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MUCINOUS BREAST CARCINOMA : A HOSPITAL BASED REVIEW

Pathology

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ABSTRACT

Background: Mucinous breast carcinoma is an uncommon form of breast carcinoma which is characterised by presence of extracellular mucin and it accounts for 1-7 % of all breast cancers. The primary objective of this study is to share our experience of clinico-pathological characteristics of this entity at a cancer hospital in South India.

Methods: The study comprises of a 3 year retrospective review of database of patients diagnosed with mucinous breast carcinoma.

Results: Out of 528 breast cancers diagnosed, 18 were mucinous carcinomas (3.4%). Amongst the 18 cases, 15 cases were pure mucinous breast carcinoma (2.84 %), rest were mixed variant of mucinous carcinoma.

Conclusions: It is concluded from this study that on morphological grounds, pure mucinous carcinomas are commoner than mixed variants. 70 % of patients presenting with stage T1-2 tumours, 60 % with no nodal metastasis and 100 % ER positivity indicate a favourable treatment outcome.

KEYWORDS

Mucinous Carcinoma, Breast, Pure, Mixed

INTRODUCTION :

The apical surface of epithelia lining the ducts in specialized organs like breast is often subject to injury during inflammation and cancer. As a defence mechanism the epithelia express mucins which have been sub classified into secreted and trans membrane forms. The secreted mucins function as a protective physical barrier by forming a mucous gel over the surface of epithelia. The trans membrane mucins, unlike their secreted counterparts, also protect the epithelial cell layer by functioning in cellular signalling pathways that promote growth and survival.[1]

Human cancers like breast carcinoma have exploited this function of mucins. Alterations in mucin expression or glycosylation accompany the development of cancer and influence cellular growth, differentiation, transformation, adhesion, invasion and immune surveillance. Aberrant overexpression of trans membrane mucins like MUC1 in breast carcinoma has been an area of research in monitoring the course of disease, to assess recurrence and prognosis and also to develop targeted therapy. [2,3,4]

Breast lesions with mucin represent a broad spectrum of entities, ranging from benign fibrocystic changes with luminal mucin to mucocele-like lesions (MLL), which can be associated with basal epithelial alterations, atypical ductal hyperplasia or ductal carcinoma in situ. Occasionally invasive mucinous carcinoma can be identified in contiguity with MLL. MLL and invasive mucinous carcinoma are characterized by large amounts of extracellular mucin.[5]

In this study we intend to share our institutional experience with mucinous carcinoma of breast and review the literature.

METHODS :

Patients diagnosed with mucinous carcinoma according to the WHO Classification of the breast 2012 [6] between 2016 and 2018 at department of Pathology, Indian Red Cross Cancer Hospital, Nellore were retrospectively included in this study. The clinico - pathological data evaluated included age at diagnosis, tumour size, TNM stage and expression of estrogen receptor (ER), Progesterone receptor (PR). This data was retrieved by inspection of patient records and was in accordance with the ethical standards of institutional research committee.

The patients in whom the diagnosis of mucinous carcinoma of breast (both pure mucinous and mixed variants) was given on histopathological examination of core and excision biopsy were only included in the study. Other pathological types were excluded from detailed study.

Descriptive statistics like mean, median and percentages were used with the help of Microsoft Office 2007 to interpret the results.

RESULTS:

During a period of 3 years from January 2016 to December 2018, a total of 528 malignant breast lesions were diagnosed of which 18 cases were confirmed to be mucinous carcinoma (3.4 %). Amongst the 18 cases, 15 cases were pure mucinous breast carcinoma (2.84 %), rest were mixed variant of mucinous carcinoma (One having admixture with invasive carcinoma of no special type, one each with papillary and signet ring cell features). The mean age at presentation was 58.72 (range 46-74) years. Premenopausal status was observed in 5 (27.8 %) patients while 13 (72.2%) patients were post menopausal.

The laterality of the lesions was right sided in 10 (55.6 %) patients and left sided in 08 (44.4%) patients.

All patients had a palpable mass in their breast. Only 10 patients underwent modified radical mastectomy with axillary node dissection following a diagnosis on tru cut biopsy while 8 patients after diagnosis were lost to follow up in our institute.

The tumour size varied greatly from 2 to 10 cm in diameter (size was T1 in 1 patient, T2 in 6 patients, T3 in 2 patients and T4 in one case). 4 patients had lymph node metastasis. No distant metastases were identified.

On gross examination, majority of specimens were well circumscribed, soft in consistency and on cut section showed gelatinous appearance. In 3 cases nipple was retracted and in one patient the tumour had direct skin extension and showed ulceration.

On microscopic examination, we identified 15 cases of pure mucinous breast carcinoma and 3 cases of mixed mucinous carcinoma. Among the mixed type, one case was accompanied by an invasive ductal component. One showed papillary pattern of arrangement while one case displayed signet ring cell morphology with intracellular mucin.

Microscopic examination of pure mucinous carcinoma showed large pools of extracellular mucin with nests and tubules of pleomorphic cells floating in the pools of mucin. These cells showed hyper chromatic to vesicular nuclei, prominent nucleoli, moderate cytoplasm

and increased N: C ratio. Delicate bands of fibro connective tissue were often present within the mucous lakes. Scattered lympho mononuclear cell infiltrate was noted in the interstitium.

Immunohistochemistry (IHC) was done on the non mucinous component of the tumour as per existing guidelines. Estrogen receptor (ER) positivity was noted in all 18 cases (100%). Progesterone receptor (PR) was expressed in 10 cases (55.55%) and was negative in 8 patients (44.45%).

Comparative analysis was done with other studies as depicted in Table 1.

Comparison Of Our Study Of MBC With Other Existing Studies:

Parameter	Ourstudy	Kashiwagi et al[8]	Dumitru et al[14]	Bagga et al[15]	Yildirim et al[16]	Lei et al[13]
Totalcases	18/528 **(3.4%)**	71/1,760 **(4%)**	25	10/658 **(1.52%)**	22/1273	125/5,297 **(2.4%)**
MeanAge(years)	58.72	61.8	62.3	63.6	49	52
Laterality Right Left	 10 (55.6%) 8 (44.4%)	 39 (54.9%) 32 (45.1%)	 10 (40%) 15 (60%)	 4 (40%) 6 (60%)	 11 (50%) 11 (50%)	 - -
Tstage T1 T2 T3 T4	 1 6 2 1	 23 38 6 4	 3 16 5 1	 - - - -	 3 14 4 1	 - - - -
Nstage N0 N1 N2 N3	 6 3 0 1	 Positive–8 Negative-63	 20 4 1 0	 Positive–6 Negative-4	 Positive–7 Negative-15	 Positive–44 Negative-81
Mstage	Absent	Absent	Absent	Absent	2patients	4patients
Lymphovascular invasion	4	8	5	6	7	44
ERpositive	100%	68%	-	-	86.36%	85.6%
PRpositive	55.55%	68%	-	-	72.72%	68.8%
SubtypePure/Mixed	15/3	48/23	3/22	2/8	16/6	48/77

DISCUSSION

Mucinous breast carcinoma (MBC) is a special type of breast cancer that is characterized by clusters of generally small and uniform cells floating in large amounts of extracellular mucin. Synonyms include colloid carcinoma; mucoid carcinoma; gelatinous carcinoma; mucinous adenocarcinoma.[6]

Based on the cellularity of the tumour, mucinous carcinomas are divided into two subtypes :

- The pure type mucinous breast carcinoma (PMBC)
- The mixed type mucinous breast carcinoma (MMBC)

It comprises approximately 4% (range : 1% to 7 %) of all invasive breast cancers. Higher incidence is observed in peri- and post-menopausal patients. Our study showed an incidence of 3.4 %.

PMBC represents approximately 2% of all malignant breast carcinomas. This type is most commonly diagnosed in women aged 55-67 years and above. 2.84 % of the cases were PMBC and mean age of MBC was 58.7 years in our study.

The origin of mucinous breast carcinoma is multifactorial and involves diet, reproductive factors and hormones.

Gross examination of this lesion shows a glistening gelatinous lesion with pushing margins and a soft consistency. Size is often variable.

Histologically mixed mucinous breast carcinoma (MMBC) contains a component of conventional invasive ductal or lobular carcinoma, and pure mucinous breast carcinoma (PMBC) shows nests of mucinous cancer cells occupying almost the entire tumour mass, and with no component of conventional invasive ductal carcinoma.[7]

The distinction between these subtypes is based on the quantification of cellularity and the amount of extracellular mucinous component. Most pathologists agree that a diagnosis of pure mucinous carcinoma should be reserved for tumours with at l east 90% mucinous component.

PMBC may be subtyped into a hypocellular variant (PMBC-A) showing a tubular, cribriform, cord- like, micropapillary or papillary growth pattern, and a hypercellular variant (PMBC-B) growing in solid nests.[8] PMBC – B shows frequent neuroendocrine differentiation which can be identified by immunohistochemistry and special stains (Grimelius).

Usually, PMBC is ER and PR positive and Androgen Receptor (AR) negative.[9] Both pure and mixed mucinous carcinomas are reported to express WT. MUC2 and MUC6 among the family of MUC genes are predominantly expressed in these lesions.[10] We found 100 % ER positivity and 55.5 % PR positivity.

Clinically the tumour does not feel firm or solid upon examination. On mammography, circumscribed and lobulated breast lesions are common findings for a mucinous carcinoma. With these findings it simulates a benign process. On ultrasonography, it is usually a complex mass with cystic and solid components and distal enhancement. Echogenicity is known to predict the histologic subtype. PMBC is isoechoic while MMBC is hypoechoic.[11]

Tissue biopsy is mandatory in evaluation of mucinous breast carcinoma. It can be obtained by core biopsy or excisional biopsy.

The main challenge on core biopsy is the differential diagnosis of mucinous carcinoma with mucocoele -like-lesion (MLL) with extravasated mucin. The presence of ducts distended by mucinous material and of myoepithelial cells adhering to the strips of cells floating in the lakes of mucin serve as important clues to differentiate benign MLL from mucinous carcinoma.[12]

It is suggested that MLL and mucinous carcinoma may represent two ends of the pathological spectrum of mucinous lesions of the breast.

NCCN Clinical Practice Guidelines in Oncology Breast Cancer v.2 2012 indicate standard treatment for a coexisting histological type should be performed in patients with MMBC. Among patients with PMBC-A, treatment for a histological type with a favourable prognosis may be selected, regardless of the presence or absence of lymph node metastasis whereas for PMBC-B, presence or absence of lymph node metastasis is taken into account.[8]

More often the treatment is based on surgery associated with post-operative hormone therapy. Since most mucinous carcinomas are negative for the protein HER2/neu, they are not treated with trastuzumab.

Existing literature shows that 75 – 97 % of patients are diagnosed with stage T1-2 tumours. Lymphatic metastasis is infrequent compared to invasive ductal carcinoma. Lack of metastases to lymph nodes is observed in 62% – 88% of patients.[13] Our study has similar findings with 70% tumours in T1-2 stage and 60 % with no nodal metastasis.

MBC shows a favourable prognosis, with a 10-year survival rate of more than 90%. Since a higher ratio of the extracellular mucin

component to the cancer cell component is associated with a more favourable prognosis, PMBC-A, PMBC-B and MMBC, in this order, would be expected to show a favourable prognosis. MMBC shows a high recurrence rate.[8]

Because of the low number of patients, no comparison was made regarding the clinico pathologic features between those with pure and mixed-type carcinomas.

CONCLUSION :

Mucinous carcinoma of breast is a rare entity with pure and mixed variants. This study consolidates its low incidence, small tumour size, low axillary node metastases and high hormone receptor positivity. More studies in India with larger data samples are required for better understanding of this particular tumour.

DECLARATIONS

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