Clinical Case Report

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Development of ipsilateral chest wall spindle cell carcinoma in a patient with invasive ductal breast carcinoma during postoperative adjuvant therapy

A case report

Kaifu Li, MD, Hua Kang, MD*, Yajun Wang, MD, Tao Hai, BSMed, Bixiao Wang, MD

Abstract

Rationale: Metaplastic breast carcinoma (MBC) is rare subtype of breast carcinoma and is regarded as ductal carcinoma that undergoes metaplasia into a glandular growth pattern. Spindle cell carcinoma (SPC) is a subtype of MBC with a predominant spindle cell component.

Patient concerns: The patient was a 52-year-old female with invasive ductal breast carcinoma who underwent a modified radical mastectomy and an axillary node dissection. A new lump was observed underneath the surgical site between the pectoralis major and pectoralis minor muscles 45 days after the patient underwent sequential postoperative chemotherapy and radiotherapy.

Diagnoses: It was speculated that the new lesion had developed during postoperative adjuvant therapy. And the new lesion was regarded as a recurrence.

Interventions: We performed a wide dissection of the tumor with negative margins. The pathology of the tumor indicated SPC. Then, the patient received chemotherapy and demonstrated a poor response.

Outcomes: Local recurrence and pulmonary metastasis developed shortly afterwards, and the patient succumbed to the disease within 5 months.

Lessons: Local recurrence with metaplastic SPC transformed from invasive ductal breast carcinoma during postoperative chemotherapy and radiotherapy is rare. The failure of subsequent chemotherapy and the progression of disease indicate the aggressive nature of SPC and its decreased sensitivity to chemotherapy and radiotherapy. Further studies must be performed to improve the prognosis of these patients.

Abbreviations: CK = cytokeratin, CT = computed tomography, EC-T = epirubicin, cyclophosphamide and paclitaxel, FEC = epirubicin, cyclophosphamide and 5-fluorouracil, MBC = metaplastic breast carcinoma, MRI = magnetic resonance imaging, SPC = spindle cell carcinoma.

Keywords: breast cancer, chemotherapy, chest wall, radiotherapy, spindle cell carcinoma

1. Introduction

Metaplastic breast carcinomas (MBCs) are regarded as ductal carcinomas that undergo metaplasia and exhibit a nonglandular growth pattern.[1,2] According to the World Health Organization, the classification of MBC is primarily based on the histological findings of purely epithelial (squamous, adenosquamous, and spindle cell carcinomas (SPCs)) and mixed epithelial and mesenchymal (carcinoma with chondroid/osseous metaplasia and carcinosarcoma) components.[3] SPC is a rare subtype of metaplastic carcinoma that constitutes 0.3% of all invasive breast malignancies.[4] Pathologically, SPC is composed of a mixture of spindle cells and epithelial cells. We present in this report an intriguing and rare case of chest wall SPC observed shortly after postoperative chemotherapy and radiotherapy in a patient with invasive ductal breast carcinoma.

2. Case presentation

A 52-year-old female presented to the Department of General Surgery of Xuanwu Hospital at Capital Medical University (Beijing, China) complaining of a lump in her right breast that had persisted for 3 weeks. The physical examination revealed a mass measuring 4.5×4 cm in the upper lateral quadrant of her right breast. A bilateral axillary examination revealed no lymphadenopathy. Sonography showed that the mass was generally well circumscribed and was internally partially anechogenic (Fig. 1A). An ultrasound examination of the bilateral axillary fossa was unremarkable. Magnetic resonance

Editor: N/A.

This work was supported by the National Natural Science Fund of China (No. 81172517) and the Beijing Municipal Health System Academic Leaders of High-level Health Personnel Program, P.R. of China (No. 2011-2-28).

The authors have no conflicts of interest to disclose.

Department of General Surgery, Xuanwu Hospital, Capital Medical University, Beijing, P.R. China.

** Correspondence: Hua Kang, Department of General Surgery, Xuanwu Hospital, Capital Medical University, No. 45 Changchun Street, Xicheng District, Beijing 100053, P.R. China (e-mail: kanghuamd@126.com).*

Medicine (2018) 97:19(e0739)

Received: 29 January 2018 / Accepted: 20 April 2018

http://dx.doi.org/10.1097/MD.0000000000010739

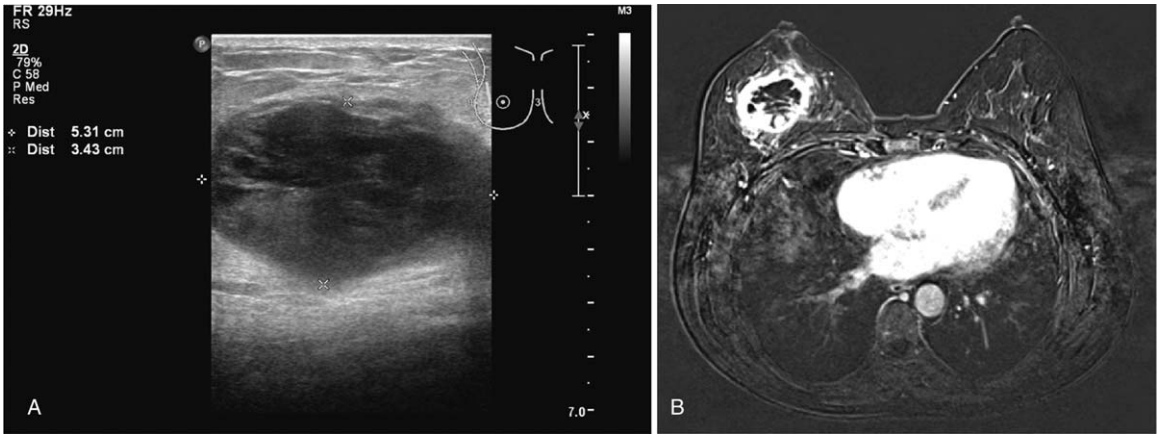

Figure 1. Preoperative images of the primary tumor. A, A transverse sonogram shows a complex cystic lesion in the patient's right breast. B, T2-weighted MR image shows a cystic mass in the patient's right breast, with significant enhancement after the injection of an enhancing agent. MR = magnetic resonance.

imaging (MRI) of the breast also revealed a cystic mass that was significantly enhanced following the injection of a contrast agent (Fig. 1B). No mass was present between the pectoralis major and minor muscles on MRI prior to surgery. An ultrasound-guided core needle biopsy of the lump was performed preoperatively and showed a middle grade atypical dysplasia. A chest X-ray revealed no manifestation of pulmonary metastasis. We performed a sentinel lymph node biopsy and a biopsy of the mass in her right breast. The frozen pathology results showed that the tumor consisted of invasive carcinoma, and of the 3 sentinel lymph nodes we dissected, 1 was positive using methylene blue. Consequently, we performed a modified radical lumpectomy and level III axillary lymph node dissection. At the final histopathological examination, the tumor was diagnosed as an invasive ductal carcinoma (Fig. 2). The deep fascial margin in the mastectomy specimen was negative. Two axillary lymph nodes were positive among the 26 that we dissected. The tumor was triple-negative and 20% positive for Ki67. The specific immunostaining markers of the tumor are shown in Table 1. We planned to give the patient EC-T chemotherapy consisting of epirubicin, cyclophosphamide, and paclitaxel. After 4 courses of EC chemotherapy had been administered, the patient received another 3 cycles of FEC chemotherapy containing epirubicin, cyclophosphamide, and 5-fluorouracil, due to her allergic reaction to paclitaxel. Then, the patient received radiation therapy of the chest wall and supraclavicular region.

Forty-five days after radiotherapy, the patient complained of persistent pain at the lateral part of the incision on her chest, where a lump was palpable. Computed tomography (CT) revealed a mass with soft tissue density between the pectoralis major and minor muscles (Fig. 3A). Sonography showed that the mass was irregular, well circumscribed, and lobulated (Fig. 3B). No significant blood flow signals were observed inside the mass. During surgery, we found that the mass was generally well circumscribed but adhered to the nearby pectoralis major and minor muscles. We performed wide excision of the tumor, with negative resection margins shown by postoperative pathology. The pathology report of the mass revealed an SPC (Fig. 4). The tumor was negative for ER, PR, and HER-2, as well as vimentin, and it was positive for cytokeratin (CK). CK5/6 and actin were partially positive. The Ki67 index was 50%. After surgery, the patient received 2 cycles of chemotherapy consisting of gemcitabine and cisplatin. However, she experienced intermittent knife-like pain in the reoperated region. Sonography indicated a

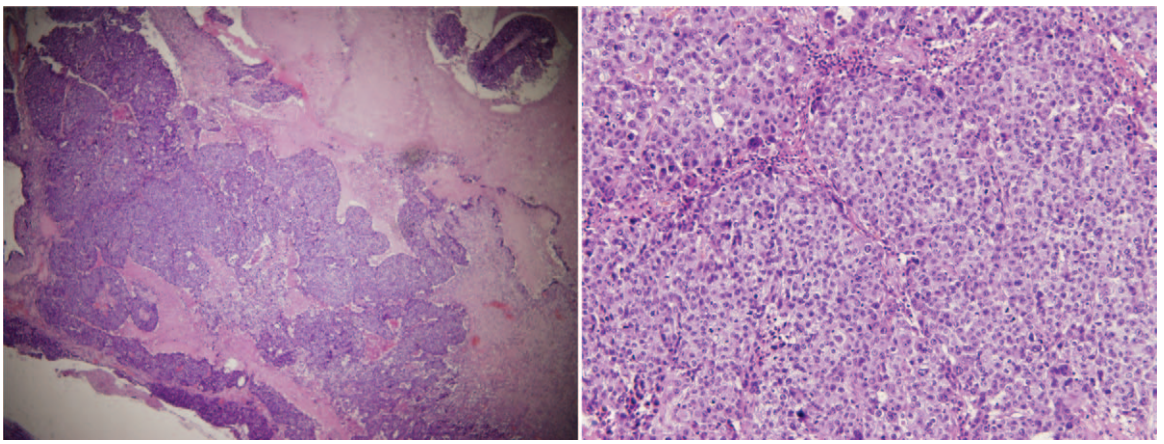

Figure 2. Hematoxylin and eosin staining of the primary tumor (A, ×40; B, ×200). Microscopically, the tumor was composed of an invasive ductal carcinoma, with medullary carcinoma properties.

Table 1

Immunostaining markers for primary tumor (PT) and SPC.

Marker	ER	PR	HER2	Ki67	E-cadherin	P120	Vimentin
PT	–	–	–	20%	+	+	+
SPC	–	–	–	50%	+ (partially)	+ (weakly)	–
Marker	CK	P53	S100	Desmin	CK5/6	Actin	ALK
PT	N/A	–	N/A	N/A	+	N/A	N/A
SPC	+	N/A	–	–	+ (partially)	+ (partially)	–

SPC = spindle cell carcinoma.

heterogeneous mass beneath the surface. An ultrasound-guided core needle biopsy was performed, and the pathology report was unremarkable. Unable to endure the adverse effects, the patient underwent another cycle of chemotherapy consisting of cyclophosphamide and oral capecitabine for several weeks. However, the pain in her chest wall gradually deteriorated, and an ulcer eventually formed. A rebiopsy of the mass indicated SPC. Meanwhile, thorax CT indicated pulmonary metastasis. The patient rejected any further treatment. Four months and 2 weeks after the second operation, the patient succumbed to pulmonary metastasis.

The patient provided written informed consent. Additionally, ethical approval was not required for this paper, as it is a case report.

3. Discussion

In this case, the most intriguing clinical feature of this patient was that the new SPC lesion was detected only 45 days after she had undergone sequential chemotherapy and radiotherapy. It is reasonable to speculate that the new lesion developed during postoperative adjuvant therapy. To the best of our knowledge, development of SPC during chemotherapy and radiotherapy for breast cancer has not been previously reported.

The clinical course of this case also raised a puzzling question regarding the origin of the SPC. Was the new lesion a new primary tumor or a local recurrence that had transformed from invasive ductal carcinoma? In this case, the SPC was positive for CK (an epithelial marker) and negative for vimentin (a mesenchymal marker), indicating the epithelial nature of the tumor. These findings might indicate an epithelial origin of the SPC. Furthermore, it was noted that MBC can be derived from ductal carcinomas through the process of metaplasia.[1,2] In a recent study, exome sequencing was performed for paired metaplastic and adjacent conventional invasive ductal carcinomas in 8 patients.[5] The study reported that the 2 tumor components had nearly identical landscapes of somatic mutation, implying a shared origin of MBC and invasive ductal carcinomas. In addition, the levels of several other markers (such as ER, PR, and Her-2) were identical to those of the primary tumor (Table 1). Therefore, the new SPC lesion might be regarded as a recurrence transformed from invasive ductal breast carcinoma. However, whether chemoradiotherapy stimulated the process of metaplasia was unknown. It is also possible that a few SPC cells, which were highly resistant to chemoradiotherapy, had undergone metaplasia in the primary tumor, and these cells may have survived chemoradiotherapy and became the predominant cell type in the recurrent lesion. Chemotherapy and radiotherapy can also induce secondary malignancies. In 1 study involving 1024 patients with lymphoma treated with chemotherapy, the incidence of secondary solid tumors was 2.54% at 5 years and 6.79% at 10 years.[6] In another study that included a cohort of 17,745 breast cancer patients, a total of 2370 secondary malignancies were observed, with a median follow-up of 13.4 years. The study showed that the incidence rates of several types of secondary malignancies (including breast cancer, leukemia, sarcoma, and lung cancer) were significantly higher in patients who were treated with chemotherapy, radiotherapy, and hormone therapy than in the general population.[7] However, it is unlikely that the new lesion was secondary to chemoradiotherapy, as 45 days are not long enough for the development of a new lesion.

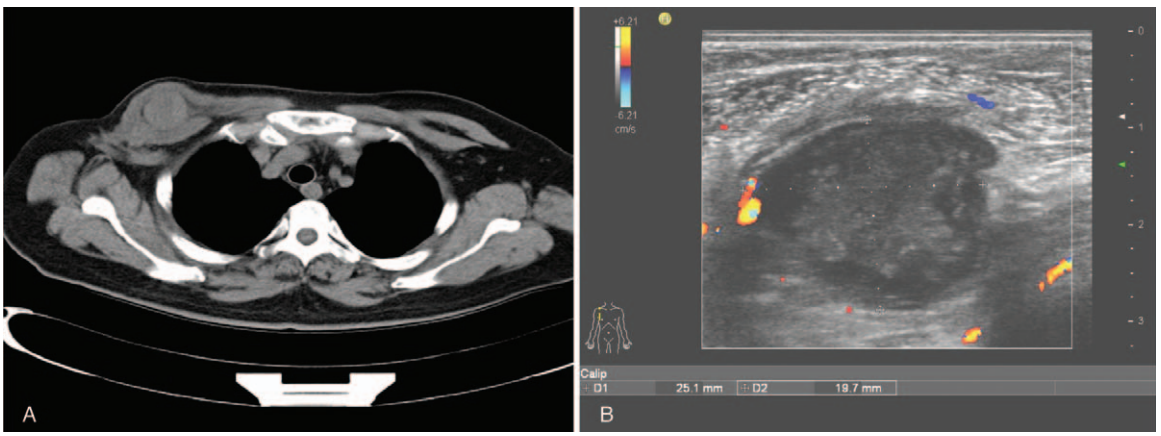

Figure 3. Images of the new tumor. A, A round mass with soft tissue density was noted between the pectoralis major and minor muscles on CT. B, The tumor was irregular, well circumscribed, and lobulated on sonography. CT = computed tomography.

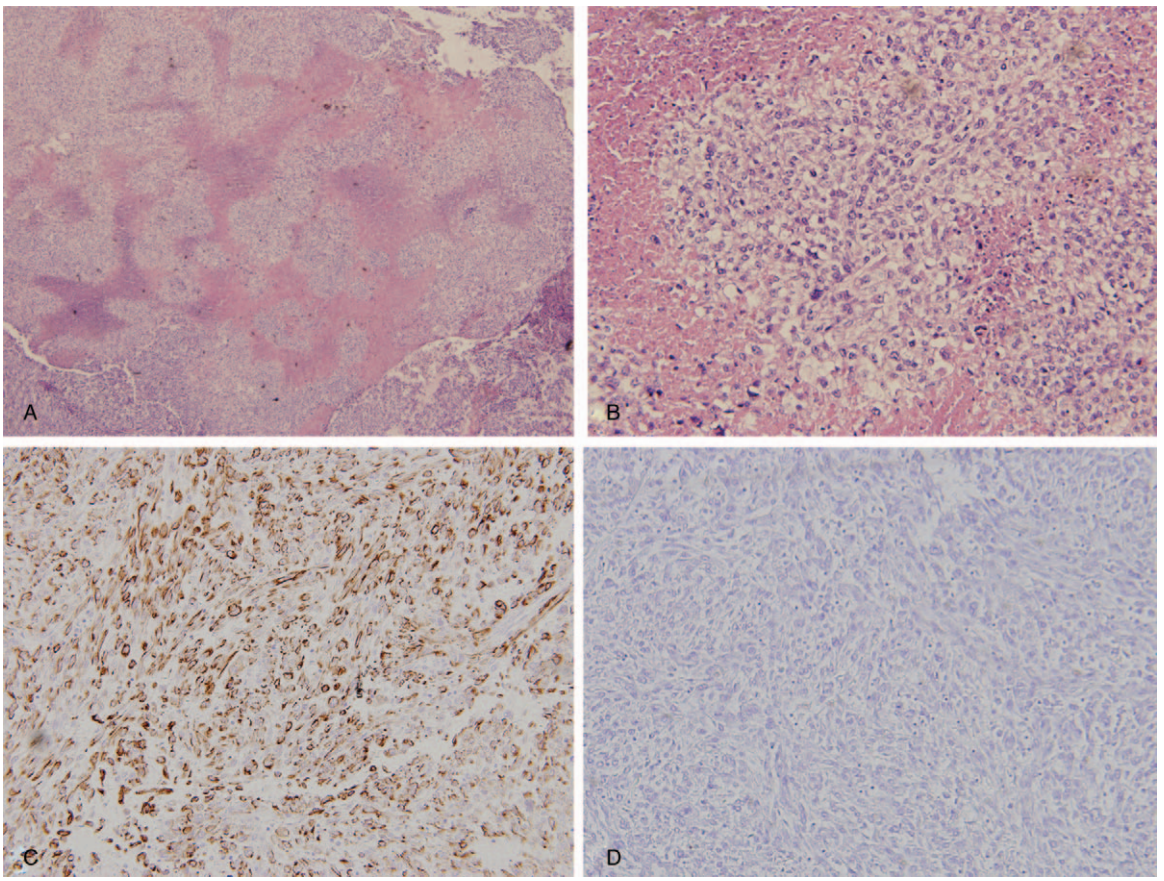

Figure 4. Histology of the SPC. A, B, Hematoxylin and eosin staining of the SPC (A, ×40; B, ×200). Microscopically, the tumor was composed of spindle-shaped cells and necrosis. C, The SPC was immunoreactive for CK. D, The SPC was negative for vimentin. CK = cytokeratin, SPC = spindle cell carcinoma.

We treated this patient in the same manner as an MBC patient. Several studies have suggested that MBC was associated with a poor prognosis compared with a control group of patients with invasive ductal carcinoma.[8–10] Currently, no guideline or consensus has been established for the treatment of MBC. Traditional chemotherapy used to treat invasive ductal carcinoma has been reported to be less effective for the treatment of MBC,[11] which was confirmed in our case. In this case, the SPC did not seem to be sensitive to an EC regimen nor to a gemcitabine plus cisplatin or capecitabine plus cyclophosphamide regimen. In addition, radiotherapy contributes to survival outcomes only for early tumors, not for late stage disease.[12] In another study, chemotherapy and radiotherapy were not associated with a positive outcome in MBC patients.[13] Furthermore, an overwhelming majority of MBCs are triple negative. Due to the rarity of MBCs, the value of Her-2-targeted therapy, which has been proven to be effective in patients for Her-2-positive breast cancer, remains to be determined. A recent study has revealed that MBCs exhibit frequent mutations in ERBB4 (36%), PIK3CA (48%), and FLT3 (60%), for which there are now targeted therapies.[13] However, few studies have investigated the value of targeted therapies for MBCs.

Due to the aggressive nature of SPC, its low sensitivity to chemotherapy and radiotherapy and the lack of targeted therapy, the treatment of SPC is still a challenge. Further studies must be performed to improve the prognosis of patients with SPC.

Author contributions

Funding acquisition: Hua Kang.
Investigation: Bixiao Wang.
Resources: Kaifu Li, Yajun Wang, Tao Hai.
Software: Kaifu Li, Tao Hai, Bixiao Wang.
Supervision: Hua Kang.
Validation: Yajun Wang.
Writing – original draft: Kaifu Li.
Writing – review and editing: Hua Kang.

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