

A Rare Case Report of Collagenous Spherulosis of Breast Diagnosed on Cytology

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Received: 01-12-2025 / Revised: 15-01-2026 / Accepted: 21-02-2026

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Conflict of interest: Nil

Abstract:

Collagenous spherulosis is an uncommon incidental finding characterized by collagen-rich spherules composed of basement membrane material. It is often associated with other benign breast lesions such as fibroadenoma, papilloma, sclerosing adenosis, radial sclerosing lesion, adenomyoepithelioma, and florid ductal hyperplasia. In cytological material, the estimated incidence of this benign condition is only approximately 0.2%. It is essential to distinguish collagenous spherulosis from atypical proliferations and malignant mimics, particularly adenoid cystic carcinoma, to prevent unnecessary therapy. Here, we present a concise review of the literature and discuss the cytological findings of a case of collagenous spherulosis that is associated with benign proliferative breast disease.

Keywords: Collagenous Spherulosis, Mucinous Spherulosis, Adenoid Cystic Hyperplasia.

DOI: 10.25258/ijcpr.18.3.158

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Introduction

Collagenous spherulosis of breast was first defined by Clement et al in 1987. [1] It is usually linked with other benign proliferative tumors of the breast. Although they are neither precancerous nor linked with malignancy, carcinoma may be coincidental within the same specimen. Almost commonly seen as incidental finding in women in third to fifth decade of life, collagenous spherulosis is not usually associated with palpable or mammographically detected mass or density. The English literature has a very limited number of reports that discuss the cytological characteristics of collagenous spherulosis. [2-4] Here, we report a case of collagenous spherulosis in a 28 year old female diagnosed on fine-needle aspiration cytology (FNAC) and discuss the cytomorphological findings.

Case Report

A 28 year old female presented with a history of painless lump in the right breast for 3 months. On examination, a diffuse nodular firm, non-tender, immobile swelling measuring approximately 1 x 0.5 cm was palpated at 9 o' clock position in the right breast. It was not attached to the overlying

skin. There was no significant menstrual and obstetric history. USG of right breast revealed a round to oval anechoic lesion measuring 10 x 6 mm with diffuse internal echoes seen at 9 o' clock position. A clinical diagnosis of galactocele/oil cyst was made. FNAC was done using a 22G needle and 20 ml syringe. Air-dried smears were stained using May-Grünwald-Giemsa (MGG) stain, while ethanol-fixed smears were stained with Papanicolaou stain. Smears examined showed moderate cellularity comprising benign ductal epithelial cells arranged in groups, papillaroid fragments and sheets admixed with spherical acellular homogenous hyaline globules in a background of few bare bipolar nuclei, lipoproteinaceous material and RBCs. The Periodic Acid Schiff (PAS) stain demonstrated significant positivity for these globules. No strongly birefringent material was observed while examining the foci with polarized light, which suggests the absence of calcium oxalate. Cytomorphological features were suggestive of a benign mammary lesion with collagenous spherulosis, which was later on confirmed on biopsy.

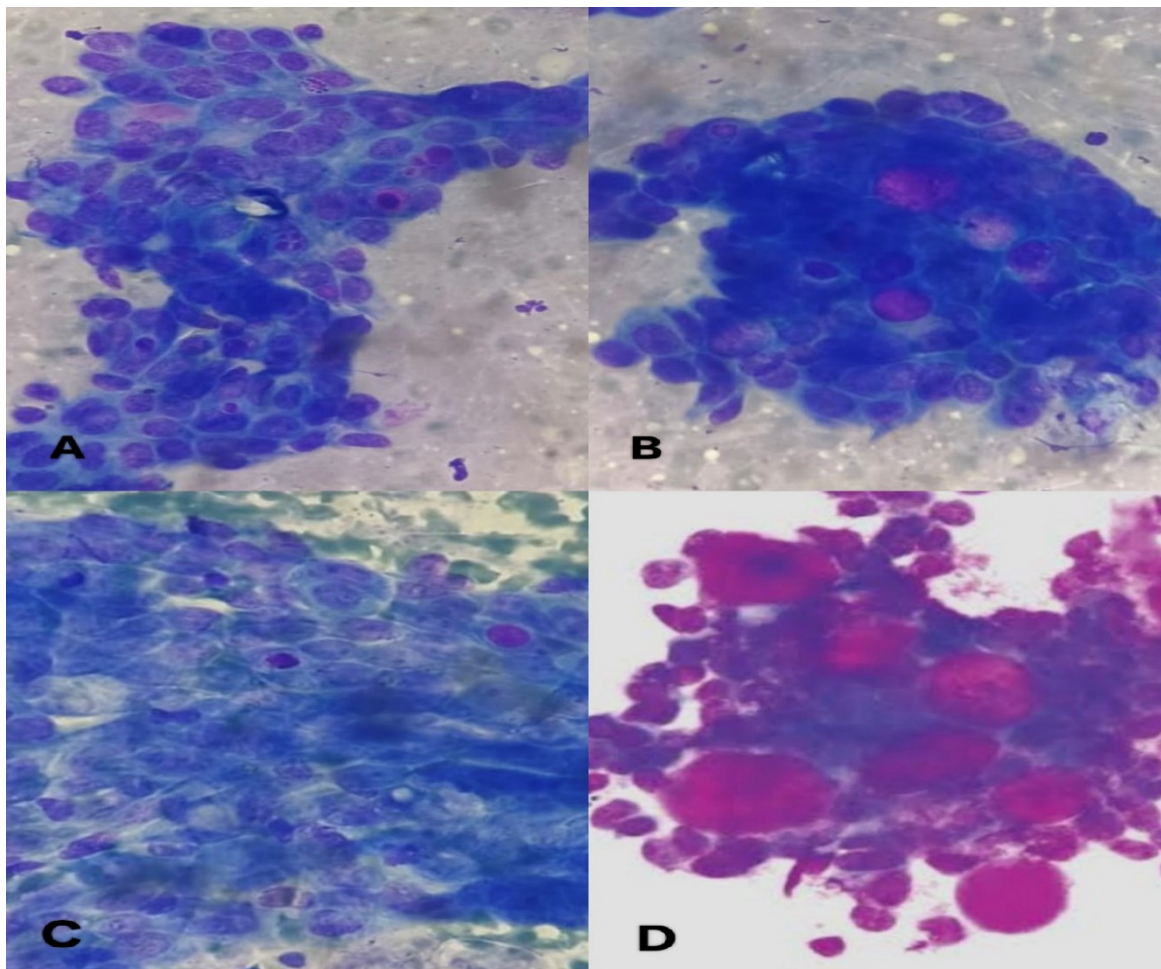


Figure 1 (A,B,C): Moderately cellular smear, comprising of tight cohesive groups, papillaroid fragments and monolayered sheets of benign ductal epithelial cells intimately mixed with many spherical, acellular homogeneous, eosinophilic hyaline globules (Leishman 100x,400x). (D): Periodic acid Schiff stain showed strong positivity for these globules (PAS 400x)

Discussion

Collagenous spherulosis (CS) of the breast is an uncommon benign lesion, with an incidence reported at less than 1% in excisional specimens and approximately 0.2% in cytology samples. [2,5] The reported cases are limited due to insufficient awareness of this entity among cytopathologists and the limited amount of diagnostic cells and spherules in the aspirated material. [5] It is often discovered incidentally, although it may occasionally present as a palpable breast mass. [6] In the present case, it manifested as a palpable mass.

It has been associated with several benign and malignant lesions, including fibroadenoma, atypical ductal papilloma, sclerosing adenosis, radial scar, ductal carcinoma in situ, lobular carcinoma in situ. [1,5] While carcinoma may be present incidentally, there is no evidence to suggest that it is a precancerous lesion. It is more usually seen in ducts than in lobules. [1,7] Due to the structural

similarities to the breast, CS has been observed in cutaneous myo-epithelial tumors such as chondroid syringoma and the salivary gland.

On cytology, spherules in MGG stain appear magenta; light pink in H and E; light green in PAP stain; their size range from 20 to 200 micrometer. Crescentic myoepithelial cells or clusters of epithelial cells surround these spherules. Diff-quick stain can reveal fibrillary quality in spherules organized in star or laminar concentric patterns. [1]

Eventually some of the spherules calcify and show up on mammography as microcalcifications. [2] Degenerative alterations could take place in spherules giving myxoid appearance. Histologic examination reveals eosinophilic or basophilic ("mucinous spherulosis") collagen-rich spherules within spaces, surrounded by flattened myoepithelial cells. Collagen spherules are stromal reactions made up of proteoglycans found in the basement membrane, including heparan sulfate, laminin, and fibronectin. They stain blue with

trichrome, pinkish red with Van Gieson, black with reticulin, and varying degrees of positive with PAS and alcian blue. Immunohistochemical (IHC) and ultrastructural studies demonstrate that these structures arise from the proliferation of myoepithelial cells and exhibit positivity for cytokeratin, S-100 protein, actin, calponin, p63, and smooth muscle myosin. [8,9]

It is important to differentiate it from malignant lesions such as adenoid cystic carcinoma (ACC) of the breast, as well as adenoid cystic hyperplasia and intraductal signet-ring carcinoma. Adenoid cystic carcinoma predominantly occurs in older women, exhibits pronounced stromal invasion, and manifests as a mass. Cytological examination reveals syncytial, multilayered, branching clusters of cells characterized by a high nuclear/cytoplasmic ratio, nuclear overcrowding, overlapping, anisonucleosis, slightly hyperchromatic nuclei, and small nucleoli. Bipolar bare nuclei are not present, and the spherules are encircled by multiple layers of cells. [10] The absence of these features in our case supports the diagnosis of collagenous spherulosis.

In challenging cases, recommending an open biopsy is advisable for accurate diagnosis. ACC demonstrates PAS-positive material within duct-like structures and Alcian blue-positive material within the pseudocyst. In CS, there is variable positivity observed for both stains.

IHC effectively differentiates these entities, as smooth muscle myosin heavy chain and calponin are consistently and strongly positive in CS, while being negative in ACC. C-kit (CD117) serves as a sensitive marker for adenoid cystic carcinoma, while it is not expressed in collagenous spherulosis. [11] Another less common pitfall is cribriform DCIS, characterized by the formation of multiple secondary lumens with round, regular spaces that exhibit sharp borders resembling those created by "cookie-cutters." Notably, no amorphous pink material is present within these lumens.

Review of referral data reveals that CS may go undetectable in around 48% of instances; alternatively, it may be misdiagnosed as atypical in 17% of cases or as in situ and/or invasive cancer in an additional 11% of cases. [12]

Pathologists have to be aware of this type of mimicry since patient therapy depends much on the classification of in situ/invasive cancer. Simple form of collagenous spherulosis calls for no therapy; nevertheless, if it is associated with cancer, treatment may be required.

Conclusion

Cytopathologists can identify collagenous spherulosis, a benign lesion, through meticulous analysis of cellular morphology. Being aware of

this entity helps the pathologist avoid misinterpretation of it as Adenoid cystic carcinoma (ACC) of breast. In challenging cases, biopsy and immunohistochemistry is indicated to distinguish it from ACC. A correlation between imaging modalities and clinical features is advised along with close follow-up.

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