

# Metaplastic Breast Carcinoma with Heterologous Mesenchymal Differentiation and Carcinoma with Pleomorphic Pattern, A Case Report and Review of Literature

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Received: 01 July 2024

Accepted: 31 July 2024

Published: 05 Aug 2024

J Short Name: AJSCCR

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## Citation:

Mori H. Metaplastic Breast Carcinoma with Heterologous Mesenchymal Differentiation and Carcinoma with Pleomorphic Pattern, A Case Report and Review of Literature. *Ame J Surg Clin Case Rep.* 2024; 8(2): 1-5

## 1. Abstract

Metaplastic carcinoma and pleomorphic carcinoma are rare malignant tumors of the breast. We have encountered a unique case of metaplastic carcinoma with heterologous mesenchymal elements such as chondroid and osseous, in 54-year-old woman. In this case, another type of ductal carcinoma with pleomorphic pattern was recognized near by the metaplastic carcinoma. The latter tumor was characterized by a proliferation of pleomorphic and bizarre giant cells. Two tumors were interpreted independent lesions. To the best of our knowledge, such case of the coincidence of two rare carcinomas has not been described. Clinicopathological features of the two types of carcinomas will be valuable for understanding of the biological behavior and histogenesis of these breast carcinomas.

## 2. Introduction

Metaplastic breast carcinoma [MBC] has been reported to account for 0.2-5% of all invasive breast carcinomas [1] and occurs mostly in woman with the median age of 50 years [2]. MBC with mesenchymal differentiation are often composed of admixture of mesenchymal components such as chondroid, osseous and rhabdomyoid together with epithelial component which can be in the forms of glandular differentiation and /or squamous differentiation [1, 3]. Meanwhile, pleomorphic carcinoma is regarded as a prognostically unfavourable lesion and represents the extreme end of the morphological spectrum of grade III infiltrating ductal carcinoma which is characterized by a proliferation of pleomorphic and bizarre, multinucleated tumor cells comprising >50% of the tumor

cells [3, 4].

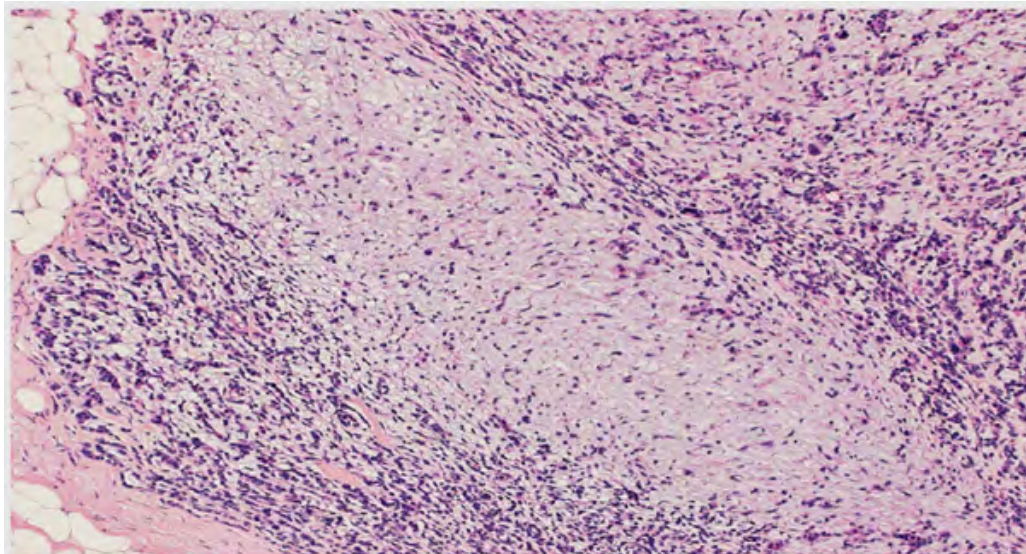
Presently, we report a unique case of two types of breast carcinomas of 54-year-old woman. Pathologically, main nodule of the breast of the patient who underwent mastectomy displayed characteristics of metaplastic carcinoma with mesenchymal differentiation with chondroid, osseous and myxoid matrix in addition to squamous metaplasia in the epithelial element. Moreover, carcinoma with pleomorphic pattern [3] with bizarre giant cells was found in an independent area. To the best of our knowledge, such case of coexistence of metaplastic carcinoma and carcinoma with pleomorphic pattern has not been described. Present case will be valuable to understand both of metaplastic carcinoma and pleomorphic carcinoma. Evidence of the clinicopathological features of the breast carcinomas is shown.

## 3. Case Presentation

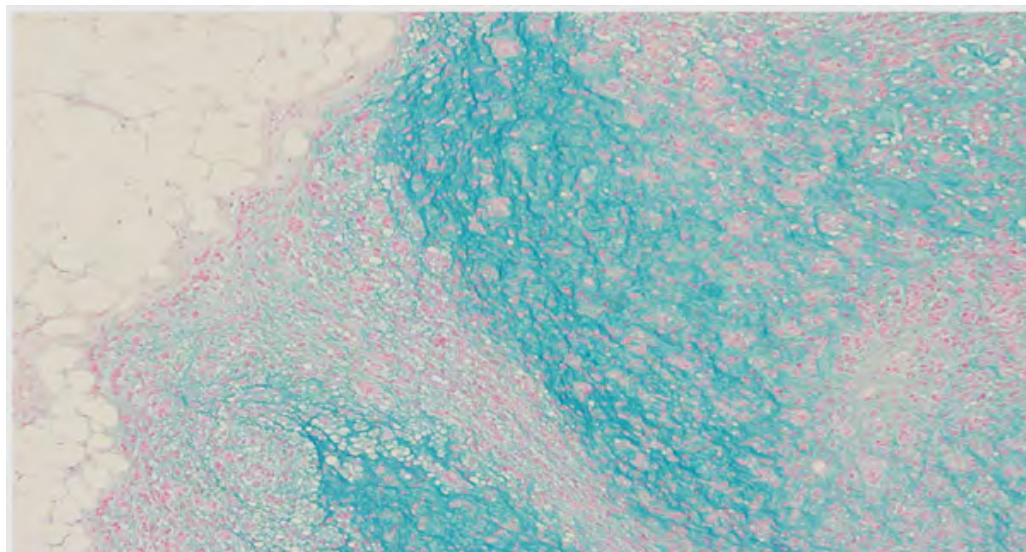
A 54-year-old woman was referred to the Department of Endocrine Surgery of Ogaki Tokushukai hospital with a lump in her right breast. Her medical history was unremarkable, and she had no history of familial breast diseases. The patient noticed a mass in her right breast 1.5 years ago. The tumor gradually enlarged, and she visited a clinic for breast oncology where an elastic hard tumor with poor mobility 50 mm in diameter was detected in right upper outer quadrant. Mammography test also showed 50mm irregular, high dens mass with obscured margins. Ultrasound imaging proved irregular, hypoechoic mass with indistinct margins. By a core needle biopsy [CNB], the mass was diagnosed as an invasive ductal carcinoma. In our hospital, MR imaging displayed

an irregular mass in the upper outer quadrant of the right breast. Furthermore, contrast-enhanced T1-weighted MR imaging exerted a rim-enhancing mass and a type III [washout] kinetic curve. Diffusion-weighted imaging [DWI] demonstrated hyperintensity in the same area. Contrast-enhanced T1-weighted MR imaging showed a heterogeneously enhancing lymph node in the right axilla. As presurgical chemotherapy, Dose-Dense EC for 4 cycles and docetaxel for 4 cycles with a month interval was performed. Then, a breast-conserving surgery + axillary lymph nodes dissection level II was carried out under general anesthesia. Pathology of the main tumorous nodule [16 x10mm] from the tissues on the mastectomy revealed that the tumorous lesion comprised neoplastic cells with small-to medium, dark nuclei and the cells were arranged in poorly formed glandular and solid nest patterns together with mesenchymal components (Figure 1). Myxomatous matrix of the MBC was positive for alcian blue stain (Figure 2). Some place of the carcinoma cells showed squamous differentiation (Figure 3). The neoplasm contained an admixture of mesenchymal compo-

nent such as chondroid, osseous and myxoid matrix (Figures 1,4). In the area of osseous matrix, both of osteoblasts and osteoclasts were also seen (Figure 4). Spindle cell proliferation was not recognized in the neoplasm. Meanwhile, a small neoplastic area [6 x 3mm] which was located near by the main nodule was characterized by a proliferation of pleomorphic and bizarre multinucleated tumor cells. The giant cells constituting 50% of the tumor cells formed indistinct glandular structures (Figure 5). No mesenchymal component was not associated in the carcinoma with pleomorphic pattern. Immunohistochemically, neoplastic cells being arranged in poorly formed glandular and solid mass was positive for E-cadherin. Mostly, carcinoma cells of MBC showed negative response for ER, PGR and HER2. However, carcinoma cells of pleomorphic pattern exhibited weakly positive response of HER2 (Figure 6). The carcinoma cells of pleomorphic pattern were positive for E-cadherin (Figure 7). They showed negative response for human chorionic gonadotropic [HCG] being an immunohistochemical marker of choriocarcinoma.

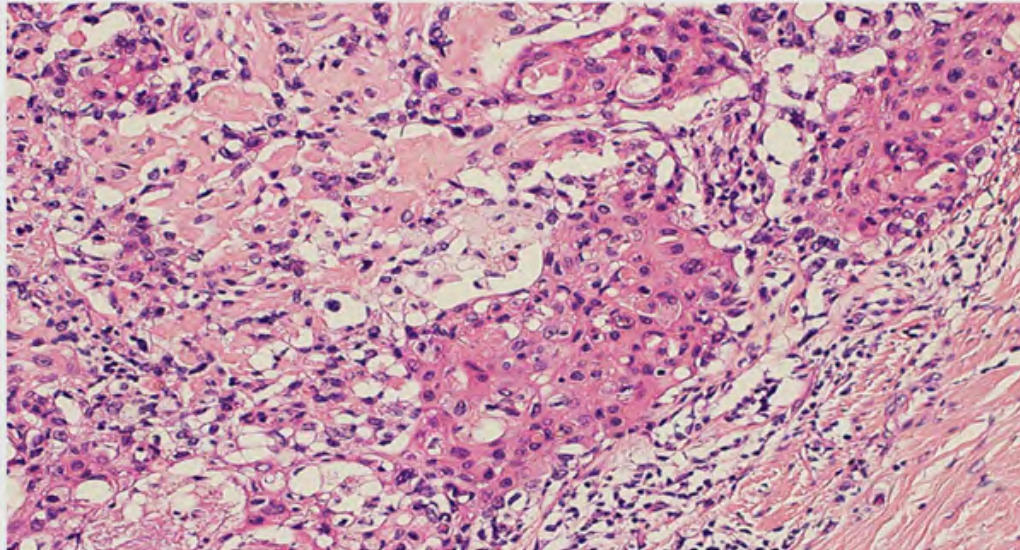


**Figure 1:** Histology of the metaplastic carcinoma. Neoplastic cells with small, dark nuclei are arranged in poorly formed glandular pattern. Myxomatous matrix is present in the center.

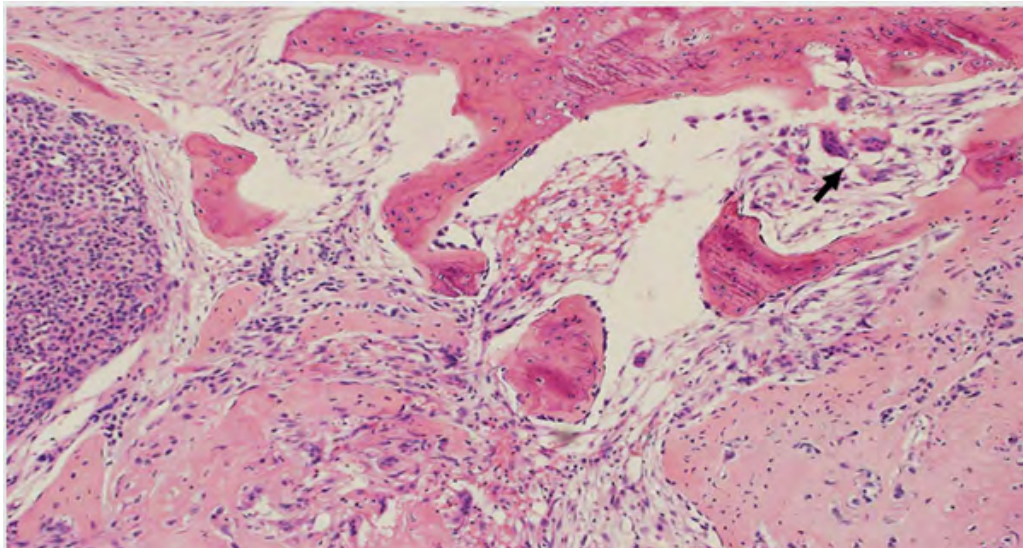


**Figure 2:** Myxomatous matrix is positive for alcian blue.

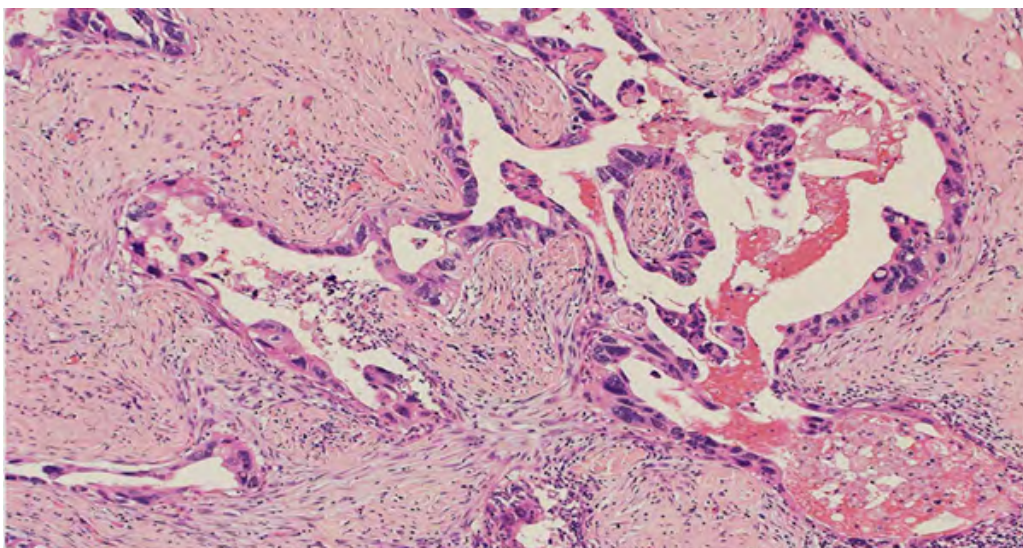




**Figure 3:** A place of carcinomatous area with squamous differentiation.

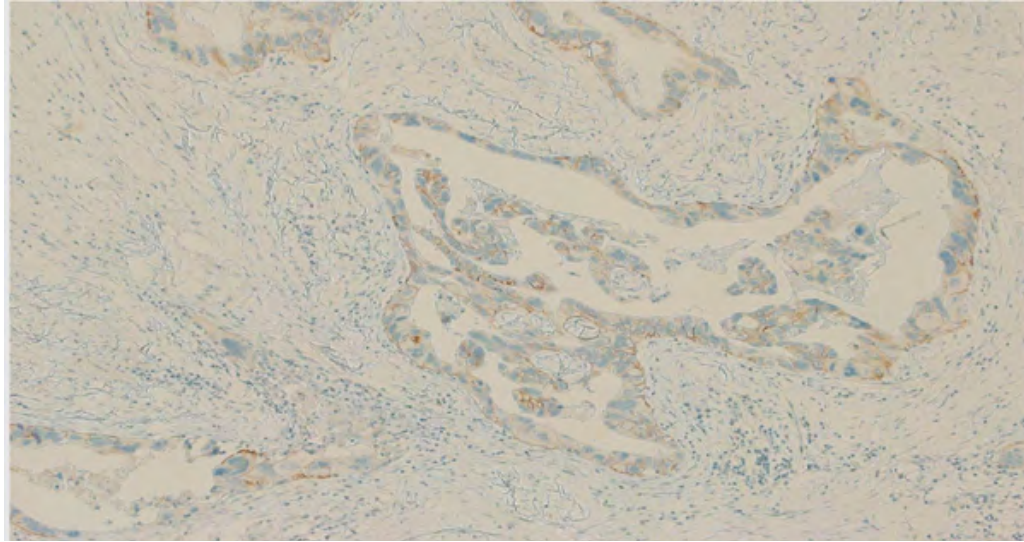


**Figure 4:** Osseous matrix with osteoblasts and osteoclasts (arrow) is present in upper side. Chondroid matrix is located in the lower side. Solid mass of cancer cells is seen in the left.

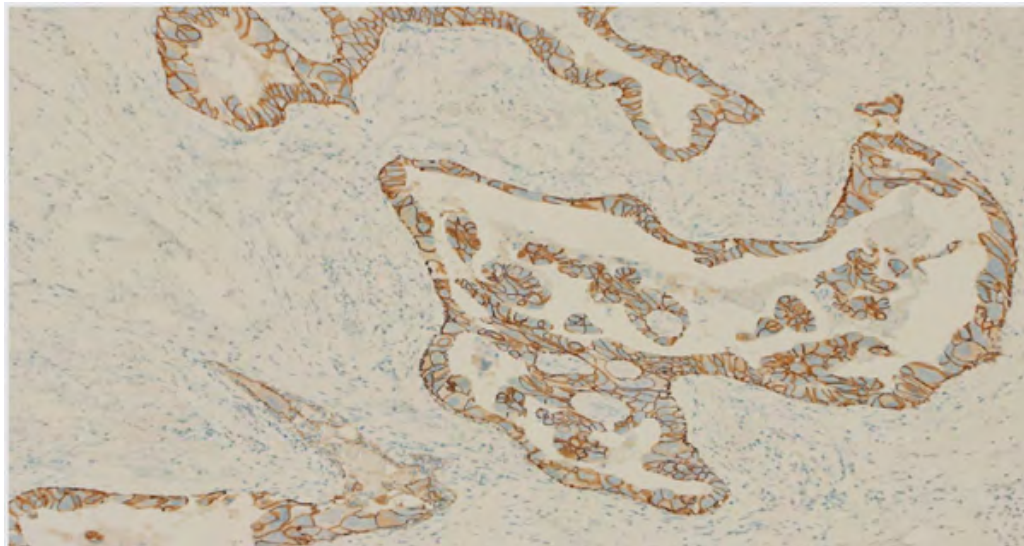


**Figure 5:** Histology of the carcinoma with pleomorphic pattern. Bizarre multinucleated giant cells form indistinct glandular structure.





**Figure 6:** Carcinoma of pleomorphic pattern has weakly positive response of HER2.



**Figure 7:** Carcinoma of pleomorphic pattern has positive response of E-cadherin.

#### 4. Discussion

In the present study, main neoplastic nodule showed histological features of solid clusters, tubules, with glandular and squamous differentiation in the carcinomatous areas. Furthermore, the tumor contained mesenchymal components such as chondroid, osseous and myxoid matrix. Such features manifested characteristics the metaplastic carcinoma with heterologous mesenchymal differentiation. Area of the carcinoma characterized by proliferation of pleomorphic and bizarre, sometimes multinucleated giant cells was diagnosed as carcinoma with pleomorphic pattern [3]. It is suggested that two rare carcinomas were present concurrently in the breast, although the lesions were close each other. To our knowledge, such coexistence of metaplastic carcinoma and carcinoma with pleomorphic pattern has not been reported. Diagnosis of pleomorphic carcinoma of the breast is not easy. Institutional Review Board of M.D. Anderson Cancer Center approved for the criteria as for the diagnosis as follows; 1] a primary invasive carcinoma of the breast; 2] at least 6-fold variation in nuclear size present in

>50% of the tumor cells examined; 3] the presence of multinucleated tumor giant cells, and 4] not more than 25% of metaplastic component, if present 5]. Present case of carcinoma with pleomorphic pattern seems to conform with the criteria. Hormone-receptor expression of ER, PGR and HER2 of both neoplasms of the metaplastic carcinoma and pleomorphic carcinoma was negative in general. However, HER2 expression was weakly positive in the present pleomorphic carcinoma. Similar case with HER2 expression was also reported in another pleomorphic carcinoma [6]. Due to the presence of giant and multinucleated tumor cells, pleomorphic carcinoma can also be misdiagnosed as invasive ductal carcinoma with osteoclast-like giant cells and invasive carcinoma with choriocarcinomatous pattern [7]. In the present case, negative expression of HCG and positive expression of E-cadherin excluded the possibility of osteoclast-like carcinoma and carcinoma with choriocarcinomatous pattern. With positive expression of E-cadherin, possibility of pleomorphic lobular carcinoma was also excluded. The molecular mechanism of metaplastic carcinoma dif-

fers from other types of breast carcinomas. It is suggested that up-regulation of cancer stem cells [CSC] and epithelial-mesenchymal transition [EMT] genes might play a crucial pathogenesis of MBC [8]. EMT activators and CSC present especially in the non-glandular components of metaplastic carcinomas [9]. On the other hand, information regarding molecular mechanism of pleomorphic carcinoma is few although limited information for the molecular pathology is present for the pleomorphic lobular carcinoma [10]. Relationship between c-erbB-2 overexpression, S-phase fraction, and Ki67 proliferation has been known in human breast cancers [11]. It was reported that c-erbB-2 positive tumors among the pleomorphic carcinomas had the highest Ki67 proliferation indices, and the majority of carcinomas manifested aneuploid or triploid DNA content [4]. Such evidences may be a hallmark of multinucleated giant cells in the pleomorphic carcinomas. Silver and Tavassoli [4] also described that 73% of cases of pleomorphic carcinomas were associated with contiguous foci of atypical ductal hyperplasia, DCIS or conventional invasive ductal carcinoma, supporting the contention that pleomorphic carcinomas represent a variant of ductal carcinoma. Accordingly, it may be possible that present carcinoma with pleomorphic pattern is related to some of preceding DCIS, although such lesions adjacent to the pleomorphic carcinoma were not found in this case. Presently, histological size of the tumor at the pathological examination after the mastectomy was much smaller than of clinical or imaged size by mammography, ultrasonic and MRI examination. This may be related to the effects of presurgical chemotherapy [Dose-Dense EC & docetaxel]. In fact, some of axillary lymph nodes were replaced by foamy cells suggesting disappearance of cancer cells by the chemotherapy, although massive necrosis was not confirmed in the tissues of metaplastic carcinoma as well as carcinoma with pleomorphic pattern.

## 5. Declarations

### 5.1. Corresponding Author

Hideki Mori is the guarantor of submission.

### 5.2. Source of Support

None.

### 5.3. Consent Statement

We obtained the informed consent from the patient by writing.

### 5.4. Ethics Approval

The report was made along the guideline of the ethics committee of our hospital.

### 5.5. Conflict of Interest

Authors declare no conflict of interest.

### 5.6. Data Availability

All relevant data are within the paper and its supporting information files.

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