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Chromosomal rearrangements in myoepithelial carcinoma of the breast that presented as metachronic double cancer with invasive ductal carcinoma in the ipsilateral breast

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Myoepithelial carcinoma of the breast is an extremely rare tumor composed entirely of malignant spindle cells with myoepithelial differentiation. The majority of previously reported cases have mainly described the clinicopathological features of the disease, and few have presented cytogenetic data. We herein present the case of a 48-year-old woman who was admitted with a left-sided breast lump in the inner upper quadrant that was initially diagnosed as a myoepithelioma with potentially malignant disorder. At 12 months after resection, she complained about a newly developed solid mass in the subareolar region of the ipsilateral breast that was diagnosed as an invasive ductal carcinoma. In addition, 16 months after the initial admission, a re-growing remnant lesion recurred in the inner upper quadrant and was ultimately diagnosed as a myoepithelial carcinoma. Lymph node metastasis of the myoepithelial carcinoma was also observed in her left axillary region 11 months after local recurrence. A cytogenetic analysis showed recurring specific chromosomal alterations both in the locally recurrent and in the lymph-node metastatic lesion: 48, XX, t(5;18)(q13;q23),del(6)(q?),+14. + mar1. To our knowledge, this is the first published report of clonal chromosomal rearrangements in myoepithelial carcinoma of the breast that presented as metachronic double cancer with invasive ductal carcinoma in the ipsilateral breast.

Keywords Breast, myoepithelial carcinoma, invasive ductal carcinoma, cytogenetic analysis, chromosomal rearrangement

Introduction

Myoepithelial cells are widely present in the breast, where they comprise part of the normal microscopic anatomy of lobules and ducts. However, myoepithelial carcinoma of the breast is an extremely rare malignant neoplasm and represents the malignant end of the spectrum of myoepithelial lesions in the breast. According to the 4th edition of the WHO Classification of Tumors of the Breast, myoepithelial lesions are composed of a pure or dominant population of myoepithelial cells and encompass myoepithelial hyperplasia, collagenous spherulosis, and myoepithelial carcinoma (1). A descriptive classification of metaplastic breast carcinoma was adopted, and myoepithelial carcinoma was classified under a phenotype of spindle cell carcinoma in metaplastic breast carcinoma. Support for a firm diagnosis of myoepithelial carcinoma comes from the identification of malignant cells emanating from the myoepithelial layer of pre-existing ducts or from the myoepithelial compartment of an epithelial–myoepithelial lesion, such as adenomyoepithelioma (2).

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Cytogenetic analyses of the myoepithelial carcinoma of the salivary gland and soft tissues have been conducted in order to evaluate the molecular events involved in the pathogenesis of these tumors (3–7). However, because of the rarity of myoepithelial carcinoma of the breast, the majority of the previously reported cases have been in the form of isolated case reports or small series, describing mainly the clinicopathological features. Only Jones et al. investigated 10 pure myoepithelial carcinomas of the breast using comparative genomic hybridization and identified relatively few genetic alterations compared with invasive ductal carcinomas of the breast (8). The present case report describes the novel cytogenetic findings of myoepithelial carcinoma that presented as double cancer with metachronous invasive ductal carcinoma in the ipsilateral breast.

Materials and methods

Case report

A 48-year-old woman presented with a recent onset of a painless left sided breast lump. Clinical examination revealed a firm 1-cm-diameter mass in the inner upper quadrant with no palpable axillary lymphadenopathy. An excisional biopsy was performed, and the lesion was initially diagnosed as a myoepithelioma with potentially malignant disorder. The margin status was histologically diagnosed as negative. Twelve months after the excisional biopsy, the patient noticed a gradually enlarging lump in the subareolar region of her left breast. The distance of the primary inner upper quadrant mass and the subareolar mass was measured to be 36 mm by CT image. Another excisional biopsy was performed, and the lesion was diagnosed as an invasive ductal carcinoma. The patient underwent additional total mastectomy and 3 axillary lymph node dissections. A histopathological examination revealed an 8-mm invasive ductal carcinoma, a 2-mm ductal carcinoma *in situ*, and no evidence of metastatic involvement of the dissected lymph nodes. The margin status of this lesion was also negative. Postoperatively, the patient was treated with 18 cycles of adjuvant molecular targeted therapy consisting of trastuzumab combined with tamoxifen as a hormone therapy. Sixteen months after the initial diagnosis of myoepithelioma, a palpable small mass was found near the excisional biopsy scar in the inner upper quadrant. The mass gradually enlarged, measuring 5 cm in diameter with dark reddish-brown color and pain that developed over the last 5 of the 16 months. A core needle biopsy was performed, and the lesion was diagnosed as a myoepithelial carcinoma. The tumor was treated by wide surgical excision. The invaded sternal and surrounding tissue as well as the costal cartilages of the first to fifth ribs was excised en bloc with the tumor. The bilateral intrathoracic arteries were identified, and the left one was ligated and excised together with the tumor. The defect of the sternum and ribs was reconstructed using the GORE DUALMESH® Patch (W. L. Gore & Associates, Flagstaff, AZ, USA), which was composed of inert biomaterial (expanded polytetrafluoroethylene), and then covered with a vertical rectus abdominis myocutaneous flap. Eleven months after this surgery, an elastic hard mass of approximately 3 cm in diameter was identified in her left axillary region. Ultrasound-guided biopsy of the left axillary lymph node revealed metastasis of the myoepithelial carcinoma. Axillary lymph node dissection was performed following post-operative external beam radiotherapy at 60 Gy.

Histopathological and immunohistochemical examination

For light microscopy, the surgically removed tumors were fixed in 10% formalin and embedded in paraffin. The dewaxed paraffin sections were then stained with hematoxylin and eosin. Immunohistochemical staining was performed using a labeled streptavidin–biotin system, and the primary antibodies used were smooth muscle actin (SMA, monoclonal; Dako, Glostrup, Denmark), CK5/6 (monoclonal; Zymed, South San Francisco, CA, USA), p63 (monoclonal; Nichirei, Tokyo, Japan), Ki-67 (monoclonal; Dako), estrogen receptor (ER, monoclonal; Nichirei), progesterone receptor (PR, monoclonal; Dako), and E-cadherin (monoclonal; Leica, Nussloch, Germany).

Cytogenetic analysis

The analyzed tumor specimens were obtained immediately after surgical excision. Portions of the tumors were treated by collagenase and cultured at 37 °C for 4 days. The chromosome slides were prepared from short-term cultured tumor cells using the standard trypsin Giemsa-banding technique. Karyotypes were described on the basis of the short system of the International System for Human Cytogenetic Nomenclature (ISCN 2009) (9).

Results

Tissue samples from each lesion were stained with hematoxylin and eosin. A microscopic examination of the specimen from the primary site in the inner upper quadrant revealed invasive and non-epithelial proliferation of spindle-shaped and small rhombus cells with a densely hyalinized matrix (Figure 1A). Moderate nuclear pleomorphism and size differentiation were seen. Six mitotic figures per 10 high-power fields were present. The immunohistochemical findings of the spindle tumor cells were diffusely positive for SMA, CK5/6, and p63 (Figure 1B, C). The labeling index of Ki-67 was more than 30% (Figure 1D). On the basis of the histological and immunohistochemical results, we considered this case to be a myoepithelioma with potentially malignant disorder.

A microscopic examination of the specimen from the subareolar region revealed typical malignant proliferation along with stromal invasion, which was diagnosed as an invasive ductal carcinoma (Figure 1E). The immunohistochemical findings were positive for estrogen receptor (ER) (2+), progesterone receptor (PR) (3+), human epidermal growth factor receptor 2 (HER2) (3+), and E-cadherin, and they were negative for SMA and p63 (Figure 1F).

A microscopic examination of the specimen from the recurrent lesion in the inner upper quadrant and the metastatic lesion in axillary lymph node revealed similar morphology to the primary lesion (Figure 1G, I). Spindle- to oval-shaped tumor cells with a storiform pattern structure were observed. The immunohistochemical findings were also the same as the specimen for the primary lesion (Figure 1H, J); therefore, the