Case Report

Significant efficacy of paclitaxel plus carboplatin (TP) as a neoadjuvant regimen for metaplastic squamous cell carcinoma of the breast: a rare case report and literature review

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Background: Metaplastic squamous cell carcinoma of the breast (MSCCB) is a rare and aggressive type of cancer. So far, no standard treatment regimen has been established due to the absence of clinical data.

Case Description: We report a case of a 48-year-old female admitted to our hospital as a result of a left breast mass with skin rupture. Core needle biopsy under ultrasonic guidance confirmed MSCCB. Immunohistochemistry revealed negative staining for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor type 2 (HER2/neu). After receiving 4 cycles of paclitaxel and carboplatin neoadjuvant chemotherapy, the patient was treated with modified radical mastectomy. Postoperative pathology revealed a Miller-Payne score of 4 and no metastasis in the axillary lymph nodes (0/13), indicating a good response to neoadjuvant chemotherapy. She recovered well post-surgery and was discharged to home after admission. No recurrence was identified during the 2 years post-surgery follow-up.

Conclusions: MSCCB is a rare and aggressive type of cancer. However, the treatment of MSCCB has not been standardized due to its rarity. Given the observation that the majority of patients with MSCCB had ER, PR, HER2-negative neoplasms, we refer to the triple negative breast cancer (TNBC) treatment protocol. TP regimen was demonstrated to be an effective treatment for TNBC. The results of this case suggest that the TP regimen is effective in neoadjuvant chemotherapy of MSCCB.

Keywords: Metaplastic squamous cell carcinoma; breast cancer; neoadjuvant chemotherapy; paclitaxel; carboplatin; case report

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Introduction

Metaplastic squamous cell carcinoma of the breast (MSCCB) is a rare tumor that exists as one of the subgroups of metaplastic breast carcinoma, which accounts for less than 0.1% of all breast carcinomas (1). Since MSCCB is a very invasive tumor, its prognosis is poor (2). Besides, the cause and underlying mechanism of MSCCB remain unclear as a result of few clinical case reports and a lack of standard treatment guidelines.

There are small series of reports of neoadjuvant chemotherapy for MSCCB in the literature. In this case, we reported a MSCCB patient who received neoadjuvant chemotherapy consisting of four cycles of paclitaxel and carboplatin (TP), with a postoperative pathology result reporting a Miller-Payne grade 4. Therefore, we herein

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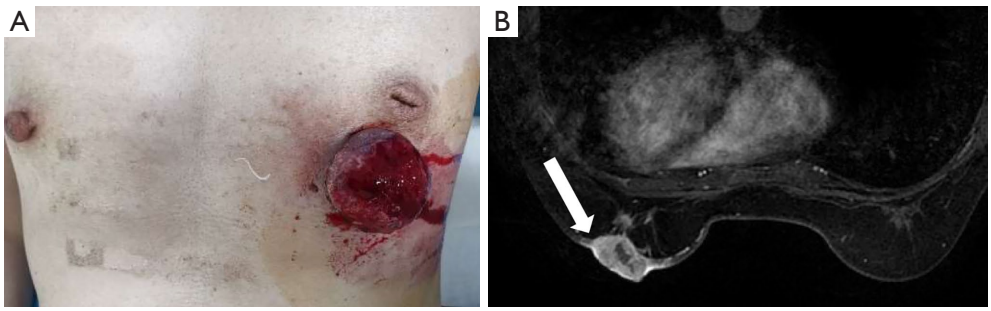

Figure 1 Examination before the neoadjuvant chemotherapy. (A) Skin ulceration with irregular margins. (B) High-density mass with an irregular margin.

report our experience with TP regimens in the case of a MSCCB and discuss the relevant literature. We present the following case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-484/rc).

Case presentation

A 48-year-old female was first presented with an occasionally found mass in the left breast in 2019. There was no previous family history of cancer. Physical examination found a 3.0 cm × 2.0 cm mass and skin ulcer in the lower quadrant of the left breast, being the ulcer with an uneven surface and bleeding (*Figure 1A*). The right breast was normal, and there were no palpable lymph nodes in the bilateral axilla.

Magnetic resonance imaging (MRI) bilateral breasts showed an irregular mass with long T1 and long T2 in the lower quadrant of the left breast, classified as BI-RADS category 5 lesions. Pricks were seen at the edge of the mass, and part of the skin surface was highlighted. The enhancement scanning was unevenly enhanced (*Figure 1B*). The serum tumor marker levels were within the normal ranges: Ferroprotein 87.2 μg/L, CA19-9 6.80 U/mL, CA15-3 16.3 U/mL, CA125 18.0 U/mL.

In order to make a definitive diagnosis, we performed a breast biopsy with an ultrasound-guided core needle biopsy, and the diagnosis of metaplastic squamous cell carcinoma was suggested. In addition, immunohistochemical staining revealed that the tumor cells were negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor type 2 (HER2/neu). However, it was strongly positive for Cytokeratin (CK), Cytokeratin 5/6 (CK5/6), and P53. Besides, the Ki-67 proliferative index was 60% (*Figure 2*). Further imaging confirmed that there was no evidence of distant metastasis.

MSCCB was an aggressive disease that behaved like poorly differentiated breast adenocarcinoma, and its clinicopathologic features were similar to the TNBC (3). Guidelines recommend the TP (paclitaxel and carboplatin) regimen as neoadjuvant chemotherapy for TNBC (4). In addition, TP regimen is often used in squamous cell carcinoma of other tissues and organs, such as lung squamous cell carcinoma (5), skin squamous cell carcinoma (6). So we chose TP regimen for this patient. Then, the patient received neoadjuvant chemotherapy based on paclitaxel (175 mg/m^2) and carboplatin (AUC 6), and efficacy evaluation every 2 cycles (21 days for 1 cycle). After 4 cycles, the left breast mass was significantly reduced, and the ulcer was healed after 4 cycles of treatment (*Figure 3A*). MRI examination revealed that the mass in the lower quadrant of the left breast was smaller than before, and the structure was disordered (*Figure 3B*), indicating a therapeutic effect of partial remission (PR). Then, neoadjuvant chemotherapy was suggested, but the patient refused due to the significantly decreased tumor size, and she requested surgical treatment. Therefore, a modified radical mastectomy with axillary clearance was performed. Postoperative pathology examination showed Miller-Payne grade 4 and no metastasis in the axillary lymph nodes (0/13). These results indicated that neoadjuvant chemotherapy had a good effect. Since then, the patient has been on regular telephone follow-up, and no signs of disease recurrence have been detected within 2 years (*Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

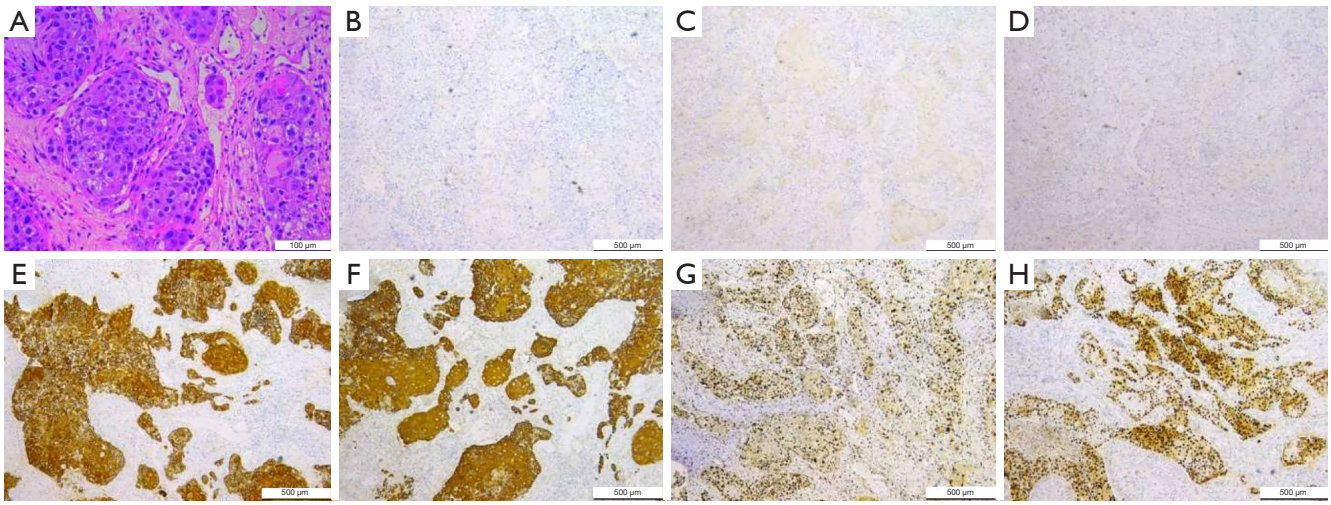

Figure 2 Histopathological examination with HE staining and IHC staining of the tumor. (A) Microscopic examination showing invasive poorly differentiated carcinoma with keratin pearls and marked squamous differentiation (HE staining, ×200). (B-H) IHC staining was used to detect the expressions of ER, PR, HER-2, CK, CK5/6, Ki-67, and P53 at the tumor (×50). (B) Negative for ER. (C) Negative for PR. (D) Negative for HER2. (E) Positive for CK. (F) Positive for CK5/6. (G) Positive for Ki-67 (60%). (H) Positive for P53. HE, hematoxylin and eosin; IHC, immunohistochemical; ER, estrogen receptor; PR, progesterone receptor; CK, Cytokeratin.

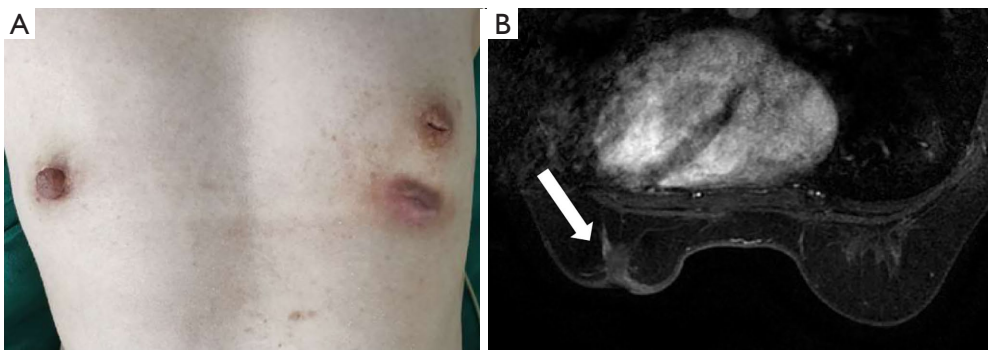

Figure 3 Examination after the neoadjuvant chemotherapy. (A) Skin ulcer healing. (B) The mass shrank and almost disappeared.

Discussion

MSCCB is a rare invasive tumor, which often occurs in middle-aged and older women with poor prognoses (7). Zhu *et al.* (7) analysis of 686 breast squamous cell carcinoma cases revealed a 5-year and 10-year overall survival of 62.1 % and 50.6 %, respectively. MSCCB usually begins with painless breast lumps, typically cystic or solid, and grows rapidly. Some MSCCB patients may have a liquefiable center caused by necrosis, which manifests as skin swelling, ulceration, pain, and other mastitis symptoms (8). Although breast squamous cell carcinoma can invade the skin, lymph node involvement is extremely rare (9). In this case, the patient presented a breast mass that had ulcerated, without lymph node metastasis, when she visited our hospital.

Although the etiology for MSCCB is not clearly defined, most authors believe it is caused by chronic cysts of the breast or squamous metaplasia of the breast ductal epithelium (10). Recent report indicated that breast squamous cell carcinoma might closely correlate with breast implants (11).

MSCCB is easily misdiagnosed or missed due to its rarity and lack of characteristic imaging features (12). The patient's MRI revealed a high-density mass with irregular and spiculated margins. This is similar to the imaging findings of invasive breast cancer. Consequently,

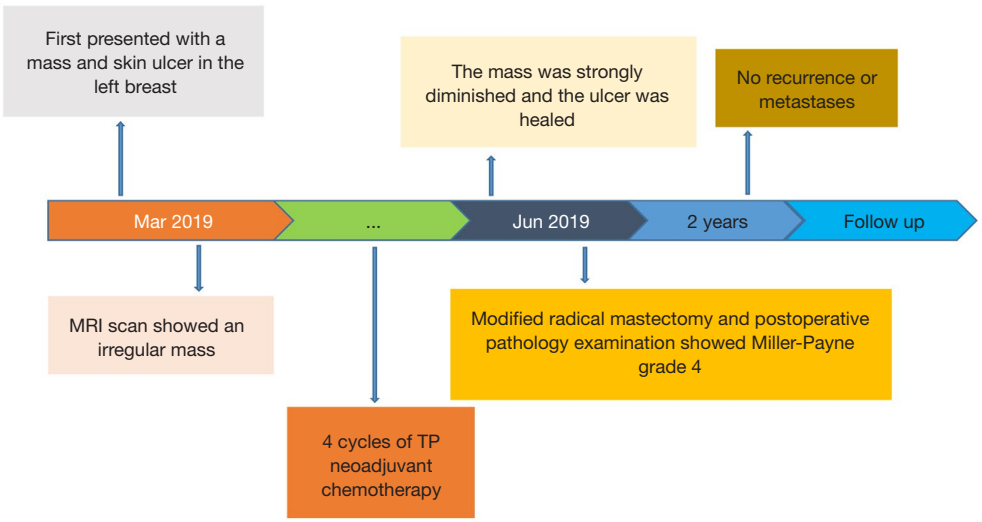

Figure 4 Timeline of interventions and outcomes. TP, paclitaxel + carboplatin.

preoperative diagnosis is challenging without biopsy support. Pathological examination of MSCCB showed that more than 90% of the tumor tissues were squamous cell components. In well-differentiated cell carcinomas, some bridges and keratinized cancer pearl were seen. It typically presents as triple-negative and high Ki-67 index (13). CK5/6 positive suggests that the tumor originates from the squamous epithelium. Additionally, the metastasis of other organs should be excluded in the diagnosis of this malignant tumor, and it should also be differentiated from breast invasive ductal carcinoma, breast angiosarcoma, and spindle cell carcinoma.

Up until now, the treatment of MSCCB has not been standardized due to its rarity. The analysis of previous studies found that the most common treatment for MSCCB is surgical excision of the tumor, combined with a comprehensive treatment program of adjuvant chemotherapy. Anne *et al.* (14) reported that a patient with breast squamous cell carcinoma received only surgical treatment, and no recurrence or metastasis was observed after 36 months of follow-up. If chemotherapy or radiotherapy can be supplemented, the therapeutic effect may be better. There is no uniform standard chemotherapy for patients with MSCCB, but it generally falls into two categories: (I) anthracycline-based chemotherapy (10); and (II) platinum-based chemotherapy (15). Details are shown in *Table 1*. Alan *et al.* (25) reported a case of pathologic complete tumor response using TAC (Paclitaxel, epirubicin, and cyclophosphamide) as neoadjuvant chemotherapy. However, some scholars have pointed out that cyclophosphamide, fluorouracil, and anthracyclines are not sensitive to breast squamous cell carcinoma (24). In addition, Pandey *et al.* (18) also confirmed that postoperative use of adriamycin and cyclophosphamide was ineffective, leading to disease progression and delayed treatments. Moreover, most breast squamous cell carcinoma is triple-negative. If anthracycline-contained regimens are ineffective, can we refer to other TNBC regimens? In the present patient, the tumor was large and ulcerated, and showed extensive inflammatory cell infiltration, which was not suitable for surgery. Therefore, we chose neoadjuvant chemotherapy to find an appropriate chemotherapeutic regimen.

GeparSixto's study confirmed that TNBC patients showed an increased pCR rate in response to neoadjuvant chemotherapy with platinum-based chemotherapy (26). The PATTERN study revealed that TP (paclitaxel plus carboplatin) was more effective than the standard-dose CEF-T (cyclophosphamide, epirubicin, fluorouracil, and docetaxel) in adjuvant chemotherapy of TNBC (27). Upon reviewing the literature, we found that the TP regimen is effective for breast squamous cell carcinoma, even for advanced patients. Although the patient did not complete the course of neoadjuvant chemotherapy, evaluation of pathologic responses after the neoadjuvant chemotherapy has achieved a good therapeutic effect. In this way, Shrestha *et al.* (22) reported a patient with large breast squamous cell carcinoma treated with a TP regimen and achieved long-

Table 1 Review of the literature on breast squamous cell carcinoma

Case	Age, years	Pathological features	Treatment options	Chemotherapy regimens	Follow-up
Bhatt *et al.* (16)	66	N/A	Adjuvant chemotherapy	(Cisplatin + ifosfamide + mitomycin-C) 4 cycles	Have an excellent disease response
Gupta *et al.* (17)	63	ER(–), PR(–), HER2(–) Ki-67 N/A	Adjuvant chemotherapy	(5FU + epirubicin + cisplatin) 6 cycles	Disease free at 1 year follow-up
Pandey *et al.* (18)	Case 1: 39	Case 1: N/A	Adjuvant chemotherapy	Case 1: Adriamycin + cyclophosphamide + paclitaxel	Case 1: Disease free at 8 months follow-up
	Case 2: 53	Case 2: ER(–), PR(–), HER2(–), Ki-67 N/A		Case 2: (Adriamycin + cyclophosphamide) 2 cycles	Case 2: recurrence and metastasis
Jakubowska *et al.* (15)	Case 1: 72	Case 1: ER(–), PR(–), HER2(–), Ki-67(+, 20%)	Adjuvant chemotherapy	Case 1: (Taxotere + Cisplatin) 5 cycles	Case 1: Distant metastases
	Case 2: 59	Case 2: ER(–), PR(–), HER2(–), Ki-67 N/A		Case 2: Cisplatin + 5-fluorouracil	Case 2: Disease free at 6 months follow-up
Cha *et al.* (10)	48	ER (–), PR(–), HER2(3+), Ki-67(+,95%)	Adjuvant chemotherapy	Doxorubicin + docetaxel + cyclophosphamide	Disease free at 4 months follow-up
Murialdo *et al.* (19)	54	ER(–), PR(–), HER2(3+), Ki-67(+,60%)	Adjuvant chemotherapy	Cisplatin + 5-fluorouracil	Disease free at 28 months follow-up
Bhosale *et al.* (9)	60	ER(–), PR(–), HER2 N/A, Ki-67 N/A	Adjuvant chemotherapy	(Paclitaxel + carboplatin) 6 cycles	Not reported
Tomasicchio *et al.* (20)	39	ER(–), PR(–), HER2(–), Ki-67(+,45%)	Adjuvant chemotherapy	Nab-paclitaxel	Without disease progression
Noda *et al.* (21)	34	ER(–), PR(–), HER2(–) Ki-67(+,>90%)	Adjuvant chemotherapy	(Adriamycin + cyclophosphamide) 4 cycles + paclitaxel 12 cycles	Disease free at 30 months follow-up
Shrestha *et al.* (22)	18	ER(–), PR(–), HER2(–) Ki-67(+,70%)	Adjuvant chemotherapy	(Paclitaxel + carboplatin) 6 cycles	Disease free at 9 months follow-up
Guo *et al.* (23)	55	ER(–), PR(–), HER2(–) Ki-67(+,50%)	Adjuvant chemotherapy	(Docetaxel + cisplatin) 3 cycles	No recurrent or metastatic
Tsung *et al.* (24)	50	ER(–), PR(–), HER2(2+, Fish negative), Ki-67 N/A	Neoadjuvant chemotherapy	(Cyclophosphamide + epirubicin + fluorouracil) 4 cycles	Neoadjuvant therapy was ineffective.
Alan *et al.* (25)	72	ER(+, ≤1%), PR(–), HER2(–), Ki-67 N/A	Neoadjuvant chemotherapy	Paclitaxel + epirubicin + cyclophosphamide	Pathological complete response
Current study	48	ER(–), PR(–), HER2(–) Ki-67(+,60%)	Neoadjuvant chemotherapy	(Paclitaxel + carboplatin) 4 cycles	Miller-Payne 4

+/–, the immunohistochemical staining of the tumor cells was positive/negative for certain antigen. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor-2; N/A, not available.

term disease-free survival. Thus, it can be seen that the TP regimen might be effective for MSCCB. However, the neoadjuvant therapy of this patient has not yet achieved a complete pathological response. Given this, we question how to improve the effectiveness of the treatment?

GBG 69-GeparSepto's study suggests that NAB-paclitaxel is more effective in improving pCR and DFS than solvent-based paclitaxel in neoadjuvant therapy for early breast cancer (28). Besides, Tomasicchio *et al.* (20) used NAB-paclitaxel as adjuvant chemotherapy for breast squamous cell carcinoma and achieved a good therapeutic response. Recently, immunotherapy has been rising rapidly and is considered an effective therapeutic. Additionally, the KEYNOTE 522's study confirmed that

TP regimen combined with PD-1 inhibitors in neoadjuvant therapy could significantly improve pCR rate in TNBC patients (29). It suggests that a combination of PD-1 inhibitors may further improve the therapeutic effect of breast squamous cell carcinoma.

In conclusion, MSCCB is a rare malignant tumor and has no established treatment method. However, through the analysis of this case and review of the literature, it is indicated that the TP regimen is an effective therapeutic option for treating MSCCB.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-484/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-484/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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