# Morphological Continuum of mucocele like tumor with its Diagnostic Dilemmas – A Case Report with Cytohistological Correlation

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**ABSTRACT**

**Introduction:** A Mucocele-like tumor is a rare breast lesion, characterized by mucin-filled cysts and extravasated mucin present in the adjacent stroma. First described by Rosen as a benign entity, it is now considered as a continuum of different pathological lesions, ranging from benign ductal hyperplasias , atypical ductal hyperplasia , ductal carcinoma in situ and mucinous carcinomas. **Case presentation:** We describe a case of Mucocele like tumor of the breast showing a morphologic and biologic continuum between a benign and malignant mucocele like tumor in a 60 year old female. This patient presented with a lump breast , in the upper outer quadrant, with ill defined margins. The lump was suspected clinicoradiologically as malignant. Fine needle aspiration cytology was suspicious of colloid carcinoma, however subsequent mastectomy showed Mucocele like tumor with spectrum of pathological lesions. **Conclusion:** This case is being presented for its rarity and is the first case being reported from India.

**Keywords:** Continuum, Mucocele like tumor, Mucinous carcinoma

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Conflict of interest**: None**

## INTRODUCTION

A Mucocele-like tumor (MLT) is a rare breast lesion, characterized by mucin-filled cysts lined by flat or low cuboidal lining epithelium with and without extravasated mucin in the adjacent stroma. [1,2,3] First described by Rosen in 1986 as a benign entity,[4] is now considered as a spectrum of various associated pathologic lesions, including benign tumor, ductal hyperplasias, ductal carcinoma in situ (DCIS), and mucinous carcinomas. [1,3,4,5]

The terms " mucocele like tumors '' and " mucocele like lesions '' are synonymous and can be classified as benign and malignant depending upon their association with carcinoma.[3] This is the first case being reported from India.

A 60 year old female, without family history of breast cancer , presented with a palpable lump in upper outer quadrant of right breast. Breast physical examination showed a 2.5 cm lump with ill defined margins, covered by normal skin, along with retracted nipple. Axillary and supraclavicular nodes were non-palpable.

A breast Ultrasonography showed an ill defined, heterogenous isoechoic, microlobulated round mass measuring 26 x 17mm at 12/1 'o' clock position; with indistinct margins along with randomly distributed cysts. Radiological aspect was not typical of a simple cyst, so the patient underwent a mamographic examination.

Mammography showed a asymmetrical increase in density with attenuated architectural distortion, along with retracted nipple with thickening of subareolar tissue. Multiple foci of round, rod like coarse calcifications were seen with few showing central lucency. It was reported as Grade IV on Breast Imaging Reporting and Data System (BI-RADS) scoring system. Fine needle aspiration biopsy yielded a thick mucoid aspirate. Smears of which showed moderate cellularity comprising of neoplastic cells arranged in loosely cohesive clusters, single files and few lying singly. Individual neoplastic cells showed nuclear enlargement with mild pleomorphism and moderate cytoplasm. Background showed wispy thick mucoid material with entangled neoplastic epithelial cells. A possible diagnosis of mucinous carcinoma was given.

A Core needle biopsy was subsequently performed, and was suspicious of carcinoma. Based on radiologic and pathologic results , a mastectomy was done.

Grossly the specimen showed no definite lump, however revealed multiple tiny aggregated cysts filled with mucoid material.

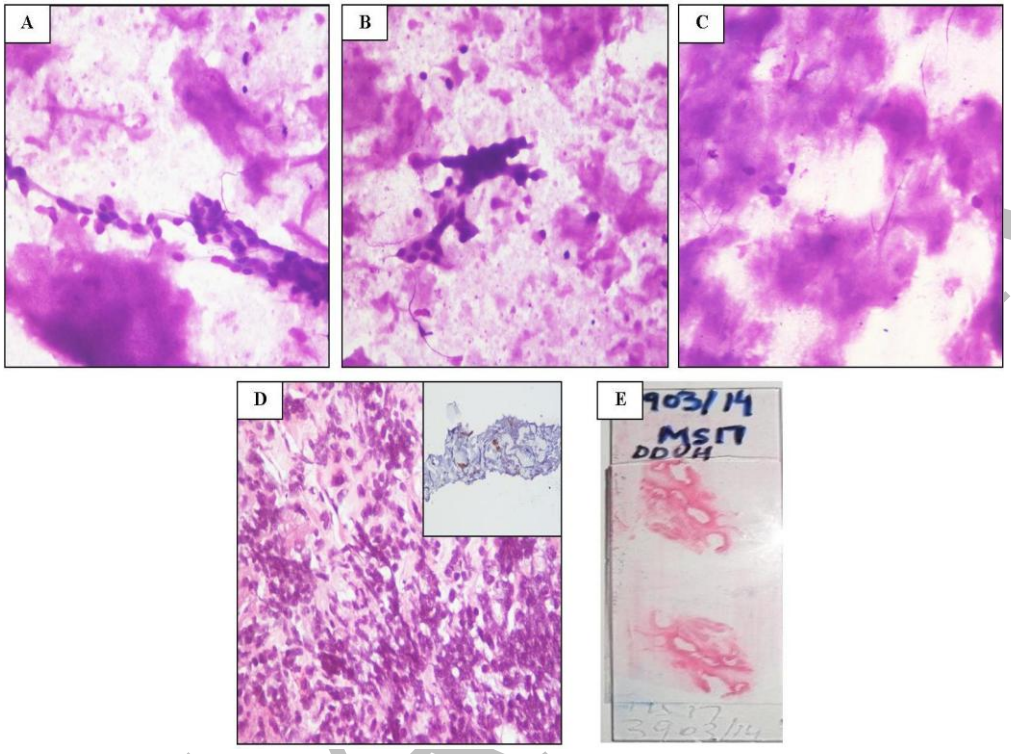


**Figure 1**

A, B ) FNAC showing loosely cohesive hyperchromatic cell clusters in a thick mucoid background. (Giemsa 40X)

C) Few hyperchromatic epithelial cells lying loosely in the mucin.( Giemsa 40X)

D) Trucut biopsy showing suspicious hyperchromatic cells. No mucin or dilated ducts identified.

( H&E 40X) Inset shows IHC of trucut biopsy with few cells showing Ki67 positivity.

E) Whole mount photograph shows cystic configuration of the lesion.( H&E )

Extensive dissection of breast specimen was done and sections from the grey white areas showed multiple foci cystically dilated ducts with inspissated secretions , at places spilled outside with foreign body giant cell reaction) along with associated flat atypical, intraductal micro papillary elements, columnar cell hyperplasia , lobular hyperplasia , cribriform hyperplasia, atypical ductal hyperplasia, and micropapillary DCIS. Numerous foci of collections and interspersed lymphocytes admixed with histiocytes and giant cells were present. Very few detached hyperchromatic epithelial cells were seen lying loosely in the extruded mucin. Intraluminal and extraluminal calcification was also noted.

The mucin in the cysts and surrounding stroma showed Alcian blue and focal Periodic acid Schiff (PAS) positivity. Immunohistochemical markers Ki 67( MMi, IgG1kappa, Mouse monoclonal biocare medical) calponin( CALP, IgG1kappa, mouse monoclonal, Dako) and smooth muscle actin (SMA) ( IA4, IgG2 kappa, Mouse monoclonal biocare medical) were used to distinguish between benign and suspicious areas. Lymph nodes resected showed non specific reactive lymphadenitis. The patient is kept on close follow up.

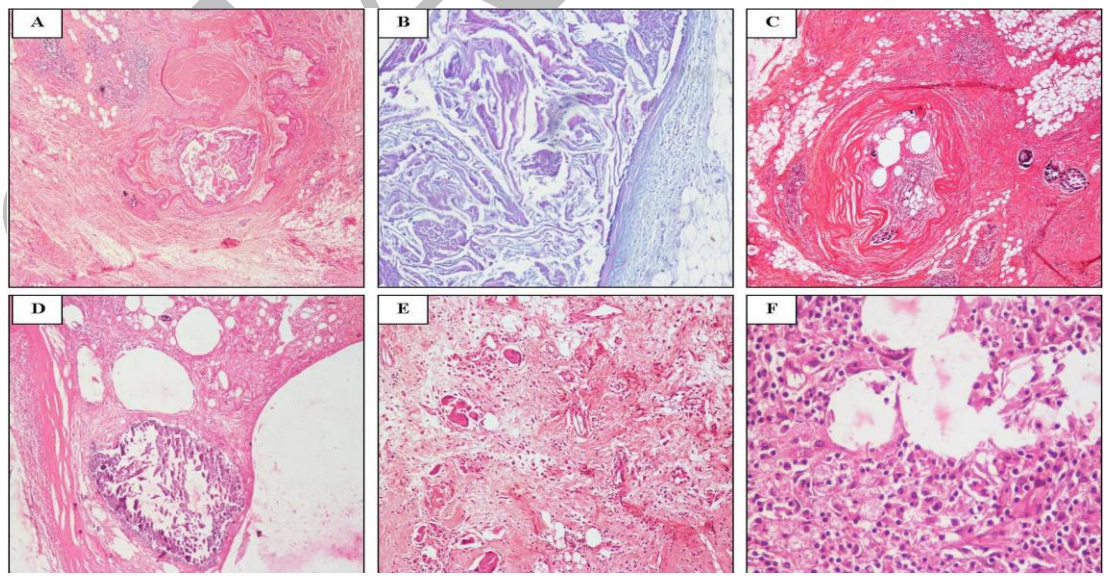

**Figure 2**

A) Histopathology showing MLT with dilated ducts filled with mucin along with extravasated mucin. Periphery of the ducts show lymphoid aggregates. ( H&E 4X)

B) Pas Alcian blue showing intra and extraluminal positivity. (40X)

C) MLT associated with intaductal and extraductal coarse calcifications.(H&E 4X)

D) Setions showing intracystic calcification. ( H&E 40X)

E) Surrounding breast parenchyma showing lymphocytes, histiocytes along with foreign body giant cell reaction in the extravasated mucin. ( H&E 40X)

F) High power view showing lymphocytic collection.(H&E 40X)

**DISCUSSION**

MLTs of the breast are described as benign lesions consisting of mucin filled cysts that have ruptured, discharging their secretions and epithelium into the surrounding breast stroma. It has been attributed to excess production of mucinous secretions or ductal obstruction, which may lead to ductal distention and to subsequent rupture with extravasation of mucin, possibly due to trauma. [2,3,5] Extravasated mucinous material into the stroma, is a typical feature of MLT. [6]

The size of MLT has been reported from incipient to 1.0cm, [2,7,8] with an occasional report of 2.0cms.[9] It usually presents as an asymptomatic/ non palpable lesion, with only 13 % having palpable masses.[5,8] The patient in the present study had a palpable lump measuring 2.5 cm , with ill defined margins, largest so far.

On screening mammogram they are seen as a nodule or as microcalcifications and based on its distribution and type, the nature of MLTs can be judged.( Table 1 ) Ultrasonographically(USG), it appears as a cluster of apparently complex cysts or hypoechoic tubular structures with no flow visualized on color doppler evaluation.[5] In this case USG and mammography pointed towards BIRAD-1V in presence of coarse

calcification along with complex cystic appearances.

MLTs may be accompanied by a spectrum of pathological findings ranging from benign to atypical to malignant. [1,2,7] Subsequent reports have shown an association with atypical hyperplasia and malignancy, and so is classified as benign or malignant depending upon their association with carcinoma. [1,3,5] ( Table 1 ) Benign lesions are associated with hyperplasias (columnar cell, usual type, with atypia ) and malignant lesions with DCIS and Mucinous carcinoma. [3,5]

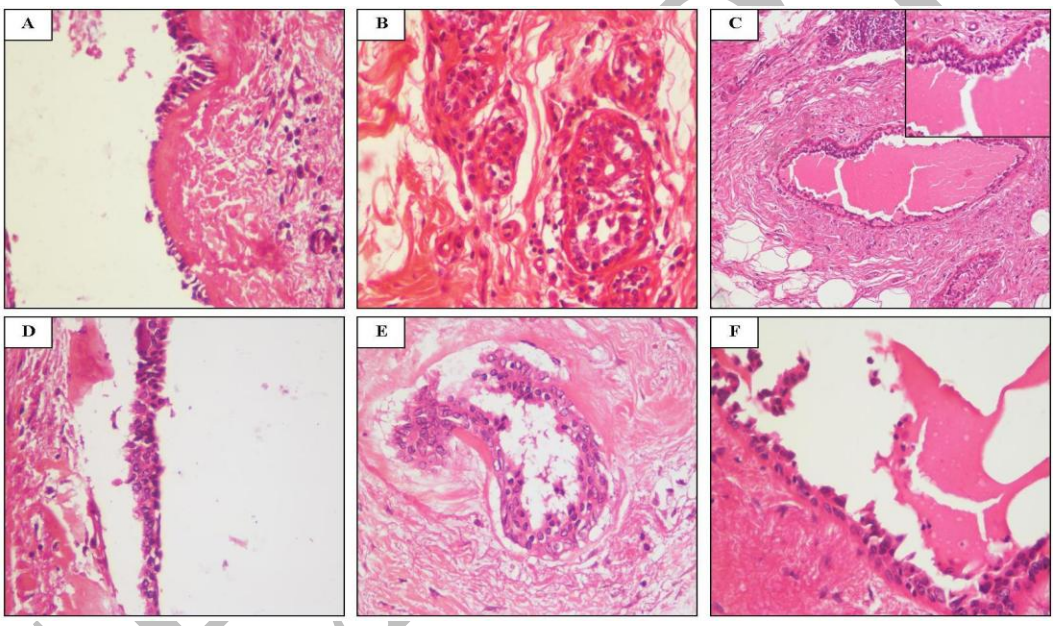


**Figure 3**

A) MLT showing a cyst lined by flattened to cuboidal to columnar lining within in a single duct presenting as a continuum. ( H&E 40X)

B) Sections showing areas with ductal hyperplasia without significant atypia. ( H&E 40X)

C) Areas showing duct filled with mucin along with columnar cell hyperplasia without atypia. (H&E 10X) Inset shows High power view of the same duct.

E) Intraductal hyperplasia with mild atypia. (H&E 40X)F) A continuum of columnar cell hyperplasia with atypia with micropapillary DCIS.(H&E 40X)

Table 1: Difference between Benign and Malignant MLTs [1,2,3,5]

| | BENIGN MLT | MALIGNANT MLT |
|---|---|---|
| **Presentation** | Usually asymptomatic, no mass | Palpable mass in majority |
| **Age, size and laterality** | No appreciable difference | No appreciable difference |
| **Mammmography appearances** | Clustered , pleomorphic calcifications with occasional lucent centered and coarse calcifications (46%). Narrow zone of extension ( 0.5-4cm ) | Segmental or diffuse, pleomorphic and coarse (71%) calcifications extending over a wide area ( 1-8.0cm ) |
| **Sonography** | Multiple cysts with calcified/non calcified nodules | Cysts with calcification |
| **Associated breast proliferations** | Hyperplasia – Columnar, Micropapillary, Usual type and typical | DCIS (including micropapillary type) and Mucinous carcinoma |

The gross pathologic findings have been described as multicystic or multiloculated lesions.[5] Grossly the specimen in our case showed no definite mass, however revealed multiple tiny aggregated cysts filled with mucoid material.

Histologically, MLT present as multiple cysts lined by flat to cuboidal to columnar lining epithelium, with a tendency to exhibit focal papillary hyperplasia and extravasation of mucin into the surrounding stroma. The lining epithelium is bland with rarity of epithelial cells in the mucin pool.

**Table 2:** Difference between MLTs and Mucinous Carcinoma on FNAC[12]

| | MLT | Mucinous Carcinoma |
|---|---|---|
| Type of aspirate | Mucoid | Mucoid |
| Cellularity | Scant | High |
| Microscopic appearance | No intact tumor cells, Rarely singly lying | Single intact cells |
| | Cohesive monolayered sheets | 3 dimensional clusters |
| | No significant atypia | Nuclear atypia |
| | Lining epithelium is bland | Mucin pools devoid of lining epithelium |
| | Epithelial cells rare in mucin pools | Numerous tumor cells in the mucin pools |
| Age of presentation | Young age group (average 34.8 years) | Older age group (average 67.8 years ) |

Malignant MLT shows associated in situ carcinoma and mucinous carcinoma with large pools of mucin devoid of lining epithelium and contains numerous tumor cells. Calcifications are often found within the mucin-containing cysts, surrounding stroma, or ductal epithelium lining the cysts, as seen in this patient. [2,5,7,10] Focal areas of columnar cell hyperplasia without atypia and micropapillary DCIS was also seen as noted by other workers.[1,6,11] Adjacent areas showed focal lobular hyperplasia, also seen in occasional studies. [7] There was also a continuum of benign to atypical to micropapillary DCIS in the same duct focally. Additional finding in our case was the presence of lymphocytes and histiocytes in the extravasated mucin, reported only in a single case study. [9]

Very few detached pleomorphic and hyperchromatic epithelial cells were seen lying loosely in intraductal mucin as well as

extruded mucin showing a focal Ki 67 positivity. This could be a focus of invasive/residual malignancy. However the areas with flattened epithelium, columnar and atypical ductal hyperplasias showed low proliferative index ( 1%).

SMA and calponin highlighted the ADH and intraductal micropapillary DCIS pattern. The DCIS with micropapillary configuration showed a downregulation of calponin/SMA in contrast with a clear upregultaion in benign areas.

In the present case FNAC was highly suspicious of mucinous carcinoma based on cytological criteria. [12] A trucut biopsy from the palpable lump showed scanty material with presence of few clusters of hyperchromatic cells, however no mucin or dilated ducts were identified.

The patient was subjected to modified radical mastectomy based on the highly suspicious radiological and cytological appearance. Total excision has been recommended by many workers in presence of MLT either on radiology or on core biopsy because of sampling phenomena, intralesional heterogeneity and coexistent atypia or malignancy.[3,7,13] Though in this case no residual frank invasive malignancy was observed on extensive dissection of the specimen, the presence of Ki 67 positivity within the lymphoid cells and few hyperchromatic cells could be a focus of residual malignancy.

Axillary nodal metastasis of mucocele-like tumor has not been reported. [5] The patient in our case also didn't present with any nodal metastasis.

Recurrences of mucocele-like tumor are rare but have been noted in the literature. A MLT with atypia, DCIS, or focal invasion is the more likely to recur, so warrants a close follow-up.

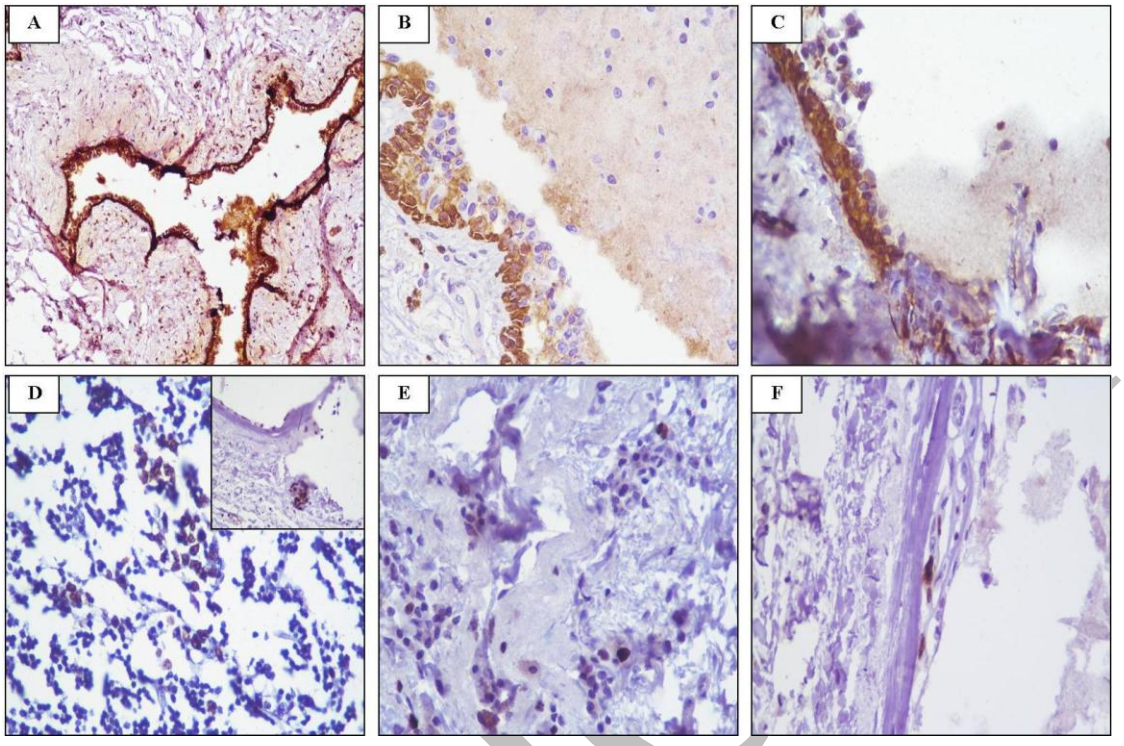


**Figure 4**

A) IHC showing positivity of calponin presenting as a benign spectrum. (40X)
B) IHC showing ductal columnar cell hyperplasia with downgrading of calponin in some atypical cells. (40X)
C) IHC showing loss of calponin in micropapillae with few loose hyperchromatic cells lying in within the intraductal mucin.( 40X)
D) Sections showing very few intraductal and extraductal hyperchromatic epithelial cells intermixed lying within the mucin with lymphoid cells showing Ki67 positivity .(40X) Inset shows proliferative marker Ki 67 positivity in a hyperchromatic epithelial cell cluster outside the duct, suspected as a focus of invasive/residual malignancy
E) Ki 67 positivity in few suspicious cells lying in the extravasated mucin. ( 40X)
F) Few intraductal cells showing Ki 67 positvity. (40X)

## CONCLUSION

This case is being presented because of its rarity, as a single breast lesion showing a morphologic continuum between benign and malignant MLTs, supporting the concept that MLTs encompasses a continuum of pathologic lesions including benign lesions, ADH, DCIS and mucinous carcinoma, coexisting within one lesion with MLT and mucinous carcinoma representing two ends of the spectrum. This is also the reason why total excision is advised in cases suggestive of benign MLT at FNAC to rule out any atypical or malignancy.

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