

Overcoming radiosurgical failure: a case of HER2-positive metastatic breast cancer responding to trastuzumab deruxtecan as third-line therapy

Michelle Vincentia Liem, Indra Wijaya*

Division of Hematology-Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia
<https://doi.org/10.22146/inajbcs.v57i3.Supplement.24268>

ABSTRACT

Submitted: 2025-09-02
Accepted : 2025-09-08

Human epidermal growth factor receptor 2 (HER2) positivity in breast cancer is associated with a higher propensity for brain metastases. Management of metastatic breast cancer (MBC) typically involves a combination of locoregional and systemic therapies. Gamma Knife radiosurgery (GKRS) is the preferred locoregional approach for selected patients. However, the outcomes of GKRS are closely linked to the control of systemic disease. Systemic therapy for HER2-positive MBC has evolved rapidly. Trastuzumab deruxtecan (T-DXd) has shown superior efficacy in the DESTINY-Breast03 (DB03) trial, leading to its recommendation as second-line therapy replacing trastuzumab emtansine (T-DM1). The trial reported a 72% reduction in progression-free survival (PFS) events (HR 0.28) and an overall response rate (ORR) of 79.7%, significantly higher than the 34.2% ORR observed with T-DM1. T-DXd has also demonstrated activity against brain metastases. This case report presents a 50-year-old woman who was diagnosed with non-luminal HER2-positive MBC with liver and bone involvement three years ago. She underwent radical mastectomy of right breast and received trastuzumab-pertuzumab-docetaxel. After one year, she had headache and vertigo; brain MRI revealed new brain metastases, while liver and bone lesions remained stable. Her treatment was switched to T-DM1. After six months, the brain MRI showed lesion progression, prompting two rounds of GKRS. Brain MRI at three months post-GKRS showed stability. T-DM1 was continued, but six months later, her neurological symptoms worsened, and imaging confirmed increased size and number of brain metastases. Treatment with T-DXd was started without additional GKRS. At both six- and nine-month follow-ups, brain MRI showed a reduction in lesion number and size, with improvement in symptoms. She remains on T-DXd with minimal toxicity and excellent performance status (WHO/ECOG 0). T-DXd administered as third-line therapy demonstrated an encouraging clinical and radiologic response with a favorable safety profile in a patient with non-luminal HER2-positive MBC.

ABSTRAK

Human epidermal growth factor receptor 2 (HER2) pada kanker payudara dikaitkan dengan kecenderungan metastasis otak yang lebih tinggi. Penatalaksanaan kanker payudara metastatik (MBC) biasanya melibatkan kombinasi terapi lokoregional dan sistemik. gamma Knife radiosurgery (GKRS) merupakan pendekatan lokoregional yang lebih disukai untuk pasien tertentu. Namun, luaran GKRS berkaitan erat dengan pengendalian penyakit sistemik. Terapi sistemik untuk MBC HER2-positif telah berkembang pesat. Trastuzumab deruxtecan (T-DXd) telah menunjukkan efikasi yang superior dalam uji coba DESTINY-Breast03 (DB03), sehingga direkomendasikan sebagai terapi lini kedua menggantikan trastuzumab emtansine (T-DM1). Uji coba melaporkan pengurangan 72% dalam kejadian kelangsungan hidup bebas perkembangan-progression-free survival (PFS) (HR 0,28) dan tingkat respons keseluruhan (ORR) sebesar 79,7%, secara signifikan lebih tinggi daripada ORR 34,2% yang diamati dengan T-DM1. T-DXd juga telah menunjukkan aktivitas terhadap metastasis otak. Laporan kasus ini menyajikan seorang wanita berusia 50 tahun yang didiagnosis dengan MBC

Keywords:

HER2-positive metastatic breast cancer;
brain metastases;
trastuzumab-deruxtecan;
Gamma Knife radiosurgery

HER2-positif non-luminal dengan keterlibatan hati dan tulang tiga tahun lalu. Dia menjalani mastektomi radikal pada payudara kanan dan menerima trastuzumab-pertuzumab-docetaxel. Setelah satu tahun, dia mengalami sakit kepala dan vertigo; MRI otak mengungkapkan metastasis otak baru, sementara lesi hati dan tulang tetap stabil. Pengobatannya dialihkan ke T-DM1. Setelah enam bulan, MRI otak menunjukkan perkembangan lesi, yang mendorong dua putaran GKRS. MRI otak pada tiga bulan pasca-GKRS menunjukkan stabilitas. T-DM1 dilanjutkan, tetapi enam bulan kemudian, gejala neurologisnya memburuk, dan pencitraan mengonfirmasi peningkatan ukuran dan jumlah metastasis otak. Pengobatan dengan T-DXd dimulai tanpa GKRS tambahan. Pada tindak lanjut enam dan sembilan bulan, MRI otak menunjukkan penurunan jumlah dan ukuran lesi, disertai perbaikan gejala. Pasien tetap menjalani T-DXd dengan toksisitas minimal dan status kinerja yang sangat baik (WHO/ECOG 0). T-DXd yang diberikan sebagai terapi lini ketiga menunjukkan respons klinis dan radiologis yang mengembirakan dengan profil keamanan yang baik pada pasien dengan MBC HER2-positif non-luminal.