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PICTORIAL REVIEW

Breast metastases from extramammary malignancies: multimodality imaging aspects

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ABSTRACT

Breast metastases from extramammary cancers are rare and usually related to poor prognosis. The extramammary tumours most frequently exhibiting breast metastases are melanoma, lymphomas, ovarian cancer, lung and neuroendocrine tumours, and sarcomas. Owing to the lack of reliable and specific clinical or radiological signs for the diagnosis of breast metastases, a combination of techniques is needed to differentiate these lesions from primary breast carcinoma or even benign breast lesions. Multiple imaging methods may be used to evaluate these patients, including mammography, ultrasound, MRI, CT and positron emission tomography CT. Clinical and imaging manifestations are varied, depend on the form of dissemination of the disease and may mimic primary benign and malignant breast lesions. Haematologically disseminated metastases often develop as a circumscribed mass, whereas lymphatic dissemination often presents as diffuse breast oedema and skin thickening. Unlike primary carcinomas, breast metastases generally do not have spiculated margins, skin or nipple retraction. Microlobulated or indistinct margins may be present in some cases. Although calcifications are not frequently present in metastatic lesions, they occur more commonly in patients with ovarian cancer. Although rare, secondary malignant neoplasms should be considered in the differential diagnosis of breast lesions, in the appropriate clinical setting. Knowledge of the most common imaging features can help to provide the correct diagnosis and adequate therapeutic planning.

INTRODUCTION

Breast metastases from extramammary malignancies are rare and usually associated to poor prognosis. Its prevalence varies from 0.5% to 6.6% of all malignant tumours in the breast.¹ However, in up to 50% of cases, the breast lesion may be the first manifestation of the primary tumour.² Treatment should be individualized and depend on the type of primary tumour and extent of disease at diagnosis.

The extramammary tumours that most frequently metastasize to the breast are melanoma, lymphomas, ovarian cancer, lung, neuroendocrine tumours and sarcomas. Clinical manifestations and imaging tests are varied, depend on the form of dissemination of the disease and may mimic primary benign and malignant mammary lesions. The suspicion and confirmation of the diagnosis are fundamental for an adequate therapeutic planning, allowing to avoid unnecessary surgeries and to provide appropriate systemic therapy.²

The aim of this pictorial essay is to review the main findings in the different imaging methods of the most common metastatic lesions to the breast.

MULTIMODALITY IMAGING ASPECTS

Owing to the lack of reliable and specific clinical or radiological signs for the diagnosis of breast metastases, a correlation of different modalities is required to differentiate these lesions from primary breast carcinomas or even from benign breast lesions. A careful clinical history is necessary, with special attention to the simultaneous or previous diagnosis of extramammary malignancy, combined with clinical examination, radiological and anatomicopathological evaluation, to ensure the correct diagnosis and management of these patients.

The form of presentation of the metastatic lesion in the breast depends on the path of dissemination of the neoplasia, whether haematogenous or lymphatic. Usually haematogenous disseminated lesions present as circumscribed

Table 1. Most common imaging findings of breast metastases from extramammary cancers

Imaging modality	Most common imaging findings
Mammography	High density, round and circumscribed masses May have microlobulated or indistinct margins No desmoplastic reaction Calcifications are uncommon
Ultrasound	Round or oval masses, with circumscribed, indistinct or microlobulated margins Skin thickening, oedema and enlarged lymph nodes (lymphatic dissemination)
MRI	Round or oval masses with intermediate signal on T_2 weighted sequences and low signal on T_1 weighted sequences (except melanoma metastases) Fast and homogeneous enhancement
CT and PET/CT	Round or oval circumscribed masses with contrast enhancement on CT and increased metabolism relative to normal breast parenchyma on PET/CT

PET, positron emission tomography.

masses, sometimes with cystic areas and calcifications, and may mimic benign masses or circumscribed malignant tumours (*i.e.* medullary, mucinous or papillary carcinoma). Lymphatic dissemination may lead to diffuse findings in the breast, such as

oedema, trabecular thickening and skin thickening, which may mimic inflammatory processes such as mastitis and special presentations of primary malignant tumours such as inflammatory carcinoma.³ Table 1 summarizes most common imaging findings.

Figure 1. A 73-year-old female patient with a palpable lump in the right breast. Mammography showed a hyperdense mass with obscured margins on upper-outer quadrant to the right breast and enlarged axillary lymph nodes (a: mediolateral oblique views). Ultrasound showed an oval hypoechoic mass with circumscribed margins (b). Biopsy showed lymphoid cells with vesicular nuclei and high mitotic index, compatible with non-Hodgkin lymphoma.

Figure 2. A 50-year-old female patient treated for non-Hodgkin's lymphoma 2 years earlier with complete remission, presented with fever and diffuse hyperaemia of the right breast (a), without response to systemic antibiotics. Ultrasound showed heterogeneous mass with indistinct margins (b). Contrast-enhanced chest CT showed a heterogeneous mass with associated oedema (c) and intense fluorine-18-labelled fludeoxyglucose uptake on positron emission tomography/CT (d). Biopsy revealed anaplastic large-cell lymphoma.

Mammography

Breast metastases can be identified in both screening and diagnostic mammograms. Usually, these lesions present as high

density, round and circumscribed masses, often mimicking benign tumours.⁴ The most common location, as in primary breast cancer, is the upper-outer quadrant, probably due to the

Figure 3. A 52-year-old female patient with history of melanoma on the left thigh 2 years earlier complained of palpable and painful lump in the right breast. Mammography (a: mediolateral oblique view) showed a round circumscribed mass in the lower-outer quadrant of the right breast (arrow). Breast ultrasound showed a hypoechoic mass with indistinct margins and mild rim vascularity on colour Doppler (b). MRI showed an irregular mass with heterogeneous enhancement (arrow) with washout kinetic curve (c). Percutaneous biopsy was compatible with metastatic melanoma.

Figure 4. A 48-year-old female patient with previous melanoma on the thumb. Mammography (a: mediolateral oblique view) showed an oval circumscribed mass in the upper-outer quadrant of the left breast. Breast ultrasound showed an oval circumscribed mass with heterogeneous echo pattern (b). Percutaneous biopsy showed metastatic melanoma.

increased blood supply in this region. Unlike primary carcinomas, breast metastases generally do not have spiculated margins, skin or nipple retraction, due to the absence of desmoplastic reaction. Microlobulated or indistinct margins may be present in some cases. Although calcifications are not frequently present in metastatic lesions, they occur more commonly in patients with ovarian cancer due to the presence of psammomatous bodies.³ However, cases with suspected microcalcifications have been reported in other metastatic tumours such as hepatocellular carcinoma, medullary thyroid carcinoma and gastric cancer.^{5,6}

Ultrasonography

As in mammography, most metastatic lesions present on ultrasound as round or oval masses, with circumscribed, indistinct or microlobulated margins.⁴ These lesions are most commonly

located superficially in the subcutaneous tissue or immediately adjacent to the breast parenchyma, a topography that is relatively rich in blood supply.⁷ Although most lesions are hypoechoic, the echotexture may be heterogeneous, presenting anechoic or hyperechoic areas, frequently associated with posterior enhancement. The Doppler study may be useful mainly in differential diagnosis with benign lesions, such as fibroadenomas and cysts.³ Unlike primary carcinomas, architectural distortion, calcifications and posterior acoustic shadow are not commonly observed in metastatic lesions. The involvement of axillary lymph nodes is also less common in metastases than in primary breast cancers.⁷ Metastases with lymphatic dissemination usually present with diffuse and heterogeneously increased echogenicity of subcutaneous fat and glandular tissue, associated with skin thickening, lymphoedema and enlarged lymph nodes, which may be indistinguishable from

Figure 5. A 39-year-old female patient submitted to surgical resection of a retroperitoneal leiomyosarcoma 1 year earlier, presented a mass in the right breast on screening tests. Mammography identified a round circumscribed mass (arrow) in the lower-inner quadrant of the right breast (a: mediolateral oblique view). Ultrasound showed a round, circumscribed, complex solid and cystic mass with internal vascularity on colour Doppler (b). Percutaneous biopsy of the lesion confirmed metastatic leiomyosarcoma.

Figure 6. A 45-year-old female patient under treatment for metastatic neuroendocrine tumour presented a new small mass on routine breast ultrasound. Breast ultrasound showed a small hypoechoic circumscribed mass (arrows) in the upper quadrants of the left breast (a), which was also identified on MRI (b). The small mass on the left breast (arrow) showed increased uptake of gallium-68 DOTATATE on positron emission tomography-CT (c), which suggest a well-differentiated neuroendocrine metastasis.

inflammatory carcinoma signs. However, in these cases, there is no evidence of primary breast mass and oedema is secondary to the mechanical obstruction of lymphatic drainage by the tumour.

Figure 7. A 77-year-old female patient with prior serous ovarian adenocarcinoma presented an oval mass with pleomorphic calcifications (arrow) at mammography (a). Breast ultrasound also showed calcifications within an oval hypoechoic mass (b). Percutaneous biopsy was positive for metastatic ovarian carcinoma.

MRI

At MRI, most metastatic lesions show intermediate signal on T_2 weighted sequences and low signal on T_1 weighted sequences, with the exception of melanoma metastases, which may show high signal on T_1 weighted images. After administration of paramagnetic contrast, intense fast and homogeneous enhancement is usually observed, with a plateau or washout kinetic curve on the delayed phase.⁸

CT and positron emission tomography/CT

In patients with known malignant neoplasms, metastatic breast lesions are often identified incidentally in routine examinations performed for systemic staging or post-therapeutic follow-up, such as CT and PET/CT. In CT, these lesions usually present as round or oval circumscribed masses with contrast enhancement.⁸ In PET/CT, any lesion with increased metabolism relative to normal breast parenchyma should be considered a suspect for malignancy. However, it is not possible to differentiate metastatic lesions from primary carcinomas by PET/CT, so complementary evaluation with dedicated diagnostic mammography and breast ultrasound should be performed to confirm the diagnosis.⁹

IMAGING FEATURES OF MOST COMMON TUMOURS

Lymphomas

Breast lymphoma occurs more frequently as a secondary involvement of a disseminated disease and, less commonly, as primary breast disease (<0.5% of cases). The most common subtypes of breast lymphoma include diffuse large B-cell lymphoma, marginal zone lymphoma (mucosal-associated lymphoid tissue lymphoma) and follicular lymphoma, all of which originate from B-cells. T-cell lymphomas are much rarer, occurring in <10% of all cases. Clinically, primary and secondary breast lymphomas often present as palpable and painful masses in the upper-outer quadrant, associated with axillary lymphadenopathy.

Figure 8. A 64-year-old female patient with lung adenocarcinoma presented with oedema of the left breast. Mammography showed skin and trabecular thickening, associated with axillary adenopathy (a). Breast ultrasound showed an ill-defined hypoechoic lesion in the upper quadrants of the left breast (b) and abnormal axillary lymph nodes. Ultrasound-guided biopsy confirmed metastatic lung adenocarcinoma in the breast.

At mammography, breast lymphoma usually appears as an indistinct mass or masses, which may be hyperechoic or heterogeneous on ultrasonography (Figure 1). As previously noted, due to the lymphatic spread of the disease, overlapping skin changes may be present (Figure 2). At MRI, breast lymphoma frequently appears as an irregular mass or masses with mild heterogeneous internal enhancement, usually presenting washout kinetic curve and restricted diffusion.¹⁰

Melanomas

Similar to lymphoma, breast melanoma may represent primary or metastatic disease. Patients who have *BRCA-2* mutations, and possibly *BRCA-1*, have an increased risk of melanoma. Melanoma often appears as a circumscribed mass or masses, without spicules or microcalcifications at mammography, and may have varied presentations on ultrasonography (Figures 3 and 4). In MRI, it can demonstrate high signal on T_1 weighted images, due to the presence of melanin or haemorrhage in the lesion.¹¹ Metastatic melanoma should also be suspected in the presence of

enlarged axillary or intramammary lymph nodes, especially in cases where the primary lesion was located in the upper limb, back or upper abdomen.

Sarcomas

Sarcomas are among the tumours that most frequently present breast metastases, especially in young females. Breast metastases of various types of sarcoma have already been described in the literature, such as rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, liposarcoma, among others.¹¹ The imaging features are similar to the other metastatic lesions in the breast, presenting more commonly as circumscribed masses (Figure 5). However, some subtypes may present more characteristic findings. Metastatic rhabdomyosarcoma of the breast is the most prevalent mammary metastasis in adolescent females and should be strongly considered in young patients with an appropriate clinical history. It may present as a focal asymmetry on mammogram, simulating an invasive lobular carcinoma. Metastases of osteosarcoma may present gross calcifications, simulating involuting fibroadenoma.¹¹

Neuroendocrine tumours

Breast neuroendocrine tumours can be categorized into three subtypes: ductal carcinoma with neuroendocrine differentiation; primary neuroendocrine tumours of the breast; or metastatic disease. Frequently, metastatic lesions appear as circumscribed masses on mammography; however, there are reports of irregular and spiculated lesions in the literature. On ultrasonography, the most common presentation is as an irregular hypoechoic mass, with internal vascularity at Doppler. At MRI, it usually shows intense post-contrast enhancement with washout kinetic curve.¹² Metastases of well-differentiated neuroendocrine tumours can be further identified in scintigraphy with indium-111 octreotide or PET/CT with gallium-68 DOTATATE (Figure 6). However, these cases should be investigated with caution to rule out primary breast lesions.

Ovarian cancer

Serous papillary carcinoma is the most common type of ovarian tumour that can metastasize to the breast and may also involve axillary lymph nodes. Occasionally, breast metastasis develops years after the initial diagnosis of primary ovarian cancer. Unlike other metastatic lesions in the breast, ovarian tumours may

present suspicious microcalcifications due to the presence of the psammomatous bodies (Figure 7).¹³

Lung cancer

Breast metastases from lung cancer appear clinically as irregular masses in most cases and may present at the time of diagnosis of lung cancer (synchronous) or after the diagnosis of lung cancer (metachronic). Synchronous metastases are more common in small-cell carcinomas, whereas metachronic metastases are more common in non-small-cell carcinomas.¹⁴ Lung cancer may still present lymphatic metastasis to the breast, simulating inflammatory process or inflammatory breast carcinoma (Figure 8).

CONCLUSION

Although rare, secondary malignant neoplasms should be considered in the differential diagnosis of breast lesions, in the appropriate clinical setting. Haematologically disseminated metastases often develop as a circumscribed mass, whereas lymphatic dissemination often presents as diffuse breast oedema and skin thickening. Knowledge of these possibilities can help the correct diagnosis of the patient and lead to more rapid and appropriate management strategies.

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