Journal Pre-proof

Sustained Tumor Response After Pembrolizumab Discontinuation Due to Severe Bullous Pemphigoid

Sofia Magno Pinto MD Gustavo Silva MD Filipa Ferro MD

PII: S0300-2896(25)00440-5

DOI: https://doi.org/doi:10.1016/j.arbres.2025.12.001

Reference: ARBRES 3928

To appear in: *Archivos de Bronconeumologia*

Received Date: 29 October 2025

Accepted Date: 5 December 2025

Please cite this article as: Pinto SM, Silva G, Ferro F, Sustained Tumor Response After Pembrolizumab Discontinuation Due to Severe Bullous Pemphigoid, *Archivos de Bronconeumología* (2025), doi: https://doi.org/10.1016/j.arbres.2025.12.001

Type of article: Clinical image

Title: *Sustained Tumor Response After Pembrolizumab Discontinuation Due to Severe Bullous Pemphigoid*

Authors and Affiliations:

Sofia Magno Pinto, MD - Pulmonology Service, Unidade Local de Saúde Santa Maria, Lisboa, Portugal

Gustavo Silva, MD - Dermatology Service, Unidade Local de Saúde Santa Maria, Lisboa, Portugal

Filipa Ferro, MD - Pulmonology Service, Unidade Local de Saúde Santa Maria, Lisboa, Portugal

Corresponding Author:

Sofia Magno Pinto
Pulmonology Service, Unidade Local de Saúde Santa Maria, Lisboa, Portugal
Avenida Professor Egas Moniz MB, 1649-028 Lisboa, Portugal
sofiamagnopinto2@gmail.com

A 63-year-old man with stage IVb squamous cell lung carcinoma (PD-L1 <1%) and brain metastases received carboplatin, nab-paclitaxel, and pembrolizumab following surgical resection of intracranial disease and whole-brain radiotherapy. After ten months of systemic therapy, he developed severe bullous pemphigoid with extensive tense bullae, erosions, and debilitating pruritus (Figure 1A, BPDAI score 96). Skin biopsy confirmed subepidermal blistering with eosinophilic infiltrate, and serology revealed markedly elevated anti-BP180 antibodies (>200 U/mL). Initial treatment with high-dose corticosteroids and mycophenolate mofetil allowed clinical stabilization; however, pembrolizumab rechallenge triggered severe relapse with widespread bullous eruption, necessitating permanent immunotherapy discontinuation and prolonged hospitalization. Addition of omalizumab ultimately achieved disease control. Remarkably, over eight months without active oncologic therapy, chest CT demonstrated progressive regression of the right upper lobe tumor and stable contralateral disease (Figure 1B), with corresponding metabolic reduction on PET-CT (SUVmax from 27.4 to 5.0). This case illustrates that severe, corticosteroid-refractory immune-related adverse events—though necessitating permanent immunotherapy withdrawal—may paradoxically signal robust immune activation with durable antitumor responses. The images highlight the clinical complexity of managing life-altering immunotherapy toxicity while maintaining prolonged tumor control through immune memory mechanisms, emphasizing that treatment discontinuation does not invariably portend disease progression and may reflect successful immune priming rather than therapeutic failure.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

Author contribution

Sofia Magno Pinto was responsible for the conception, data collection, and drafting of the manuscript. All co-authors reviewed and approved the final version.

Artificial Intelligence Involvement

No part of this manuscript has been produced with the help of artificial intelligence software or tools.

Ethics and Informed consent

Written informed consent for participation and publication of clinical details and images was obtained from the patient. All identifying information has been omitted to ensure anonymity.

REFERENCES

1. Update of Incidence, Prevalence, Survival, and Initial Treatment in Patients With Non–Small Cell Lung Cancer in the US. Ganti AK, Klein AB, Cotarla I, Seal B, Chou E. JAMA Oncology. 2021;7(12):1824-1832. doi:10.1001/jamaoncol.2021.4932.

2. Association of Bullous Pemphigoid With Immune Checkpoint Inhibitor Therapy in Patients With Cancer: A Systematic Review. Asdourian MS, Shah N, Jacoby TV, Reynolds KL, Chen ST. JAMA Dermatology. 2022;158(8):933-941. doi:10.1001/jamadermatol.2022.1624.

3. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. Schneider BJ, Naidoo J, Santomasso BD, et al. Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2021;39(36):4073-4126. doi:10.1200/JCO.21.01440.

4. Analysis of the Clinical Characteristics of Pembrolizumab-Induced Bullous Pemphigoid. Wang J, Hu X, Jiang W, et al. Frontiers in Oncology. 2023;13:1095694. doi:10.3389/fonc.2023.1095694.

5. Association of Bullous Pemphigoid With Immune Checkpoint Inhibitor Therapy in Patients With Cancer: A Systematic Review. Asdourian MS, Shah N, Jacoby TV, Reynolds KL, Chen ST. JAMA Dermatology. 2022;158(8):933-941. doi:10.1001/jamadermatol.2022.1624.

FIGURE

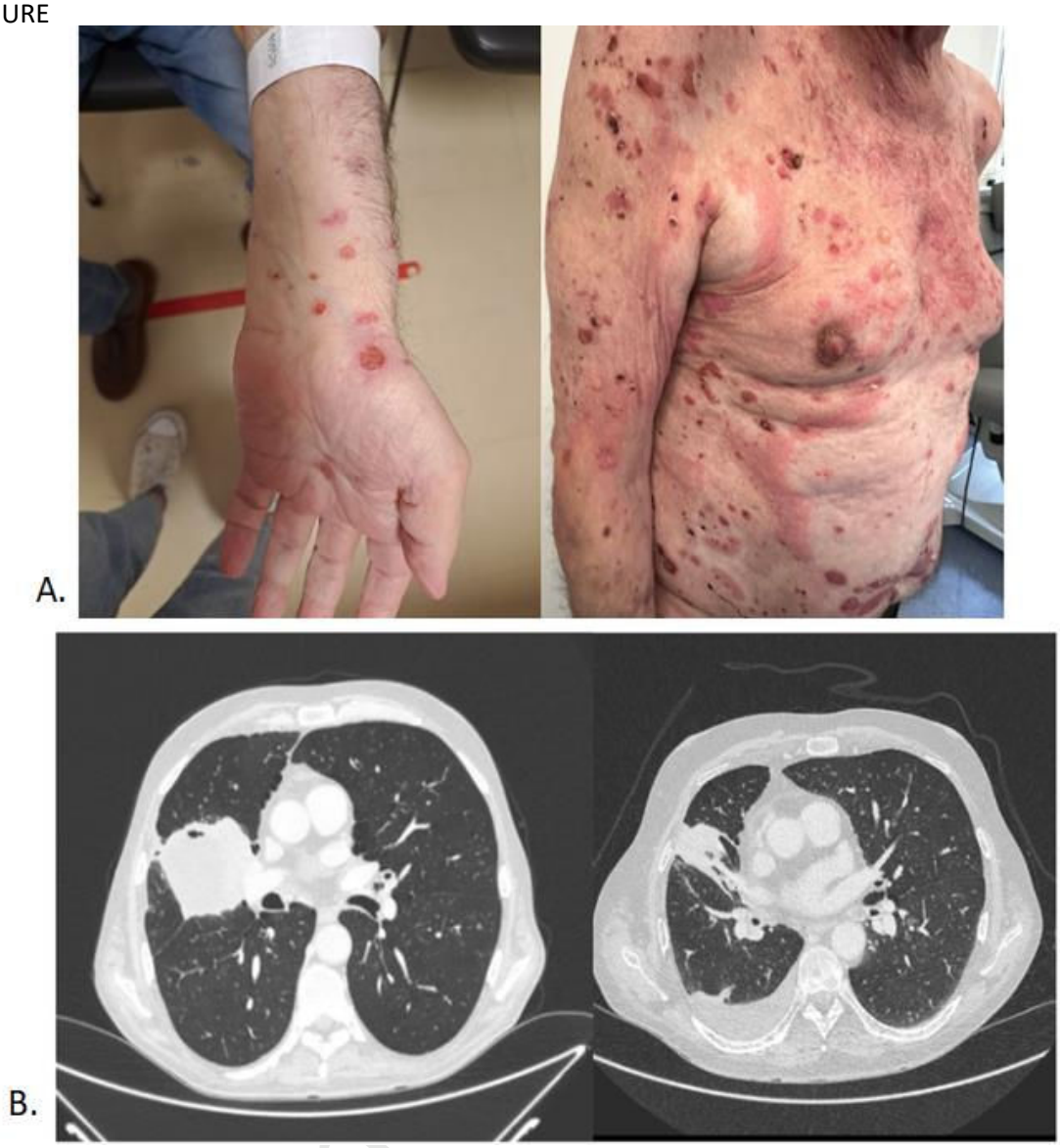

Figure 1. A. Evolution of dermatological lesions between May (left) and September (right) of 2024. B. Evolution of primary pulmonary lesion between march 2023 (left), before treatment, and february 2025 (right), 5 moths wihout pembrolizumab.