

Successful Trastuzumab Deruxtecan Treatment After Adjuvant Trastuzumab-Induced Heart Failure: A Case Report

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Case Report

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Abstract

Background: Trastuzumab-induced cardiotoxicity is a well-recognized complication that may lead to discontinuation of adjuvant HER2-targeted therapy. Evidence regarding subsequent treatment strategies for recurrence in patients with a history of trastuzumab-related heart failure remains limited.

Case presentation: A woman with HER2-positive early breast cancer received adjuvant trastuzumab after surgery. Her baseline left ventricular ejection fraction (LVEF) was in the 60% range. During therapy, she developed acute heart failure with LVEF decline to 30%, requiring a one-week hospitalization and discontinuation of trastuzumab. Her cardiac function gradually recovered to the 60% range under standard heart failure management. Approximately 43 months later, she developed recurrence with liver metastases and multiple lymph nodes metastasis. Her cardiologist didn't allow re-anti-HER2 therapy, and we kept chemotherapy without anti-HER2 drugs. Two years later, given her recovered cardiac function and disease progression, trastuzumab deruxtecan (T-DXd) was started. She received 13 cycles over 10 months, achieving durable tumor response without cardiac deterioration.

Conclusion: This case illustrates that T-DXd can be a feasible and effective option for recurrent HER2-positive breast cancer in patients with prior trastuzumab-induced heart failure, when cardiac function has sufficiently recovered and careful cardio-oncology monitoring is ensured.

Introduction

Trastuzumab is a key component of adjuvant therapy for HER2-positive breast cancer; however, cardiotoxicity remains a clinically significant adverse event, occasionally necessitating treatment discontinuation. Although many patients experience recovery of cardiac function, the optimal management of recurrent disease in individuals with a history of trastuzumab-induced heart failure is unclear. Trastuzumab deruxtecan (T-DXd) has demonstrated substantial efficacy in metastatic HER2-positive breast cancer¹⁾²⁾, yet data regarding its use in patients with prior cardiotoxicity are scarce. We report a case of recurrent HER2-positive breast cancer successfully treated with T-DXd following recovery from trastuzumab-induced heart failure in the adjuvant setting.

Case Presentation

A 79-year-old woman had a history of right breast cancer treated 23 years ago with mastectomy and axillary lymph node dissection, followed by 5 years of adjuvant endocrine therapy.

Seven years before the current presentation, an annual screening examination revealed a chest wall mass. Cytology demonstrated Class V malignant cells. A CT scan and positron emission tomography-computed tomography (PET-CT) scan didn't show distant metastasis. She underwent chest wall tumor resection and repeat axillary lymph node dissection, which identified seven metastatic lymph nodes. Pathology confirmed hormone receptor-positive, HER2-positive recurrent breast cancer.

Adjuvant chemotherapy consisted of dose-dense doxorubicin and cyclophosphamide (ddAC) for four cycles, followed by weekly paclitaxel for 12 cycles combined with trastuzumab and pertuzumab (HP). After completion of paclitaxel, trastuzumab and pertuzumab were continued. During the second cycle of HP maintenance, she developed new-onset dyspnea. Echocardiography revealed a left ventricular ejection fraction (LVEF) of 33%, consistent with severe chemotherapy-related cardiac dysfunction. She required hospitalization and treatment by the cardiology service. HER2-targeted therapy was discontinued. Cardiac function recovered gradually and it took seven months for the cardiac function to recover to the 60% range. Radiotherapy was done and endocrine therapy was continued.

Four years after surgery, surveillance imaging revealed a new hepatic lesion, and metastatic recurrence was diagnosed. We consulted cardiology regarding the safety of re-initiating HER2-targeted therapy; however, approval was not granted. Liver biopsy demonstrated hormone receptor–positive, HER2-negative. Treatment was changed to fulvestrant plus a CDK4/6 inhibitor, but tumor markers continued to rise and imaging showed progression of hepatic metastases.

Because the patient strongly wished to avoid alopecia, treatment was switched to eribulin; however, disease progression (PD) was observed. Weekly paclitaxel plus bevacizumab was then initiated, but again resulted in PD with further hepatic enlargement. With limited remaining options and considering the lower reported cardiotoxicity compared with trastuzumab, trastuzumab deruxtecan (T-DXd) was selected.

Four months after initiating T-DXd, the patient developed drug-related interstitial lung disease (ILD), which improved with treatment interruption. Therapy was resumed at a reduced dose. Importantly, her cardiac function remained stable throughout T-DXd treatment, without decline in LVEF or heart failure symptoms. She achieved a sustained response for 10 months.

After progression, treatment was changed to docetaxel, followed by vinorelbine, but neither achieved disease control. She remained ambulatory at her final treatment visit but died at home one week later.

Discussion

Trastuzumab-related cardiotoxicity is characterized by non-structural, non-necrotic myocardial dysfunction, in contrast to anthracycline-induced injury. Because trastuzumab does not cause myocyte death or fibrosis, the resulting decline in left ventricular ejection fraction (LVEF) is typically reversible³⁾⁴⁾. Several prospective studies have demonstrated that most patients experience complete recovery of LVEF within weeks to months after discontinuation of trastuzumab and initiation of guideline-directed heart failure therapy⁵⁾.

The HER-SAFE trial⁶⁾ further confirmed that trastuzumab cardiotoxicity is functionally reversible, showing that patients whose LVEF recovered could discontinue heart failure medications without subsequent deterioration in cardiac function. These findings support the concept that recovery of LVEF reflects true

myocardial recovery, and that re-introduction of HER2-targeted therapy may be feasible in selected patients.

In our case, the patient's LVEF improved after cessation of trastuzumab and heart failure treatment, consistent with the known reversible pattern of trastuzumab-induced cardiomyopathy.

The cardiotoxicity profile of trastuzumab deruxtecan (T-DXd) appears to be more favorable than that of trastuzumab⁷⁻⁹). Although T-DXd contains the same anti-HER2 antibody backbone, its antibody–drug conjugate (ADC) structure limits myocardial exposure to the cytotoxic payload. Internalization of the ADC occurs predominantly in HER2-expressing tumor cells, and is minimal in cardiomyocytes, resulting in reduced HER2 signaling inhibition in cardiac tissue compared with trastuzumab.

Across the DESTINY-Breast clinical trials, declines in left ventricular ejection fraction (LVEF) were uncommon (approximately 1–3%), and cases of symptomatic heart failure were exceedingly rare. Importantly, patients with baseline LVEF < 50% or significant cardiac disease were excluded from these trials, leaving limited evidence regarding the safety of T-DXd in patients with pre-existing cardiomyopathy.

In real-world practice, T-DXd is generally well tolerated from a cardiac standpoint, with interstitial lung disease (ILD) representing the primary dose-limiting toxicity¹⁰⁾¹¹). In our case, despite a history of trastuzumab-induced cardiomyopathy, the patient maintained stable cardiac function throughout T-DXd therapy, without decline in LVEF or development of heart failure symptoms, achieving a sustained response for 10 months.

Conclusions

In summary, recovery of cardiac function allowed safe re-introduction of HER2-directed therapy, and trastuzumab deruxtecan achieved a durable response without further cardiac deterioration. This rare case underscores the critical role of cardio-oncology in guiding treatment for patients with concomitant cancer and cardiovascular disease.

Discontinuation of HER2-targeted treatment due to fear of cardiotoxicity places patients at an oncologic disadvantage.

Patient Perspective

Although the patient could not provide a direct perspective, her treatment course reflected a strong desire to maintain quality of life and remain engaged with her family. She often expressed her hope to live long enough to see her grandchild, a wish that was ultimately fulfilled. According to her family, she deeply appreciated being able to continue treatment while preserving her daily functioning. After her passing, her family visited the clinic to convey their gratitude, expressing that the care she received allowed her to spend meaningful time with her loved ones during the final stage of her life.

Declarations

Ethics approval and consent to participate

This case report describes routine clinical care and did not require institutional ethics committee approval. All diagnostic and therapeutic procedures were performed in accordance with the ethical standards of our institution and with the Declaration of Helsinki and its subsequent amendments. Because the patient is deceased and all identifying information has been fully anonymized, consent to participate was waived according to journal policy.

Consent for publication

The patient is deceased. All identifying information has been fully anonymized. According to journal policy, consent for publication was waived.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

(I) Conception and design: The author (II) Provision of patient care and clinical data: The author (III) Collection and assembly of data: The author (IV) Data analysis and interpretation: The author (V) Manuscript writing: The author (VI) Final approval of the manuscript: The author

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Availability of data and materials

All data generated or analyzed during this case report are included within the published article. No additional datasets are available.

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