Collagenous spherulosis, classic and mucinous/degenerative types with associated microcalcifications and underlying mass/density

Collagenous spherulosis is an uncommon benign change (occurs in less than 1-2% of all biopsies) typically associated with the other benign proliferative lesions (papilloma, sclerosing adenosis, radial sclerosing lesion, adenomyoepithelioma, florid ductal hyperplasia, etc.) and characterized by presence of intraluminal spherules (Am J Surg Pathol 1987;11:411, J Clin Pathol 2004;57:83). Several more recent studies describe association with in situ ductal and lobular neoplasms (Pathologica 2002;94:317, Am J Surg Pathol 1995;19:1366, Am J Surg Pathol 2006;30:20). Carcinoma may be coincidentally present within the same specimen, and rarely may be involved by collagenous spherulosis; however, it has been suggested that if this should occur, these are most likely independent processes (Pathologica 1993;85:123, Pathologica 1994;86:234, Am J Surg Patho. 1995;19:1366, Pathologica 2002;94:317). To date no association with a neoplastic process has been firmly established and there is no evidence to indicate that collagenous spherulosis is a precancerous lesion. Collagenous spherulosis presents almost always as incidental finding, and is only rarely associated with palpable or mammographically detected mass or density. It usually is multifocal, forming small and not grossly visible lesions (1 to 3 mm in size). The other most commonly used names are adenoid cystic hyperplasia and mucinous spherulosis. On histologic examination, intraluminal clusters of eosinophilic or rarely basophilic (“mucinous spherulosis”), collagen rich spherules within spaces, surrounded by flattened myoepithelial cells are present. The spherules consist of basement membrane material and can calcify (25% of
cases of collagenous spherulosis had associated calcifications in our study) (Am J Surg Pathol 2006;30:20). Associated calcifications may lead to more frequent identification of collagenous spherulosis by mammography (Rosen’s Breast pathology, p. 130, Am J Surg Pathol 2006;30:20). The stimulus for spherule formation is still unclear but association with radial scars and fibrotic lesions suggests that localized pattern of fibrosis may serve as prompting environment. Collagenous spherulosis may be encountered in cytology specimens, especially in association with intraductal papillomas and benign proliferative lesions, where it presents as hyaline pink globules surrounded by benign myoepithelial cells in Giemsa stained smears associated with proliferative epithelium (Cytopathology 2002;13:116). Mucinous spherulosis may appear as cribriform structures with lightly basophilic material embedded in loosely mucinous acellular background and spherules are intermediate to large and are either naked or surrounded by rare myoepithelial cells. Diff-Quik stain shows fibrillary radial appearance (Diagn Cytopathol 2006;34:626). Upon re-review of referral material, collagenous spherulosis may go unrecognized in about 48% of cases; however, it could also be misdiagnosed as atypical in 17% of cases, or in situ and/or invasive carcinoma in an additional 11% of cases (Arch Pathol Lab Med. 1995;123:626). Myoepithelial cells surrounding collagenous spherules stains for smooth muscle actin, smooth muscle myosin heavy chain, p63 and calponin but no immunoreactivity is noted by c-kit/CD117, which is typically positive in cells in adenoid cystic carcinoma. The main differential diagnosis and pitfall is adenoid cystic carcinoma (Pathol Int 2004;54:332, Modern Pathol 2006;19:1351, J Cytol 2010;27:69). In adenoid carcinoma denser and tightly nodular material is rarely degenerated; and adenoid cystic carcinoma shows more obvious stromal invasion and forms mass. Luminal cells are
frequently positive for CD117+ and calponin and smooth muscle actin are typically negative, although occasionally adenoid cystic carcinoma may have associated collagenous spherulosis-like structures in some parts of tumor. Another less common pitfall is cribriform DCIS, which forms multiple secondary lumens with round, regular spaces having sharp borders that appear to be made from “cookie-cutters” but no amorphous pink material is present within these lumens. We encountered in our study a relatively high number of an erroneous interpretation of collagenous spherulosis associated with lobular neoplasm (4/15 of our cases) as cribriform DCIS. Pathologists must remain vigilant to this form of mimicry, because classification of in situ carcinoma of the breast carries important clinical implications for patient management, especially if diagnosed on core needle biopsy. LCIS involving collagenous spherulosis can be morphologically distinguished from DCIS by careful evaluation of the nature of the cells forming the spaces, the contents of lumens, and the cohesive properties of atypical cells. Moreover, in LCIS involving collagenous spherulosis, the atypical lobular cells do not directly abut spaces that contain spherules; instead a layer of myoepithelial cells intervenes. E-Cadherin immunostaining and myoepithelial markers could be also utilized in equivocal cases (Am J Surg Pathol 2006;30:20). Collagenous spherulosis in its simple form requires no treatment, but treatment may be necessary if it is associated with malignancy.