COLLAGENOUS SPHERULES OF THE BREAST: A DIAGNOSTIC ENIGMA

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ABSTRACT

INTRODUCTION

Collagenous spherule (CS) is an enigmatic finding in a breast lesion involving the lobular acini and ductules and is defined with the presence of eosinophilic intraluminal collagen rich spherules measuring 20-100 microns in diameter, surrounded by flattened myoepithelial cells.[1] It is an uncommon incidental finding in less than 1-2% of biopsies associated with various benign and malignant diseases occurring in isolation or multifocally.[2] A major growing concern surrounding collagenous spherules is that it might be misinterpreted as atypical ductal hyperplasia (ADH), cribriform ductal carcinoma in situ (DCIS), cribriform carcinoma or adenoid cystic carcinoma of breast.

We present a case of mobile cystic mass of the breast reported as fibrocystic disease of the breast with focal areas showing adenosis and hyperplastic changes with multiple ducts displayed a peculiar change with the presence of extracellular concentric hyaline material present within the intraluminal space, diagnostic of collagenous spherules.

KEYWORDS

Collagenous, Spherules, Hyperplasia.

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INTRODUCTION: The term collagenous spherules are first reported by Clement et al in 1987, to describe this change within the lumina of breast acini and ductules.[3,4] It is a very rare finding, will typically develop in women between the ages of about 40 to 55, occurring in only 1%-2% of biopsies for hyperplastic breast lesions.[5] The presence of the multiple intraluminal spherules, surrounded by an epithelial and myoepithelial proliferation, gives the involved ducts a cribriform appearance. This can lead to a misdiagnosis of atypical ductal hyperplasia (ADH), cribriform ductal carcinoma in situ (DCIS), cribriform carcinoma or adenoid cystic carcinoma.[4] We report an unusual case of a multifocal collagenous spherulosis of the breast in association with proliferative breast disease posing a diagnostic enigma of cribriform DCIS in a 45-year-old woman.

CASE REPORT: A 45-year-old lady came to the surgical OPD with a lump in the right breast since 20 days. The lump was 5x3 cm, tender, mobile, and soft to firm in consistency in upper inner quadrant in right breast. FNAC was advised to confirm a diagnosis of fibroadenosis. Aspiration revealed 5 mL of clear fluid, which on centrifugation showed only sheets of histiocytes and neutrophils with scanty ductal epithelial cells. A diagnosis of cystic lesion of breast with infection was given and advised lumpectomy for further evaluation. Gross examination of the mass showed an irregular fibrofatty mass measuring 6x4x0.5 cm. Cut surface showed multiple cystic spaces, the largest measured 1.5x1.0 cm. Microscopy showed fibroadenomatoid changes with adenosis and epitheliosis, apocrine metaplasia, cystic spaces showing stratification and forming cribriform like pattern with eosinophilic concentric collagenous spherules in the centre. Duct ectasia with a collection of sheets of acute inflammatory cells and histiocytes are seen.

DISCUSSION: Collagenous spherules of the breast is a circumscribed spherule composed of epithelial and myoepithelial proliferation forming sieve like spaces almost filling the terminal ducts or acini. The theory based on ultrastructural observation is stromal invagination into cellular lobules. It is also characterised by presence of eosinophilic intraluminal collagen rich spherules measuring 20-100 microns in diameter, and demonstrates a concentric and radiating fibrillar patterns. The collagen deposition in a spherule is due to secretion of extracellular material by the proliferative myoepithelium which includes mucopolysaccharides and basement membrane materials.[1] Clement et al also showed that the hyaline material in the intra luminal space was rich in collagen. Some authors also called them as mucinous spherules.[3] But, Mooney et al., described both the lesions collagenous and mucinous spherulosis as related lesions. CS is considered as an end-stage lesion resulting from transformation of its predecessor, mucinous spherulosis of the early stages.[6] The use of various histological stains can determine that the spherules are rich in collagen, and will usually also show that the spherules contain varying amounts of acidic mucin, elastin, membrane-like materials, and PAS-positive proteins.[7]

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Breast collagenous spherulosis is originally described in the breast, but it is now reported in skin and salivary gland neoplasms. It is an incidental microscopic finding, which may occur in isolation or multifocally.[8] The present case had multifocal areas indicating the proliferation from multiple sites. It typically never presents as a mass but occurs in association with other benign and malignant breast diseases, which presents as a mass. The present case showed an infected irregular soft to firm, tender mass measuring 6x4x0.5 cm. (Fig 1) Collagenous spherulosis could present as a mammographically suspicious mass or density and could be associated with microcalcifications.[8] But the present case did not show any such microcalcific changes.

Fig. 1: Irregular Fibrofatty Mass Measuring 6x4x0.5 cm

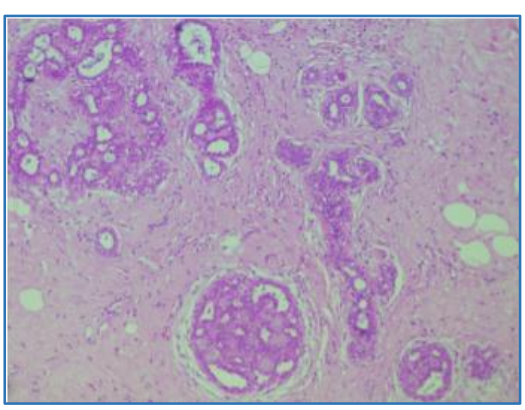

Fig. 2: Hyperplastic Changes with Multiple Foci of Collagenous Spherules (10X)

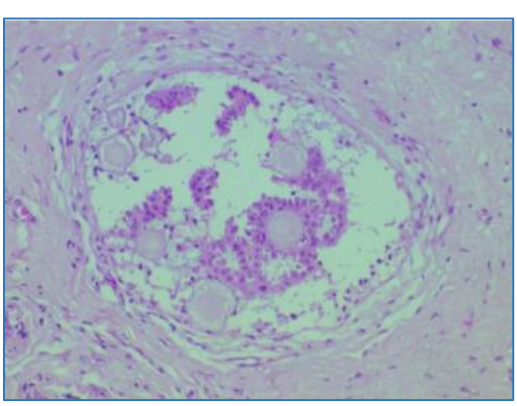

Fig. 3: Collagenous Spherules (40X)

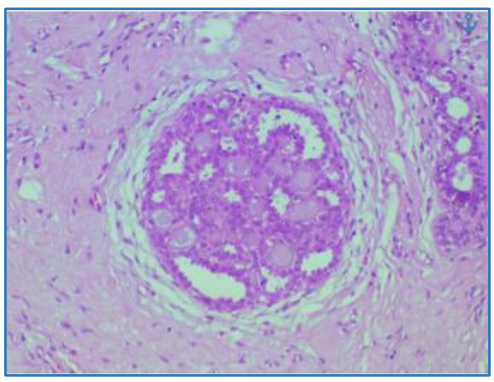

Fig. 4: Collagenous Spherules (40X)

The differential diagnosis of cribriform pattern poses quite a characteristic diagnostic challenge in a spectrum of benign and malignant proliferations in the breast. The term Cribriform was used in 1933 to describe the pattern of proliferation in ductal carcinoma in situ (DCIS). The term was derived from latin word "Cribrum" means sieve or pierced with holes.[9] Currently, the term is used to refer to the proliferation inside the ductules which is perforated by round spaces or fenestrations. In the breast, invasive cribriform carcinoma, cribriform ductal carcinoma, adenoid cystic carcinoma and collagenous spherules all can present with sieve like architecture on low power examination. Careful examination on high power and immunohistochemistry is mandatory for the diagnosis in difficult cases.

In cribriform pattern of adenoid cystic carcinoma, the cribriform spaces are formed by myoepithelial tumour cell proliferation and are often filled with eosinophilic or basophilic like material. If these pseudo glandular spaces are prominent due to abundant basement membrane lesions, it could be mistaken for collagenous spherules. In CS, eosinophilic collagen typically forms a ring like structure encompassing basement membrane material or less commonly basophilic mucinous material. The present case typically presented with concentric laminated eosinophil like material in association with proliferation of ducts with no atypia, hence identification was not difficult. The diagnosis becomes difficult when it is associated with lobular neoplasia or ductal hyperplasia. Immunohistochemical markers like c-Kit, calponin, smooth muscle actin can be used to differentiate both the entities.[9]

Similarly, DCIS cribriform may have intraluminal mucin, but lacks fibrillar or laminated appearance, myoepithelial component restricted to peripheral layer of duct and nuclei slightly enlarged compared to normal.[10] Also, the often 'radiating' appearance of collagenous spherulosis cells differ in appearance from the disorganised appearance, cellular debris, and flocculent mucin found in many in situ breast cancers.[9]

The possible mechanism involving the formation of collagenous spherules is by collision of a hyperplastic lesion (epitheliosis) inside the ductules, and its association with malignancy warns the pathologists not to assume it as benign process. Cardesi et all reported collagenous spherulosis might be associated with lobular breast

carcinoma around 20%-25% of the time, and with atypical ductal hyperplasia in less than 1% of cases.[9] Stephenson TJ et al described two cases of collagenous spherules with invasive carcinomas of unusual histological types, one with intracystic papillary carcinoma, one with comedo ductal carcinoma in situ and one with atypical ductal hyperplasia.[11] Since atypical hyperplasia in the breast is considered predictive of relatively high risk of later carcinoma development, the finding of collagenous spherulosis with atypical hyperplasia should suggest a long term followup.[12]

CONCLUSION: Collagenous spherules presenting as palpable masses in association with hyperplastic lesion in a fibrocystic disease, caused a diagnostic enigma, of whether its presence is related to a precancerous lesion. A long term followup is recommended in this study as it showed proliferation from both the layers of ducts. Only further more studies on series of patients need to be done to prove the prognostic value and significance. But they definitely create a diagnostic enigma as they mimic many malignant lesions which need to be differentiated on the basis of histopathology and IHC.

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