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Original Article

Pathology Section

Metaplastic Carcinoma of Breast: A Rare Pathological Entity- A Study of 10 Cases from Tertiary Care Centre in Northern India

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ABSTRACT

Introduction: Metaplastic Carcinoma of Breast (MCB) is a rare heterogeneous neoplasm characterised by a mixture of adenocarcinoma with dominant areas of spindle cells, squamous and other mesenchymal differentiation. The reported incidence is 0.2% of all breast cancers.

Aim: To study the clinicopathological presentation, pathologic features and differential diagnosis of MB.

Materials and Methods: This retrospective cross-sectional descriptive study included 10 cases of MCB who underwent mastectomy and biopsies at BPS GMC Khanpur Kalan, Sonipat, Haryana, India from March 2013 to February 2020. Data were analysed by Microsoft Office Excel Datasheet 2019.

Results: Out of 10 cases, five cases were MCB Not Otherwise Specified (NOS) type, four cases were MCB with mesenchymal differentiation and one case showed rhabdomyosarcomatous differentiation. The right breast was involved in nine cases. The mean size of tumour was 8 cm with range of 3 to 16 cm. Five patients were treated by modified radical mastectomy and axillary dissection, four patients had lumpectomy and one patient underwent mastectomy. Half of the patients were below 40 years with the mean age being 36.8 years and range of 21-60 years. On Immunohistochemistry (IHC), 90% (9/10) cases were triple negative.

Conclusion: The MCB, although rare has to be diagnosed and excised at the earliest as the prognosis is predicted to be worse similar to other triple negative breast carcinomas. Ductal Carcinoma in Situ (DCIS) at the tumour periphery and co-expression of vimentin and cytokeratin would help to clinch the diagnosis in difficult situations.

Keywords: Carcinosarcoma, Mastectomy, Neoplasm, Osteosarcoma, Rhabdomyosarcoma

INTRODUCTION

In 1973, Huvos AG et al., first described the metaplastic carcinoma of the breast [1]. It is a rare and histologically a diverse subtype of breast carcinoma. There has been limited research as it was not recognised as a distinct subtype until 2000. It accounts for less than 1% of all breast cancers [1-3]. Multiple types of MCB have been described, in 2012 World Health Organisation (WHO) Classification of Tumours of the Breast, broadly as: a) No special type- low-grade adenosquamous carcinoma, fibromatosis like metaplastic carcinoma, squamous cells carcinoma, and spindle cell carcinoma; b) With mesenchymal differentiation- (chondroid, osseous and other mesenchymal differentiation); and c) Mixed metaplastic carcinoma [4].

Clinicopathological features: The MCB is often seen in 5th or more decade women and present as a palpable breast mass [1,4]. These are characterised by large size and rapid growth. The imaging characterisitcs of lesions can be simliar to Invasive Ductal Carcinoma (IDC) and benign lesions on mammography, sonography, and Magnetic Resonance Imaging (MRI). The imaging spectrum can be from circumscribed, round or oval shapes lesions on mammogram to lobular, circumscribed, hypoechoic solid mass with posterior acoustic enhancement on ultrasound with MRI T2 hyperintensity [5]. These lesions usually show Oestrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal growth factor Receptor 2 (HER2neu) negativity. Axillary lymph nodes can be invoved in 8-40% of cases [6]. Comparing with IDC, MCB shows poor prognosis with 5-year survival rates as 49-68% [7].

In this study, authors have discussed clinicopathologic presentation, pathologic features and differential diagnosis of this rare type of breast cancer.

MATERIALS AND METHODS

This was a retrospective cross-sectional descriptive study done in Pathology Department of BPS GMC Khanpur Kalan, Sonipat, Haryana, India from March 2013 to Feburary 2020, analysis of the data was done in March 2020. Institutional Ethical Commitee (BPSGMCW/RC/180/IEC/16) permission was taken. Considering the descriptive observational study of this rare subtype of breast carcinoma, convenient sampling of 10 cases (as total revcieved) of MCB who underwent mastectomy and biopsies during the study duration was taken.

Data from clinical history, imaging and operative details of histopathologically proven MCB cases was retrieved from medical record section as available for study inclusion. Cases data with patient history of previous exposure to chemotherapy or radiotherapy was excluded from the study. Histopathology blocks and IHC slides of panel comprising of ER and PR, HER2/neu as done in all cases and cytokeratin, vimentin, p63, S100 and desmin as done in different respective cases were retrieved from histopathology section of Pathology department. WHO Classification of Tumour of the Breast, 2012 has been used for characterisation of cases [4]. Data was studied, associated and summarised.

STATISTICAL ANALYSIS

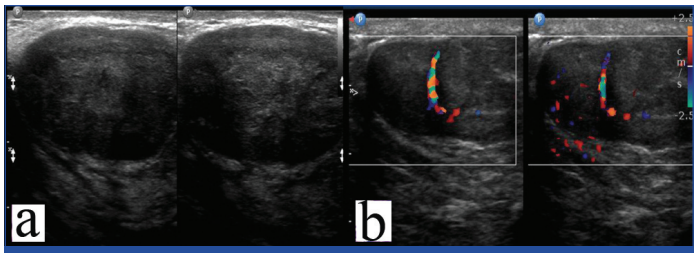
Mean and median were calculated. Data were analysed by Microsoft Office Excel Datasheet 2019.

RESULTS

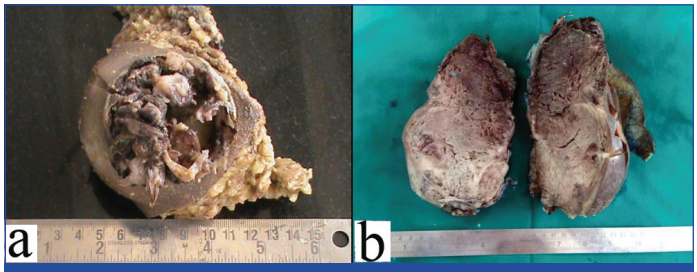
Right breast was involved in nine out of the ten cases. The lesions ranged from 3-16 cm with mean as 8 cm and the duration of lesion was upto six months in most of the cases. Half of the patients were below 40 years with mean age being 36.8 years and age range of 21-60 years. Two patients were postmenopausal and others had normal menstrual history and none of the patient had family history of carcinoma breast. The Ultrasonography (USG) of lesions (as available) showed well defined, homogenous, round to hypoechoic lesions with internal vascularity on Doppler mimicking benign

lesions [Table/Fig-1a,b] (Case No. 10). Five patients were treated by modified radical mastectomy and axillary dissection, one patient was treated by mastectomy with axillary clearance and four patients underwent lumpectomy. Grossly, the large MCB cases showed ulceration and cut surface showed infiltrative grey white tumour with areas of necrosis and firm glistening cartilaginous and bony areas [Table/Fig-2a,b], (Case No 3 and 6). Cases No 1-5, 6-9 and 10 were of MCB, NOS type, MCB with mesenchymal differentiation and with rhabdomyosarcomatous differentiation respectively [Table/Fig-3].

On histological examination, four cases (Case No. 1-4) of MCB NOS type contained malignant IDC component, histological grade III admixed with high-grade spindle sarcomatoid elements with giant cells [Table/Fig-4a]. Case No. 5 showed tumour composed of polygonal cells with increased N/C ratio, hyperchromatic nuclei, eosinophilic cytoplasm and at places showed keratinisation and intercellular bridges [Table/Fig-4b,c]. Four cases (Case No. 6-9) showed MCB with mixture of heterologous myxoid and chondroid elements and large areas of necrosis. Case No. 6-8 showed MCB with chondrosarcomatous areas [Table/Fig-4d] and Case No. 9 showed osteosarcomatous tumour area with osteoid production [Table/Fig-5a]. Case No. 10 showed MCB with rhabdomyoblastic differentiation [Table/Fig-5b-d]. The detailed immunohistochemical profile of the subtypes is shown in [Table/Fig-6].



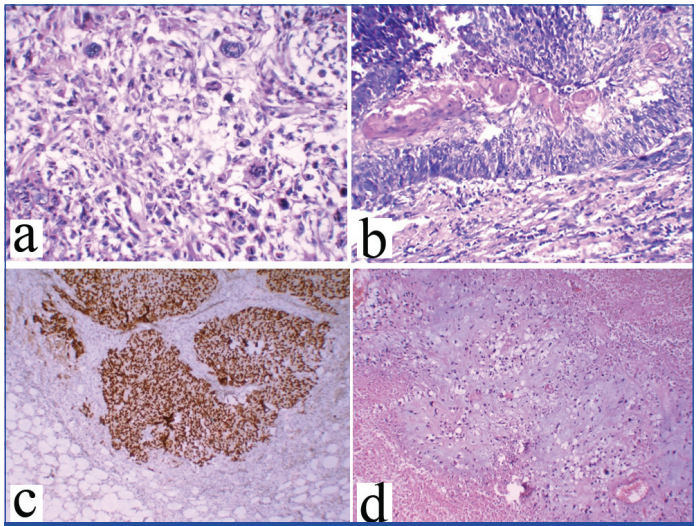
[Table/Fig-1]: Case No 10 (a and b) Grey scale USG images showing well defined lobulated hypoechoic mass lesion measuring 3×2.5 cm in right breast which shows internal vascularity on Doppler images.



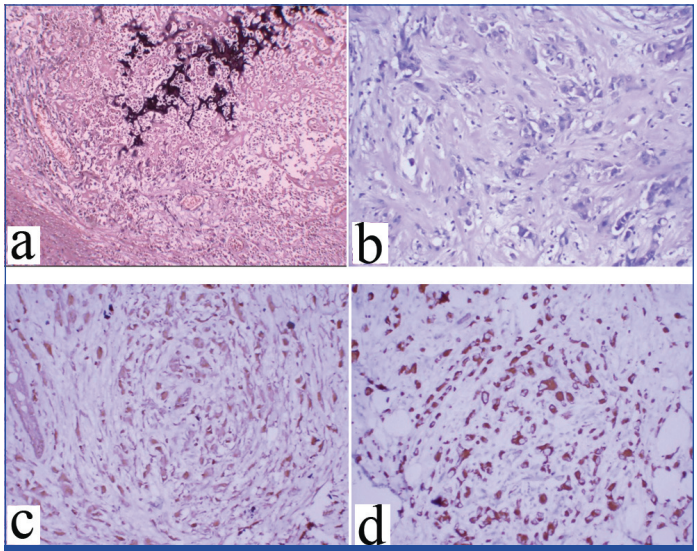
[Table/Fig-2]: Gross images- a) Case No 3, Carcino-sarcomatous MCB- Large, ulcerated growth measuring 7×5.5×5 cm; b) Case No 6, Matrix producing MCB- cut surface showing infiltrative grey white tumour measuring 16×16×8 cm with areas of necrosis and firm glistening chondroid areas.

Case No.	Subtype	Age (in years)/ Sex	Laterality and duration of lesion (in Months)	Type of specimen and gross findings	Size*(cm)	Nodal status
1-5	**MCB (NOS)** Carcino-sarcoma (1-4)	28/F	Left and 3	Mastectomy with axillary tail dissection and grey white infilterative tumour	5	0/5
		26/F	Right and 2	Lumpectomy	3	-
		41/F	Right and 4	MRM with axillary lymph nodes dissection and large, ulcerated growth	8	2/10
		36/F	Right and 6	MRM with axillary lymph nodes dissection and large areas of haemorrhage and necrosis	7	0/12
	MCB (NOS) Squamous cell carcinoma (5)	21/F	Right and 2	Lumpectomy and grey white infilterative tumour	4	-
6-9	**MCB with mesenchymal differentiation** (Osteo and Chondrosarcomatous differentiation) (4)	60/F	Right and 4	MRM and large areas of necrosis and calcified areas	16	-
		41/F	Right and 6	Lumpectomy	6	-
		50/F	Right and 6	MRM with lymph node dissection and large areas of haemorrhage and necrosis	12	2/11
		42/F	Right and 12	MRM and large bony hard calcified areas	10	-
10	**MCB with Rhabdomyosarcomatous differentiation (1)**	26/F	Right and 6	Lumpectomy	3	-

[Table/Fig-3]: Clinicopathological features of MCB subtypes.
*Largest dimension, MRM: Modified radical mastectomy



[Table/Fig-4]: a) Case No 3- MCB NOS subtype showing malignant cells in sheets and nest with occasional multi-nucleated giant cells and mitosis (H&E, 20X); b) Case No 5 MCB NOS subtype showing squamous cells with hyperchromatic nuclei, keratinization and intercellular bridges (H&E, 10X); c) Staining with p63 (IHC, 10X); d) Case No 6- MCB with mesenchymal differentiation showing malignant cells with chondrosarcomatous area (H&E, 10X).
H&E: Hematoxylin and eosin; IHC: Immunohistochemistry



[Table/Fig-5]: a) Case No 9, MCB with mesenchymal differentiation showing Osteo-sarcomatous area and osteoid production (H&E, 10X);); b-d) MCB with rhabdomyosarcomatous differentiation Case No 10- b) showing rhabdomyoblastic cells infiltrating the breast parenchyma (H&E, 10X); c) Staining with desmin (IHC, 20X); d) Cytokeratin (IHC, 20X).
H&E: Hematoxylin and eosin; IHC: Immunohistochemistry

Case No	Subtypes	ER	PR	HER2/neu	Pan CK	p63	S100	Desmin	Vimentin
1-5	**MCB (NOS)** Carcino-sarcoma (4)	-	-	-					
		-	-	-	+				
		-	-	-					
		+	-	+	+				
	MCB (NOS) [Table/Fig-5b,c] Squamous cell carcinoma (1)	-	-	-		+			
6-9	**MCB with mesenchymal differentiation** (Osteo and Chondrosarcomatous differentiation) (4)	-	-	-	+				+
		-	-	-	+	+	+		
		-	-	-	+				+
		-	-	-			+		
10	**MCB with Rhabdomyosarcomatous differentiation (1)** [Table/Fig-6b-d]	-	-	-	+	-		+	

[Table/Fig-6]: Immunohistochemical profile* of MCB subtypes.
*As Available in different subtypes; (-): Negative for marker, (+): Positive for marker; ER: Oestrogen receptor, PR: Progesterone receptor; CK: Cytokeratin

DISCUSSION

There are major challenges in classification of MCB and its differentials due to the rarity and histological diversity [5]. Though actual pathogenesis of MCB is still unknown but few theories clarified the histomorphological diversity of this tumour, including genetic and non genetic mechanisms with reports suggested origin from cancer stem cells or myoepithelial progenitors [8]. Few reports also suggested the theory of epithelial to mesenchymal transition causing transformation of the carcinomatous component into the sarcomatous component [9].

In present study, authors had evaluated 10 MCB cases for their clinicopathological and immunohistochemical profile. Half of the patients were below 40 years with mean age being 36.8 years and age range of 21-60 years. In contrast Western series reported MCB in women older than 50 years of age [6,10,11]. Young age group shows spindle cell proliferation and warrants differential diagnosis of rare sarcoma. It is difficult to differentiate low-grade spindle cell metaplastic carcinoma with key morphologic features as irregularly fat infiltration, entrapped ducts with variable atypia and plump atypical spindle cell nuclei exhibiting cytokeratin immunoreactivity on IHC [12]. In this study, irregular infiltration of fat and breast parenchyma was observed as shown in MCB squamous cell carcinoma and rhabdomyoblastic differentiation cases. DCIS was also observed in two cases. Several antibodies like High Molecular Weight Cyto-Keratin (HMW CK) (34bE12), CK5/6, smooth muscle actin, muscle-specific actin and p63 have been described useful in supporting the diagnosis and hypothesis of derivation from myoepithelial cells with p63 expression may be seen in both epithelial and spindle cell components [5,6,13]. Moderate atypical metaplastic carcinomas is to be distinguished from malignant phyllodes tumour and sarcoma as the treatment and prognosis both differ significantly [12,14]. Certain features as Leaf like architecture, stromal cell CD34 expression and lack of cytokeratin expression favours diagnosis of phyllodes tumour [8]. Immunohistochemical panel as proposed by Hicks DG and Tang P consisting ER, PR, HER2, Epidermal Growth Factor Receptor (EGFR) and cytokeratin 5/6 (CK 5/6) as a surrogate for molecular classification was widely accepted in identifying breast carcinomas with basal-like immunophenotype and categorisation of MBC [9,10,13]. A 90% cases were found to be Triple Negative Breast Carcinomas (TNBC) and didn't exhibited positivity to ER, PR or HER2 and only one case showed immunopositivity with ER and HER2 neu while negative for PR. These findings were in concordance with previous studies [Table/Fig-7] [15-20]; concluding that rare nuclear reactivity MCB for ER and PR hormone receptors in range of 0 to 17% [11,17-21]. The rate of HER2 overexpression has been shown variable in different studies ranging from 4-19.6% and up to 72% in one of the study [21,22]. Triple negative features of MCB in range from 77-96 % have been described in few studies. The p63 positivity in majority of squamous cell carcinoma cases and EGFR overexpression in up to 80% of cases of MCB have been reorted in few studies [22-25]. The axillary lymph nodal metastasis in MCB has been reported lower than that of IDC as incidence being 15-36% [20]. In this study, out of four MRM specimens with lymph node dissection, two showed lymph node metastasis.

There are still lot of controvesies regarding prognosis of MCB; however most of the studies showed its more aggressive behaviour than IDC [7]. In a study comparing 29 cases of MCB with 4,851 cases of IDC, Park HS et al., found comparable survival rates of stage I-III of MCB to those of IDC wth incidence of MCB stage IV disease at the diagnosis and recurrence being higher [26]. In present study, two cases of matrix producing MCB showed recurrence within six month. Younger age presentation, skin invasion, squamous cell carcinoma subtype and nodal spread have been described as poor prognostic factors of MCB. Few studies reported insignificant role of subtypes in MCB prognosis [2]. Association of phenotypic diversity of breast cancer with differences in risk factors, biological behaviour,

Authors and publication year	No. of cases	Diagnosis (Subtypes and No. of cases)	Conclusions
Rungta S and Kleer CG 2012 [15]	1	Metaplastic carcinoma with spindle cell differentiation (1)	34bE12 and cytokeratin 5/6 as most sensitive and specific in Immunohistochemical diagnosis of metaplastic carcinomas
Dewasi N et al., 2014 [16]	2	Spindle cell carcinoma (2)	MCB are rare and have poor prognosis and need to be excised at the earliest
Altaf FJ et al., 2014 [17]	7	Squamous cell carcinoma (3) Spindle cell sarcoma (1) Choriocarcinoma (3)	Younger age affected, all cases were Triple negative with majority of cases developed early local recurrence and metastasis over follow-up
Muthusamy RK and Mehta SS 2016 [18]	2	Spindle cell sarcoma (2)	MCB are extremely rare malignancy with divergent differentiation and controversial histogenesis, need extensive sampling of tumour, Co-expression of Vimentin and Cytokeratin helps in diagnosis
Boler D et al., 2016 [19]	7	Spindle cell carcinoma (2) Mixed epithelial and mesenchymal type (3) epithelial type (2)	85% were triple negative, more efforts should be made to find potential molecular targets to pass beyond small series
Mohanty S et al., 2018 [20]	9	Carcinosarcoma (3) Squamous cell carcinoma (3) Adenosquamous carcinoma (2) ILC with osseous metaplasia (1)	All were triple negative, poor prognosis and refractoriness to conventional chemotherapy, multi-institutional studies are needed to evaluate a new treatment paradigm with multitargeted combination therapy to improve survival outcome.

[Table/Fig-7]: Review of literature of metaplastic carcinoma of breast [15-20].

clinical outcome, histologic grades and response to therapy has been described by Perou CM et al., [8]. However, few believed in role of subtypes in prognosis describing more favourable outcome for fibromatosis-like spindle cell tumours and low likelihood of axillary metastasis in tumours with predominantly sarcomatous morphology [12,18]. Mastectomy and radiation therapy has been recommended for MCB equal or larger than 5 cm or with 4 or more metastatic axillary lymph nodes (irrespective of size of the tumour). Adjuvant radiation should always be considered as part of the multimodality therapy for MCB irrespective of the its subtype [7].

Limitation(s)

Though authors have studied maximum number of cases comparing previous studies in past, limitation of rarity of this disease further warrants advanced scientific exploration to have more light in the unexposed perspective of this rare pathlogical entity.

CONCLUSION(S)

Divergent differentiation and histogenesis of metaplastic carcinoma of the breast have been described which is a rare histological subtype of breast cancer with aggressive nature and poor prognosis. It should always be included in the differentials of breast carcinomas with spindle cell subtype. Extensive sampling of tumour tissue should be done to rule out the presence of adjoining focus of DCIS, fat infiltration with IHC being quite helpful in the narrowing the differentials.

REFERENCES

[1] Huvos AG, Lucas JC Jr, Foote FW Jr. Metaplastic breast carcinoma: Rare form of mammary cancer. N Y State J Med. 1973;73:1078-82.
[2] Rauf F, Kiyani N, Bhurgni Y. Metaplastic carcinoma of breast, an intriguing rarity. Asian Pac J Cancer Prev. 2006;7(4):667-71.
[3] Patrikar A, Maimoon S, Mahore S, Akhtar MA, Wilkinson A. Metaplastic carcinoma of breast (carcinosarcoma variant): A case report. Indian J Pathol Microbiol. 2007;50(2):396-98.
[4] Reis-Filho JS, Lakhani SR, Gobbi H, Sneige N. Metaplastic carcinomas. In: Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, eds. WHO Classification of Tumours of the Breast. Lyon, France: IARC Press; 2012:48-52.
[5] Gunhan-Bilgen I, Memis A, Ustun EE, Zekioglu O, Ozdemir N. Metaplastic carcinoma of the breast: Clinical, mammographic, and sonographic findings with histopathologic correlation. AJR Am J Roentgenol. 2002;178:1421-25.
[6] Oberman HA. Metaplastic carcinoma of the breast: A clinicopathologic study of 29 patients. Am J Surg Pathol. 1987;11(12):918-29.
[7] Lai HW, Tseng LM, Chang TW, Kuo YL, Hsieh CM, Chen ST, et al. The prognostic significance of metaplastic carcinoma of the breast (MCB)-A case controlled comparison study with infiltrating ductal carcinoma. Breast. 2013;22(5):968-73.
[8] Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000;406:747-52.
[9] Ennessy BT, Gonzalez-Angulo AM, Stemke-Hale K, Gilcrease MZ, Krishnamurthy S, Lee JS, et al. Characterisation of a naturally occurring breast cancer subset enriched in epithelial-to-mesenchymal transition and stem cell characteristics. Cancer Res. 2009;69:4116-24.
[10] Hicks DG, Tang P. Molecular classification of breast carcinoma: Is immunohistochemistry a viable alternative to other molecular methodologies? Connection. 2009;13:31-34.
[11] Lim KH, Oh DY, Chie EK, Han W, Im SA, Kim TY, et al. Metaplastic breast carcinoma-clinicopathologic features and prognostic value of triple negativity. Jpn J Clin Oncol. 2010;40(2):112-18.
[12] Lee AH. Recent developments in the histological diagnosis of spindle cell carcinomas, fibromatosis and phyllodes tumour of the breast. Histopathology. 2008;52(1):45-57.
[13] Adem C, Reynolds C, Adlakha H, Roche PC, Nascimento AG. Wide spectrum screening keratin as a marker of metaplastic spindle cell carcinoma of the breast: An immunohistochemical study of 24 patients. Histopathology. 2002;40(6):556-62.
[14] Tse G, Tan PH, Lui P, Putti TC. Spindle cell lesions of the breast-The pathologic differential diagnosis. Breast Cancer Res Treat. 2008;109(2):199-207.
[15] Rungta S, Kleer CG. Metaplastic carcinomas of the breast: Diagnostic challenges and new translational insights. Arch Pathol Lab Med. 2012;136(8):896-900.
[16] Dewasi N, Bhattacharya D, Sarker P, Das M, Ghosh S, Ghosh T. Metaplastic carcinoma of breast. Journal of Pathology of Nepal. 2014;4(7):594-96.
[17] Altaf FJ, Mokhtar GA, Emam E, Bokhary RY, Mahfouz NB, Amodi SA, et al. Metaplastic carcinoma of the breast: An immunohistochemical study. Diagn Pathol. 2014;9:139.
[18] Muthusamy RK, Mehta SS. Metaplastic carcinomas of Breast. IOSR-JDMS. 2016;15(8):81-84.
[19] Boler D, Kara H, Saglican Y, Tokatb F, Uras C. Metaplastic carcinoma of the breast: A case series and review of the literature. Journal of Oncological Sciences. 2016;2:38-42.
[20] Mohanty S, Devi YS, Nongrum DL, Singh LJ, Sekar V, Das DS. Metaplastic carcinoma of breast: A series of nine cases from a regional cancer center in Northeast India. Oncol J India. 2018;2:69-74.
[21] National Cancer Registry Kingdom of Saudi Arabia, Ministry of health: Cancer Incidence Report. 2004. Report.
[22] Abd El-Rehim DM, Pinder SE, Paish CE, Bell J, Blamey RW, Robertson JF, et al. Expression of luminal and basal cytokeratins in human breast carcinoma. J Pathol. 2004;203(2):661-71.
[23] Weigelt B, Kreike B, Reis-Filho JS. Metaplastic breast carcinomas are basal-like breast cancers: A genomic profiling analysis. Breast Cancer Res Treat. 2009;117:273-80.
[24] Carter MR, Hornick JL, Lester S, Fletcher CD. Spindle cell (sarcomatoid) carcinoma of the breast: A clinicopathologic and immunohistochemical analysis of 29 cases. Am J Surg Pathol. 2006;30(3):300-09.
[25] Reis-Filho JS, Milanezi F, Carvalho S, Simpson PT, Steele D, Savage K, et al. Metaplastic breast carcinomas exhibit EGFR, but not HER2, gene amplification and overexpression: Immunohistochemical and chromogenic in situ hybridisation analysis. Breast Cancer Res. 2005;7:1028-35.
[26] Park HS, Park S, Kim JH, Lee JH, Choi SY, Park BW, Lee KS. Clinicopathologic features and outcomes of metaplastic breast carcinoma: Comparison with invasive ductal carcinoma of the breast. Yonsei Med J. 2010;51(6):864-69.

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