Mucinous Carcinoma Breast- Experience of a Tertiary Care Centre of North India

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ABSTRACT

Introdction: Breast cancer is the most common cancer in woman globally and in India. 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. Pure mucinous carcinoma are rarer and account for 2% of all breast cancers. Pure mucinous carcinoma are generally associated with low rates of local and distant recurrences and excellent 5 year disease free survival rates. Aims and Objectives: The purpose of this paper is to share the last 10-year experience regarding mucinous breast carcinoma, of the Department of Pathology of our institute which is a tertiary care centre of North India.

Material and Methods: A 10-year (July 2006 – June 2016) retrospective review of database of patients diagnosed with breast cancer was performed. The medical records of 10 patients with invasive mucinous breast cancer who underwent surgery were retrieved and their clinical data, surgical treatment and pathological findings were reviewed.

Results: A total of 658 patients underwent mastectomy for invasive breast cancer during the 10 year study period. Out of 658 patients, ten were diagnosed with mucinous carcinoma (1.52%). Amongst the ten, only two were pure mucinous breast carcinoma (0.30%), rest were mixed variant of mucinous carcinoma. The mean age at presentation was 63.6 (range 43–90) years. The tumor size ranged between 3 to 7.5 cm in its greatest dimension. Medium sized vessels showed calcification in tunica media (Monckeberg sclerosis) in two cases. Six out of ten patients had lymph node metastases with no distant metastases.

Conclusions: Mucinous carcinoma of the breast is a rare entity, the reported incidence of pure mucinous carcinoma being 2% of all breast cancers. Traditionally, pure mucinous carcinoma has a far better prognosis than the mixed variety. Much lower prevalence of mucinous carcinoma especially pure or classic form was seen in our institutional study and more than half of the cases of mucinous carcinoma showed lymph node metastasis with no distant metastasis.

Keywords: Mucinous, carcinoma, breast, Pure, mixed

INTRODUCTION

Invasive breast cancer is the most common carcinoma in women, accounting for 23% of all cancers in women globally¹ and now the most common cancer in Indian women, having recently overtaken cervical cancer in this respect.² Mucinous breast cancer, also called colloid breast cancer, is a rare histological type that is characterized by nests of cells floating in lakes of mucin partitioned by delicate fibrous septae containing capillary blood vessels. It accounts for 1 to 7% of all breast cancers.³⁻⁵ MC usually occurs in elderly and the median age at diagnosis is older than 55 years.¹ Mucinous breast carcinoma (MMBC) and pure mucinous breast carcinoma (PMBC) based on whether the tumor is with or without a component of invasive carcinoma

of no special type. A pure mucinous tumour is composed of more than 90% mucinous carcinoma.⁶ Pure mucinous breast carcinomas are rare and account for about 2% of all primary breast carcinomas.¹ The purpose of this paper is to share the last 10 year experience regarding mucinous breast carcinoma, of the Department of Pathology of our institute which is a tertiary care centre of North India.

MATERIAL AND METHODS

This study was done in Pathology department of a tertiary care centre of North India. A 10-year (July 2006 - June 2016) retrospective review of database of patients diagnosed with breast cancer was performed. The prevalence of various pathological types of breast cancer based on database of our institution was determined. The medical records of 10 patients with invasive mucinous breast cancer who underwent surgery were retrieved and their clinical data, surgical treatment and histopathology reports along with the histopathology slides were reviewed in detail. The available cytology reports and smears of patients were also reviewed. The patients in whom the diagnosis of mucinous carcinoma of breast (both pure mucinous carcinoma and mixed variants) was given on histopathology were only included in the study. Patients of breast cancer of other pathological types were excluded from the detailed study. All procedures done and methods used in this study were in accordance with the ethical standards of institutional research committee.

STATISTICAL ANALYSIS

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

RESULTS

A total of 658 patients underwent mastectomy for invasive breast cancer during the 10 year study period. Amongst which five were male patients and rest were females. Most common histopathological diagnosis was Invasive carcinoma of no special type (93.47%) followed by lobular (3.34%), and other rare varieties. Out of 658 patients, ten were diagnosed with mucinous carcinoma (1.52%). Amongst the ten, only two were pure mucinous breast carcinoma (0.30%), rest were mixed

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variant of mucinous carcinoma having admixture with invasive carcinoma of no special type. The mean age at presentation was 63.6 (range 43-90) years. All (100%) patients had a palpable mass in their breast. The laterality of the lesions was left-sided in 06 (60%) patients and right-sided in 04 (40%) patients. All patients underwent modified radical mastectomy. On gross examination, the majority of tumours were well circumscribed, and had a relatively soft consistency. Nipple was retracted in two cases, while nipple and areolar area was ulcerated in four cases. The tumor size ranged between 3 to 7.5 cm in its greatest dimension. Cut section showed variable mucoid material in all the cases and characteristic gelatinous and glistening appearance. (figure-1) On microscopic examination, we identified 8 cases of mixed type mucinous breast cancer. Only two case was of "pure" mucinous breast carcinoma (hypocellular variant). Histopathology sections of pure mucinous carcinoma showed cell clusters of variable size and shape, having minimal nuclear atypia, floating in lakes of mucin separated by delicate fibrous septae (figure-2). Mixed variants showed admixture with invasive carcinoma of no special type and mucinous



Figure-1: Gross photograph of cut section of a case of mucinous carcinoma breast showing mucoid material and characteristic glistening and gelatinous appearance of the tumour tissue.



DISCUSSION

Mucinous carcinoma of the breast is a rare histologic type of mammary neoplasm. Invasive tumours with atleast 90% extracellular mucin surrounding the tumour epithelial islands are classified as pure mucinous carcinomas while the "mixed" type is a tumor where 50-90% of the area is mucinous and also admixing most commonly with regular invasive duct carcinoma.¹ The pure mucinous carcinomas are further



Figure-2: Microphotograph of a case of pure mucinous carcinoma showing small clusters and individual cells floating in large amount of mucin. H and E, X100



Figure-3: Microphotograph of a case of mucinous carcinoma showing medial calcific sclerosis(Monckeberg sclerosis) in a vessel wall. H and E. X400



Figure-4: Microphotograph of a case of mucinous carcinoma showing Periodic Acid Schiff staining (PAS) positivity in mucinous areas. PAS, X100

subdivided into hypercellular and hypocellular variants. Mucinous carcinoma comprises of 1% to 7% of all invasive breast cancers.²⁻⁴ Pure mucinous breast carcinomas are rarer and account for about 2% of all primary breast carcinomas.¹ In our study mucinous carcinoma accounted for 1.52% (10/658) of all invasive breast cancers diagnosed during the ten year study period, whilst pure mucinous carcinoma comprised of only 0.30% (2/658). Mucinous carcinoma has higher incidence in perimenopausal and postmenopausal age groups and usually occurs in women more than 55 years.⁵ In our study age of the patients diagnosed with mucinous carcinoma ranged from 43 to 90 years. Pure mucinous carcinoma was diagnosed in 90 year and 75 year old female. The cytological diagnosis of mucinous carcinoma is based on a combination of the characteristic morphology and abundant extracellular mucin. On FNAC, aspirate usually yields visible jelly like mucin and cut sections of mastectomy specimens show variable mucoid material and characteristic gelatinous and glistening appearance. The lake of mucin bathing bland tumor cells is a very distinctive clue to the identification of mucinous carcinoma. The presence of only mucin does not warrant a diagnosis of mucinous carcinoma as other breast lesions i.e. mucocele like lesions (MLL) also show extracellular mucin. The presence of ducts distened by mucinous material and of myoepithelial cells adherent to the strips of cells floating in lakes of mucin serve as important clues to differentiate benign MLL from mucinous carcinoma.⁶ The diagnosis of mixed mucinous carcinoma in eight of our cases was made based on following cytological features. i.e one or more smears lacking mucin, one or more smears more cellular and nuclear atypia much more higher than in typical pure mucinous carcinoma, nucleoli unduly prominent and presence of necrosis. So, extracellular mucin and large numbers of pleomorphic cells strongly suggests a mixed Mucinous Carcinoma-Infiltrating Duct Carcinoma. It is important to distinguish pure mucinous carcinomas from "mixed" mucinous carcinomas, as the prognosis of pure mucinous carcinoma is much better than for mixed one. Pure mucinous carcinoma are generally associated with low rates of local and distant recurrences and excellent 5 year disease free survival rates ranging from 80% to 100% in different studies.5,7-9 Mixed mucinous carcinomas have far worse prognosis and high incidence of lymph node metastasis than do pure mucinous carcinoma.^{10,11} Only 2-14% of the pure variety7,10-13 show axillary node metastasis compared to 45-64% of the mixed type.7,10 Late distant metastasis may occur in pure mucinous carcinoma.14,15 Half of our cases of mixed mucinous carcinoma showed lymph node metastasis whilst cases of pure mucinous carcinoma showed lymph node metastasis in all the lymph nodes removed during surgery. It has been suggested in some studies that specific subtypes of pure mucinous carcinoma - those with a micropapillary pattern demonstrate significantly worse prognosis with greater vascular invasion and lymph nodes metstasis.^{16,17} A subset of pure mucinous breast carcinomas with large cell clusters and neuroendocrine differentiation as defined by immunoreactivity to synaptophysin and chromogranin are labelled as hypercellular or type B mucinous carcinoma.14,18 One study found out that neuroendocrine differentiation was associated with a favourable histology and a good outcome¹⁹ while others did not find this association^{20,21} As mucin comprises the major component of the tumor volume, tumor size in the staging system may not be a significant factor¹⁸ We didn't find any correlation with the tumour size and node positivity. Similarly some studies have not found any correlations between tumor size and the incidence of axillary nodal metastases,^{22,23} however few have documented that the incidence of node positivity was directly related to tumor size7,8 Mucinous carcinoma is positive for oestrogen and progesterone receptors5, while androgen receptors are expressed at low levels²⁴ and HER2 is not amplified.²⁵ Pure and mixed mucinous carcinomas are reported to express WT1.26 Mucinous tumours are of luminal A molecular subtype and transcriptionally distinct from grade and molecular subtype matched invasive carcinoma of no special type.1 Calcifications seen rarely in conjunction with mucinous tumors frequently correspond to the invasive ductal component of the cancer in a mixed mucinous tumor.^{27,28} The finding of medial calcific (monckeberg) sclerosis in two of our cases is incidental and has never been reported in the past. The primary treatment in patients suffering from mucinous breast carcinoma is surgery with post-operative radiotherapy, chemotherapy and endocrine therapy. Adjuvant endocrine therapy is indicated for hormone responsive tumors.¹⁷ and it is very effective in mucinous carcinoma breast as almost all mucinous carcinomas are estrogen and/ or progesterone-receptor positive

CONCLUSION

Mucinous carcinoma of the breast is uncommon, the reported incidence of pure mucinous carcinoma being 2% of all breast cancers. Traditionally, pure and mixed variants of mucinous carcinoma have been described. Pure mucinous carcinoma has a far better prognosis than the mixed variety noted in several studies. Much lower prevalence of mucinous carcinoma especially pure or classic form was seen in our institutional study and more than half of the cases of mucinous carcinoma showed lymph node metastasis. However more studies, especially from India, with large sample size with long follow-up are necessary, to achieve an improved understanding of this particular tumour and to document the demographic and geographical variations.

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