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*Case Report*

# Early Complete Metabolic Response to Chemotherapy Plus Osimertinib-Based Therapy in Non–Small-Cell Lung Cancer (NSCLC): A Case Report

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## Abstract

Complete metabolic responses to first-line osimertinib-based therapy in advanced Epidermal Growth Factor Receptor (EGFR)-mutated Non–Small-Cell Lung Cancer (NSCLC) are uncommon and the presence of multiple primary malignancies may complicate treatment response assessment. We report a 53-year-old woman with a history of stage IIIA luminal A breast cancer in remission who presented with cough, dyspnea on exertion and weight loss and was diagnosed with advanced EGFR L858R–mutated lung adenocarcinoma with extensive baseline disease on FDG PET/CT. Treatment with carboplatin, pemetrexed and osimertinib resulted in a complete metabolic response after four cycles. Eight months later, new hypermetabolic lymphadenopathy was detected; biopsy confirmed recurrent HER2-low breast carcinoma rather than lung cancer progression. This case reinforces the importance of tissue confirmation in patients with prior malignancies to correctly guide treatment and prevent inappropriate management decisions.

**Keywords:** Non-Small-Cell Lung Carcinoma; Epidermal Growth Factor Receptor (EGFR); Second Primary Cancer; Osimertinib; Neoplasm Recurrence

## Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with Non–Small-Cell Lung cancer (NSCLC) accounting for the majority of cases. The identification of actionable driver mutations, particularly in the Epidermal Growth Factor Receptor (EGFR), has transformed the therapeutic landscape, enabling the use of targeted therapies with improved clinical outcomes. Among these, Osimertinib has become the standard first-line treatment for patients with advanced EGFR-mutated NSCLC due to its demonstrated efficacy and central nervous system activity [1,2].

Despite these advances, the interpretation of disease status during oncologic follow-up remains challenging, particularly in patients with a history of prior malignancies. The increasing use of FDG PET/CT has improved the sensitivity for detecting metabolically active disease; however, its lack of specificity may lead to diagnostic ambiguity. Hypermetabolic lesions identified on PET/CT are not tumor-specific and may reflect a wide spectrum of conditions, including inflammatory processes, treatment-related changes or distinct malignancies. In this context, differentiating true disease progression from the emergence of a second primary malignancy represents a critical clinical challenge with direct therapeutic implications. Misclassification may result in inappropriate treatment modifications, premature discontinuation of effective therapies or delays in initiating the correct oncologic management. This issue is particularly relevant in patients with prior cancer diagnoses, in whom the probability of developing additional primary tumors or experiencing recurrence is significantly increased.

**Case Description**

A 53-year-old woman with a medical history of type 2 diabetes mellitus, systemic arterial hypertension and hypothyroidism, 24-year history of tobacco use, with a smoking index of 24 pack-years. Her oncologic history was notable for stage IIIA Luminal A left breast cancer, receiving neoadjuvant treatment with 4 cycles of doxorubicin/cyclophosphamide + 12 weeks of paclitaxel, followed by radical left mastectomy with complete pathological response and subsequently 5 years of adjuvant tamoxifen. During her last year of follow-up, the patient reported a dry cough, dyspnea on exertion and unintentional weight loss of 7 kg. She was evaluated by pneumology with a chest CT scan, which identified a pulmonary nodule in the right main bronchus. A study protocol was initiated and a bronchoscopy with transbronchial biopsy was performed, whose histopathological study reported primary pulmonary adenocarcinoma, with positive immunohistochemistry for TTF-1 and Napsin A and the presence of the EGFR L858R mutation (exon 21).

To assess baseline tumor activity and disease extent, an FDG PET/CT scan was performed, demonstrating hypermetabolic cervical, axillary and mediastinal lymphadenopathy, as well as a right parahilar solid lesion associated with a ground-glass pattern and subsolid nodules. Multiple hypermetabolic foci were also identified in the axial skeleton bone marrow with blastic changes, along with bilateral pleural effusion with right-sided predominance (Fig. 1).

Given that the patient was a candidate for first-line treatment according to the FLAURA-2 regimen, she received carboplatin, pemetrexed and Osimertinib. After four cycles of therapy, follow-up FDG PET/CT demonstrated a complete metabolic response, showing a hypodense area in the right main bronchus without increased metabolic uptake, consistent with complete response to treatment [3]. Complete resolution of the previously identified lymphadenopathy and bone lesions was also observed (Fig. 1).

Eight months later, follow-up FDG PET/CT revealed new hypermetabolic lesions. Biopsy of a right axillary lymph node confirmed metastatic poorly differentiated invasive ductal carcinoma (grade II), HER2-low positive, consistent with breast cancer recurrence. The patient is currently receiving pemetrexed and Osimertinib in combination with trastuzumab deruxtecan; after three cycles and a fourth cycle with trastuzumab deruxtecan plus carboplatin, follow-up FDG PET/CT demonstrated a near-complete partial metabolic response (Fig. 2) [4].

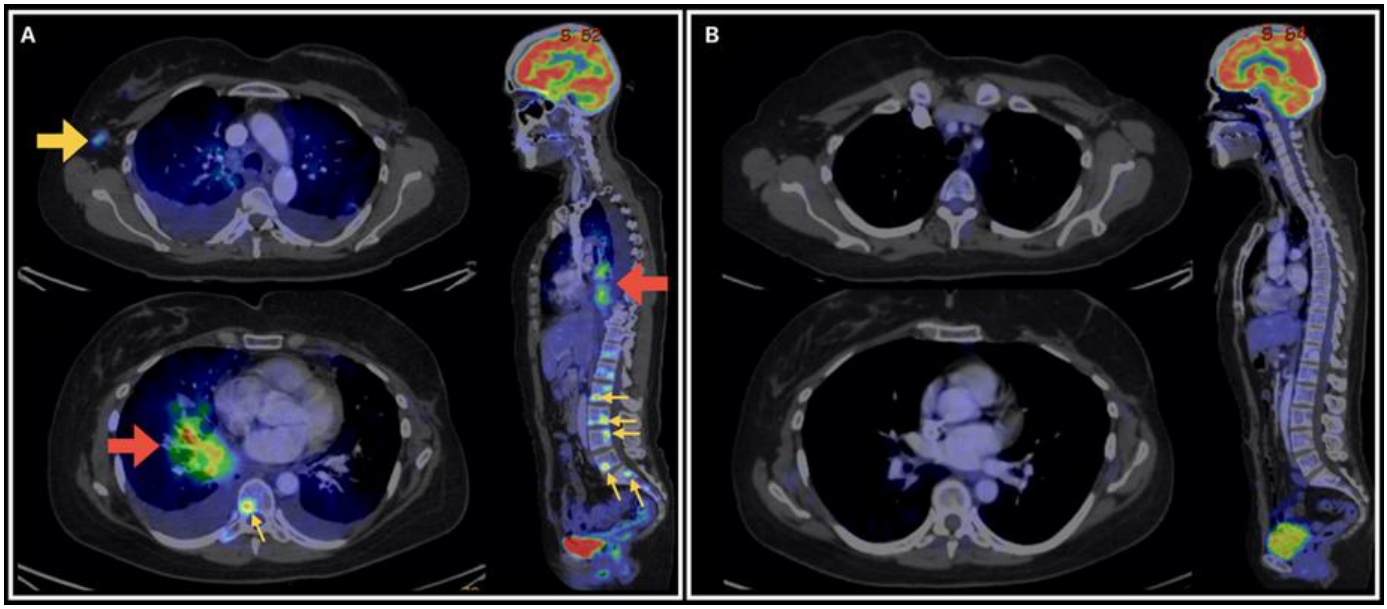


**Figure 1:** Baseline FDG PET/CT versus complete metabolic response. (A) Baseline FDG PET/CT demonstrating extensive metastatic disease, including axillary lymphadenopathy (yellow arrow), a right parahilar solid lesion (red arrows) and multiple hypermetabolic foci in the axial skeleton (thin yellow arrows); (B) Follow-up FDG PET/CT after four cycles of carboplatin-pemetrexed-Osimertinib showing complete metabolic response, with hypodensity of the right main bronchus without increased FDG uptake, complete resolution of axillary lymphadenopathy and complete resolution of bone lesions.

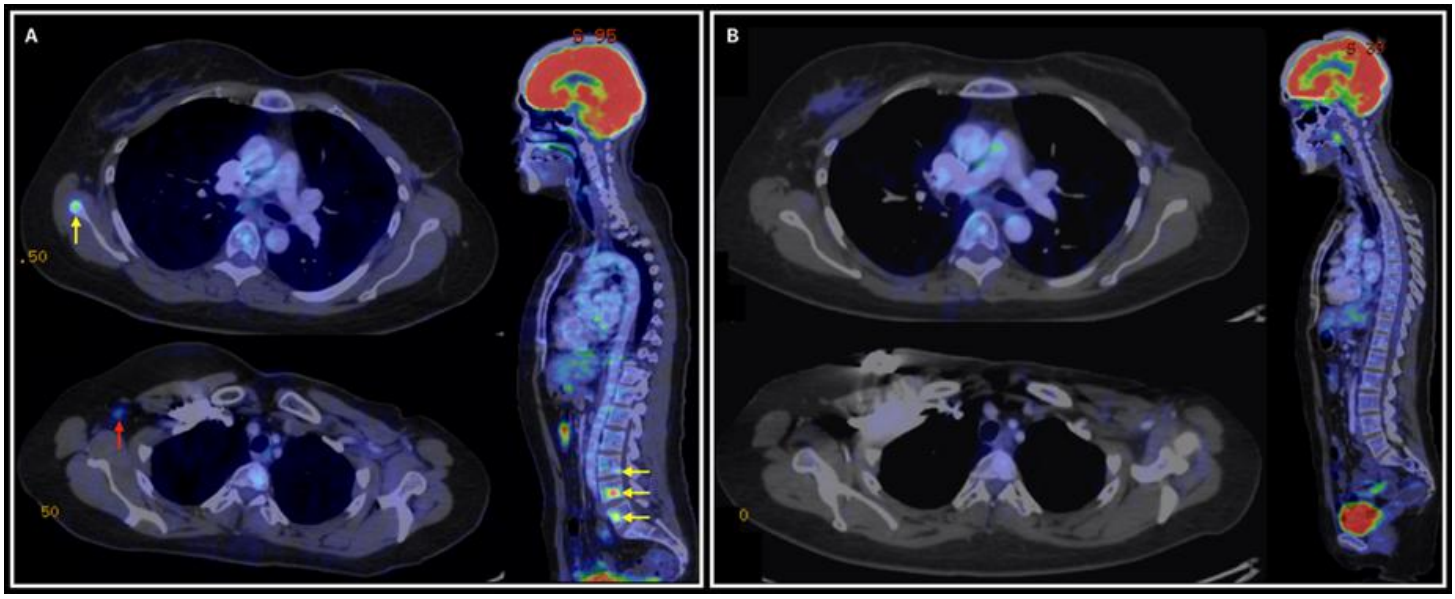


**Figure 2:** Breast cancer recurrence and treatment response. (A) FDG PET/CT at 8 months showing new hypermetabolic lesions in the lumbar vertebrae and right scapula (yellow arrows) and right axillary lymphadenopathy (red arrow); biopsy confirmed HER2-low breast carcinoma recurrence; (B) Follow-up FDG PET/CT after trastuzumab deruxtecan-based therapy demonstrating near-complete partial metabolic response with resolution of right axillary lymphadenopathy and scapular lesion and reduced metabolic activity in vertebral blastic lesions.

## Discussion

In the pivotal FLAURA-2 trial, platinum-based chemotherapy plus osimertinib achieved an objective response rate of approximately 80 %, with a statistically significant improvement in progression-free survival of 24.7 months in patients with the L858R mutation. However, complete metabolic responses were reported in only 2 of 276 patients treated with osimertinib plus platinum-pemetrexed. This finding, together with real-world data, underscores that even in the setting of highly selective targeted therapies, achieving a complete response remains an uncommon outcome [3,4].

The rapid and profound response observed in this case, documented by complete resolution of tumoral metabolic activity after only four cycles, reinforces the role of platinum-based chemotherapy plus osimertinib as a first-line treatment and suggests that elective and sustained inhibition of the EGFR signaling pathway may result in early, deep and clinically meaningful responses, even in advanced disease settings with extensive involvement. In addition, the favorable tolerability profile described for this regimen is consistent with the patient's clinical course, allowing adequate treatment adherence and a positive impact on quality of life [5].

## Conclusion

This case highlights the efficacy and clinical impact of platinum-based chemotherapy plus osimertinib as first-line therapy in EGFR-mutated lung cancer, demonstrating that complete metabolic responses, while rare, are achievable. It also emphasizes the critical importance of tissue biopsy confirmation when new lesions appear in patients with a history of multiple malignancies, as this case illustrates that assumptions of disease progression can lead to inappropriate treatment decisions such as treatment modifications, premature discontinuation of effective therapies or delays in initiating the correct oncologic management. This issue is particularly relevant in patients with prior cancer diagnoses, in whom the probability of developing additional primary tumors or experiencing recurrence is significantly increased.

## Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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**Data Availability Statement**
Not applicable.

**Ethical Statement**
The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

**Informed Consent Statement**
Informed consent for publication was obtained from the patient involved in this case report, as documented in the manuscript.

**Authors' Contributions**
All authors contributed equally to this paper.

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