COMPARATIVE STUDY OF METAPLASTIC BREAST CARCINOMA (MBC) AND IDC-NOS: A 7 YEARS RETROSPECTIVE ANALYSIS IN A TERTIARY CARE CENTRE OF WESTERN ODISHA

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ABSTRACT

BACKGROUND

Metaplastic breast carcinoma is a heterogeneous group of uncommon aggressive type of breast cancer, accounting for 0.2% to 5% of all invasive mammary carcinoma. It is used to denote tumour with mixed epithelial and sarcomatoid components, primary squamous or mixed adenocarcinoma and squamous cell carcinoma. This study was undertaken with an objective to know the incidence of MBC (Metaplastic breast carcinoma) in our population, analyse them with respect to different clinicopathological parameters and to determine different biological behaviour with that of Invasive ductal carcinoma of Breast (Not otherwise specified) IDC-NOS.

MATERIALS AND METHODS

This study was conducted in the Department of pathology, VIMSAR, Burla from July 2010 to July 2017. 5 cases of MBC and 441 cases of IDC-NOS were retrospectively reviewed. Clinical presentation, pathological findings and type of surgery were evaluated.

RESULTS

All patients were female with median age of 50 years in case of MBC, whereas in case of IDC-NOS, patients presented in earlier age i.e. from 25 years and eldest one was 85 years old. All the tumours were unilateral with median size of 8 cm (6cm-10cm) in case of MBC. IDC-NOS patients were presented with unilateral mass, but some patients presented with multifocal mass with median size of 4cm (2cm-6cm). All patients had undergone modified radical mastectomy. Out of 5 cases of MBC, 3 patients had metaplastic squamous cell carcinoma, one had heterologous metaplastic carcinoma with chondroid metaplasia another one had matrix producing metaplastic carcinoma. Out of 5 patients, 3 cases showed lymph node metastasis. All the tumours were triple negative. In case of IDC-NOS, 8cases (1.81%) were triple negative.

CONCLUSION

MBC are large sized tumours as compared to IDC-NOS, usually triple negative with high ki-67 scores indicating aggressiveness and lack of response to usual hormonal therapy. Large series of patients are needed to develop potential therapy for sub groups of the disease.

KEYWORDS

Invasive Ductal carcinoma of Breast-Not otherwise specified (IDC-NOS), Metaplastic Breast Carcinoma(MBC), Triple Negative Breast Carcinoma.

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BACKGROUND

Metaplastic Breast carcinoma (MBC) is a rare type of breast carcinoma that has heterogeneous histological elements admixed with adenocarcinoma. MBC differs from typical adenocarcinoma in several pathological and clinical aspects.[1]

MBC accounting for 0.2%-5% of all invasive mammary carcinoma.[2]

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The term metaplasti breast carcinoma is used by many authors to denote tumours with mixed epithelial and sarcomatoid components as well as primary squamous cell carcinoma or mixed adenocarcinoma and squamous cell carcinoma. Sarcomatoid component of the tumour is classified into monophasic, composed of spindle cell only or biphasic admixed with a carcinomatous element.[3]

Microscopic structural changes that diverge from glandular differentiation present as squamous, spindle cell, chondroid and osseous morphology. This phenotypic alteration is an expression of genotypic properties that are not typical of normal mammary epithelial and myoepithelial cells but results from a process of genetic dedifferentiation. This phenomenon is called as epithelial to mesenchymal Transition, (EMT).[4,5]

With regards to nonductal components MBC is often pathologically subdivided into several distinct subtypes

which includes squamous, spindle cell, matrix producing, carcinosarcoma etc.[6]

There are no established criteria regarding the extent of metaplasia required to diagnose MBC and the extent of metaplastic component can range from about 10% to 100% of the tumour mass.[7]

The 2012 WHO classification of tumours of breast divided MBC into subtypes based upon the morphologic components of the tumours. The majority of MBC are triple negative for Oestrogen Receptor (ER),Progesterone Receptor (PR) and human epidermal growth factor receptor2 (HER2) expression(TNBC) and may express cytokeratin 5/6(CK5/6) and Epidermal Growth Factor Receptor(EGFR).

MBC tends to present as a large tumour mass with low axillary lymph node metastasis and poor prognosis.[8,9]

Diagnosis of MBC has been raised its importance because this neoplasm is usually triple negative and resistant to conventional endocrine therapy for hormone receptors as compared to IDC-NOS. In general MBC represents larger tumour size, lesser lymph node involvement as compared to IDC-NOS.

Purpose of our study is to compare the clinical presentation, outcomes and response to hormone therapy of MBC with that of IDC-NOS.

MATERIALS AND METHODS

We retrospectively studied the data of invasive breast carcinoma and MBC in the department of pathology, VIMSAR Burla between July 2010 to July 2017.

Inclusion Criteria

All the female patients with carcinoma breast were included in our study group.

Exclusion Criteria

Male patient with carcinoma breast, female patients who were receiving neoadjuvant chemotherapy before surgery were excluded from our study group.

We compared the clinicopathological features between IDC NOS and MBC. We documented age of the patients, subtype, tumour size, nodal status. Modified BR grade, status of ER, PR and HER2/neu over expression were calculated and compared. Immunohistochemical evaluation of ER, PR and Her 2/neu of all the cases were done by 10% NBF fixed paraffin embedded tissue section by using monoclonal antibodies and by Dako envision FLEX/HRP detection reagent. Reporting of ER/PR was done by quick scoring system and CAP/ASCO guideline. Her 2 status was determined in formalin fixed paraffin embedded tissue by assessing protein expression on the membrane of the tumour cells using immunohistochemistry.

Five years recurrence free survival (RFS) and overall survival (OS) rate in both the groups were calculated and compared. RFS rate is free from local recurrence and distant recurrence

Statistical Analysis

Statistical analysis was performed with the use of software package SPSS. P value of <0.5 was considered significant.

RESULTS

We diagnosed 5 cases of metaplastic carcinoma of breast in a period between July 2010 to July 2017. Total number of cases of carcinoma breast (IDC-NOS) in that period was 441. The incidence rate of MBC was 1.01%. All 5 cases presented with MBC were above 50 years of age group. All the cases of MBC were female with median age in between 50 years to 70 years whereas in case of IDC-NOS age of the patient was in between 25 years to 80 years. Max. No. of patients (265) presented with IDC-NOS were below 50 years age group (60.09%) (Table I). MBC Patients presented with mass in the breast with rapid growth over a short period of time (2-6 months). All the tumours were unilateral. All the patients had undergone modified radical mastectomy (MRM). Average tumour size in case of MBC was 8cm (6cm-10cm), but in case of IDC-NOS average size of tumour was 4cm(2cm -6cm) (Table II). One patient had undergone FNAC preoperatively and was diagnosed correctly as metaplastic squamous cell carcinoma (Table III). Out of 5 cases, 3 cases were diagnosed as metaplastic squamous cell carcinoma, one case was diagnosed as matrix producing carcinoma another case was of heterologous metaplastic carcinoma with chondroid metaplasia. Among 5 cases of MBC, 3 cases showed lymph node metastasis (Table II), out of which 2 cases were metaplastic squamous cell carcinoma and another one was matrix producing carcinoma. Out of 441 IDC-NOS cases, 399 patients showed lymph node involvement by metastatic adenocarcinoma (90.47%),in case of metaplastic carcinoma of breast we found 60% cases with lymph node metastasis ($p<0.5$) (Table II) Immunohistochemical evaluation ER, PR and HER -2 /neu of MBC were done on 10% NBF paraffin embedded tissue section and the result came out as triple negative in all 5 cases of MBC. 8cases (1.81%) of IDC-NOS showed Triple negative ($p<0.5$) (Table V). Triple positive was seen in 5 cases (1.13%) (Table V). Luminal A type was seen in 198 (44.89%) cases of IDC-NOS. In our study, all MBC were triple negative (basal like) and display its unique characteristic like large size and rapid growth. In our study, all MBC cases were GR III, whereas maximum number of IDC NOS were GR II (58.27%). (Table-VI).

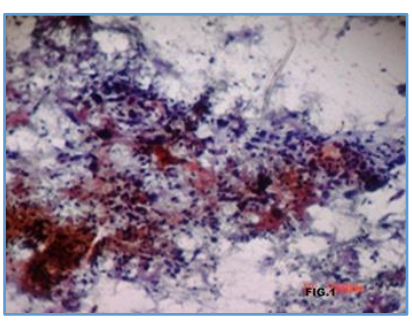

Figure 1. FNAC Smears of Metaplastic SquamousCell Carcinoma (Pap x 400)

Smear showing pleomorphic ductal epithelial cell intermingled with malignant squamous cells in a necrotic background.

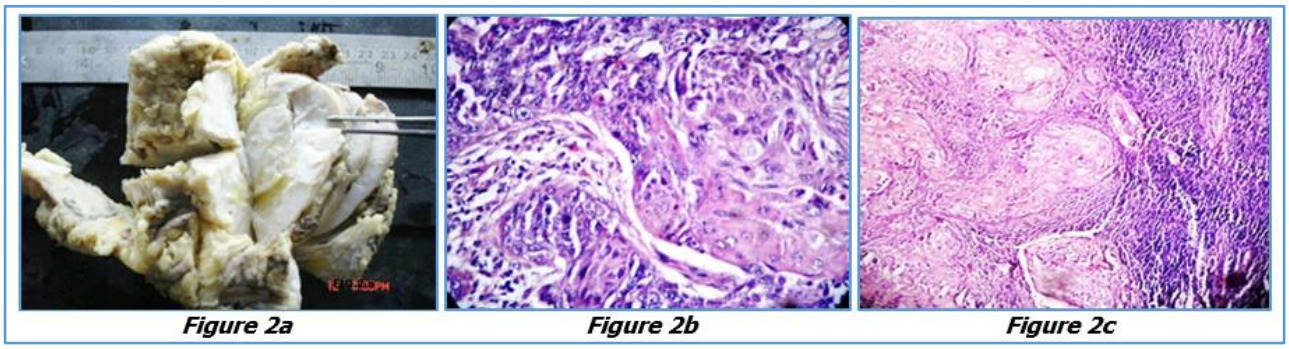

Figure 2. Gross and Microsection of Metaplastic Squamous Cell Carcinoma

2(a). Mastectomy specimen- cut surface showing growth with multiple small cysts.
2(b). Poorly differentiated ductal carcinoma with squamous metaplasia. (H&E x 400)
2(c).Lymph node showing metastatic squamous cell carcinomatous deposit.

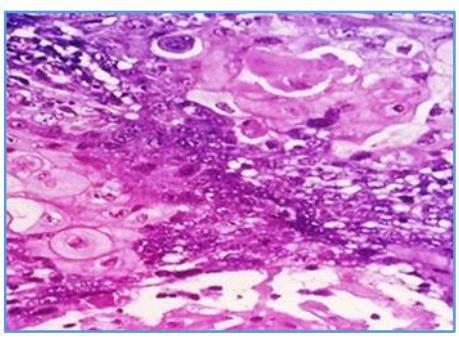

Figure 3a. Well differentiated squamous cell carcinoma from the wall of cystic cavity (H&E x 100)

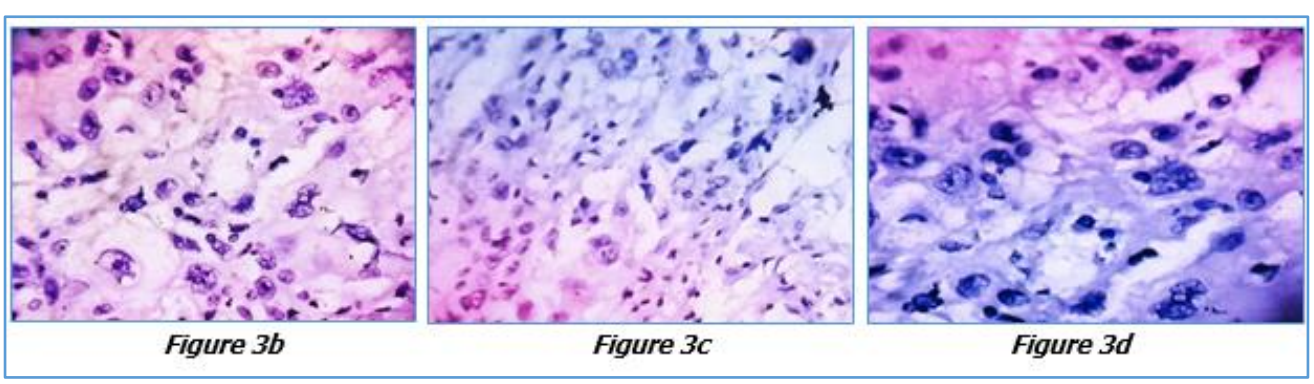

Figure 3b, 3c, 3d. ER/PR and Her2neu are triple negative (x 400)

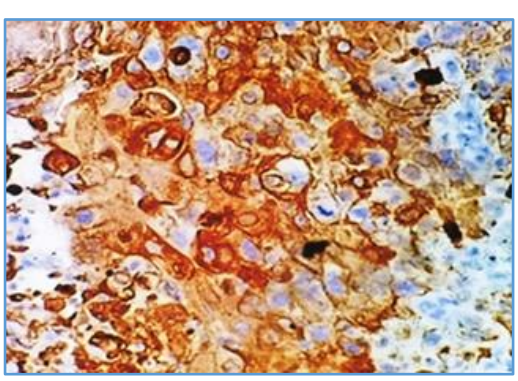

Figure 3e. CK5/6 positive (x 400)

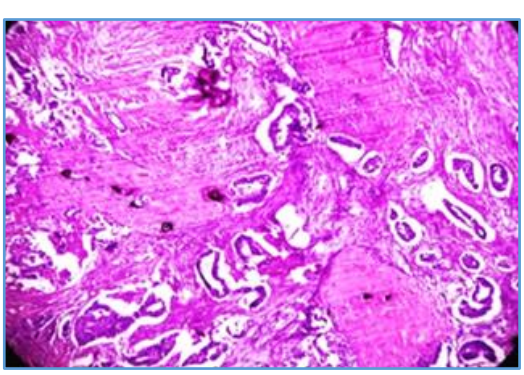

Figure 4. Matrix Producing Metaplastic Carcinoma (H&E x 400)

Showing moderately differentiated ductal carcinoma with direct transition to osseous stromal matrix.

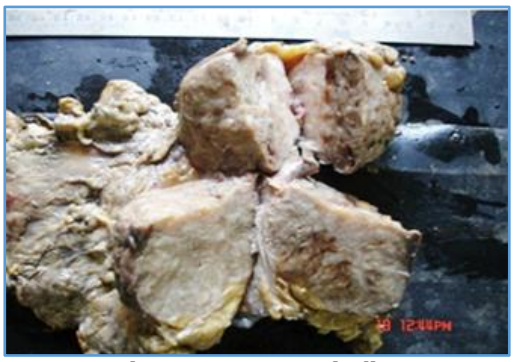

Figure 5a. Gross Finding

Mastectomy specimen- Cut surface greyish white, glistening, solid. Cut section was gritty.

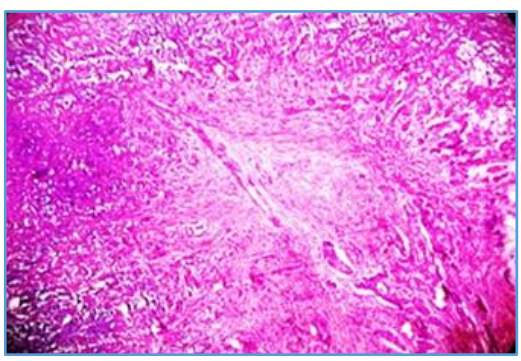

Figure 5b. (H & E x 100)

Moderately differentiated ductal carcinoma showing chondroid metaplasia with an intervening spindle cell zone.

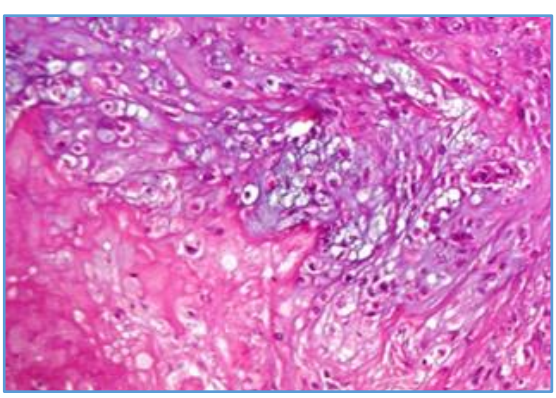

Figure 5c. Microsection (H&E x 400) Heterologous metaplastic carcinoma with chondroid metaplasia.

Age Group	IDC-NOS	Percentage	MBC	Percentage
21-30	08	1.81	0	0
31-40	85	19.27	0	0
41-50	172	39.00	0	0
51-60	100	22.67	03	60
61-70	51	11.56	02	40
71-80	10	2.26	0	0
81-90	05	1.13	0	0

Table 1. Age of Presentation of IDC-NOS & MBC

	IDC-NOS	MBC
No. of cases within 7yrs.	441	5
Maximum no. of cases	(≤ 50yrs.) 265 (60.09%)	(≥ 50yrs.) 5 (100%)
Lymph node Positivity	399 (90.47%)	3 (60%)
Average size	4cm	8cm
Focality	Multifocal 152 (34.46%)	Unifocal 100%
Triple Negative (TNBC)	8cases (1.81%)	All (100%)

Table 2. Comparison of Clinicopathological Features of MBC & IDCNOS

Type of Investigation	Tumour Type	No. of cases	Percentage
USG	Malignant	5	100
	Benign	0	0
Mammography	Malignant	5	100
	Benign	0	0
FNAC	Ductal carcinoma	4	80
	Metaplastic carcinoma	1	20

Table 3. Preoperative Evaluation of MBC

Histologic Subtype	No. of cases	Percentage
Squamous cell Carcinoma	3	60%
Metaplastic Carcinoma with mesenchymal differentiation	1	20%
Matrix Producing carcinoma	1	20%

Table 4. Histologic Sub Type of MBC

Molecular Classification	No. of cases	Percentage
Luminal A	198	44.89%
Luminal B	170	38.54%
Her 2 over-expression	65	14.73%
Triple negative (Basal Like)	8	1.81%

Table 5. Molecular Classification of IDC-NOS & MBC

Grade	IDC-NOS		MBC	
	No. of Cases	Percentage	No. of Cases	Percentage
GradeI	88	19.95%	-	-
GradeII	257	58.27%	-	-
GradeIII	96	21.76%	5	100

Table 6. Histologic Grade of IDC-NOS & MBC

Comparative Study	Lymph Node Positivity
Current study	60%
GM Tse et al	56%
Hyung Seok Park	31%
Yiquion Zhang	20.8%

Table 7. Comparison with other Study

DISCUSSION

Metaplastic breast carcinoma accounts for 0.2% - 5% of all invasive mammary carcinoma[2]. In our study, out of total 441 cases of invasive breast carcinoma 5 cases were diagnosed as MBC.

Metaplastic breast carcinoma is a rare neoplasm of breast. In our study, it constitutes 1.01% of all breast carcinoma which is consistent with literature.

Most metaplastic carcinoma are sporadic, but there may be a slight propensity for metaplastic spindle cell carcinoma to arise from pre-existing lesions such as papilloma, complex sclerosing lesion and nipple adenoma.[10] MBC is composed of mixed group of neoplasm containing both glandular and nonglandular pattern with epithelial and/or mesenchymal components.Epithelial type of MBC is further classified into 1-squamous cell carcinoma 2-Adenocarcinoma with spindle cell differentiation 3-Adenosquamous carcinoma whereas mixed type of MBC is classified into five types according to cytopathological features which are1-spindle cell, 2- squamous cell,3-matrix producing carcinoma,4 –carcinosarcoma,5- MBC with osteoclastic giant cells.[11]

DCIS is present adjacent to metaplastic carcinoma in 11% to 65% cases and usually but not always has high or intermediate nuclear grade. The presence of DCIS strongly supports diagnosis of metaplastic carcinoma. Rarely lobular carcinoma in situ (LCIS) or atypical ductal hyperplasia (ADH) can be present.[12]

Heterologous metaplastic carcinoma is characterised by differentiation into elements with mesenchymal phenotype such as cartilage or bone. Zone of spindle cell metaplasia usually intervene between the adenocarcinomatous and heterologous elements. In general carcinoma with heterologous metaplasia tend to retain an epithelial component which may be glandular and/or suamous.[13]

Matrix producing carcinoma is a variant of heterologous metaplastic carcinoma composed of overt carcinoma with direct transition to cartilaginous and/or osseous stromal matrix without an intervening spindle cell zone or osteoclastic cells.[14] In our study we found one case of matrix producing metaplastic carcinoma with direct transition to cartilaginous matrix.

Metaplastic carcinoma spindle cell with or without squamous metaplasia show variety of histologic appearances depending on the proportion of spindle cell and squamous components. MBC with spindle cell metaplasia assumed a spindle cell growth pattern that resembles fibrosarcoma.[15] The distinction between spindle cell carcinoma and primary sarcoma of the breast is difficult in the lesion having minimal epithelial component. The lesion might be mistaken for fibrosarcoma or malignant fibrous histiocytoma because of minimal epithelial component and storiform growth pattern.[16]

A common pattern of metaplastic carcinoma is focal squamous metaplasia in typical invasive ductal carcinoma. When squamous metaplasia is the predominant pattern a spectrum of differentiation may be found. Mature keratinizing epithelium, sometimes keratohyaline granule as well as adenocarcinoma can be associated with transition to spindle cell, pseudosarcomatous areas. The term adenosquamous carcinoma is often used for tumour showing both squamous and glandular component with moderate to high cellularity and nuclear atypia. Mitotic activity is usually moderate to high and areas of necrosis may be present.[17]

In a major Chinese cancer centre study by yiqian Zhang et al[18] they got spindle cell carcinoma as the most common variant, G M Tse et al[19] found in their study metaplastic carcinoma with sarcomatoid component was the most common type of MBC (70.58%) but in our study, (Table.IV), we got metaplastic squamous cell carcinoma as the most common type of MBC. we had small number of case study in 7 years period in our population group. Yiqian Zhang found highest lymph node metastasis rate in squamous cell carcinoma (25.9%) cases, GM Tse et al found 56% with axillary lymphnode metastasis. We had also found 2cases (40%) of metaplastic squamous cell carcinoma having lymph node positivity (Table.VII). Hyung Seok, Park et al[20] found in their studies the incidence of triple negative MBC cases was 84%, in our study we found 100% cases of MBC was triple negative.

Survival Analysis

The median followup time of MBC and IDC cases was 36 months and 60 months respectively. Five-year recurrence free survival rate of IDC was 85.2% and overall survival (OS) was 92.6%. Our study correlates with study of Hyung Seok,Park et al[20]. In case of MBC, median survival rate is 33 months. Five years recurrence free survival rate was 36.2%. It correlates with study of Mariotto A et al.[21]

CONCLUSION

Results of our study are consistent with the literature.MBC are large sized tumours, usually triple negative breast cancer indicating aggressiveness and lack of response to hormonal therapy. Our present knowledge of MBC is limited. The rarity and heterogeneity of MBC in biological and morphological features need further studies. The prognosis of MBC still remains controversial. Large series of patients are needed to find and rest new biomarkers to develop potential targeted therapy for subgroups of disease.

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