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Case Report

# Management of Trastuzumab Deruxtecan-Induced Heart Failure and Pneumonitis in a Patient with HER2-Positive Metastatic Breast Cancer

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## Abstract

We report a case of a 49-year-old female with HER2-positive metastatic breast cancer treated with trastuzumab deruxtecan (T-DXd) after progression on multiple prior lines of therapy. Following the third cycle, she developed dyspnea and was admitted to the coronary intensive care unit with heart failure and pulmonary edema. Echocardiography revealed an ejection fraction (EF) of 10-15%. Imaging demonstrated unilateral pleural effusion and bilateral pulmonary infiltrates. Clinical findings were attributed to T-DXd-induced heart failure, bicytopenia, and pneumonitis. Despite initial improvement with corticosteroid therapy, long-term follow-up revealed worsening thrombocytopenia and development of severe pneumonitis, leading to discontinuation of T-DXd. The patient ultimately succumbed to sepsis. This case highlights the importance of vigilant monitoring and management of cardiopulmonary adverse events in patients receiving T-DXd.

**Keywords:** Fever of Unknown Origin, Macrophage Activation Syndrome, Child

## INTRODUCTION

Trastuzumab deruxtecan (T-DXd) is a HER2-directed antibody-drug conjugate approved for the treatment of HER2-positive metastatic breast cancer, particularly in patients with disease progression following standard therapies (1). Clinical trials, including the DESTINY-Breast01 and DESTINY-Breast03 studies, have demonstrated its significant efficacy in improving progression-free and overall survival in heavily pretreated patients (2). However, treatment-related adverse events such as interstitial lung disease (ILD)/pneumonitis, hematological toxicities, and cardiotoxicity necessitate careful patient monitoring and management (3).

This case report discusses the clinical challenges and management of a patient with HER2-positive metastatic breast cancer who developed T-DXd-induced cardiopulmonary complications. It emphasizes the need for a multidisciplinary approach and highlights the importance of long-term follow-up to manage adverse events effectively (4).

## Case

A 49-year-old woman with HER2-positive metastatic breast cancer was initiated on T-DXd after progression on multiple prior lines of therapy. The patient tolerated the first three cycles without complaints. Two weeks after the third cycle, she presented to the emergency department with progressive dyspnea and was admitted to the coronary intensive care unit for heart failure and pulmonary edema.

Echocardiography revealed a severely reduced ejection fraction (10-15%). Laboratory findings showed neutropenia and thrombocytopenia. Thoracic CT demonstrated a unilateral pleural effusion and bilateral pulmonary infiltrates (**Figure 1**). Based on clinical, imaging, and laboratory findings, the diagnosis was T-DXd-induced heart failure, bicytopenia, and pneumonitis. The patient was started on corticosteroid therapy (1 mg/kg/day), leading to significant clinical improvement. Follow-up CT performed 10 days later revealed complete resolution of the pleural effusion and pulmonary infiltrates, and repeat echocardiography showed an improved EF of 30-35%. Corticosteroid tapering was initiated 14 days after treatment.

Despite initial improvement, the patient's thrombocytopenia deepened over time. She developed severe pneumonitis requiring high-dose corticosteroid

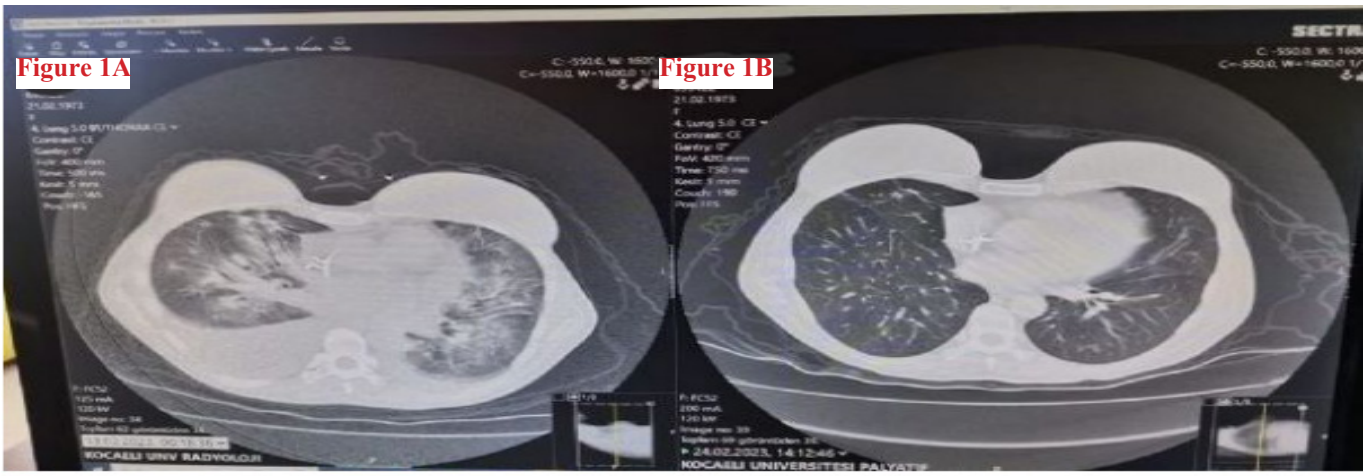


**Figure 1**. A: Thorax CT image taken in the emergency room, B: Thorax CT image taken on the 10th day of steroid treatment

therapy. Given the nearly complete tumor response but significant toxicities, T-DXd was permanently discontinued. Unfortunately, the patient developed sepsis and passed away, underscoring the need for ongoing vigilance and robust supportive care in such cases.

## DISCUSSION

T-DXd has demonstrated significant efficacy in HER2-positive metastatic breast cancer; however, its use is limited by potential cardiopulmonary and hematological toxicities (1). ILD/pneumonitis is reported in approximately 10-15% of patients treated with T-DXd (2). Cardiotoxicity, although less frequently reported, remains a significant concern, particularly in patients with prior anthracycline exposure or baseline cardiac dysfunction (5).

The patient's severe pneumonitis aligns with the 10-15% incidence reported in DESTINY-Breast studies. However, the fatal outcome highlights the importance of early detection and aggressive management (2). While less common, the observed heart failure is consistent with reported cardiotoxicity rates in T-DXd-treated patients, emphasizing the need for baseline and serial echocardiographic assessments (3).

To mitigate such toxicities, a proactive monitoring strategy should include baseline echocardiography, pulmonary function tests, and CT imaging (6). During treatment, echocardiography should be performed every 6-8 weeks during initial cycles, and thoracic CT should be conducted at least every 12 weeks or earlier if symptoms arise (6). Regular CBC monitoring is essential to detect hematological abnormalities early (3).

Management strategies for ILD/pneumonitis include high-dose corticosteroids (1-2 mg/kg/day), which remain the cornerstone of treatment. Early initiation is critical to prevent progression to life-threatening stages (7). For cardiotoxicity, optimization of heart failure therapies, including diuretics and beta-blockers, alongside T-DXd discontinuation, is essential for recovery (5).

This case underscores the importance of a multidisciplinary approach involving oncologists, cardiologists, and pulmonologists to manage the complex toxicities associated with T-DXd. Furthermore, educating patients on recognizing early symptoms of adverse events can facilitate timely interventions (7).

Conclusion This case demonstrates the challenges of managing T-DXd-induced toxicities, including severe pneumonitis and heart failure. Despite initial improvements, long-term outcomes were compromised due to persistent toxicities, ultimately resulting in fatal sepsis (2). Future studies should focus on refining monitoring protocols and identifying predictive markers for adverse events to enhance the safety and efficacy of T-DXd.

## CONCLUSION

This case illustrates the significant challenges in managing trastuzumab deruxtecan-induced cardiopulmonary toxicities in patients with HER2-positive metastatic breast cancer. Despite marked initial tumor response, the development of severe pneumonitis, heart failure, and subsequent fatal sepsis underscores the critical importance of vigilant monitoring and early intervention for adverse events. Multidisciplinary collaboration, proactive surveillance with cardiac and pulmonary assessments, and prompt initiation of supportive therapies are essential to optimize patient safety. Future research should aim to establish more refined risk stratification tools and monitoring protocols to prevent and mitigate life-threatening toxicities associated with novel antibody-drug conjugates like T-DXd.

## DECLARATIONS

This case report was conducted in accordance with the ethical standards of human research and the principles set forth in the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the patient's legal guardians for publication of the case details and accompanying images. All efforts have been made to ensure patient anonymity, and no identifying information has been disclosed.

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## REFERENCES

1. Modi S, Saura C, Yamashita T, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. *N Engl J Med.* 2020;382(7):610-621. doi:10.1056/NEJMoa1914510
2. Rugo HS, Im SA, Cardoso F, et al. Efficacy and safety of trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: results from DESTINY-Breast03. *J Clin Oncol.* 2023;41(2):201-210.
3. Li BT, Smit EF, Goto Y, et al. Trastuzumab Deruxtecan in HER2-Mutant Non-Small-Cell Lung Cancer. *N Engl J Med*. 2022;386(3):241-251. doi:10.1056/NEJMoa2112431
4. Saura C, Modi S, Krop I, et al. Trastuzumab deruxtecan in previously treated patients with HER2-positive metastatic breast cancer: updated survival results from a phase II trial (DESTINY-Breast01). *Ann Oncol*. 2024;35(3):302-307. doi:10.1016/j.annonc.2023.12.001
5. Tolaney SM, Wardley AM, Zambelli S, et al. Monitoring strategies for trastuzumab deruxtecan-associated toxicities. *J Clin Oncol*. 2020;38(3):197-204.
6. Cardinale D, Colombo A, Lamantia G, et al. Anthracycline-induced cardiomyopathy: clinical relevance and response to pharmacologic therapy. J Am Coll Cardiol. 2010;55(3):213-220. doi:10.1016/j.jacc.2009.03.095
7. Emens LA, Middleton G. The interplay of immunotherapy and chemotherapy: harnessing potential synergies. Cancer Immunol Res. 2015;3(5):436-443. doi:10.1158/2326-6066.CIR-15-0064