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"Tally of the Jelly": A Comprehensive Case Series of 8 Intriguing Encounters of Mucinous Breast Carcinoma

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Abstract: ***Background: Mucinous carcinoma (MC) (also called colloid carcinoma). Mucinous carcinoma accounts for 2% of all breast carcinomas often occurs in older women with a median patient age of 71 years. They commonly present as a lobulated, well circumscribed masess on mammography, sonography, and MRI imaging. Metastasis in these types of carcinomasis very rare. Often the Capella type A shows histopathological patterns like micropapillary, Papillary, rarely tubular and Cribriform type. Aim of the Study: To present the diverse histomorphologies associated with mucinous breast carcinoma and explore impact of pattern on clinical behavior. Materials and Methodology: A retrospective observational study was conducted in the Department of Pathology, Topiwala National Medical College, from January 2019 till July 2023, for 4.5 years. During this period, out of total 221 modified radical mastectomies(MRM)done 8cases were MC, accounting for 3.6 %. Results: Of these 8 cases, 1 was pure mucinous carcinoma showing > 90% mucin component and remaining 7 had 50% to 90% mucin. The mean age of presentation was 61.75 years, range (42 years – 79 years)and all presented with palpable lumps in their breast. Laterality of breast was 50% on left and 50% on right. Size of smallest tumor was 2.5 cm to largest being 11 cm in dimension. Axillary Lymph node metastases seen in 2 cases. Majority patients presented in stage IIA (4 nos), 3 cases II B, 1 case III A.***

Keywords: Breast, Mucinous carcinoma, micropapillary, signet ring, apocrine

1. Introduction

Mucinous carcinoma (MC) of breast is a relatively rare subtype of breast cancer accounting for 2% of all breast carcinomas.MC appears mammographically as a well circumscribed or lobulated mass and may mimic a benign process. While [5,6,12,17]. Sonographically most tumors are hypoechoiec in density, MRI reveals a persistent enhancement pattern and hyperintensity on T2 weighted images

According to latest WHO classification of tumors of the breast, mucinous carcinomas are special type of breast cancer. There are 2 histologic subtypes: mixed mucinous carcinoma where ductal carcinoma is associated with the colloid component, and the more prognostically favorable pure mucinous carcinoma where the > 90% mucin surrounds the tumor tissue and constitutes a mechanical barrier limiting cell invasion and virulence. The heterogenous microscopic patterns associated with Mixed MC seen are Papillary, Micropapillary, Solid Variant of Papillary, Infiltrating duct Carcinoma ordinary type and rarely Tubular,Cribrifirm and lobular type.

MC are usually seen in postmenopausal women.[1,2,9]and represents an excellent prognostic histologic variant, due to its positivity to Estrogen, Progesterone receptors, and negativity to HER2 receptors.{17} Regional lymphnode involvement and distant metastasis is rare.[3 ,7,8] The etiology of Mucinous Breast Carcinomas is multifactorial and shares common breast cancer risk factors; nevertheless, data suggests that some aspects related to reproductive events (e.g. late menarche, early menopause, childlessness) contribute less to MC risk than that of ordinary breast cancer[9,]

2. Aim of the Study

To present the diverse histomorphologies associated with mucinous breast carcinoma and explore impact of pattern on clinical behaviour.

3. Material and Methods

A retrospective observational study was conducted in the Department of Histopathology, Topiwala National Medical College, from January 2019 till July 2023, for 4.5years. During this period, we received total 221 MRM specimens of which 8 cases were diagnosed as MC . The specimens fixed in 10% neutral buffered formalin were subsequently grossed, paraffin embedded and stained with hematoxylin and eosin for histopathological study to assess histological type, tumor grade, axillary lymph node status, lymphovascular invasion, perineural invasion and surgical margin status; WHO guidelines (Edition V). Immunohistochemical (IHC) test were applied to evaluate estrogen receptor (ER), progesterone receptor (PR), Ki67, and human epidermal growth factor receptor 2 (HER2/neu) expression with PathnSitu & Biogenex.

4. Results

We identified 8 patients with diagnosis of MC in MRM along with axillary dissections. 7 women were in postmenopausal and 1 in perimenopausal age group at the time of diagnosis. The mean age of presentation was 61.75 years, (range 42 years – 79 years). All cases presented with clinically palpable breast lumps. Laterality of breast was 50% on left and 50% on right side.

Tumor size was T2 in 5 patients (smallest 2.5cm) and T3 (largest 11cm) in 3 patients. Axillary lymphnode metastasis found in 2 patients. Maximum4 cases presented in stage IIA, 3 cases in II B, and 1 in case III A.

Table 1: TNM staging of study patients

Clinical features	No. of patients
Tumor size (T)	
T1 (0.1-2 cm)	0
T2 (2-5 cm)	5
T3 >5cm	3
T4 extension to the chest wall/skin	0
Nodal status (pN)	
pN0	6
pN1	1
pN2	1
pN3	0
Stage (TNM)	
I	0
II	7
III	1
IV	0

Table 2: Integrated table of clinical features & diagnostic data of study population

Cases	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Ageat presentation (In years)	72	79	60	44	56	71	42	66
Duration	1 year	1 year	3 months	6 months	3 years	1 year	3 months	5 months
Laterality	Left	Left	left	right	right	left	Right	Right
USG BIRADS SCORE	IV C	IV	V	VI	IV	IV	VI	IV
(IHC)	Not available	ER + PR+ HER2 2+ KI67=20-25%	ER + PR _ HER2 1+ KI67=80-90%	ER- PR- HER2- KI67>90%	ER+ PR+ HER2 -	ER+ PR+ HER2-	ER+ PR+ HER2-	ER+ PR+ HER2 2+ KI67=5-10%
TNM Stage	IIB	IIA	IIIA	IIA	IIA	IIB	IIB	IIA
Tumor Size & Nodal Status	T3N0	T2N0	T3N2	T2N0	T2N0	T2N0	T3N0	T2N1
% of Mucin	>90%	60%	50%	50%	50%	80%	50%	50%
Final Histopathological Diagnosis	90%, PURE	MIXED, Apocrine CA	MIXED IDC NOSGr 1	MIXED IDC NOS Gr 3	MIXED Papillary CA	MIXED Intracystic, Papillary	MIXED-IDC NOS Gr 2	MIXED-IDC NOS Gr2

On gross examination, two tumors were encysted whereas 06 well circumscribed ranging from 2.5cm-11 cm in dimension. 5 cases had admixed solid firm areas,while 2 predominantly solid-cystic areas and one tumorwas entirely cystic with multiloculations. 5 masses showed obvious gelatinous mucin.Nipple retraction, areas of hemorrage and necrosis was noted in 6 cases. All masses had radiological concordance.

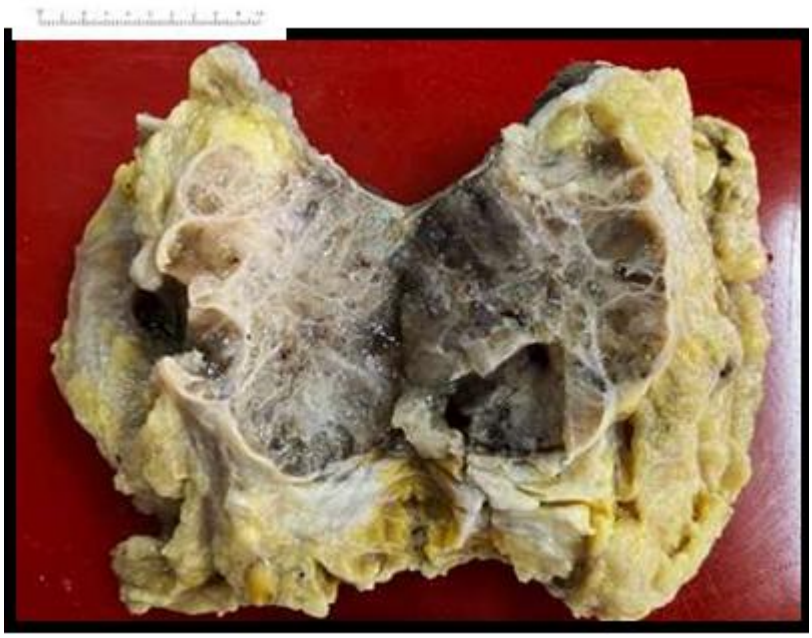

Figure 1: Well encapsulated purely cystic mass of 11x5.5x7cm, multiloculated cysts filled with brownish gelatinous material

5. Microscopic Examination

A complete tranverse slice of the tumor in largest dimension along with perimetric borders, and tumor size in 3 dimensions were examined under microscope to assess the approximate proportion of tumor cells to that of mucin.

We identified one Pure Mucinous Carcinoma, characterized by over 90% mucin content associated with well-differentiated papillary morphology with intermediate nuclear grade. The other 7 masses exhibited Mixed Mucinous Carcinoma with heterogenous variety in the solid areas. A single case showed nodules of cells with apocrine differentiation separated by abundant mucin also containing perineural invasion. Two prominently cystic tumors had mural nodules of micropapillae and well differentiated papillary fronds each, with large extracellular mucin and moderate degree of tumor infiltrating lymphocytes. Two tumors displayed cribriform and complex papillary histology, accompanied by large areas of infarctoid necrosis. We encountered very unusual histomorphological variants such as apocrine carcinoma and ductal carcinoma with signet ring differentiation in the Mucinous Breast Carcinoma.

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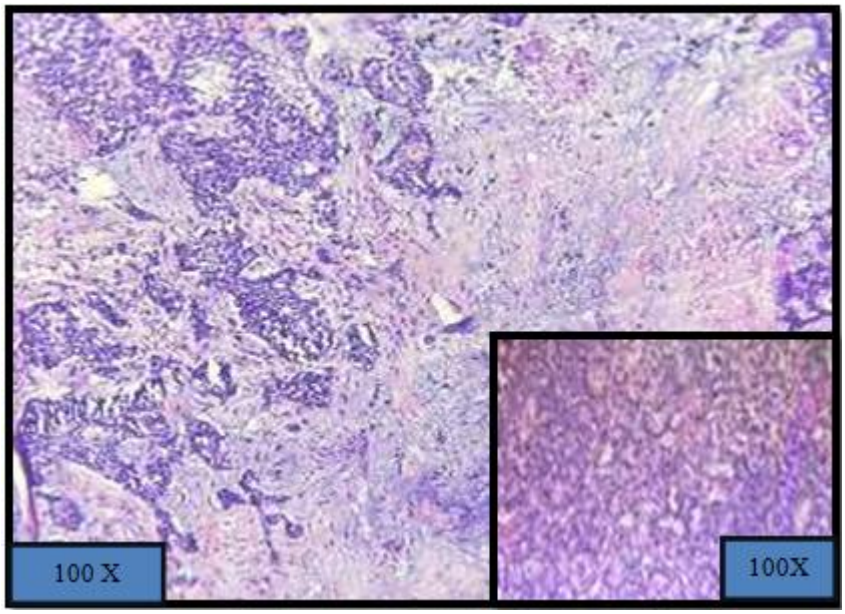

Figure 2: Invasive cribriform histology with large extracellular mucin. Inset showing higher magnification.

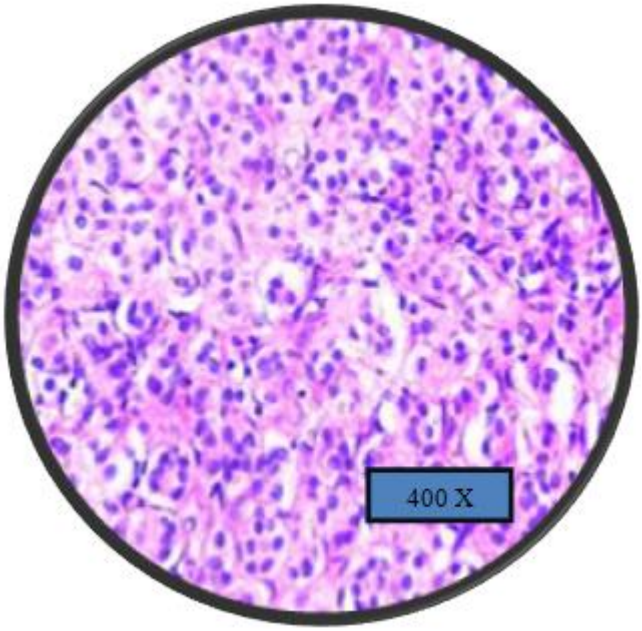

Figure 3: Showing signetring differentiation

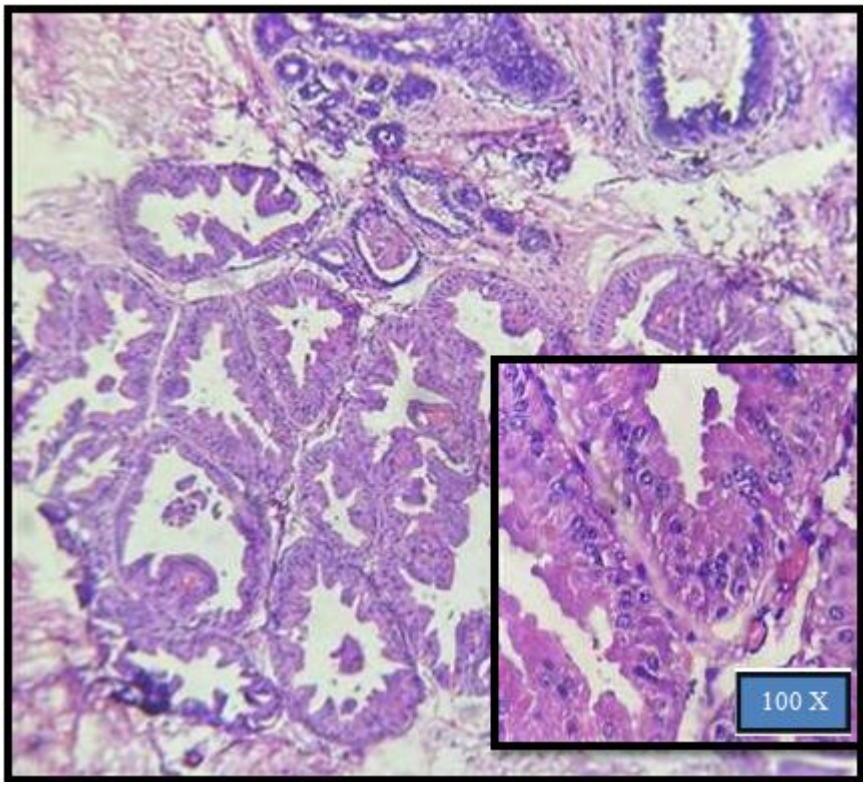

Figure4: Low power view of apocrine differentiation associated with mucin. High Power in Inset

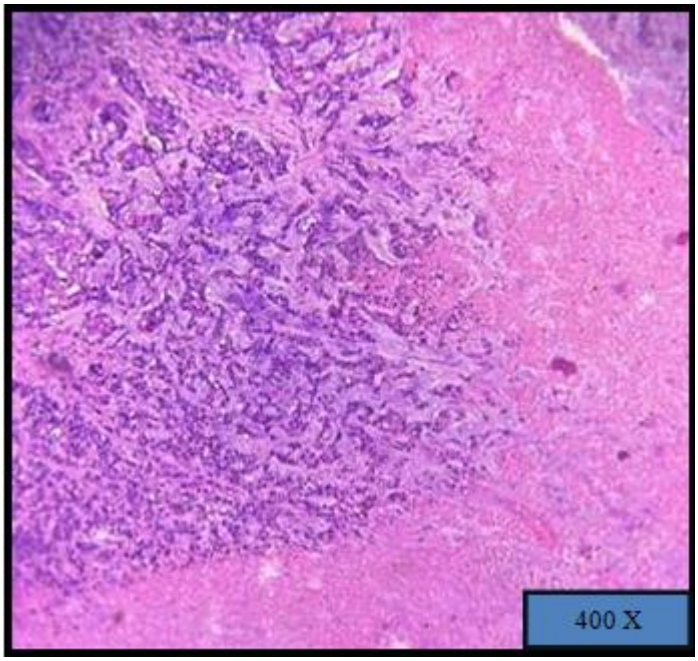

Figure 5: Showing high power view of papillary carcinoma with extracellular mucin and infarctiodnecrosis.

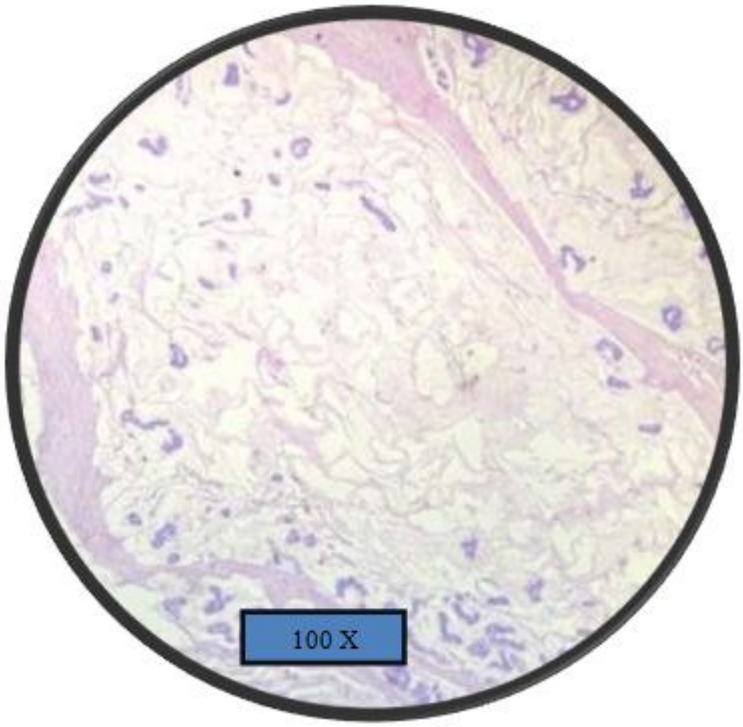

Figure 6: Multiloculated Pure Mucinous Breast Carcinoma with micropapillae floating in ocean of mucin. Locules lined by thin to delicate fibrous septae.

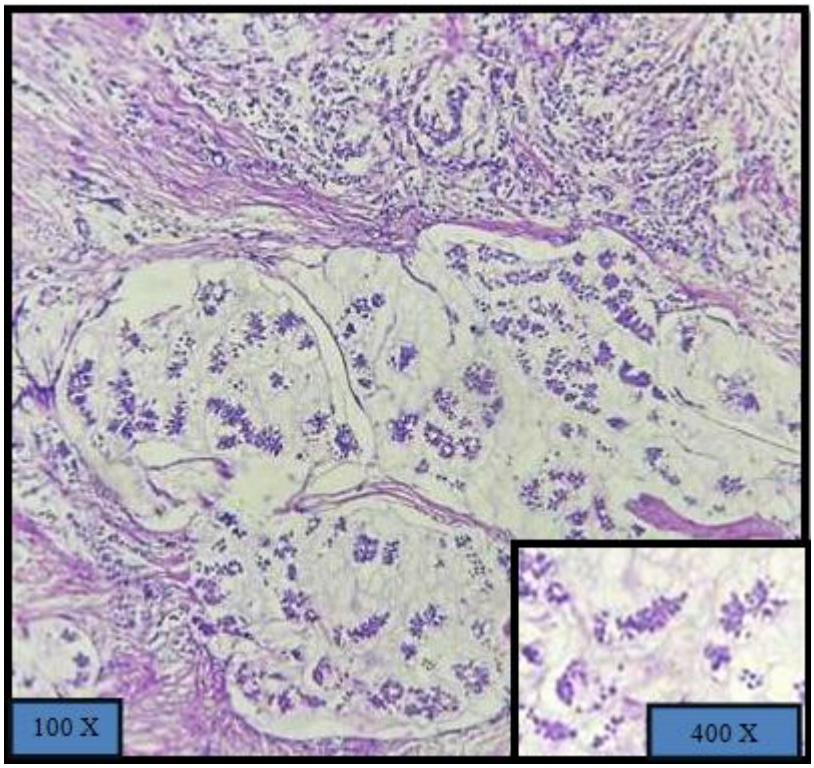

Figure 7: Solid Cystic tumor showed Micropapillaein abundant mucin

7. Immunohistochemitry Profiles (IHC)

IHC was available in 7 out of 8 patients. Six MC exhibited strong ER, PR expression in over 60 to 90% tumor cells. One patient was triple negative. One case had ER positive but PR negative. Majority i.e 5/7 tumors did not express Her2neu, while 2 cases were indeterminate expression. However in both these patients FISH results were unavailable to us. Ki67 proliferative index results were found in only 4 patients, revealing a high index in 3 and low in 1 patient.

8. Discussion

Mucinous Carcinoma Breast is rarely seen in clinical practice, representing about 4% of all diagnosed invasive breast cancer.[2] In our study we got 3.6% of MC. They prevails mainly in postmenopausal women and usually affects older patients compared to other breast cancer types, and is exceptionally rarely diagnosed in younger women under 35 years of age (1%)[3]. Mean age of presentation in our study is 61.75years.

Literature does not present much data regards to histomorphological diversity in associated with mucin.

Mucinous carcinoma of the breast is characterized histologically by clusters of tumor cells suspended in pools of extracellular mucin.[17]In cystic variant the mucin lakes are partitioned by delicate fibrous septa containing capillary blood vessels.

Based on the cellularity Capella et al. classified MCs into type A which are relatively hypocellular with a large amount of extracellular mucin, whereas type B are hypercellular consists of large epithelial clumps or sheets that often show neuroendocrine differentiation.[19]Our Study contained two cases of Capella A type MC and remaining majority were Capella type B however none exhibited any neuroendocrine features.

Pure MCs may have foci with micropapillary pattern consisting of morula- like clusters suspended in tight mucin pools. [4,17] They usually exhibits more nuclear atypia than conventional MCs, and they may have hobnailcells; psammomatous calcifications.[1,17] Compared with conventional Pure MC, those with micropapillary pattern tends to occur at a younger age, [4]and has more frequents lymphovascular emboli and lymph node metastasis.Besides the common histologies we also found unusual rare variety of apocrine differentiation in one case and signet ring cells admixturewithin ordinary invasive breast cancer inside Mixed MC.

MCs are of the luminal A molecular subtype and transcriptionally distinct from grade and molecular subtype – matched IBCs of no special type(NST).[17]Similar pattern of gene expression is observed in Neuroendocrine Carcinomas.Pure mucinous carcinomas harbor a low level of genetic instability and rare recurrent amplifications, and the genomic profiles of the tumor components of mixed mucinous tumors are remarkably similar to those of pure mucinous carcinomas. More than 90% of pure mucinous carcinomas are diploid, whereas only 42% of mixed mucinous carcinoma are diploid .[19]

Typically, MC is positive for ER and PR ,while androgen receptors are expressed at a low level, and HER2 is not amplified . Our study was in keeping with literature data , however we encountered a maverick single case of Triple Negative Mixed MC with high Ki67 index and no axillary or distant metastasis. Pure and Mixed MC are reported to

express WT. Mucinous breast carcinoma expresses predominantly MUC2 and MUC6 among the family of MUC genes [2].

Mucinous breast cancers are usually associated with smaller tumor size.[5,13,14] Although in our study the largest tumor was 11cm diameter. T size appears to be insignificant independent factor associated with the severity of the disease because the mucin component comprises the majority of the tumor mass as per American Joint Committee on Cancer (AJCC) [3,14,15]

Table 3: Comparison of present study with other study

Study	Our Study	AdrianDumitru et.al[1]	Budzik M P et.al[2]	Ranade A et. al [7]	Lei L et al[14]
Total no of cases mucinous carcinoma	8	25	24	100	125
Duration (years)	4.5	5	2	10	10
Pure	1	3	15	45	48
Mixed	7	22	9	55	77
Tumor size(cm)	2.5 – 11	2- 19	0.7 - 4	0.2- 9.5	Largest tumor dimension 4.4cm
TNM- Stage I	0	4	4	Not done	Not done
Stage II	7	9	9		
Stage III	1	12	11		
Stage IV	0	0	0		

Four of our cases doing well after chemotherapy completion,FEC Flurouracil,Epirubicin, Cylophosphamide based regimen, remaining cases not available.

The effect of chemotherapy on patients with mucinous carcinoma remains under discussion[18].

9. Conclusion

Mucinous Breast Carcinoma is rare and recognized as special subtype with favorable prognosis. Histopathological evaluation is mandatory for definite diagnosis, and also of the associated morphological varieties which may impact the overall prognosis. Rare breast cancers vary by treatment regimens and outcomes. Therefore larger data samples with longer follow necessary to achieve an improved health and healing in these cancers.

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