



Original Research Article

Pitfalls in cytological diagnosis of mucinous carcinomas of breast

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ARTICLE INFO

Article history:

Received 15-09-2020

Accepted 16-11-2020

Available online 20-02-2021

Keywords:

Carcinoma

Breast

Cytology

ABSTRACT

Introduction: Mucinous (colloid) carcinoma (MC) of the breast is relatively rare and accounts for 1-6% of all breast cancers. Traditionally, pure mucinous tumors and mixed infiltrating ductal carcinomas with a mucinous component have been described. Pure mucinous carcinoma of the breast has a favorable prognosis than the mixed variety noted in several studies. The common age of presentation is the postmenopausal group. Cytological diagnosis of these tumors is challenging.

Materials and Methods: A retrospective study was conducted at our institute. 22 cases consisting of both mixed and pure mucinous carcinomas diagnosed by cytology and verified on histopathology between January 2007 and November 2015 were included in the study. All cytology and histopathology slides were reviewed.

Results & Discussion: A total of 22 cases were evaluated. The age ranged from 34-78 years. The left breast was involved in 12 cases and the right breast in 10 cases. 19 cases were diagnosed as mucinous carcinoma on cytology. However 12 of these cases were reported as pure mucinous carcinoma on biopsy. All these cases displayed abundant mucin, small nuclei and/or regular nuclear outlines on cytology. 7 cases turned out to be mixed tumors on histopathology. Sparse mucin, large nuclei, irregular nuclear outlines or the presence of nucleoli were found in mixed mucinous carcinomas but not in pure tumors. Three cases were diagnosed as infiltrating ductal carcinoma (IDC) on cytology. One of these patients had 2 nodules, diagnosed on histopathological examination as IDC and mucinous carcinoma. Out of the other two cases, 1 case was diagnosed as cellular variant of mucinous carcinoma and another case as mixed carcinoma on biopsy. Cellular variant of mucinous carcinoma can mimic low grade ductal carcinoma on cytology. A thorough examination of the slides for mucinous material and few thin capillary fragments provide a valuable diagnostic clue.

Conclusion: The distinction between pure and mixed mucinous carcinoma is important, because patients with the former type have a much favorable prognosis, with a low propensity for lymph node and distant metastasis. Cytopathological identification of patients with pure mucinous carcinomas may be performed only in a limited number of cases. The various differential diagnosis should always be kept in mind while dealing with lesions associated with mucin. However the age of presentation, clinical features and radiological findings can help to further categorize the various mucinous lesions.

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1. Introduction

Mucinous (colloid) carcinomas (MCs) of the breast are comparatively rare and account for 1-6% of all

breast cancers. These tumors tend to have a low to intermediate nuclear grade, however tumors with high nuclear grade and mucin production as best described as invasive ductal carcinomas-no special type (IDC-NST) with mucin production (Mixed IDC-NST and special type).¹⁻³ MCs of breast have a better prognosis as compared to

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the mixed variety. WHO further categorizes MCs into type A (hypocellular with large amounts of extracellular mucin) and type B (hypercellular with larger epithelial clusters showing neuroendocrine differentiation) subtypes. The common age of presentation is the postmenopausal group.^{2,4,5} Cytological diagnosis of these tumors is challenging. Cytological diagnosis of MC is rendered based on a combination of abundant extracellular mucin and certain characteristic morphological features. The aspirate generally yields a jelly like mucinous material.^{6,7} The background of pools of mucin with scattered bland tumor cells aids in identification of MC.

2. Materials and Methods

A retrospective study was conducted at our institute. 22 cases consisting of both mixed and pure mucinous carcinomas diagnosed by cytology and verified on histopathology between January 2007 and November 2015 were included in the study. Fine needle aspiration (FNA) was performed using 23 gauge needle and a 10 ml syringe. Smears were fixed in 95% ethanol for Papanicolaou stain. Air dried smears were fixed in 100% methanol for Giemsa stain. All cytology slides were retrieved and reviewed. Histopathology slides and blocks were also reviewed.

3. Results

A total of 22 cases were evaluated. The age ranged from 34-78years. The left breast was involved in 12 cases and the right breast in 10 cases. A total of 19 cases were diagnosed as mucinous carcinoma on cytology. However 12 of these cases were reported as pure mucinous carcinoma on biopsy. All these cases showed small round nuclei along with abundant extracellular mucin. 7 cases turned out to be mixed tumors on histopathology. Sparse mucin, large pleomorphic nuclei with prominent nucleoli were found in mixed mucinous carcinomas but not in pure tumors. Three cases were diagnosed as infiltrating ductal carcinoma (IDC) on cytology. One of these patients had 2 nodules, diagnosed on histopathological examination as IDC and mucinous carcinoma. Out of the other two cases, 1 case was diagnosed as cellular variant of mucinous carcinoma and another case as mixed carcinoma on biopsy. Cellular variant of mucinous carcinoma can mimic low grade ductal carcinoma on cytology. A thorough examination of the slides for mucinous material and few thin capillary fragments provide a valuable diagnostic clue.

4. Discussion

MC is a rare morphological type of breast carcinoma, with better prognosis than IDC-NST. It usually affects elderly women. On fine needle aspiration cytology (FNAC), it is very important to differentiate MC from other mucin containing neoplastic and non neoplastic lesions of breast.

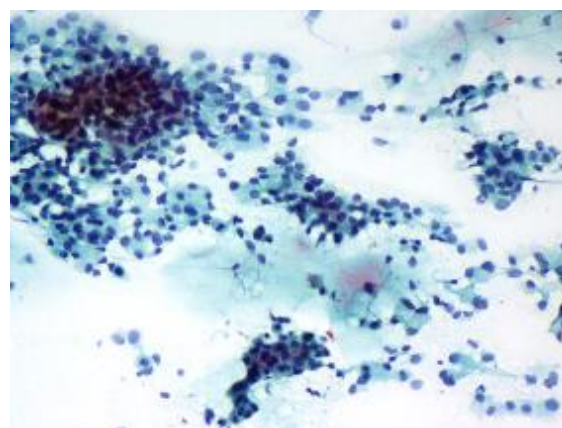


Fig. 1: Mucinous carcinoma with singly scattered and clusters of cells in a background of mucin [Pap x200]

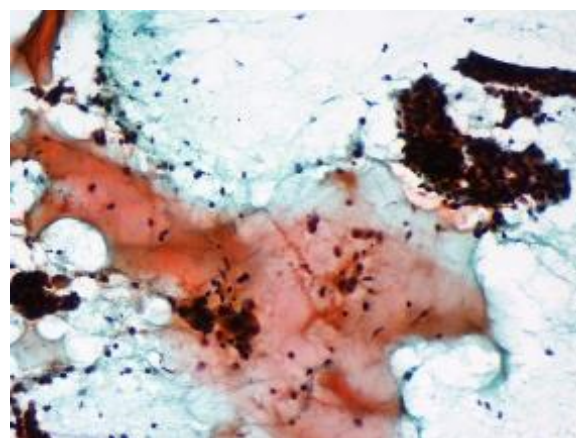


Fig. 2: Cohesive and occasional branching clusters in a background of mucin may mimic myxoid changes in a fibroadenoma [Pap x100]

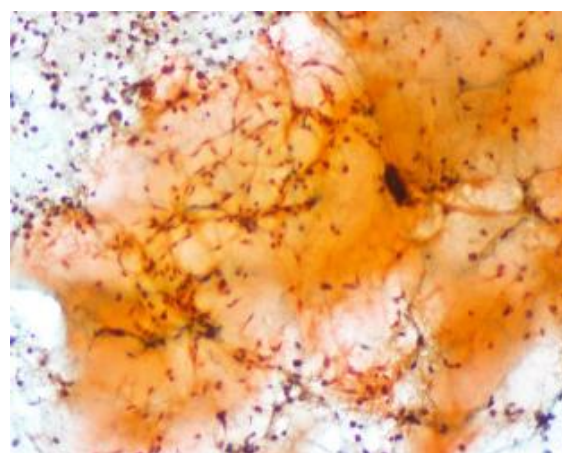
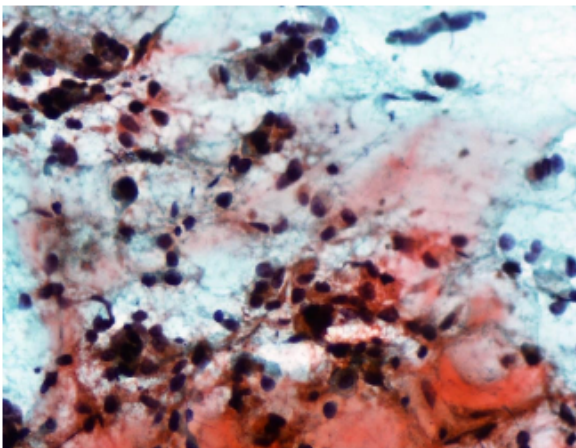
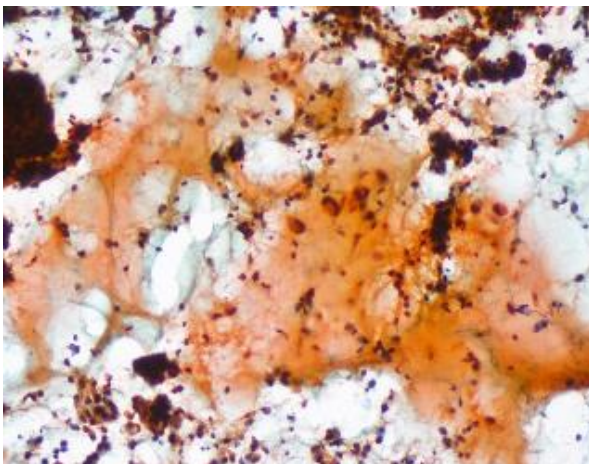


Fig. 3: Fine branching capillaries in a background of mucin [Pap x100]

Table 1: Cytological differential diagnosis of mucinous carcinomas

Mucinous lesions	Cytological features
Benign mucocele-like lesions, Mucinous cysts Fat necrosis	Abundant mucous in the background, scant cellularity, rarely intact single tumor cells/ cohesive monolayered clusters which lack nuclear atypia. Can be misinterpreted as mucin, hypocellular, smears with clusters/singly scattered foam cells with no significant nuclear atypia, inflammatory, necrotic background, vascularized fibrous tissue fragments may also be seen
Mucocele-like lesion with Atypical ductal hyperplasia or with ductal carcinoma in situ Mucinous sperulosis	Scant cellularity with single cells or monolayered sheets and features overlapping with mucinous carcinoma. Ductal carcinoma in situ can show varying degree of cellularity Acellular smears with mucinous hyaline background, may contain isolated myoepithelial cells
Myxoid changes in fibroadenoma	Markedly cellular smears with dyscohesive cell clusters, variable atypia may be seen, with stromal fragments and oval bare nuclei. Metachromasia of stromal fragment on Giemsa staining.
Infiltrating ductal carcinoma with mucinous component Lobular carcinomas with mucinous features	Cellular smears with pleomorphism which is marked, with necrosis and relatively small amount of background mucin. Small uniform cells with scanty cytoplasm arranged in linear dyscohesive pattern in a background of mucin rich smears, no marked pleomorphism, no necrosis

**Fig. 4:** Mixed IDC and mucinous carcinoma with cells showing marked pleomorphism [Pap x200]**Fig. 5:** Mixed IDC and mucinous carcinoma [Pap x100]

The various differential diagnosis are discussed below. [Table 1]

Mucocele-like tumors of the breast were originally described by Rosen in 1986. They occur due to overproduction of mucin from the epithelial cells with obstruction of the mammary ducts. They were described as benign lesions which had markable resemblance to pure MCs. These lesions on cytology show abundant mucin in the background with a few clusters and sheets of benign epithelium lacking nuclear atypia.^{8,9} Intact single cells are not present. In contrast, MCs show high cellularity, abundant singly scattered and clusters of tumour cells with mild to marked nuclear atypia. A mucinous cyst is characterized by cystically dilated mucin filled ducts often associated with rupture and extravasation of mucin into the stroma.^{3,4,9} However malignancy cannot be excluded solely on the basis of FNAC. Detailed histopathological examination of the surgically excised specimen is often recommended.

It is more difficult to make a definitive diagnosis in mucocele like tumors with concomitant atypical ductal hyperplasia or ductal carcinoma in situ, since the cellular polarity and atypia may be prominent, as in mucinous carcinoma.^{2,10}

Fat necrosis of the breast parenchyma may be misinterpreted as mucin. There is infiltration of histiocytes, multinucleated giant cells and degenerated RBCs in the intermediate stage of fat necrosis. These hypocellular smears show clusters and singly scattered foam cells with no nuclear atypia.^{1,5,11} Careful interpretation along with radiological and clinical correlation is often helpful.

Mucinous sperulosis can also mimic MCs on cytology. Often smears show scattered cellular debris in a dirty background. Sometimes three-dimensional group of cohesive epithelial cells showing hyperchromatic nuclei

and inconspicuous nuclei are also found raising the suspicion of malignancy.^{12,13} Few can also show a mucinous background. Classical round spheres with well defined borders often solves the diagnostic dilemma and needs to be accurately recognized on cytology.

Myxoid changes in fibroadenoma can also mimic mucinous carcinoma. Clinically myxomatous fibroadenoma(M-FA) shows a rapid growth and a relatively larger size. On cytological examination, M-FA can be differentiated from carcinomas based on the absence of marked nuclear atypia and metachromasia in the mucus components, a useful features which is seen on Giemsa staining.^{3,14}

Mixed tumors (invasive ductal carcinoma with mucinous component) generally yield cellular smears which on cytology show pleomorphism which is marked, necrosis and relatively small amount of background mucin. Features on cytology indicative of a mixed tumor include one or more smears totally without mucin, or scanty amounts of mucin or necrosis. However several studies have reported pure mucinous carcinoma usually show abundant mucin on all smears, no pleomorphism or necrosis.^{1,2,15}

5. Conclusion

It is important to distinguish between pure and mixed IDC with mucinous component as patients with the former type have better prognosis, with a low potential for lymph node and distant metastasis. With the help of FNAC, identification of patients with pure mucinous carcinomas may be possible only in a few cases. Mucin on cytology can be associated with various benign and malignant lesions. The cytology findings of the entire spectrum of mucinous lesions of the breast must kept in mind while dealing with lesions associated with mucin. However the age of presentation, clinical features and radiological findings can help to further categorize the various mucinous lesions.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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Cite this article: Shivamurthy A, Jaiprakash P, Vasudevan G, Kudva R, Valiathan M. Pitfalls in cytological diagnosis of mucinous carcinomas of breast. *Indian J Pathol Oncol* 2021;8(1):100-103.