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REVIEW

Mesenchymal tumours of the breast and their mimics: a review with approach to diagnosis

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Summary

Mesenchymal tumours of the breast comprise a broad spectrum of entities that frequently pose diagnostic challenges to surgical pathologists. Metaplastic carcinoma and phyllodes tumour are site-specific mimics that account for the majority of tumours in the breast with a sarcomatoid appearance. Although uncommon, mammary tumours with fibroblastic, adipocytic or vascular differentiation may be encountered, spanning the spectrum from benign to malignant. Tumours with histiocytoid morphology are potential traps due to bland cytomorphology and resemblance to reactive processes. This comprehensive review provides a diagnostic approach to specific challenging mesenchymal tumours of the breast and their mimics, with a discussion on the salient morphological, immunohistochemical and molecular features that allow accurate diagnosis and will help the pathologist avoid potential pitfalls.

Key words: Breast; mesenchymal breast tumours; metaplastic carcinoma; phyllodes tumour; fibroblastic tumours; adipocytic tumours; vascular tumours; histiocytoid morphology; spindle cell; soft tissue; sarcoma.

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INTRODUCTION

Mesenchymal tumours of the breast may present a challenge to the practising pathologist, in part, owing to their site-specific mimics. Metaplastic carcinoma and phyllodes tumour account for the majority tumours with spindle cell/sarcomatoid morphology. As well as covering these entities, this review will provide a diagnostic approach to specific challenging fibroblastic, adipocytic, vascular and histiocytoid tumours that can present as mammary lesions.

METAPLASTIC CARCINOMA

Clinical presentation

Although metaplastic carcinoma is rare, accounting for less than 1% of primary tumours of the breast, it is a frequent source of diagnostic difficulty. Metaplastic carcinoma arises in the same age group as other forms of invasive carcinoma. Some studies have found that it is slightly more common in African American and Hispanic women.[1] Patients tend to present with higher tumour size and stage than conventional invasive mammary carcinoma (approximately 3–4 cm).[1,2] Rapid growth in a short span of time is common. Large lesions can be tethered to the skin and/or chest wall.

Radiologically, metaplastic carcinomas are less likely to show the characteristic imaging features of malignancy. They tend to have a rounded or oval shape with circumscribed margins, which suggest benignity. Spiculated margins and pleomorphic linear calcifications are uncommon. Coarse internal calcifications may hint at heterologous chondroid or osseous elements, if present. Cystic change may be present in tumours with squamous differentiation.[3]

Pathology

Metaplastic carcinoma represents a heterogeneous category of tumours with various forms of differentiation along a multitude of cell lines. This group includes squamous cell carcinoma, adenosquamous carcinoma and tumours showing complete or partial transition to mesenchymal elements, including spindle cell/sarcomatoid carcinoma, metaplastic carcinoma with pseudosarcomatous metaplasia, matrix-producing carcinoma and carcinosarcoma.[4–11] There is no general consensus on subclassification within this group. Metaplastic carcinoma more often originates from poorly differentiated invasive ductal carcinoma; however, rarely, it can arise from invasive lobular carcinoma. The amount of metaplasia may vary from small microscopic foci to complete replacement of the glandular component. There is currently no consensus on the minimum extent of metaplasia qualifying for a diagnosis of metaplastic carcinoma.[12]

Metaplastic carcinoma with squamous differentiation

The most common form of metaplastic carcinoma is invasive ductal carcinoma with squamous metaplasia. Both keratinising and non-keratinising types have been well described, including some tumours with prominent keratin pearls, and the extent of this may vary.[7] An acantholytic variant has been described which shows a pseudoglandular appearance that may be mistaken for angiosarcoma.[13] The majority of the pure squamous carcinomas show central cystic change. Pure squamous cell carcinoma should be distinguished from squamous cell carcinoma of the overlying skin by appropriate sampling. The distinction from mucoepidermoid carcinoma can be made by observing a lack of mucin cells.[7]

Spindle cell carcinoma

Spindle cell carcinoma is characterised by spindle-shaped cells arranged in a variety of architectural patterns, including storiform, fascicular, fasciitis-like or haphazard (Fig. 1A).[5,9,11] The degree of cytological atypia may vary

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from striking pleomorphism to deceptively bland. Usually some degree of nuclear atypia is observed, at least focally. Although macroscopically often circumscribed, microscopically the tumours tend to be infiltrative, with spindle cells encircling benign ducts. The mitotic rate is variable; some cases may not show any appreciable mitotic activity.[5] Necrosis may be present. Many tumours show an inflammatory infiltrate that is most commonly lymphoplasmacytic. The inflammation may be so prominent as to raise the possibility of an inflammatory myofibroblastic tumour.[5] Fibromatosis-like carcinoma is a subtype that is a potential trap, owing to its bland cytology and superficial resemblance to fibromatosis, with similar nodular and finger-like projections (Fig. 1B).[14] Fibromatosis-like carcinoma may arise *de novo* or within papillary or sclerosing lesions.[15] Despite its low-grade histological appearance, the recurrence rate is high and there is a small risk of haematogenous metastasis.[14,15]

Although it is prudent to scrutinise microscopic slides for foci of epithelial differentiation, often this is not present despite extensive sampling.[9,11] When present, the epithelial component is often seen as nests or cords of squamous cells, sometimes merging imperceptibly with the spindle cells.[5] This would suggest that some spindle cell carcinomas represent sarcomatoid squamous carcinoma, whereas others are thought to have myoepithelial differentiation.[11,16] In the absence of an *in situ* component or recognisable epithelial differentiation, immunohistochemistry is invaluable in establishing the diagnosis (see below).

Low-grade adenosquamous carcinoma

Low grade adenosquamous carcinoma is a rare subtype of metaplastic carcinoma composed of well-differentiated infiltrative glands with varying degrees of squamous differentiation within a collagenous spindle cell stroma.[17–19] The glands show bland cytomorphology and have an ovoid to compressed shape with elongated lumina, and long slender extensions that insinuate between benign breast ducts and lobules (Fig. 1C).[17–19] Often they have a tear-drop morphology resembling syringomatous tumours of the nipple, and some have proposed a relationship to syringoma.[20] There is commonly a prominent lymphoid cuff surrounding the tumour. The spindle cell stroma is variably cellular and merges with the epithelial component in areas. Osteocartilaginous metaplasia can rarely be present.[17,18] Low grade adenosquamous carcinoma has been reported in association with papillomata, adenomyoepithelioma and sclerosing lesions.[17–19] Rarely, the tumours may be multiple.[21]

Metaplastic carcinoma with (heterologous) mesenchymal differentiation

Carcinomas within this group show varying degrees of heterologous mesenchymal elements. Most commonly, this takes the form of osseous or cartilaginous differentiation, but rhabdomyoblastic, fibrosarcomatous and even neuroglial differentiation have been reported (Fig. 1D).[4,6–8,11,12] Often an admixture of cartilaginous and osseous differentiation is seen. These tumours may show a prominence of osteoclast-type giant cells, which are often situated around zones of stromal haemorrhage, reminiscent of aneurysmal bone cyst.[7] 'Matrix-producing carcinoma' is a special subtype within this group that describes an overt carcinoma with direct transition to a chondroid or osseous component without an intervening spindle cell zone.[4] The heterologous elements may appear histologically bland to frankly sarcomatous. The carcinoma component is most commonly high grade invasive ductal carcinoma. Matrix-producing carcinoma is an aggressive tumour with decreased locoregional recurrence-free survival and distant recurrence-free survival compared to invasive ductal carcinoma.[4,10]

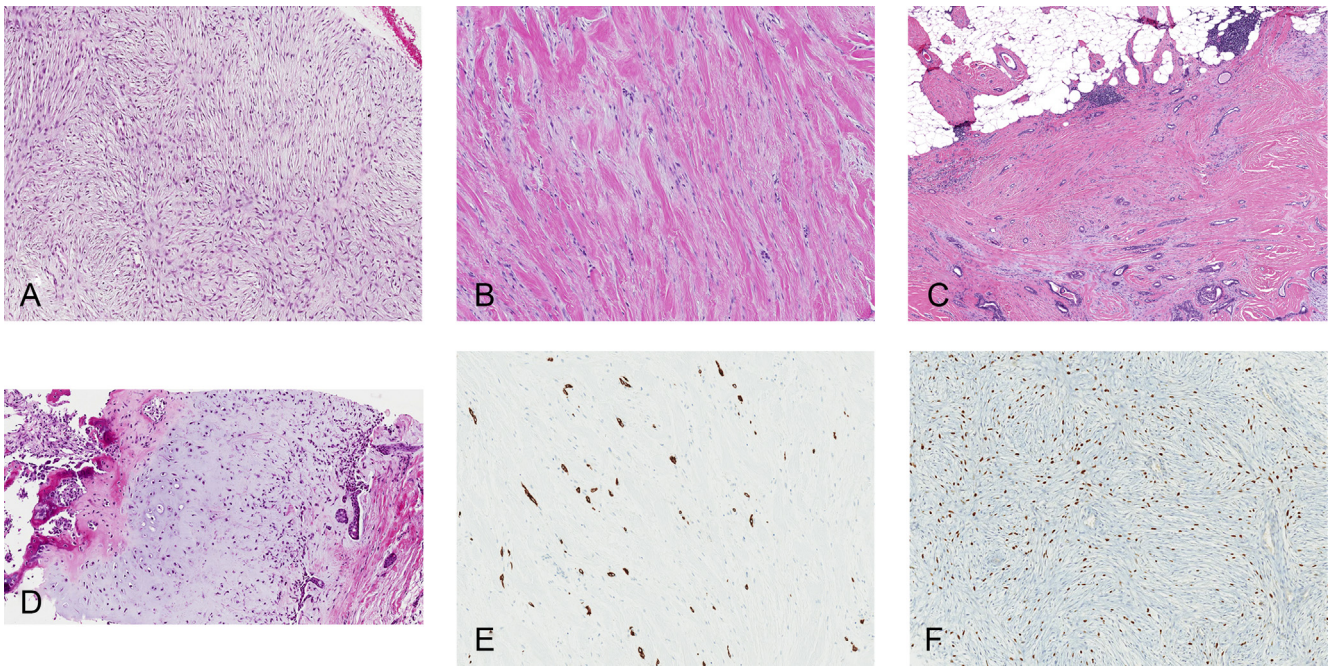

Fig. 1 (A) Spindle cell carcinoma with a storiform architecture. (B) Fibromatosis-like carcinoma resembling spindle cell carcinoma. (C) Low grade adenosquamous carcinoma with bland cytomorphology. (D) Metaplastic carcinoma with chondro-osseous differentiation. (E) Cytokeratin 7 in fibromatosis-like metaplastic carcinoma. (F) p63 immunostain in spindle cell carcinoma.