COMBINED EPITHELIAL-MYOEPITHELIAL LESIONS OF THE BREAST

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KEYWORDS

• Fibrocystic breast disease adenoma • Pleomorphic adenomyoepithelioma carcinoma
• Adenoid cystic spherulosis • Adenomyoepithelial adenosis

ABSTRACT

Epithelial-myoepithelial proliferations of the breast are a heterogeneous poorly defined group of lesions characterized morphologically by dual differentiation into ductal (luminal) and myoepithelial cells. They include neoplastic and non-neoplastic entities that have overlapping morphologic features that may give rise to diagnostic difficulty. Many of these entities are low grade or of uncertain malignant potential but the biology of some of these rare lesions remains to be elucidated. This article discusses the differential diagnosis of epithelial-myoepithelial lesions of the breast and highlights the morphologic features of some of these entities.

OVERVIEW

Epithelial-myoepithelial lesions of the breast (also known as adenomyoepithelial lesions of breast) comprise a heterogeneous group of entities, some of which are rare. Their clinical behavior shows a spectrum ranging from benign through borderline to malignant. Currently, no unifying classification system exists and precise definitions of some of the various nosologic entities are lacking. Problems with existing classifications include overlapping morphologic features between hyperplastic and neoplastic disorders, diverse morphology within each diagnostic category, description of the same entity under different names in the literature, and poor clinical follow-up data available due to the rarity of many of these lesions. The current World Health Organization (WHO) classification of breast tumors lists most of these lesions as "epithelial-myoepithelial" lesions,[1] with myoepithelial carcinoma also included in the category of metaplastic carcinoma. This review discusses the differential diagnosis of epithelial-myoepithelial lesions of the breast (**Box 1**), excluding lesions composed exclusively of cells of myoepithelial lineage. Because even normal breast tissue is composed of both epithelial and myoepithelial cells, and so too are many of the common well-defined benign proliferative entities familiar to most pathologists (papilloma, fibrocystic changes, fibroadenoma, tubular adenoma [TA], and so forth), these processes are excluded from this review.

ADENOSIS AND ADENOMYOEPITHELIAL ADENOSIS

OVERVIEW

Adenosis of common, or usual, type is a localized exaggerated synchronous hyperplasia of both ductal luminal cells and myoepithelial cells out of step with the surrounding breast tissue. It affects a wide age range but is more common after the fourth decade. Adenosis of usual type is seen as an incidental finding in the context of fibrocystic changes, sclerosing adenosis, and adenosis nodules (ANs) and within papillomas and fibroadenomas.

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Box 1
Differential diagnosis of epithelial-myoepithelial lesions of the breast

Benign

- Adenosis of usual type and variants
  - Sclerosing adenosis
  - Atypical apocrine adenosis
  - Blunt duct adenosis
  - Tubular adenosis
  - AMEA
- AN or tumor
- Collagenous spherulosis (CS)

Low malignant potential

- Adenomyoepithelioma (AME)
- Pleomorphic adenoma (PA)
- Adenoid cystic carcinoma (ACC)

Malignant

- AME with malignant progression
  - Myoepithelial malignancy: epithelioid, sarcomatoid, carcinosarcoma-like
  - Epithelial malignancy: carcinoma, sarcomatoid carcinoma, carcinosarcoma-like
  - Combined epithelial and myoepithelial malignancy
- PA with malignant progression
  - Carcinoma ex PA
  - Myoepithelial carcinoma ex PA
  - True malignant mixed tumor (dual-lineage malignancy)
- ACC—solid basaloid poorly differentiated type

Thus, it presents clinically as mammographically detected calcifications, increased stromal density, or a mass detected on imaging studies or by palpation. The authors regard this usual type of adenosis as part of the spectrum of fibrocystic changes rather than as a specific entity. Other specific variants of adenosis are listed in **Box 1**. A full discussion of all of these variants is outside the scope of this review. This discussion focuses on a distinct rare subtype of adenosis, termed *AMEA*, that is reported to occur in association with AME,[2–6] but whether or not it is a hyperplastic or neoplastic disorder, a precursor lesion for AME, or a variant of tubular AME is unclear. Unfortunately, there is little attention paid to AMEA in the current WHO classification of breast tumors.[1]

GROSS FEATURES

No specific gross features have been described because AMEA is usually an incidental microscopic finding. Occasionally, it presents as a localized focus of thickening, a nodular or multinodular mass lesion. AMEA usually presents along with a gross nodule of AME but a single case of AMEA presented as an irregular spiculated mass on mammography.[7]

MICROSCOPIC FEATURES

Adenosis of usual type is encountered commonly in breasts containing fibrocystic changes and sclerosing adenosis and goes largely unnoticed in routine pathology. The morphology of usual-type adenosis is well known and is not discussed further. The distinct entity of AMEA is characterized by a proliferation of tubular glands along with myoepithelial hyperplasia sometimes forming multiple layers around the tubule (**Fig. 1**). A thick basal lamina is constantly present. The luminal epithelial cells may have apocrine features acquiring abundant eosinophilic granular cytoplasm often associated with apical cytoplasmic blebs.[4] The myoepithelial cells are often enlarged, have abundant clear cytoplasm, and encircle the crowded tubular acini. The high-power features closely resemble those of the well-differentiated epithelial-myoepithelial carcinoma of salivary gland or the tubular variant of AME of the breast. At low magnification, however, the lesion lacks the mass effect of AME. Nevertheless, some cases are associated with an adjacent AME, suggesting that AMEA is either a variant growth pattern of AME or a precursor lesion.

Immunohistochemical staining of AMEA highlights the dual epithelial and myoepithelial composition. The luminal ductal epithelial component stains for low molecular weight keratins, Cam

Key Features
ADENOMYOEPITHELIAL ADENOSIS

- AMEA is an incidental microscopic finding usually occurring in association with AME.
- There is a prominent layer of myoepithelial cells with clear cytoplasm.
- Thick basement membranes are a key feature of AMEA.
- Apocrine differentiation of the luminal cells is typical.
- AMEA may be the precursor lesion of AME.