

Case Report

Long-Term and Sustained Remission of Advanced Triple-Negative Breast Cancer with Large Chest Wall Lesions after Transient Chemoimmunotherapy: A Case Report

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Keywords

Triple-negative breast neoplasms · Immunotherapy · Toripalimab · Thoracic wall

Abstract

Introduction: We report a case of advanced triple-negative breast cancer (TNBC) with special clinical manifestations, in which a durable remission was achieved after short-term administration of toripalimab combined with chemotherapy. The progress, advantages, and unique experience of chemoimmunotherapy in TNBC were examined. **Case Presentation:** A patient with TNBC with local recurrence 2 years following surgery, with inoperable large chest wall lesions and positive PD-L1 as the main manifestations, was treated with toripalimab plus paclitaxel (albumin-bound) for 5 months and achieved a partial remission. Twenty-five months after the discontinuation of treatment, the chest wall lesions exhibited a slow but continuous decline, until they achieved a nearly complete remission; however, the patient eventually died from cancer progression. **Conclusion:** Typically, chest wall recurrence in TNBC has a poor prognosis; however, recurrence was rapidly controlled, sustained remission was achieved after immunotherapy combined with chemotherapy, and the curative effect continued after drug withdrawal, which is a rare occurrence. Thus, the tailing effect of immune checkpoint inhibitors was confirmed in the treatment of TNBC.

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Introduction

Triple-negative breast cancer (TNBC) is ER-, PR-, and Her-2-negative breast cancer and accounts for 15–20% of all breast cancers [1]. It is aggressive and has a high probability of visceral and brain metastasis. Recurrence with metastasis usually occurs within 3 years following surgery and the prognosis is worse compared with other types of breast cancer [2]. Here, we report a case of advanced TNBC with specific clinical manifestations, in which a durable remission was achieved following short-term treatment with toripalimab combined with chemotherapy. We examined the progress, advantages, and our unique experience with chemoimmunotherapy for TNBC. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000543292>).

Case Presentation

The patient was a 64-year-old female of Han nationality, with no family history of breast cancer, smoking, drinking, or other underlying diseases or comorbidities. In May 2018, a breast ultrasound was performed during a physical examination and a 2-cm mass was detected on the medial side of the right breast at a location of 3 o'clock. Breast needle aspiration cytology revealed adenocarcinoma cells. A modified radical mastectomy for right breast cancer was performed on May 21, 2018. Pathology indicated invasive carcinoma of no specific type, World Health Organization grade III, a size of $2.3 \times 1.8 \times 1.4 \text{ cm}^3$, ipsilateral axillary lymph node 5/16 (+), and a negative resection margin. The results of immunohistochemistry were as follows: ER (–), PR (–), HER-2 (–), Ki-67 (60%+), E-cad (+), CK5/6 (partial +), β -catenin (+), and P120 (membrane+). Following surgery, the AC-T regimen (doxorubicin 100 mg d1 + cyclophosphamide 1,000 mg d1 q3w, 1–4 cycles; paclitaxel 300 mg d1 q3w, 4–8 cycles) was followed for eight courses in other hospitals. The final course of adjuvant chemotherapy was administered in January 2019 and the patient refused postoperative radiotherapy.

The patient experienced right chest wall pain and discomfort beginning in June 2020. In August 2020, because of aggravated pain, the patient visited our hospital for the first time. A physical examination revealed a subcutaneous soft tissue mass on the right side of the sternum body of the chest wall near the surgical scar, with an unclear boundary, deep into the chest wall, with tenderness (–), and intact skin. The patient refused a chest wall biopsy. A chest computed tomography (CT) scan was performed on August 14, 2020, and revealed a huge soft tissue shadow ($7.4 \times 6.2 \text{ cm}^2$) inside and outside of the right chest wall, protruding to the phrenic angle, and invading the rib cortex. A small amount of encapsulated effusion was observed in the right pleural cavity (Fig. 1a). Consequently, local recurrence of breast cancer with chest wall, sternum, and rib invasion was diagnosed. The 2018 surgical specimens were procured and they tested positive for PD-L1: TC+ (positive ratio of tumor cells) 26–49% using the detection antibody VENTANA PD-L1 (SP263). Whole-body bone imaging on August 17, 2018, revealed metastasis to the right 6th anterior rib (Fig. 2). On August 21, 2020, toripalimab (Suzhou Zhonghe Biomedical Technology Co., Ltd; trade name: Tuoyi) 240 mg d1 plus paclitaxel (albumin-bound) (232 mg d1, 8 q3w) treatment was administered for six courses combined with zoledronic acid (4 mg q4w) for bone protection. The final course of chemotherapy was administered in January 2021. Following treatment, chest wall discomfort was rapidly relieved. After two courses of treatment, the tumor shrank rapidly, the subcutaneous soft tissue tumor regressed significantly, and the right pleural effusion disappeared, as evidenced by a CT scan. A PR was confirmed (Fig. 1b) and the lesions continued to shrink after four and six courses of treatment (Fig. 1c), which was well-tolerated, with mild nausea and anorexia. Furthermore, no chemotherapy-related bone marrow suppression or immune-related side effects were observed.

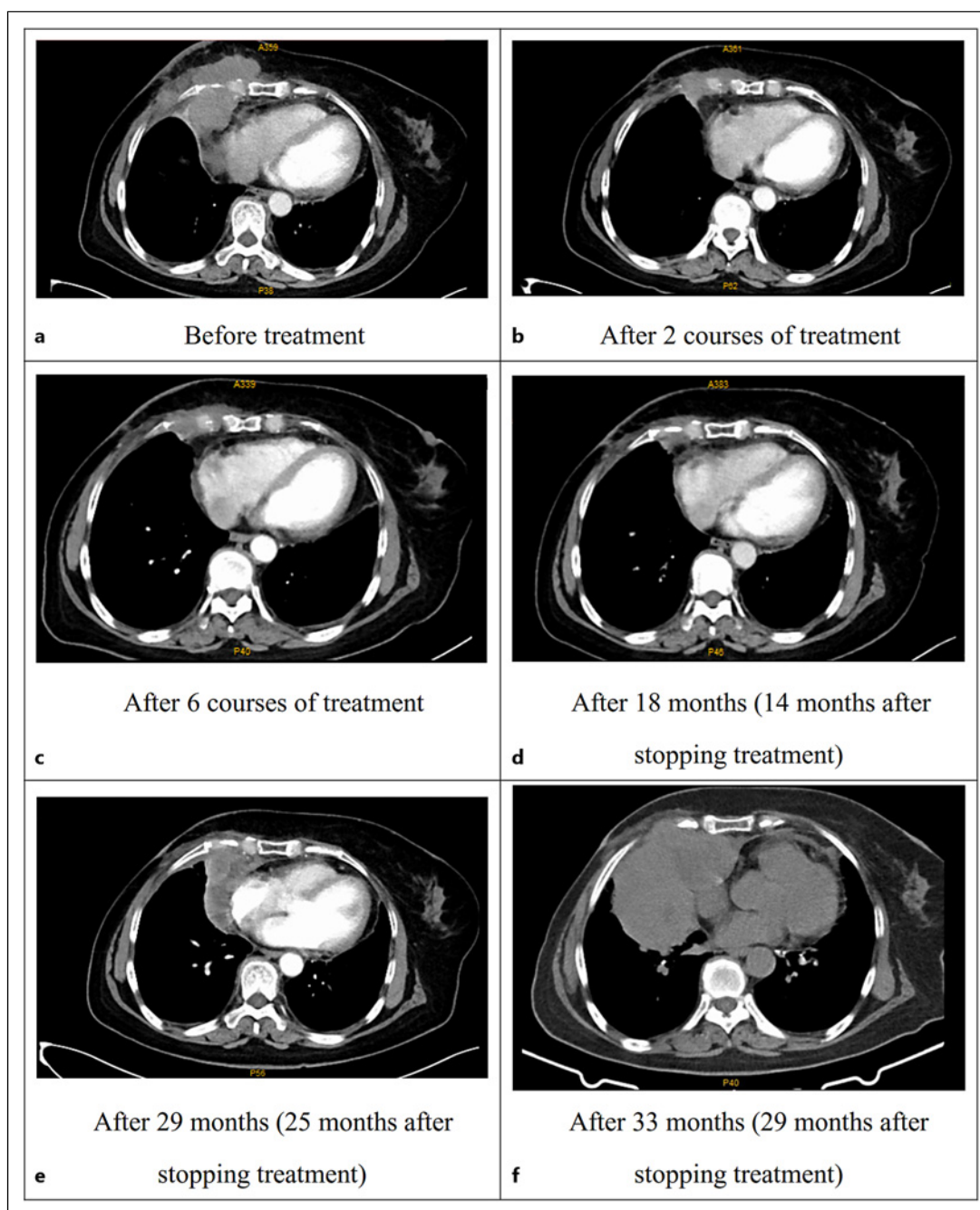


Fig. 1. a–f Comparison of chest CT in different treatment periods.

Because of poor patient compliance, immune maintenance therapy, radiotherapy, and bone protection agent maintenance were not performed. Follow-up observation from January 2021 and repeat CT scans every 3 months revealed that the lesions on the right chest wall continued to shrink. Fourteen months after discontinuation of all treatments, CT re-examination (February 22, 2022) indicated that the soft tissue lesions in the chest wall were close to complete remission, residual rib lesions were observed, and no pleural effusion was evident (Fig. 1d). During this period, the patient had a normal life without discomfort and an ECOG PS of 0 points. On January 31, 2023, a CT scan revealed that the lesion in the chest wall

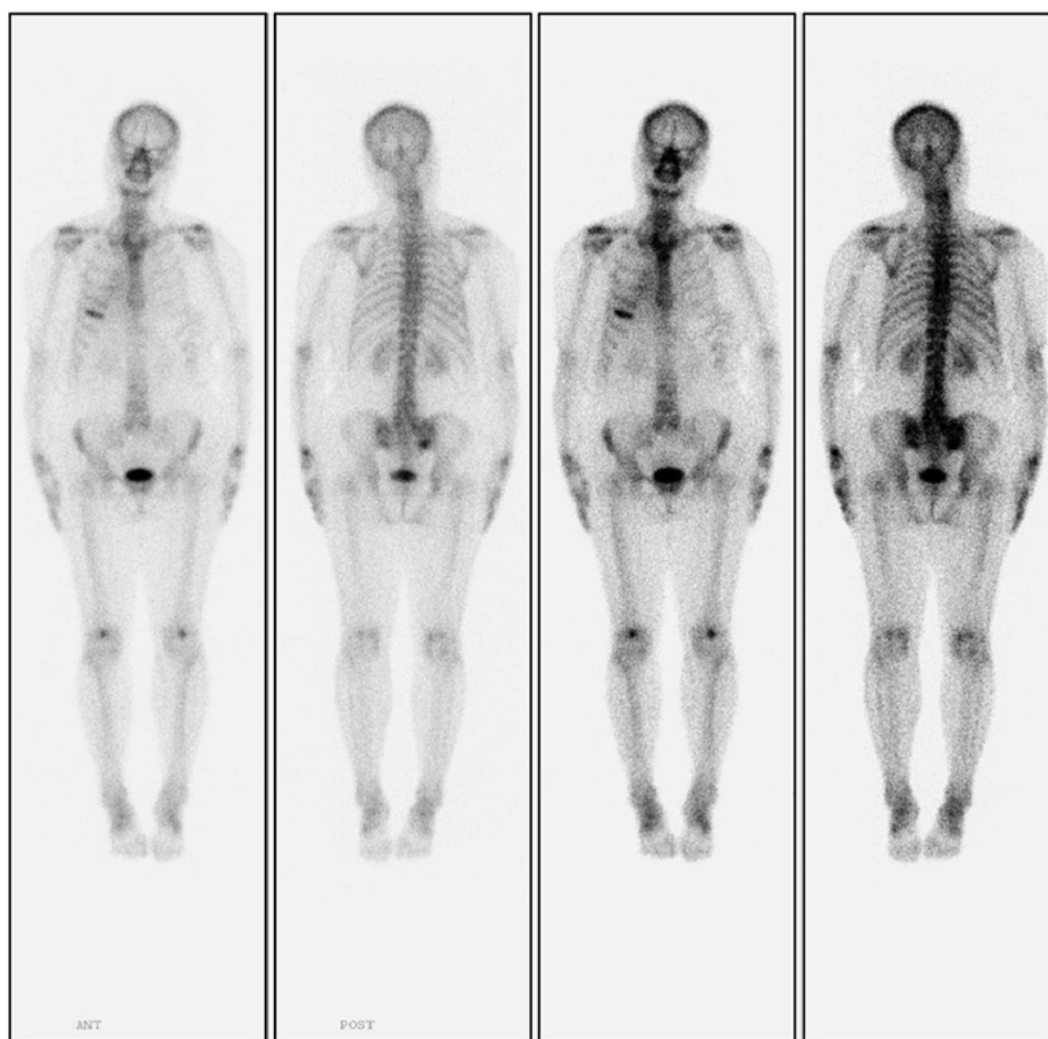


Fig. 2. Whole-body bone imaging (before treatment).

had progressed (Fig. 1e). On May 10, 2023, a CT reexamination revealed that the lesion in the chest wall had progressed significantly and reappeared as a right pleural effusion (Fig. 1f). The patient consistently refused anticancer treatment and ultimately died on August 24, 2023. The progression-free survival after first-line treatment was 29 months and the overall survival time following recurrence was 3 years. During these 3 years, the patient received only 5 months of antitumor therapy. Despite complete cessation of treatment, the patient still achieved a progression-free survival period of 2 years.

Conclusion

Generally, chest wall recurrence in TNBC is associated with a poor prognosis; however, in this particular case, the recurrence was quickly managed and a sustained remission was achieved following a combination of immunotherapy and chemotherapy. Remarkably, the therapeutic effect persisted even after the discontinuation of treatment, which is an unusual occurrence.

Discussion

Under the influence of various high-risk factors (5 positive axillary lymph nodes, high proliferative index, and no postoperative radiotherapy), this case developed local recurrence 2 years after radical resection, but no visceral or other distant metastases were observed. This does not represent the behavioral characteristics of typical TNBC. Instead of skin ulceration, large chest wall lesions showed rapid and sustained remission after the initiation of chemoimmunotherapy, which is very rare and encouraging in TNBC.

Compared with the other subtypes, TNBC tumor tissue has more abundant peripheral infiltrating lymphocytes, a higher tumor mutational burden, and PD-L1 expression, which comprise the immune microenvironment that is conducive to the onset of immune checkpoint inhibitors (ICIs) [3]. The objective response rate (ORR) of single-agent ICIs (atezolizumab and pembrolizumab) during first-line treatment of TNBC is approximately 24% and the median survival time is 18 months [4, 5]. The combination of chemotherapy with ICIs enhances the positive immunomodulatory effects of chemotherapy and is a focus of current clinical studies of immunotherapy for TNBC [6]. Patients with PD-L1 positivity and those receiving first-line treatment have demonstrated advantages in their response to therapy [7]. In the ANASTASE real-world study, the ORR of atezolizumab combined with paclitaxel (albumin-bound) as first-line treatment for PD-L1 positive TNBC patients was 42.3%, with a median PFS of 6.3 months [8]. In the KEYNOTE-355 study, the ORR of pembrolizumab combined with chemotherapy as first-line treatment for PD-L1 CPS ≥ 10 TNBC patients was 52.7%, with a median progression-free survival of 9.7 months and a median overall survival of 23 months, which indicates superiority over chemotherapy alone [9]. The efficacy data for immunotherapy ranks among the highest in breast cancer and even solid tumors; however, no statistically significant difference was observed in TNBC patients with a CPS ≥ 1 .

This case study involved a large soft tissue lesion of the chest wall with insignificant skin involvement, but deep bone and pleura involvement. TNBC chemotherapy with chest wall recurrence has a short response time and is prone to distant metastasis, which may result in complex complications, such as chest wall skin ulceration, infection, and bleeding. Although TNBC is more sensitive to chemotherapy compared with other subtypes, it is more likely to develop resistance, whereas ICIs combined with chemotherapy are promising candidates for circumventing resistance. In the present case, the combination of ICIs and chemotherapy was administered as first-line treatment and the rapid remission of huge lesions and obvious local invasion was a rare event. Toripalimab (the import drug that was not used for economic reasons) is an anti-PD-1 monoclonal antibody and the first domestic ICI to be marketed in China as of December 17, 2018, and later in the USA on October 28, 2023. Phase III TORCHLIGHT studies indicate that the combination of toripalimab and paclitaxel (albumin-bound) administered as first-line therapy for PD-L1 positive TNBC has an ORR of 66%, a median PFS of 8.4 months, and a median OS of 32.8 months [10].

The selection of chemotherapy drugs also significantly influences treatment efficacy. In this case, the use of albumin-bound paclitaxel, which utilizes a targeted nanoparticle albumin-bound technology, addresses the challenges of poor solubility and the need for solvent coadministration that may cause hypersensitivity reactions, while enabling higher dosing. In the IMpassion 130 study, atezolizumab combined with paclitaxel (nab-bound) as first-line treatment for TNBC showed a median response of 7.4 months and a 1-year progression-free survival rate of 24% [11]. However, in the IMpassion 131 study, the combination of atezolizumab with paclitaxel as first-line treatment for TNBC did not show a statistically significant improvement in progression-free survival compared with single-agent paclitaxel [12].

Based on these findings, in September 2020, the FDA issued a warning to healthcare professionals that the combination of atezolizumab and paclitaxel is not effective against previously untreated advanced TNBC.

After >2 years of treatment discontinuation, the progression-free survival of the patient in the present study was 29 months and the chest wall lesions continued to shrink until nearly completely absent. It is uncommon for chemotherapy alone to achieve this effect, which reflects the overall situation for TNBC patients.

There were some limitations to this case study: (1) the patient's breast cancer surgery occurred in 2018. Based on current diagnostic and treatment guidelines, as well as data from evidence-based medicine, the absence of neoadjuvant therapy is a significant missed opportunity. If the patient had received neoadjuvant chemotherapy, the likelihood of achieving a pathologic complete response would have been quite high, potentially leading to less extensive surgical resection and a better prognosis. This perspective is also supported by a retrospective study conducted by Gentile et al. [13]. (2) No distant metastases were detected in the internal organs and other areas, which is in contrast to typical advanced TNBC, and therefore, limits the study's generalizability. The control of local residual soft tissue and bone lesions may be strengthened by radiotherapy, but it is almost impossible to achieve complete regression from the follow-up effects of previous immunotherapy. (3) Because of compliance issues, postoperative adjuvant radiotherapy was not performed, which is the primary reason for the local recurrence. (4) Regarding good tolerance and no apparent side effects, the prognosis may be improved further if ICIs were continuously administered for 2 years. (5) Chest wall biopsy was not repeated after recurrence. Without follow-up biopsies, confirmation of a continued response, and evaluating potential treatment resistance were limited. No breast cancer susceptibility gene (BRCA^{1/2}) test was conducted (although there was no family history of breast cancer). Because the proportion of BRCA mutations is higher in TNBC, the complete response rate of chemotherapy in mutated TNBC is significantly higher compared with that in non-TNBC [14], which explains the unique efficacy in this case from a perspective other than PD-L1. This assay also supports the subsequent application of PARP inhibitors; however, poor compliance has never been an excuse for insufficient communication between doctors and patients, which is constantly reviewed. Another interpretation of "real world" medical care may not be covered by clinical trials and evidence-based medicine. Because "real world" medical care inadvertently excludes the interference of other treatment modalities on the treatment results, we examined the possibility of chemoimmunotherapy for TNBC alone and explored additional strategies and models for breakthrough treatments.

Acknowledgments

Written informed consent was obtained from the patient's relatives for the publication of this report.

Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the daughter of the deceased patient for the publication of this case report and the accompanying images.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Chanjuan Chen and Wei Chen carried out the studies, participated in collecting data, and drafted the manuscript. Chanjuan Chen and Xiaonan Pang performed the statistical analysis and participated in the study design. Mingjun Zhang, Fanfan Li, and Wangying Zhang participated in data acquisition, analysis, or interpretation and drafted the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

The datasets used and/or analyzed for the current study are available from the corresponding author upon reasonable request. The decision to withhold the data from this study is not publicly available because of privacy or ethical restrictions. However, interested parties may request access to the data directly from the corresponding author (Wei Chen, 274309229@qq.com).

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