

Interventional chemoembolization for the treatment of severe ulcerative bleeding caused by advanced breast cancer: A report of two cases

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Abstract. Local ulcerative cutaneous hemorrhage resulting from breast cancer profoundly affects the quality of life of patients, at times even posing a threat to life. While early diagnosis rates of breast cancer have shown improvement, some patients may present at an advanced stage upon consultation. Presently, there is no standardized treatment approach for these patients. In this context, the present study presented two case studies detailing the use of interventional embolization chemotherapy for addressing severe local ulcerative hemorrhage associated with breast cancer. Post-treatment, there was a notable amelioration in the mammary ulceration among the patients, an elevated hemoglobin level compared with baseline and a consequent enhancement in their overall quality of life. These cases may serve as valuable references for the management of such clinical situations.

Introduction

Breast cancer ranks as the predominant type of cancer among women and stands as a primary contributor to cancer-related mortality, making it one of the foremost causes of morbidity and mortality among women globally (1). Advanced breast cancer, categorized under stages III and IV, encompasses

either inoperable, locally advanced, or metastatic breast cancer. Such advanced stages are often synonymous with a poor prognosis, where systemic therapy is the conventional treatment modality (2). The median overall survival time is ~3 years, with the 5-year survival rate hovering at ~25% (3,4).

In the context of advanced breast cancer, cutaneous ulceration can manifest and is frequently accompanied by intermittent or continuous bleeding. This complicates the clinical picture, profoundly impairing the patient's quality of life and, in severe instances, leading to potentially fatal anemia. Digital subtraction angiography-guided inferior artery embolization has been introduced as a therapeutic option for mammary hemorrhage conditions (5). Enhanced therapeutic outcomes are observed when this technique is synergized with arterial infusion and chemotherapy. In line with this, we present two case studies of advanced breast cancer patients experiencing intense skin ulceration bleeding, who were successfully managed through interventional chemoembolization.

Case report

Case 1. A 45-year-old female patient was admitted to Jinshazhou Hospital of Guangzhou University of Chinese Medicine (Guangzhou, China) due to a right breast mass found 2 years previously and right breast ulceration for 4 months. The patient had noticed a right breast mass in February 2021 but did not pay sufficient attention to the lesion. Breast ulceration occurred in October 2022, resulting in herbs being applied to the wound, although this had no beneficial effects and the patient came to the hospital in February 2023 for further treatment. Physical examination on admission revealed ulceration of the right breast, with an ulcerated surface area of ~18x16 cm, accompanied by a foul smell, visible blood, fluid seepage and a tendency to bleed easily (Fig. 1A). Physical examination on admission in February 2023 showed a hemoglobin (HGB) level of 8.8 g/l (normal range, 13.0-17.5 g/l). On the same day, the patient underwent a PET/CT examination that showed the following results: i) Multiple nodules were identified in the right breast,

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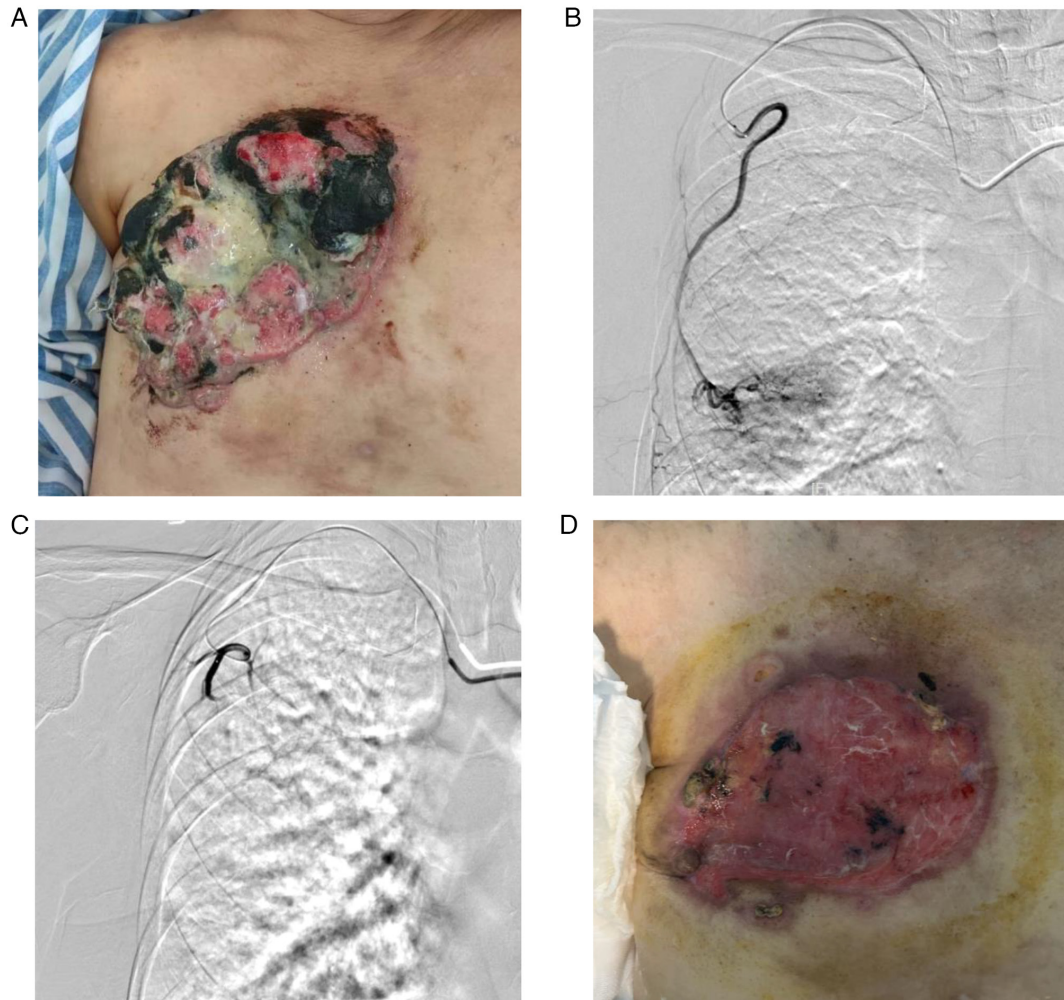


Figure 1. Tumor changes and interventional surgery. (A) The breast ulcerated and bleeding. (B) The vessels of the tumor area became thick and tortuous. (C) The blood vessels were occluded after embolization. (D) The mammary gland wound stopped bleeding and developed granulation tissue.

with lamellar focal hypermetabolic lesions. These were consistent with the manifestations of right breast cancer. Lesions were predominantly clustered near the skin, right nipple, right chest wall and sternum body; ii) a multitude of hypermetabolic lymph nodes were observed, indicative of multiple lymph node metastases. These were situated in various locations, including the deep surface of the right pectoralis muscle, right axillary region, bilateral pulmonary hila, mediastinum, retroperitoneal area, right side of the common iliac artery, left clavicular area, left cervical zones IV and V, and right cervical zones II, III, and V; iii) both lungs exhibited multiple nodular formations with augmented glucose metabolism, suggestive of multifocal pulmonary metastases; iv) multiple nodular, hypermetabolic foci were discerned in the liver, which were interpreted as multiple hepatic metastases; and v) extensive bone metastases were evident throughout the skeletal system, accompanied by pathological fractures of the lumbar vertebrae at levels 2 and 4. The diagnoses at admission were: i) Stage IV breast cancer; ii) lung metastasis; iii) liver metastasis; iv) multiple bone metastases; and v) pathological fractures of lumbar vertebrae 2 and 4. At admission, 2023, the patient underwent a needle biopsy of the breast mass. The puncture was successful without bleeding at the puncture site. Pathological examination showed an invasive adenocarcinoma, estrogen receptors (ER+), progesterone

receptors (PR+), and human epidermal growth factor receptor 2 (HER2+++; Fig. 2). As the patient's breast wound continued to ooze blood and the HGB level declined to 6.9 g/l at 3 days post-admission, 840 mg pertuzumab and 450 mg trastuzumab were administered as intravenous targeted therapy. Arterial perfusion embolization of the right lateral thoracic artery was performed at 4 days post-admission, with intraoperative angiography showing that the vessels in the tumor area had become thick and tortuous (Fig. 1B). Accordingly, 90 mg docetaxel and 200 mg carboplatin were injected through the arterial catheter and embolized the right lateral thoracic artery with a 560- μ m gelatin sponge and embolized microspheres (Fig. 1C). A week after the procedure, the patient exhibited marked improvement in the breast wound, with a noticeable reduction in its size and diminished blood oozing. Furthermore, the HGB levels showed a progressive increase. By the 20th day post-chemoembolization, the ulcers in the patient's breast wound had significantly healed, displaying no signs of odor, blood oozing or effusion. New granulation tissue had also formed (Fig. 1D), and the HGB level had risen to 94 g/l. On the 21st day post-chemoembolization, the patient's overall condition was substantially improved, and there was a significant enhancement in the quality of life. Subsequently, regular antitumor therapy, including targeted therapy, chemotherapy and radiotherapy, was continued.

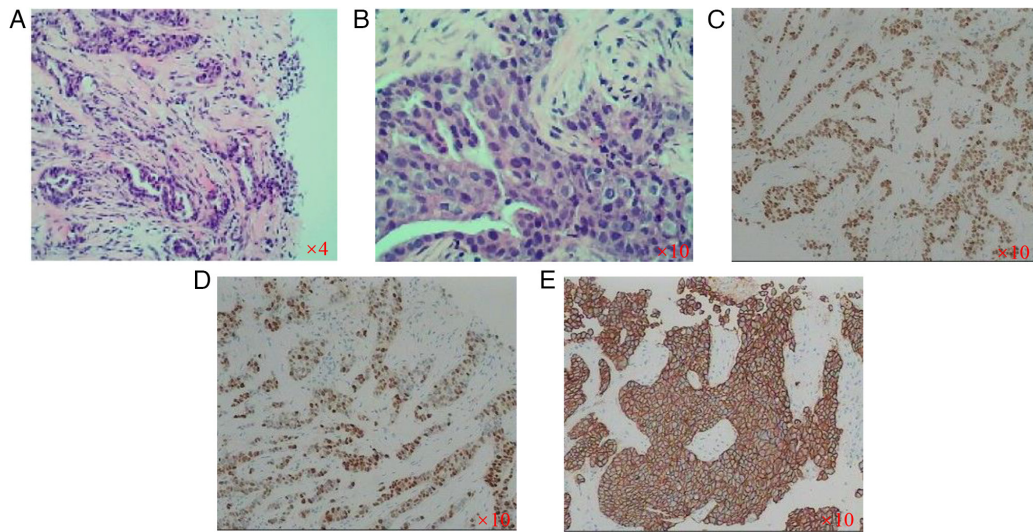


Figure 2. Pathological and immunohistochemical results. (A and B) Invasive breast cancer. (C) ER(+), (D) PR(+), (E) HER2(+++). ER, estrogen receptors; PR, progesterone receptors; HER2, human epidermal growth factor receptor 2.

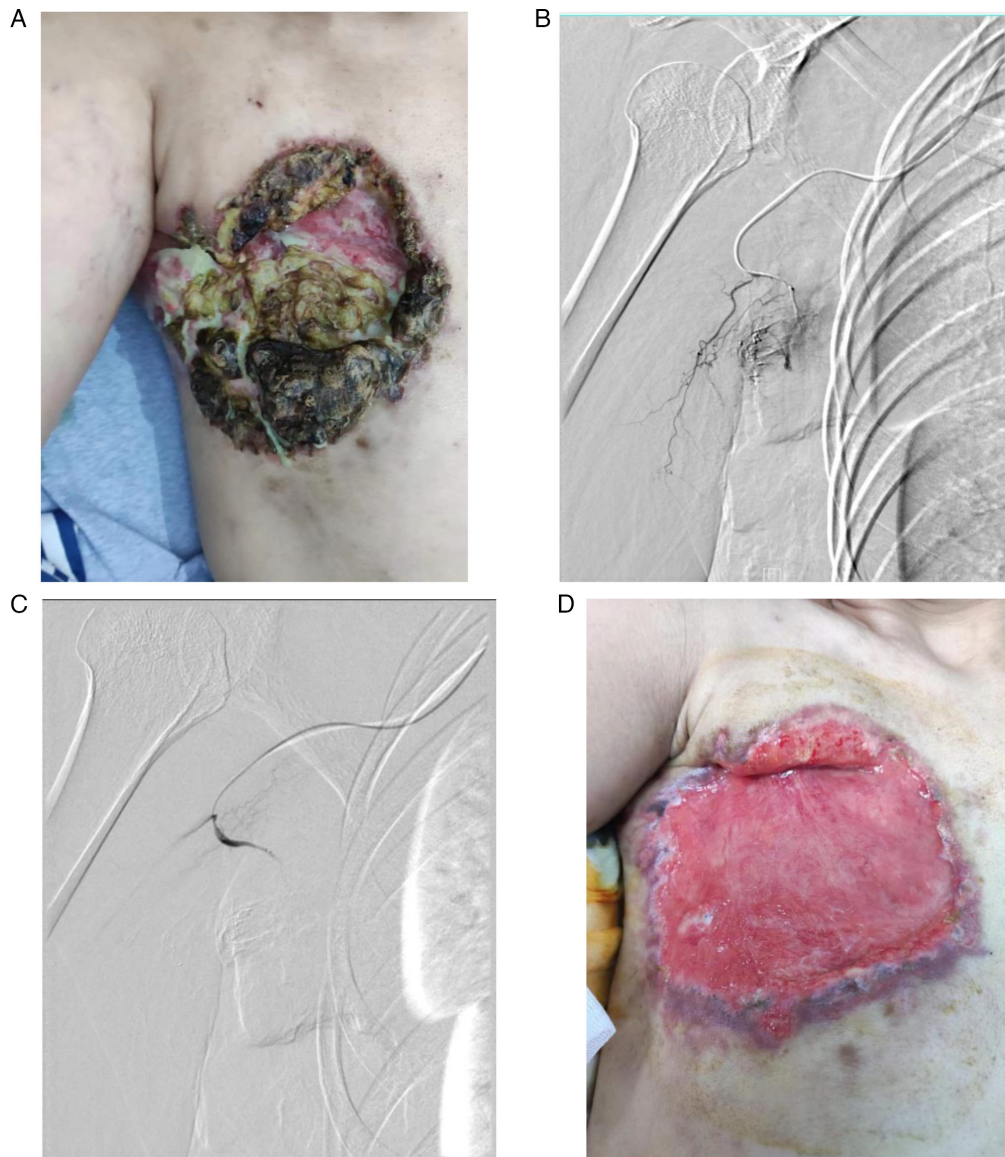


Figure 3. Changes of tumor and interventional surgery (A) A large amount of necrosis was observed in the breast wound, accompanied by bleeding. (B) The right dorsal thoracic artery was tortuous and thickened. (C) The blood vessels were occluded after embolization. (D) The wound healed gradually.

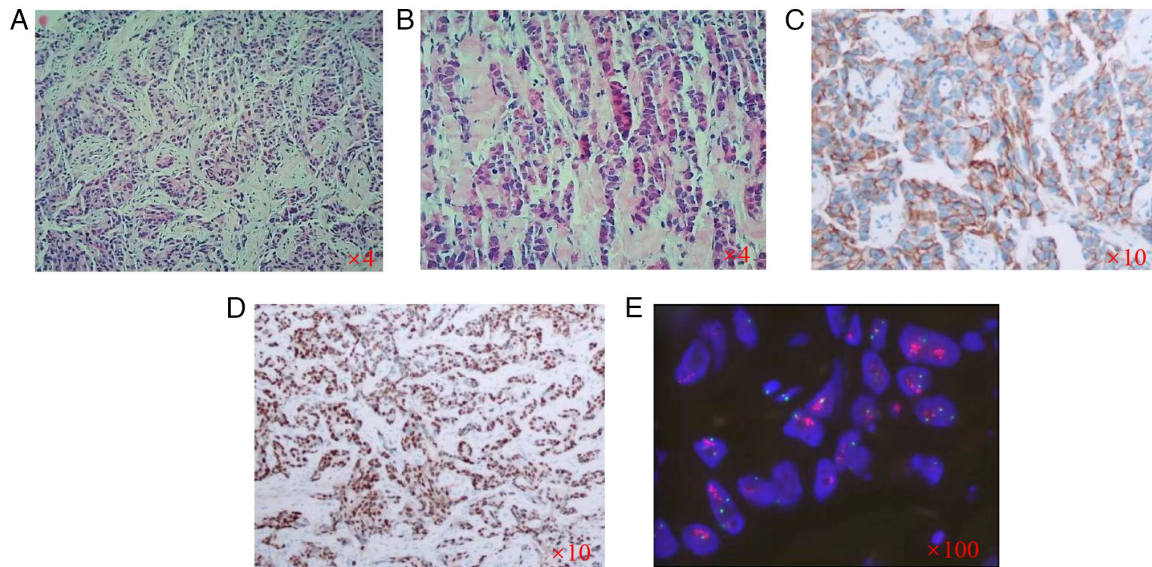


Figure 4. Pathological and immunohistochemical (A and B) Invasive ductal carcinoma of the breast. (C) ER(+), (D) HER2(++). (E) Fluorescence *in situ* hybridization(+): HER2 signal mean=18.7, CEP17 signal mean=1.8 and HER2/CEP17 signal mean=10.3. The color represents a positive HER2 signal. ER, estrogen receptors; PR, progesterone receptors; HER2, human epidermal growth factor receptor 2.

Case 2. The patient was a 44-year-old female. A physical examination in April 2021 revealed a right breast mass and axillary lymph node enlargement, although antitumor therapy was not received. The patient came to Jinshazhou Hospital of Guangzhou University of Chinese Medicine in December 2022 at which time ulceration was observed from the right nipple to the axilla. The ulceration area was $\sim 15 \times 12$ cm with an unclear boundary and was associated with oozing of blood and yellow secretions and an odor (Fig. 3A). At 1 day post-admission, the HGB level was 7.5 g/l. A CT scan was performed on admission that showed the following results: i) Presence of right breast cancer with local skin rupture. The lesion was observed to have invaded both the breast tissue and the overlying skin anteriorly. Posteriorly, it extended into the soft tissue of the chest wall, affecting the right major and minor pectoral muscles as well as the adjacent ribs and costal cartilage, nearing the pleura; ii) multiple lymph node metastases were identified in several regions: The bilateral supraclavicular fossae, axillary areas, internal mammary chain, mediastinum, retroperitoneum, and the area at the right cardiophrenic angle; iii) multiple metastatic tumors were discerned in various locations including the subcutaneous soft tissue proper, right major and minor pectoral muscles, deltoid, latissimus dorsi, and serratus anterior; iv) multiple metastatic tumors in both lungs; v) multiple bone metastasis of the sternum, right scapula, humerus head and multiple bilateral ribs, thoracic 1, lumbar two vertebrae and accessories; and vi) a metastatic tumor of the left lobe of the liver. The diagnoses at admission were: i) Stage IV breast cancer; ii) multiple bone metastases; iii) lung metastases; and iv) liver metastases. As shown in Fig. 4, pathological examination of a breast biopsy showed invasive breast cancer, ER(+), PR (+), HER2(++), and fluorescence *in situ* hybridization(+). The biopsy procedure was smooth with no postoperative bleeding. Due to continuous bleeding of the ulcerated part of the breast, the patient's hemoglobin decreased to 58 g/l. At 6 days post-admission, arterial interventional chemotherapy embolization into the right dorsal thoracic artery was

performed. The angiogram revealed a tortuous and thickened right dorsal thoracic artery (Fig. 3B). Subsequently, 60 mg doxorubicin and 1 g cyclophosphamide were administered directly into the artery serving the tumor area. To embolize the dorsal thoracic artery, a 350- μ m gelatin sponge and embolized microspheres were utilized, continuing until the vessels were suitably occluded. A follow-up angiogram confirmed vascular occlusion (Fig. 3C). Post-procedure, the patient's HGB level steadily rose to 9.2 g/l. Due to financial constraints, the patient declined anti-HER2 medications but underwent interventional chemoembolization every 21 days. As evidenced by Fig. 3D, this intervention resulted in a consistent reduction of wound oozing in the mammary gland and subsequent wound healing. Currently, the patient remains in favorable health and persists with regular antitumor therapy in the Fifth Department of Oncology, Jinshazhou Hospital of Guangzhou University of Chinese Medicine.

Discussion

Among solid tumors, breast cancer registers the highest incidence of malignant wounds, with a prevalence rate of $\sim 47\%$ (6). Contemporary therapeutic interventions for hemorrhagic malignant wounds attributable to breast cancer predominantly encompass calcium alginate, local hemostatic agents, non-adhesive dressings, and sclerosing agents such as Moes paste and 10% formalin (5,7). Presently, substantive evidence supporting the utilization of interventional embolization hemostasis for malignant wounds in breast cancer remains elusive. Nonetheless, notable cases in the literature shed light on its potential. For instance, Leung *et al* (8) documented a case where preoperative embolization was employed as a preemptive measure against intraoperative hemorrhage stemming from a vascular phyllodes breast tumor. Similarly, Atzori *et al* (9) relayed the successful execution of transcatheter arterial embolization in managing

a locally advanced breast cancer case presenting with critical bleeding.

In patients with breast cancer, transcatheter arterial chemoembolization (TACE) is used mainly to treat liver metastasis of breast cancer (10-12). A notable study by Li *et al* (13) elucidated the superiority of TACE over systemic chemotherapy in treating breast cancer patients with liver metastasis. Additionally, the influence of hormone receptors on the efficacy of interventional embolic chemotherapy has been documented, suggesting their role as pivotal determinants in therapeutic outcomes for breast cancer patients (14). Notably, both cases discussed in the present study exhibited positive hormone receptor status, potentially contributing to the observed favorable therapeutic outcomes. Intra-arterial perfusion emerges as a variant of systemic chemotherapy, distinguished by its localized perfusion attributes. This method ensures a heightened drug concentration within tumor cells compared with adjacent tissues. The direct interaction between the drug and tumor cells, coupled with an extended action duration, arguably confers superiority over traditional intravenous chemotherapy approaches (15,16). Epirubicin (EPI) in combination with paclitaxel, when utilized as neoadjuvant chemotherapy administered via arterial perfusion, has been heralded for its commendable efficacy and minimal toxicological implications (17). Similarly, Fiorentini *et al* (18) reported the beneficial outcomes and low toxicity profile associated with the use of EPI in conjunction with either mitomycin or docetaxel as frontline agents for breast cancer treatment, again leveraging arterial perfusion. However, despite accumulating reports advocating for vascular interventional treatments in breast cancer (19-21), such modalities have yet to secure a formal endorsement within the standard breast cancer treatment guidelines.

Research indicates that the internal mammary artery predominantly supplies breast tumor. Consequently, in interventional therapy, a catheter is usually placed in this artery, followed by the subclavian artery (20,22). Consistent with this approach, the TACE procedures in the two cases presented in the present study focused on the subclavian branch of the external thoracic artery.

In conclusion, interventional chemoembolization for treating breast ulceration caused by advanced breast cancer has a good effect.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

YHT, XW and XL were involved in the patient's treatment management process, and HCZ and WSW performed

interventional surgery. YHT and XL confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by The Ethics Committee of Jinshazhou Hospital of Guangzhou University of Chinese Medicine (Guangzhou, China; approval number JSZ-IEC-SL-KT-20230506).

Patient consent for publication

Written informed consent was obtained from the patients for publication of the present case reports and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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