METAPLASTIC CARCINOMA OF THE BREAST: A CLINICOPATHOLOGICAL STUDY

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ABSTRACT

INTRODUCTION

Metaplastic carcinoma of the breast (MCB) denotes a heterogeneous group of rare malignant tumour of the breast expressing epithelial and/or mesenchymal tissue within the same tumour.

AIMS

To evaluate the clinicopathological features of 11 cases of metaplastic breast carcinoma in surgically excised malignant breast tumours in 8 years from April 2008 to March 2016.

MATERIALS AND METHODS

Total 284 consecutive cases of malignant breast lumps were removed surgically during study period, out of which 11 cases were diagnosed to have metaplastic breast carcinoma and were studied for its clinical features, size, site, gross morphological features, histopathological diagnosis, ER, PR, HER2 status, lymph node status.

OBSERVATIONS

Out of total 11 cases, 4 cases showed epithelial (tumour expressing adenocarcinoma and squamous cell carcinoma or squamous cell carcinoma alone), 6 cases showed biphasic (tumour expressing carcinoma and sarcomatoid or spindle cell component) and 1 case showed monophasic (tumour exclusively of sarcomatoid or spindle cell component). The mean age of the patient was 44 years, 8 cases were triple ER/PR/HER2 negative. Largest tumour size was 16 cm with mean size of 7 cm. Only 3 cases showed lymph node metastasis on histopathology.

CONCLUSION

In our study of metaplastic breast carcinoma, patients were found to be younger–mean age 44 years, as compared with other studies of metaplastic breast carcinomas. Clinically, they had bigger size of tumour–mean 7 cm, at presentation, aggressive course with low regional lymph node metastasis-27.3%. Most of these cases were triple negative (72.7%) for ER, PR and HER2 on immunohistochemical study.

KEYWORDS

Tumours of Breast, Rare Breast Cancers, Metaplasia.

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INTRODUCTION: These rare tumours of the breast have pathological features of both carcinoma and non-epithelial cellular component and were described under various terms which include carcinosarcoma, pseudosarcomatous metaplasia, sarcomatoid carcinoma, fibrosarcoma like squamous cell carcinoma and spindle cell carcinoma.¹⁻³ The term metaplastic breast carcinoma (MBC) was proposed by Huvos et al for all mixed carcinomas of the breast.⁴ MBC is a rare subtype and invasive breast cancer which accounts for less than 1% of all breast malignancies.⁵

Financial or Other, Competing Interest: None. Submission 04-04-2016, Peer Review 18-04-2016, Acceptance 26-04-2016, Published 28-04-2016. Corresponding Author: Dr. Sunil Vitthalrao Jagtap, Professor, Department of Pathology, KIMS, University, Karad, India. E-mail: drsvjagtap@gmail.com DOI: 10.18410/jebmh/2016/372 The WHO working group on the breast tumours recently adopted a descriptive classification of MBC which includes low grade adenosquamous carcinoma, fibromatoid like metaplastic carcinoma, spindle cell carcinoma, metaplastic carcinoma with mesenchymal differentiation and mixed metaplastic carcinoma.^{6,7}

MATERIALS AND METHODS: The retrospective, analytical study was done at a tertiary care center for a period of 8 years from April 2008 to March 2016. The clinical data was collected from medical records. The standard protocol was prepared for clinicopathological features which included age, sex, clinical presentation, breast mass site, quadrant, tumour size, FNAC, mammography and histopathological tissue diagnosis.

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The routine haematoxylin and eosin staining method was used for histological section studying. The reporting was done by a pathologist.

Inclusive criteria - all the cases having palpable breast lump diagnosed to have metaplastic carcinoma on histopathological examination were included in this study. Exclusion criteria - all other type of malignancies apart from metaplastic breast cancer were excluded.

Gross features of resected specimen were studied. Microscopic findings with histopathological finding were seen and grading of tumour was done by Modified Richardson and Bloom grading system. The immunohistochemical study, further treatment plan and followup were noted. The antibodies ER/PR, HER2 were assessed using DAKO immunohistochemistry reagents. Other immunohistochemical markers were done wherever required.

RESULTS: A total of 284 consecutive cases diagnosed as malignant breast carcinoma were studied of which 11 cases of metaplastic breast carcinoma were included in the study. The detailed clinicopathological features of all cases of metaplastic breast carcinoma are given in table 1.

				1	1							
Case No.	1	2	3	4	5	6	7	8	9	10	11	
Diagnosis	IBC NST+ Sarcoma	IBC NST+ Sq. Diff	High grade Sarcoma	IBC NST+ Malignant chondroid	IBC NST+ High Grade Sarcoma	IBC NST+ Chondroid Diff	IBC NST+Sq Diff.	IBC NST+ Matrix producing	IBC NST+RMS	IBC NST+ Sq Diff.	Pure SCC	
Age (years)	42	40	36	45	50	33	45	33	50	50	60	
Duration (month)	6	4	2.5	6	6	7	6	4	3	5	4	
Side	R	L	L	R	L	L	R	L	L	R	L	
Size (cm)	3.5x2x1.5	4.5x1.5x1	16x12x4	9x9x6.5	8x5x3	4.5x3x2	9x7x2 3x2x1	5x3x2	7.5x6.2x2	3.5x3.5x2	3x3x1	
Quadrant	LOQ	UOQ	UOQ+LOQ	UOQ	UIQ+LIQ	LIQ	UIQ & LIQ	UOQ	UIQ	CENTRAL	UOQ	
Mobile/Fixed	Mobile	Mobile	Mobile	Fixed to skin	Mobile	Fixed to skin	Mobile	Mobile	Fixed to tissue	Mobile	Mobile	
Unifocal/ multifocal	Uni	Uni	Uni	Uni	Uni	Uni	Multi	Uni	Uni	Uni	Uni	
Epithelial component	IBC NST-II	IBC NST-II	IBC NST-II	IBC NST-II	IBC NST-III	IBC NST-II	IBC NST-II	IBC NST-II	IBC NST-III	IBC NST-III	Squamous cell Ca.	
Mesenchymal component	Spindle cells	Sq diff	Sarcoma	Chondroid	sarcoma	Chondroid	Sq diff	Matrix	Rhabdoid	Sq diff	-	
Other specific features	-	-	Recurrence axillary mass	Lung & Liver mets	-	-	-	-	Axillary mass	-	Lung mets+malig Pleural effusion	
Axillary LN(Involved/ total)	0/10	4/4	0/1	1/5	0/27	0/3	0/15	0/5	2/8	0/16	0/3	
ER/ PR/ HER2, others	-/-/-	+/+/-	-/-/-, CK+, Vimentin+	-/-/-	-/-/-	-/-/-	-/-/-	-/-/+, EMA+, S100+	-/-/- Myogenin+, MyoD1+	-/-/+	-/-/-CK+	
	Table 1: Clinicopathological Features of all Cases of Metaplastic Breast Carcinoma											

IBC NST–Invasive Breast Carcinoma No Special Type, Sq diff –Squamous differentiation, diff-differentiation, SCC– Squamous cell carcinoma, R-Right, L–Left, LOQ–Lower outer Quadrant, UOQ–Upper Outer Quadrant, UIQ–Upper Inner Quadrant, LIQ–Lower Inner Quadrant, LN–Lymph Node, mets-metastasis, RMS-rhabdomyosarcoma.

Clinical Features: All 11 cases in our study were females. Age range of patient was from 33 to 60 years with mean age of 44 years. Clinically, all presented with lump in breast with duration ranging from 2.5 months to 6 months. Patient usually gave history of rapid growth of lump in short duration. Nipple discharge was noted in 1 case. Skin ulceration was seen in 2 cases and fixity to skin and underlying tissue was seen in 3 cases. On followup, one case (case number 3 from table 1) presented with local recurrence twice in short duration, first at the site of operation and later as a huge axillary mass.

The left breast was involved in 7/11 cases and right in 4/11 cases. FNAC was available in all cases and showed positivity for malignant cells. On sonomammography, 5 cases showed calcifications. The tumour size varied from 3 cm to 16 cm with mean size of 7 cm. Out of total 11 cases, 3 cases showed axillary nodal metastasis and 2 cases showed evidence of distant metastasis, one in both lung and liver and other with malignant pleural effusion (small lung metastasis).

DISCUSSION: Metaplastic carcinoma represents a group of unrelated invasive breast cancers displaying differentiation of the tumour cells into squamous or mesenchymal looking elements.

Most benign and malignant tumours of the breast arise from glandular epithelium. However, in some cases glandular epithelium differentiates into non-glandular mesenchymal tissue which is called as metaplasia. Such differentiation may become significant component of the tumour and gives specific distinct entity. Metaplastic breast carcinoma is often histologically subdivided into several distinct subtypes which include squamous, matrix producing, carcinosarcoma, spindle cell, metaplastic breast carcinoma with osteoclastic giant cells, metaplastic breast carcinoma with chondroid differentiation etc. The pathological classification of metaplastic breast carcinoma is challenging due to the diversity of the histological patterns and rarity of diagnosis. The preoperative diagnosis of breast lump is usually done with the help of FNAC and sonomammographic features. In diagnosing benign or malignant epithelial lesions of the breast fine needle aspiration cytology has been successful. However, breast lesions with a mesenchymal component are rarely encountered in FNA posing a diagnostic dilemma.8

In almost one half of the cases, the diagnosis is not possible by FNAC to show both ductal carcinoma and metaplastic carcinoma elements as study by Doshi et al.⁹ In our study, all cases were reported as positive for malignant cells, but in 3 cases the differentiation was difficult to detect whether it is related to high grade invasive breast carcinoma or high grade sarcoma. Thus, final differentiation was done on histopathology and immunohistochemical study.

In preoperative core needle biopsies, accurate diagnosis of MBC can be a challenging.¹⁰ Tumour heterogeneity is presumably the major contributing factor to the challenge. Therefore, surgical excision is the necessary procedure to achieve the final diagnosis.

In our study, the cases of metaplastic breast carcinoma were divided as shown in table 1. The mean age of presentation was 44 years with range from 33 years to 60 years. All the cases in our study were female. The left side breast was commonly involved and one case showed multicentric tumour lump. The clinical presentation of MBC has several differences from the presentation of other invasive breast carcinomas. MBC more commonly presents as a rapidly growing mass, and it has been consistently reported to present larger than typical breast cancers. Metaplastic breast carcinoma reported in western studies shows that the common age for occurrence is older than 50 years of age.^{11,12} In the present study, patients with metaplastic breast carcinoma presented at a younger age than other international studies.

In our study, the size of breast tumour ranged from 3 cm to 16 cm with mean of 7 cm. The metaplastic breast carcinoma are generally present to larger size than typical breast cancers and usually more than 2 cm and shows rapidly growing mass.^{1,13} Despite larger tumour size, the axillary nodal metastasis rate is between 6-26%.^{13,14} Present study showed axillary nodal metastasis in 3 cases (27.3%), while 8 cases showed no nodal involvement; however, two cases showed distant metastasis, one to both in lung and liver and other in lung with malignant pleural effusion.

According to previous WHO classification of tumours of breast, the metaplastic breast carcinomas are divided into two types on histological features as⁵: a) Epithelial type metaplastic breast cancer and b) Mixed type metaplastic breast cancer.

Accordingly, in our study on histopathology subtype, all cases showed epithelial component and 6 cases (54.5%) showed biphasic (epithelial and mesenchymal component). When mesenchymal component is predominant in tumour, in such cases finding of malignant epithelial component is difficult requires and extensive sampling and immunohistochemical confirmation. When spindle cell atypical in metaplastic breast carcinoma with prominence it must be distinguished from malignant phyllodes tumour and primary or metastatic sarcoma.¹⁵ The distinction between metaplastic carcinoma and malignant phyllodes tumours of the breast is critical because the treatment and prognosis differ significantly.

Squamous cell carcinoma is an extremely rare variant of breast cancer.¹⁶ The case 11 (Table 1) pure squamous cell carcinomas on microscopic examination showed malignant squamous cells, large polygonal cell with dyskeratosis, abundant keratin and large areas of necrosis. The possibility of metastasis from another primary site was excluded before diagnosis of primary squamous carcinoma of breast. Adenosquamous carcinomas were composed of invasive breast carcinoma admixed with areas of malignant squamous differentiation in case no 2, 7, 10 (Table 1).

Immunohistochemistry was done for ER, PR, HER2 in all cases. The triple negative cases were 72.7%. The reported series shows most of cases were triple negative.^{12,17} Reported data shows metaplastic breast carcinoma rarely shows nuclear reactivity for ER and PR hormone receptors which range from 0 to 17%.^{11,12,17} In our study, ER positivity was seen in 9% and PR positivity in 9%. The mesenchymal/stromal element requires additional immunohistochemistry study for its specific diagnostic confirmation. All the cases in our study underwent modified mastectomy. Additional chemotherapy radical and radiotherapy was given as per requirement of the cases. It has been reported that the lack of ER, PR, and HER2 expression makes endocrine therapy and molecularly targeted therapy ineffective. Therefore, adjuvant and/or neoadjuvant chemotherapy have become the mainstay of management, although no therapeutic regimen has proven to be effective.

MBC has been reported to have a poorer prognosis than invasive breast carcinoma.^{18,19} Although comparable prognoses have been reported in cases with matched stages, recognition of metaplastic breast carcinoma on histopathological finding is required as it is an aggressive type of breast cancer with poor prognosis. So further effective comprehensive therapeutic regimen to treat these patients will be required.²⁰

CONCLUSION: Metaplastic breast carcinoma is an extremely rare subtype of invasive breast cancer. Careful evaluation of breast specimens during histopathological

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examination is essential. The cases of metaplastic breast carcinoma in our study were having large tumour size, high rate of ER, PR and HER2 negativity on immunohistochemical study and involvement of axillary nodal metastasis was low as compared to other invasive breast cancers. Metaplastic breast carcinoma in our study presented at a younger age than other studies done in western countries.

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