

An Update of Mucinous Lesions of the Breast

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KEYWORDS

• Breast • Mucinous carcinoma • Mucocele-like lesion • Solid papillary carcinoma

Key points

- A diverse group of entities in the breast are associated with extracellular mucin production.
- The most important differential diagnosis is between mass-forming mucocelelike lesions and mucinous carcinoma.
- Mucocelelike lesions may be associated with benign proliferative and nonproliferative changes, atypia, and neoplasia, and inadequate sampling at biopsy is a concern.
- Mucinous carcinoma may be pure or mixed with other histologic subtypes and in its pure form is associated with a good prognosis.
- Solid papillary carcinoma often exhibits neuroendocrine and mucinous features and in some cases, may be a precursor to mucinous carcinoma.

ABSTRACT

Mucinous lesions of the breast include a variety of benign and malignant epithelial processes that display intracytoplasmic or extracellular mucin, including mucocelelike lesions, mucinous carcinoma, solid papillary carcinoma, and other rare subtypes of mucin-producing carcinoma. The most important diagnostic challenge is the finding of free-floating or stromal mucin accumulations for which the significance depends on the clinical, radiologic, and pathologic context. This article emphasizes the differential diagnosis between mucocelelike lesions and mucinous carcinoma, with a brief consideration of potential mimics, such as biphasic and mesenchymal lesions with myxoid stroma (“stromal mucin”) and foreign material.

OVERVIEW

Mucins are a family of high molecular weight, heavily glycosylated proteins that are classified

into 2 groups: membrane-bound mucins (eg, MUC1, MUC3, and MUC4) involved in signal transduction and gel-forming secreted mucins released into the extracellular space (eg, MUC2, MUC5AC, MUC5B and MUC6).¹ At least 18 mucin genes have been cloned to date.² The classic mucin genes are primarily expressed by epithelial cells.³ A membrane-bound mucin, MUC1, is found at the apical surface of most normal breast epithelium, whereas its polarity is lost and its expression increased in neoplastic epithelium.⁴ Secreted mucins are produced by various benign and malignant lesions of the breast. Mucinous carcinoma characteristically produces MUC2 (gel-forming intestinal-type secretory mucin) and MUC6 (pyloric gland-type secretory mucin), a finding uncommon in other mammary adenocarcinomas.¹ Secreted mucins are neutral or acidic and the chemical composition determines reactivity on special stains, such as periodic acid-Schiff, Alcian blue, and mucicarmine.^{5,6}

In the older literature, proteoglycan-rich extracellular matrix secreted by connective tissue cells was referred to as “connective tissue mucin” or

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“stromal mucin,” but this is a misnomer, as there are biochemical differences between the 2 families of glycoproteins. Nevertheless, prominent “myxoid” stromal change is morphologically similar to extracellular mucin on a macroscopic and microscopic level, related in large part to the hydrophilic, gel-forming properties of proteoglycans.⁶


This review is focused on mammary epithelial lesions with extracellular mucin production, especially mucocelelike lesions (MLLs) and mucinous carcinoma, with a brief consideration of biphasic and mesenchymal lesions with myxoid stroma and other mucin mimics as they relate to the differential diagnosis.

MUCOCELELIKE LESIONS



Key Points
MUCOCELELIKE LESIONS

- MLLs consist of ruptured mucinous cysts and extravasated mucin.
- The cysts may be lined by flat-to-columnar epithelium or involved by usual, atypical or neoplastic epithelial proliferations. Large, granular calcifications are often present within the mucin.
- Mucinous carcinoma is the most important consideration in the differential diagnosis of an MLL, especially if the lesion is associated with intraductal neoplasia, abundant stromal mucin, and/or floating epithelium.
- MLLs without evidence of atypia on core needle biopsy have a rate of upgrade to malignancy on excision of less than 5%.
- Excision has been traditionally recommended; however, conservative management may be possible in selected incidental or small benign lesions.



Pitfalls
MUCOCELELIKE LESIONS

! The presence of strips or clusters of epithelium floating within the mucin of an MLL involved by atypical ductal hyperplasia or ductal carcinoma in situ may raise consideration for mucinous carcinoma. Epithelial displacement is favored if the floating epithelium is scant, associated with myoepithelial cells, or contiguous with the cyst lining.

MLL was first described by Rosen⁷ in 1986 as a benign lesion analogous to mucocele of the minor salivary glands. Rosen⁷ defined this lesion as benign mucin-filled cysts lined by flat or cuboidal epithelium frequently associated with rupture and mucin extravasation. It is now appreciated that MLLs arise in the setting of various pathologic processes, including benign proliferative and nonproliferative changes, atypical ductal hyperplasia (ADH), and in situ or invasive carcinoma. The biology of the lesions depends on the nature of the lining epithelium, which may be hyperplastic, atypical, or neoplastic.^{8,9} Therefore, “mucocelelike lesion” is best considered a descriptive term, insufficient on its own as a diagnosis without further classification of the underlying process.

GROSS FEATURES

An MLL may present as a palpable breast mass, a mammographic abnormality, or an incidental finding. The most common presentation is indeterminate microcalcifications on screening mammography.^{10–12} The microcalcifications are typically described as clustered and pleomorphic, but also may be coarse and eggshell-shaped or fine and linear or granular. If a mass lesion is present, it is usually a single round or lobulated mass with circumscribed or indistinct borders or possibly multiple masses with a “rosarylike” appearance.¹¹

Grossly, there may be well-defined multiloculated cystic nodules or ill-defined shiny areas with a gelatinous cut surface. Yellow flecks or gritty texture are found in lesions with prominent calcifications. Most lesions measure between 0.5 and 1.0 cm.⁸

MICROSCOPIC FEATURES

MLLs consist of cysts with mucinous contents and extravasated mucin within the surrounding stroma. In benign lesions, the cysts are lined by attenuated, flat-to-cuboidal epithelium (**Figs. 1 and 2**). With rupture, strips of epithelium detach from the cyst wall and float within the mucin. Mucin collects as pools within the stroma. Large, granular calcifications are often present within the mucin and are characteristic (**Figs. 3 and 4**). Some lesions are associated with chronic inflammation and stromal fibrosis (see **Fig. 2**). The epithelium commonly exhibits areas of columnar cell change or proliferative change ranging from usual ductal hyperplasia to ADH (see **Fig. 2; Figs. 5–9**).

MLLs may be associated with neoplastic proliferations that warrant a diagnosis of in situ or invasive carcinoma. Ductal carcinoma in situ (DCIS)

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