International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 02 Issue 04 April 2022

Page No: 274-279

DOI: https://doi.org/10.47191/ijmscrs/v2-i4-04, Impact Factor: 5.276

Micropapillary Variant of Invasive Mucinous Carcinoma - A Case Report and Review of Literature

Dr. Unnimaya K S[1], Dr. Jaimie Anandan[2], Dr. Lilarani Vijayaraghavan[3]

[1]Junior resident, Department of Pathology, Government medical college, Thiruvananthapuram, Kerala, India.

[2]Assistant professor, Department of Pathology, Government medical college, Thiruvananthapuram, Kerala, India.

[3]Professor and Head of the Department, Department of Pathology, Government medical college, Thiruvananthapuram, Kerala, India.

ABSTRACT

Invasive micropapillary variant of mucinous carcinoma breast is an under-recognized category which shares features of both pure mucinous carcinoma and invasive micropapillary carcinoma. Due to its greater propensity for nodal metastasis and angioinvasion, the prognosis in this subtype is worser than pure mucinous carcinoma breast. Here we report a case of invasive micropapillary variant of mucinous carcinoma breast in a 43-year-old female.

ARTICLE DETAILS

Published On:
18 April 2022

Available on:
https://ijmscr.org

INTRODUCTION

Invasive micropapillary variant of mucinous carcinoma is a special histological subtype of mucinous carcinoma breast. It shows combination of features of both mucinous carcinoma and invasive micropapillary carcinoma breast. Unlike other subtypes of mucinous carcinoma breast, these tumours exhibit frequent nodal metastasis and angioinvasion, which warrants more aggressive treatment. Greater awareness of this variant is required among pathologists and clinicians for a better patient overall survival.

CASE REPORT

We here describe a case of micropapillary variant of invasive mucinous carcinoma breast.

A 43year, old female with no significant previous medical history, presented with a palpable lump in her right breast. Physical examination revealed a hard lump with irregular margins in the upper outer quadrant and measured around 3 x 2 cm. Three axillary lymph nodes were palpable, which were fixed and largest measured 1 x 1 cm. Mammography revealed a well-defined irregular lesion with spiculated margin, BIRADS 5, in the superolateral quadrant of right breast with axillary lymph nodes. Then a fine needle aspiration cytology was performed and a diagnosis of carcinoma breast IAC CODE 5 was made. Later trucut biopsy was taken and the histopathological report was suspicious of mucinous carcinoma breast. Following this right modified radical mastectomy was done. On gross examination, identified an ill circumscribed pale grey white lesion with mucinous appearance measuring 4 x 3.5 x 3.5cm, well away from all the margins. On microscopy, a neoplasm composed of cells arranged in micropapillary pattern surrounded by abundant extracellular pools of mucin is seen (Fig.1), individual cells being moderately pleomorphic with scant to moderate eosinophilic cytoplasm and pleomorphic vesicular nucleus with coarse clumped chromatin (Fig.2). Also seen occasional hobnailing of cells (Fig.3) and extensive psammomatous calcification (Fig.4, Fig.5).

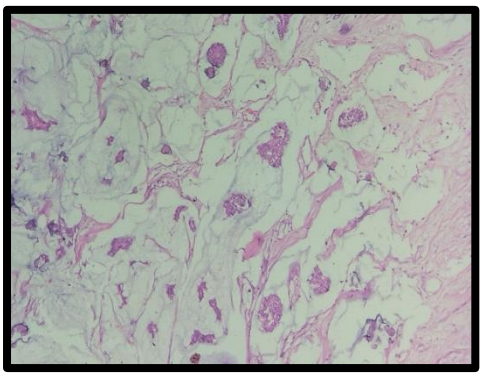
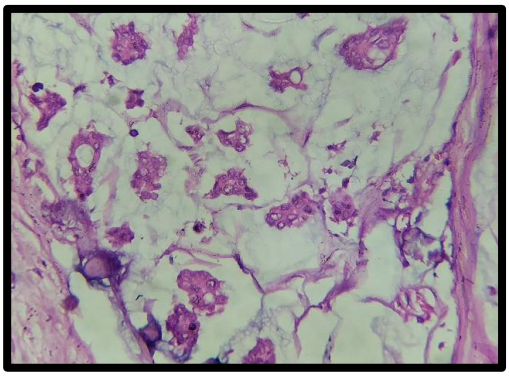

Fig. 1 (40x) & Fig. 2 (100x): Histologic features characteristic of Invasive micropapillary variant of mucinous carcinoma of the breast; micropapillary clusters within mucin filled stromal compartments.

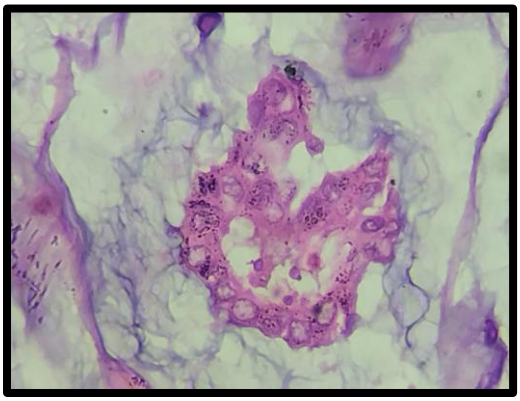

Fig 3: Micropapillae showing reversed polarity and hobnail cells (400x).

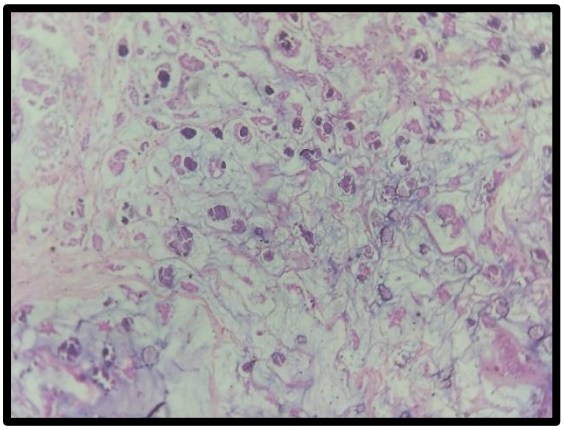
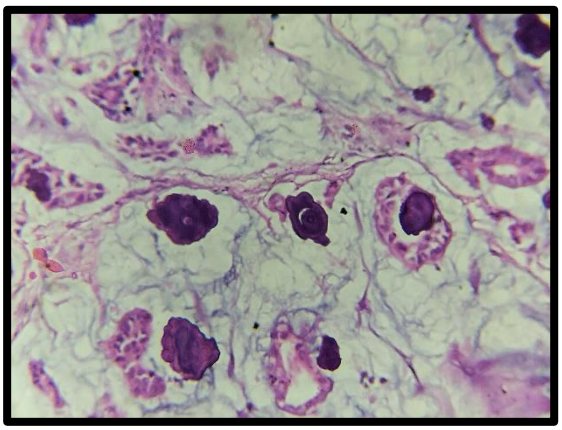

Fig 4 (40x) & Fig 5 (100x) showing numerous psammamatous calcification

5 out of 12 lymph nodes show metastasis from the neoplasm (Fig.6). On immunohistochemical examination, ER (Fig.7) and PR (Fig.8) shows positive expression and Her 2Neu shows negative expression. EMA shows staining in the peripheral border of micropapillary cluster (Fig.9) and Ecadherin shows staining of central pseudolumina (Fig.10).

A diagnosis of invasive micropapillary variant of mucinous carcinoma breast was given.

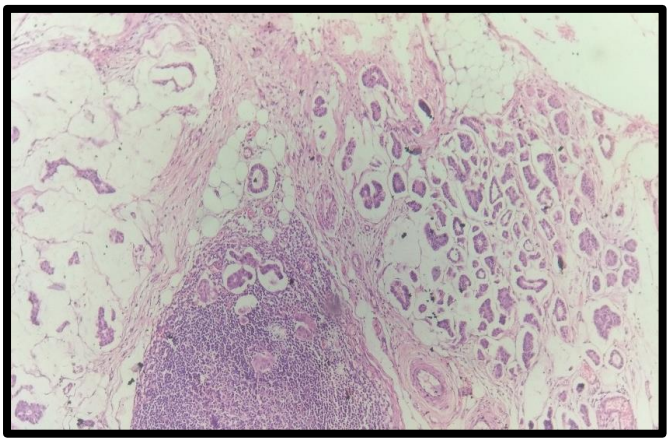

Fig 6: Lymph node metastasis with features similar to primary tumour.

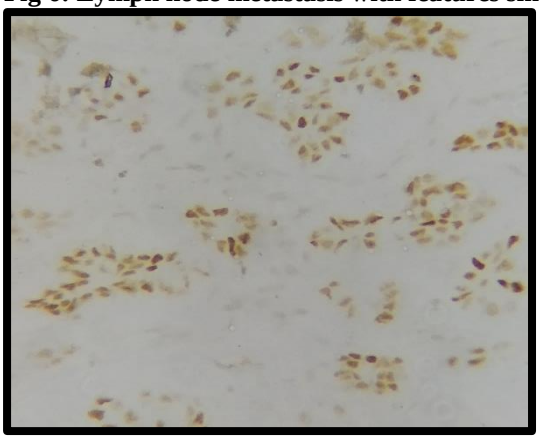

Fig 7: Positive immunostaining with PR

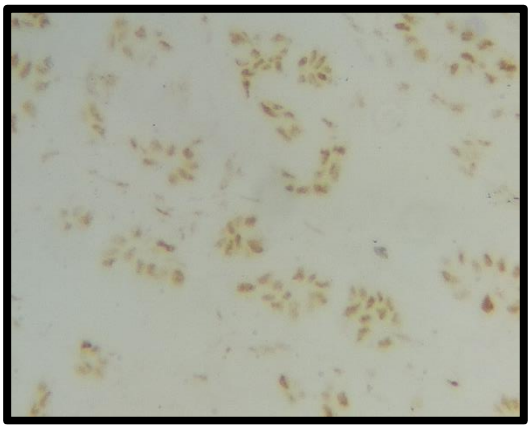

Fig 8: Positive immunostaining with ER

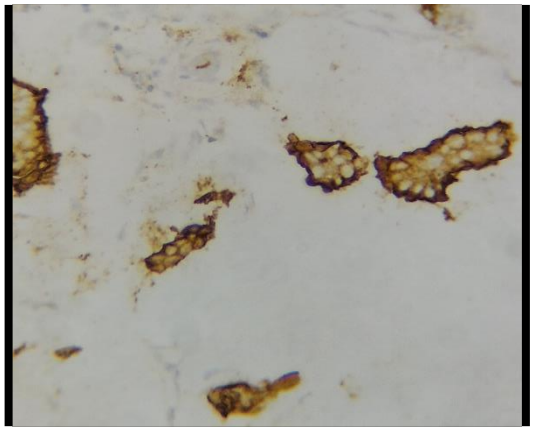

Fig 9: Immunostaining with EMA in the peripheral border of micropapillary cluster

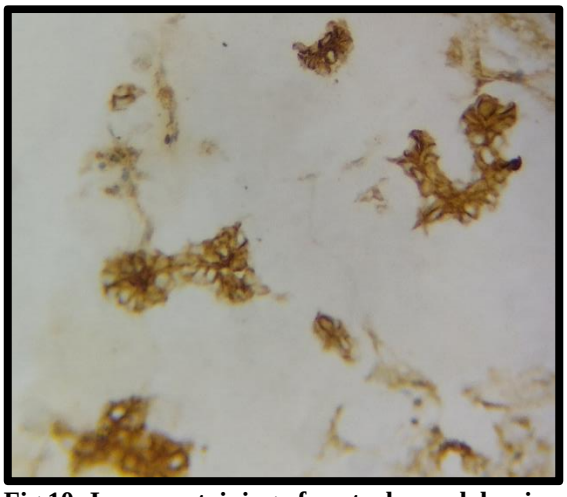

Fig 10: Immunostaining of central pseudolumina and loss of peripheral labelling with E cadherin

DISCUSSION

Mucinous carcinomas of the breast are usually indolent tumours affecting the elderly, with low propensity for angioinvasion and nodal metastasis. [1] These tumours are subclassified into pure mucinous carcinoma which has > 90% mucin component and mixed mucinous carcinoma which has 10- 90% mucin component. Generally, pure mucinous carcinoma may be hypocellular variant or hypercellular variant with neuroendocrine differentiation. [2] Apart from these two, there is another rarely recognized variant of pure mucinous carcinoma, known as invasive micropapillary variant of mucinous carcinoma breast.[3–5] This entity has a micropapillary architecture with a predilection for nodal metastasis and angioinvasiveness.[6] Literature consider this as a hybrid of pure mucinous carcinoma and micropapillary carcinoma. Interestingly its clinical behaviour and morphology are straddled between these two.[5]

It was first described in 2002 by Wai Kuen Ng.[7] It accounts for <1% of all breast cancers. Invasive micropapillary variant of mucinous carcinoma accounts for < 1% of all breast cancers and 12-35% of all pure mucinous carcinoma.[5,8,9] But the reported cases are far less due to its underrecognition.[9] The affected individuals belong to a wide age group, 28-80 years (mean 55years) and half of them are in the pre- or perimenopausal age group.[1] Patients usually present in T1-T4 stage. The common site being upper outer quadrant followed by central quadrant of breast.[10]

Cytologically, Invasive micropapillary variant of mucinous carcinoma shows moderately cellular smear with cells arranged in cohesive clusters and micropapillae, with occasional abortive branches, in a background of thick mucin.[7] Tumour cells are usually of low grade, occasionally with additional features of nuclear hobnailing and intracytoplasmic vacuoles. Many a times psammomatous calcification is seen. Cell block preparations show characteristic micropapillary or pseudoacinar cellular arrangement. Immunohistochemical studies on cell block sections with EMA shows cytoplasmic positivity but fails to demonstrate reverse polarity. Studies suggest that this could be due to distortion of membrane antigen during specimen processing.[7,11]

Histologically, the characteristic feature of Invasive micropapillary variant of mucinous carcinoma is the presence of neoplastic cells arranged in a pattern similar to invasive micropapillary carcinoma within abundant mucin filled stromal compartments. [1,10]Like micropapillary carcinoma, Invasive micropapillary variant of mucinous carcinoma show retraction cleft between micropapillae and stroma. These micropapillae have scalloped edges, lined by cells with inverted luminal border showing reversed polarity and the cells appear to be of higher nuclear grade than other mucinous carcinoma subtypes. Other defining features include hobnailing of the cells and extensive psammomatous calcification.[3,4,12] Unlike other subtypes of pure mucinous carcinoma, Invasive micropapillary variant of mucinous carcinoma shows a propensity for nodal metastasis and angioinvasiveness. Studies have found that mucin in the interface between tumour cells and stroma has a role in reducing angioinvasiveness.[13,14] This protective effect is reduced in Invasive micropapillary variant of mucinous carcinoma due to the diminished amount of mucin around the micropapillary cluster.[10]

Invasive micropapillary variant of mucinous carcinoma usually belong to luminal subtypes with frequent expression of ER, PR and low rate of expression of HER-2. But when compared to cases of pure mucinous carcinoma, HER2 expression is significantly higher in Invasive micropapillary variant of mucinous carcinoma.[9] In the study by Liu et al, HER2 status was identified as an independent predictor for unfavourable overall survival and recurrence free survival. Immunohistochemical study by EMA demonstrates characteristic reverse polarity of the micropapillary structure. While, E-cadherin demonstrates dyscohesive micropapillary structure by staining central pseudolumina and loss of peripheral labelling. [1]

Molecular studies describe Invasive micropapillary variant of mucinous carcinoma as genetically heterogenous. It shows genetic alterations intermediate between those of mucinous carcinoma and micropapillary carcinoma. Usually, ER positive breast disease harbour frequent PIK3CA and TP53 mutations. But in mucinous carcinoma breast only lower rate of PIK3CA and TP53 mutations are encountered. They also lack concurrent 1q gains and 16q losses which are commonly observed in the ER positive breast cancers.[15,16] On the other hand in micropapillary carcinoma PIK3CA and TP53 mutations are frequently detected and they show complex copy number profiles and recurrent gains of 8q.[17] As said earlier, Invasive micropapillary variant of mucinous carcinoma have intermediate genetic alterations. Similar to mucinous carcinoma, Invasive micropapillary variant of mucinous carcinoma lack mutations involving PIK3CA and TP53. Akin to micropapillary carcinoma, some Invasive micropapillary variant of mucinous carcinoma show complex pattern of copy number alterations and 16q losses. A subset of Invasive micropapillary variant of mucinous carcinoma shows simple copy number profiles and lacked concurrent 1q gains and 16q losses similar to mucinous carcinoma.[18] Frameshift mutations in CUX1 gene, which has a tumour suppressor role, has been identified in some cases of Invasive micropapillary variant of mucinous carcinoma.[18] Loss of function mutations involving CUX1 gene results in PI3K pathway activation. Study by Pareja et al postulates that some Invasive micropapillary variant of mucinous carcinoma demonstrate genetic features of micropapillary carcinoma with 16q loss and alterations of PI3K pathway via loss of function mutation of CUX1.[19] All these molecular studies suggest that some Invasive micropapillary variant of

mucinous carcinoma might be mucinous carcinomas that acquired genetic alterations of micropapillary carcinoma in their evolution and others could be micropapillary carcinoma that acquired mucin production. One could say, Invasive micropapillary variant of mucinous carcinoma may not belong to a histological subtype, but rather a convergent phenotype originating from mucinous or micropapillary carcinoma.[16]

Prognosis of Invasive micropapillary variant of mucinous carcinoma is better than micropapillary carcinoma but worser than other subtypes of pure mucinous carcinoma due to its propensity for nodal metastasis and angioinvasiveness. Overall survival and disease-free survival in Invasive micropapillary variant of mucinous carcinoma are impacted by their nodal status, amount of mucin around micropapillary cluster, irregularity of tumour border and tumour stage.

CONCLUSION

In summary, Invasive micropapillary variant of mucinous carcinoma occupies intermediate portion of a spectrum of breast carcinoma phenotype with pure mucinous carcinoma at one end and invasive micropapillary carcinoma at the other end. Invasive micropapillary variant of mucinous carcinoma, which is now identified as a subtype of pure mucinous carcinoma has a clinical behaviour and propensity for nodal metastasis and angioinvasion intermediate between pure mucinous carcinoma and micropapillary carcinoma. Previous studies emphasises that presence of this micropapillary architecture in pure mucinous carcinoma modifies its biologic behaviour and has to be managed more aggressively than other subtypes of pure mucinous carcinoma. Therefore, awareness of this underrecognized category and its accurate diagnosis is important for patient management.

REFERENCES

I. Collins K, Ricci A. Micropapillary variant of mucinous breast carcinoma: A distinct subtype. *Breast Journal*. 2018;24(3). doi:10.1111/tbj.12935

II. Tan PH, Ellis I, Allison K, et al. The 2019 World Health Organization classification of tumours of the breast. *Histopathology*. 2020;77(2):181-185. doi:10.1111/his.14091

III. Asano Y, Kashiwagi S, Nagamori M, et al. Pure Mucinous Breast Carcinoma with Micropapillary Pattern (MUMPC): A Case Report. *Case Reports in Oncology*. 2019;12(2). doi:10.1159/000501766

IV. Yuan JP, Yan HL, Gao LK, Liu L, Rao J. Mucinous variant of invasive micropapillary carcinoma of breast: Report of two cases and literature review. *International Journal of Clinical and Experimental Pathology*. 2017;10(10).

V. Barbashina V, Corben AD, Akram M, Vallejo C, Tan LK. Mucinous micropapillary carcinoma of the breast: An aggressive counterpart to conventional pure mucinous tumors. *Human Pathology*. 2013;44(8). doi:10.1016/j.humpath.2013.01.003

VI. Kim HJ, Park K, Kim JY, Kang G, Gwak G, Park I. Prognostic significance of a micropapillary pattern in pure mucinous carcinoma of the breast: Comparative analysis with micropapillary carcinoma. *Journal of Pathology and Translational Medicine*. 2017;51(4). doi:10.4132/jptm.2017.03.18

VII. Ng WK. Fine-needle aspiration cytology findings of an uncommon micropapillary variant of pure mucinous carcinoma of the breast: Review of patients over an 8-year period. *Cancer*. 2002;96(5). doi:10.1002/cncr.10747

VIII. Madur B, Shet T, Chinoy R. Cytologic findings in infiltrating micropapillary carcinoma and mucinous carcinomas with micropapillary pattern. *Acta Cytologica*. 2007;51(1). doi:10.1159/000325678

IX. Liu F, Yang M, Li Z, et al. Invasive micropapillary mucinous carcinoma of the breast is associated with poor prognosis. *Breast Cancer Research and Treatment*. 2015;151(2):443-451. doi:10.1007/s10549-015-3413-4

X. Shet T, Chinoy R. Presence of a micropapillary pattern in mucinous carcinomas of the breast and its impact on the clinical behavior. *Breast Journal*. 2008;14(5). doi:10.1111/j.1524-4741.2008.00616.x

XI. Madur B, Shet T, Chinoy R. Cytologic findings in infiltrating micropapillary carcinoma and mucinous carcinomas with micropapillary pattern. *Acta Cytologica*. 2007;51(1). doi:10.1159/000325678

XII. Bhattacharjee K, Valiathan M. Mucinous Carcinoma of the breast with micropapillary pattern and psammomatous calcification: A case study. *Journal of Pathology of Nepal*. 2021;11(1). doi:10.3126/jpn.v11i1.30950

XIII. CAPELLA C, EUSEBI V, MANN B, AZZOPARDI JG. Endocrine differentiation in mucoid carcinoma of the breast. *Histopathology*. 1980;4(6). doi:10.1111/j.1365-2559.1980.tb02957.x

XIV. Komaki K, Sakamoto G, Sugano H, Morimoto T, Monden Y. Mucinous carcinoma of the breast in Japan. A prognostic analysis based on morphologic features. *Cancer*. 1988;61(5). doi:10.1002/1097-0142(19880301)61:5<989::AID-CNCR2820610522>3.0.CO;2-E

XV. Lacroix-Triki M, Suarez PH, Mackay A, et al. Mucinous carcinoma of the breast is genomically distinct from invasive ductal carcinomas of no

special type. *Journal of Pathology*. 2010;222(3). doi:10.1002/path.2763

XVI. Pareja F, Lee JY, Brown DN, et al. The Genomic Landscape of Mucinous Breast Cancer. *Journal of the National Cancer Institute*. 2019;111(7). doi:10.1093/jnci/djy216

XVII. Natrajan R, Wilkerson PM, Marchiò C, et al. Characterization of the genomic features and expressed fusion genes in micropapillary carcinomas of the breast. *Journal of Pathology*. 2014;232(5). doi:10.1002/path.4325

XVIII. Pareja F, Selenica P, Brown DN, et al. Micropapillary variant of mucinous carcinoma of the breast shows genetic alterations intermediate between those of mucinous carcinoma and micropapillary carcinoma. *Histopathology*. 2019;75(1). doi:10.1111/his.13853

XIX. Wong CC, Martincorena I, Rust AG, et al. Inactivating CUX1 mutations promote tumorigenesis. *Nature Genetics*. 2014;46(1). doi:10.1038/ng.2846