

THYROID TUMORS

Medullary thyroid carcinoma (MTC) is an uncommon thyroid cancer and has been reported to metastasize to the breast.137 All patients were women with persistent elevated calcitonin level after treatment and the failure of other imaging modalities to detect residual disease.137 Distant metastasis occurred late, usually to the breast. Metastatic MTC gland can have an infiltrating pattern that mimics infiltrating lobular carcinoma of breast.138 Immunohistochemical studies showed that the
neoplastic cells were positive for CK7, neuroendocrine markers, calcitonin, and TTF-1 but negative for ER and PgR.

Papillary and follicular carcinoma of the thyroid may rarely metastasize to the breast.24 Only a few reports of metastatic papillary thyroid carcinoma to the breast have been published.139-142 The majority of the cases showed conventional morphology; however, one case showed the histologic features of tall cell variant 141 (Fig. 36.11). An anaplastic component arising within papillary carcinoma metastatic to the breast was also reported 142. Thyroid carcinoma is positive for TTF-1, thyroglobulin, and PAX8, effectively excluding a diagnosis of breast carcinoma.

OTHER CARCINOMAS

Salivary gland carcinomas such as mucoepidermoid and acinic cell carcinomas, neoplasms not often considered as a source of metastatic tumor, have been rarely reported to metastasize to the breast.12,125,143 Metastases from medulloblastoma 143 and neuroblastoma 144 have been reported in children and adults.

HEMATOPOIETIC MALIGNANCIES

Secondary spread of lymphomas to the breast is reported to account for approximately 0.07% of all breast malignancies (see also Chapter 35). However, these secondary lymphomas compose the largest group (17%) of tumors that can involve the breast.5,145,146 Wiseman and Liao 147 defined the clinical criteria for the diagnosis of primary breast lymphoma when the breast is the clinical site of the first major manifestation of the lymphoma. They also state that ipsilateral lymph nodes may be involved if they develop simultaneously with the primary breast tumor. Previous reports document a right-sided predominance. However, one study has shown equal involvement of the right and left breast.145 The presence of B symptoms (fever, night sweats, and weight loss) is uncommon.

The most common histologic type reported in the literature when primary and secondary cases are grouped together is diffuse large B-cell lymphoma (Fig. 36.12), which represents 45% to 90% of all cases.4 Burkitt-type lymphoma and mucosa-associated lymphoid tissue–type lymphoma have also been documented.7,145-147 Secondary involvement of the breast with a T-cell lymphoma...
FIG. 36.11 Metastasis from thyroid papillary carcinoma. A, Tumor infiltrates the breast parenchyma and is intermixed with benign breast tissue. B, Tumor shows papillary architecture, vascular stroma, and occasional psammoma body formation. C, Tumor cells show nuclear features of papillary carcinoma such as intranuclear inclusions and multiple nuclear grooves. D, Thyroglobulin and thyroid transcription factor-1 are positive in tumor cells, reinforcing the diagnosis of metastatic thyroid carcinoma.

Metastatic Tumors in the Breast

has been reported in only a few cases. Immunohistochemistry and polymerase chain reaction (PCR) for immunoglobulin heavy chain clones or translocations are often helpful.

Leukemia occasionally involves the breast. The morphology of the blasts or more differentiated cells may give a clue to the diagnosis, but a high index of suspicion may be needed to make the correct diagnosis if there is no clinical history. Myeloma rarely involves the breast. The plasmacytoid morphology and pattern of infiltration around lobules can suggest the diagnosis. Demonstration of light chain restriction is important in establishing the correct diagnosis. CD38 and CD138 are especially useful markers of plasma cell differentiation, but neither is specific.

SARCOMAS

Both primary and metastatic sarcomas in the breast are rare. Sarcoma is more commonly seen as a component of metaplastic carcinoma or phyllodes tumor. Metastatic sarcoma to the breast includes uterine leiomyosarcoma, synovial sarcoma, hemangioendothelioma, alveolar soft part sarcoma, Ewing sarcoma, low-grade endometrial stromal sarcoma, and malignant fibrous histiocytoma. These tumors may be difficult to distinguish from primary mammary sarcomas and some metaplastic mammary carcinomas. Given the known limitations of a core needle biopsy, accurate diagnosis becomes very difficult unless there is a prior history of the sarcoma. Clear cell sarcoma of soft tissue, also called melanoma of soft parts, is an excellent example that can be a diagnostic pitfall. This rare type of sarcoma has morphologic similarities to malignant melanoma, but distinct genetic profile of chromosomal translocation of t(12;22)(q13;12), resulting in fusion gene EWSR-ATF1. The tumor is located in deep soft tissues of the extremities, limb girdles, or trunk. The malignant cells are spindled or epithelioid arranged in fascicular or solid sheetlike pattern, but can also have alveolar pattern. Without a prior history, tumor located in breast having an epithelioid morphology can easily be mistaken for primary mammary carcinoma (Fig. 36.13). However, these tumors are strongly positive for S100 and HMB45 and variably positive for MiTF and Melan-A. AE1/3 can rarely be positive (up to 3%), and CAM5.2 is typically negative.
Prognosis

The appropriate treatment option can be challenging in metastatic breast carcinomas. There is little information in the literature regarding what is considered the best practice. In the study by Vaughan and coworkers, 61% of patients underwent some form of resection, but only 22% of these patients had their resection with curative intent. Surgical debulking or excision for palliative purposes may be appropriate in widely metastatic disease. Metastases to the breast have been associated with poor prognosis, with most patients dying within 1 year of diagnosis. Vaughan and coworkers reported a mean survival time of 17.8 months after the diagnosis of a breast metastasis of nonhematologic origin. Median survival in a review of 27 cases of melanoma metastases to the breast was 12.9 months. Metastatic disease in the breast is a marker for disseminated metastatic spread and, therefore, indicates a poor prognosis. Mastectomy may be performed to obtain local control of bulky, ulcerated metastatic lesions. Wide excision can be supplemented by radiotherapy to the breast for radiosensitive neoplasms, and axillary dissection may be performed, especially if the lymph nodes appear to be grossly involved. Patients with smaller metastasis not causing problems with local control and not having clinical evidence of axillary metastases may be treated with extensive surgical resection.

SUMMARY

The correct identification of metastatic tumors in the breast is of vital importance to proper patient management. Recognition depends on the pattern of breast involvement, including lack of an in situ component, unusual tumor cell morphology, and disseminated lymphangitic spread. The analysis should begin with obtaining the patient history, and in most instances, the evaluation should be the work-up of tumors of unknown origin when patients lack a history of a prior extramammary neoplasm.

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