

Extreme Response in Metastatic Squamous Cell Lung Cancer with a Single Dose of Pembrolizumab: A Case Report

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Case Report

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Abstract

Introduction: Squamous cell lung cancer (SqCLC) is an aggressive subtype of non-small cell lung cancer (NSCLC), frequently associated with distant metastases. Although immune checkpoint inhibitors improve survival, complete responses after a single dose are exceedingly rare.

Case presentation: A 77-year-old Turkish male with hypertension and type 2 diabetes presented with acute left arm weakness. He was a never-smoker with a history of urothelial carcinoma. Brain MRI revealed right paracentral and cerebellar metastatic lesions, while thoracic imaging showed multiple pulmonary nodules. Histopathology confirmed metastatic SqCLC with a PD-L1 tumor proportion score of 40%. The patient underwent craniotomy and stereotactic radiosurgery, followed by one cycle of gemcitabine, carboplatin, and pembrolizumab. Treatment-related toxicities (grade 2 fatigue, neutropenia, mild infection, and grade 1 skin toxicity) resolved with supportive care. Despite clinical stability, the patient declined further therapy. Follow-up imaging demonstrated complete resolution of all lesions. At 24 months, he remains in complete remission.

Conclusions: This case illustrates a rare, durable complete response—including intracranial disease—after a single cycle of chemoimmunotherapy, highlighting the potential role of individual tumor-immune interactions in exceptional outcomes.

Introduction

Lung cancer remains the leading cause of cancer-related deaths worldwide, posing a significant burden in terms of both morbidity and mortality. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases, with squamous cell lung cancer (SqCLC) being the second most common subtype, representing 25–30% of NSCLC cases (1, 2). SqCLC is strongly associated with smoking and is histologically characterized by keratinization and intercellular bridges (2). While treatment approaches have traditionally relied on platinum-based chemotherapy, the advent of immunotherapies has transformed therapeutic paradigms (3).

Brain metastases occur in approximately 10–20% of patients with NSCLC either at the time of diagnosis or during disease progression, and they are generally considered a limiting factor for overall survival (4, 5). These metastases are most commonly localized in the cerebral hemispheres, though they can also be found—albeit less frequently—in the cerebellum and brainstem (5). By causing significant neurological impairments, brain metastases substantially affect both the quality of life and prognosis of patients (6).

Immunotherapies have emerged as a promising area in the treatment of NSCLC. Pembrolizumab is an immune checkpoint inhibitor that targets the human programmed death-1 (PD-1) receptor, reactivating the immune system to enable T cells to recognize and eliminate tumor cells (7). Clinical trials have demonstrated that pembrolizumab improves progression-free survival and overall survival in patients with NSCLC, offering an effective treatment option either as monotherapy or in combination therapy, particularly in those with high PD-L1 expression (8, 9). However, immune-related adverse events (irAEs) are frequently reported during pembrolizumab treatment. Among these, cutaneous toxicities are relatively common and can range from mild rashes to severe dermatological reactions (10).

This case report presents a patient with SqCLC and brain metastases who achieved a complete response following a single dose of pembrolizumab, with cutaneous toxicity as the only reported adverse effect. Such early and profound responses to immunotherapy in SqCLC have been rarely reported in the literature. Although local treatments played a key role in initial intracranial disease control, the sustained absence of recurrence together with

the complete resolution of extracranial lesions following a single systemic treatment cycle suggests a systemic immune-mediated antitumor effect.

Case Presentation

A 77-year-old male presented to the emergency department with acute complaint of weakness in the left arm in May 2023. His medical history included Type 2 Diabetes Mellitus and essential hypertension, and he was non-smoker. His family history was unremarkable. The patient also had a surgical history of transurethral resection (TUR) for invasive urothelial carcinoma without muscularis propria invasion in January 2021.

To evaluate his neurological symptoms, contrast-enhanced cranial MRI was performed, which revealed a paracentral mass lesion was seen in the right cerebral hemisphere and a metastatic lesion in the lateral part of the right cerebellar hemisphere (Figs. 1A-B). Thoracic CT was performed to identify the primary lesion and showed thickening in the costal and diaphragmatic pleura in both hemithoraces, consistent with asbestosis plaques. Lobulated solid mass lesions and scattered nodules were detected in both lungs, measuring 25 mm in the superior segment of the right lower lobe and 19 mm in the posterobasal segment of the left lower lobe (Fig. 2A-B). PET-CT showed additional lesions. Levetiracetam and anti-edema therapy were initiated, and the patient subsequently underwent surgical excision of brain tumor. Pathological examination revealed CK-7 positive, p40 positive and TTF-1 negative squamous cell carcinoma metastasis and the disease was staged as stage IV. The PDL-1 tumor proportion score (TPS) was 40%. Postoperative imaging showed no residual lesion at the resection site, while the metastatic lesion in the cerebellar hemisphere remained unchanged. Stereotactic radiosurgery (27 Gy in 3 fractions) was applied to the resection cavity and the metastatic focus. The patient was administered gemcitabine (1250 mg/m²), carboplatin (AUC 5) and pembrolizumab (200 mg). On day 8 day of the cycle; he was complained about grade 2 fatigue and grade 2 neutropenia which is resulted in mild upper respiratory tract infection that controlled oral antibiotherapy and three days of G-CSF support. In addition, grade 1 skin immune-related skin toxicity was observed at physical examination and resolved within two weeks with topical treatment (Fig. 3). Although the toxicities were managed appropriately, the patient declined further treatment despite comprehensive discussions regarding the need for continued therapy. Importantly, no additional local or systemic anticancer treatment was administered after the first cycle of chemoimmunotherapy. The patient was subsequently followed with regular physical examinations and contrast-enhanced thoracic and abdominal CT scans. Follow-up imaging revealed no residual or detectable lesions in either the lungs or the brain (Fig. 1C-D and 2C-D). Complete remission was maintained in both intracranial and extracranial sites throughout long-term follow-up. The patient remains alive and disease-free at 24 months of follow-up.

Discussion

This case suggests that the unusually strong responses to immunotherapies, independent of dosage, may stem from patient-specific immune biology, indicating the need to reconsider current treatment paradigms. Similar outcomes have been reported in the literatur, showing rapid and durable responses with single or limited doses of immunotherapies. Machida et al reported a case with a complete tumor response after a single dose of pembrolizumab, despite the discontinuation of treatment due to Stevens-Johnson syndrome. In that case, it was suggested that suppression of the transcription factor Nr4a1 enhanced cytotoxic CD8⁺ T cell activity while reducing regulatory T cell function, thereby contributing both to the development of irAEs and to a robust antitumor immune response. Monitoring of cytokine and mRNA levels reflecting immune activation provided insights into the underlying biological mechanisms (11).

In another case report by Kondo et al., a 79-year-old patient with advanced adenocarcinoma and 100% PD-L1 expression in tumor cells developed severe immune-related hepatitis (grade 3) after a single dose of pembrolizumab. Treatment was discontinued, and systemic corticosteroid therapy (prednisolone) was initiated, leading to normalization of liver function tests. During follow-up, the disease remained in remission for 1.5 years without any additional treatment. Notably, a deep and durable tumor response was achieved with only a single dose of pembrolizumab. Dense infiltration of CD138-positive plasma cells within the tumor microenvironment, supported the potential role of B cells and plasma cells in immunotherapy response (12). Similarly, in our case, a complete response was achieved following a single dose of pembrolizumab, accompanied by the development of immune-related skin toxicity. These findings support the concept that immunotherapy can induce durable responses in selected patients, possibly driven by individual variations in immune activity.

Another case report described a patient with advanced metastatic lung adenocarcinoma who developed multiple irAEs following a single dose of pembrolizumab, ultimately resulting in death, despite the presence of a complete pathological response on autopsy. Three weeks after treatment, the patient developed autoimmune thyroiditis, hepatitis, myositis, myocarditis, pneumonitis, and myasthenia gravis. Despite initiation of high-dose corticosteroids, intravenous immunoglobulin (IVIG), and infliximab, the patient rapidly progressed to respiratory failure and died. Autopsy findings revealed widespread immune-mediated tissue damage characterized by CD8+ T lymphocyte and histiocyte infiltration, while no residual tumor was detected in either the primary site or metastatic lesions. This case is particularly striking in demonstrating that immunotherapy can, in some individuals, trigger fatal immune responses while simultaneously achieving extraordinary antitumor efficacy (13). Ahdi et al. reported a rare case of renal cell carcinoma in which multiple autoimmune complications developed following a single dose of pembrolizumab (14). Similarly, Martinez-Calle et al. presented a case of multiple myeloma in which fulminant myocarditis occurred after a single dose of pembrolizumab combined with lenalidomide and dexamethasone (15). These reports highlight that even minimal exposure to pembrolizumab may result in severe immune-related toxicity in susceptible individuals.

Although surgical resection and stereotactic radiosurgery are effective local treatment modalities for brain metastases, durable intracranial disease control without any additional systemic therapy is uncommon in metastatic squamous cell lung cancer. In our case, the sustained absence of intracranial recurrence, together with the complete resolution of extracranial disease after a single cycle of pembrolizumab-based therapy, suggests a potential contribution of systemic immune activation beyond local treatment effects.

Comparable and remarkable cases in the literature further support that even a single administration of immunotherapy may induce profound, durable, and in some instances, pathologically confirmed complete responses in selected patients. In the cases reported by Watanabe, Kato, and Tokuyasu, long-lasting tumor responses were achieved without additional systemic treatment, despite the development of immune-related pneumonitis, across diverse histological subtypes including large cell neuroendocrine carcinoma, adenocarcinoma, and pleomorphic carcinoma (16–18). In the case described by Matsumura et al., although immunotherapy was discontinued due to an irAE following a single dose of pembrolizumab-based chemoimmunotherapy, a pathological complete response (pCR) was confirmed after surgery (19).

In the case of metastatic thymoma reported by Shen et al., multiple irAEs after a single dose of pembrolizumab, accompanied by a marked tumor response (20). Similarly, Jin et al. described a pathological complete response (pCR) after one cycle of anti-PD-1 therapy combined with chemotherapy in MSI-high gastric cancer (21). Durable responses have also been reported in penile squamous cell carcinoma and pancreatic cancer, particularly in the

presence of high tumor mutational burden or PD-L1 expression (22,23). These findings collectively indicate that immunotherapy may exert profound antitumor effects even after very limited exposure.

A summary of published case reports in which a complete or durable response was achieved following a single dose of pembrolizumab, along with the corresponding irAEs, is provided in Table 1. These cases support the notion that minimal exposure to immunotherapy may be sufficient to induce sustained responses in selected patients, possibly due to individual differences in immune responsiveness.

This case represents a rare instance of squamous cell lung cancer in which a complete response was achieved in all tumoral lesions, including brain metastases, after a single cycle of pembrolizumab. The sole immune-related adverse event was limited to cutaneous toxicity, which responded rapidly to topical treatment. Similar durable responses after a single dose of immunotherapy have been reported across different tumor types, suggesting that limited exposure may be sufficient in selected individuals. These dramatic responses are related to interpatient variability of immune response. In this context, beyond established biomarkers such as tumor molecular profile, PD-L1 expression, and TMB, the patient's intrinsic immune responsiveness may also influence treatment outcomes.

This case highlights an exceptional and durable response following a single cycle of chemoimmunotherapy in metastatic squamous cell lung cancer. While local treatments were essential for initial intracranial disease control, the long-term complete remission observed across all disease sites without further therapy supports the hypothesis that systemic immunotherapy may induce profound and lasting antitumor immune responses in selected patients. Systematic documentation of such exceptional responses and their validation in larger case series may contribute to the identification of novel predictive biomarkers for immunotherapy efficacy.

Declarations

Statement of Ethics

This study adhered to the principles of the Declaration of Helsinki.

Ethical approval for this study was waived by the Istanbul University Istanbul Faculty of Medicine Clinical Research Ethics Committee, in accordance with institutional guidelines stating that case reports without experimental interventions do not require formal ethics approval.

Consent to Publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest to disclose.

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Author Contributions

All authors contributed substantially to the conception, drafting, and critical revision of the manuscript, approved the final version, and agree to be accountable for all aspects of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Consent to Participate

Written informed consent was obtained from the patient for participation in this study.

Authors' contributions

All authors (S.Ç., N.A.) were involved in the diagnosis and treatment process of the patient. S.Ç. drafted the manuscript. The other authors contributed to the preparation of the manuscript and approved the final version. All authors are accountable for the scientific content of the work.

Clinical trial number

Not applicable.

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Table

Table 1: Published case reports describing complete or durable tumor responses following a single dose of pembrolizumab, along with the associated immune-related adverse events (irAEs).

No	Reference number	Authors	Year	Diagnosis / Histology	Age	Sex	PFS	irAE
1	11	Machida et al.	2022	Stage IIIb squamous cell lung cancer	68	Male	>1 year	Stevens-Johnson syndrome
2	12	Kondo et al.	2022	NSCLC adenocarcinoma	79	Male	18 months	Grade 3 immune-related hepatitis
3	13	Fuentes-Antrás et al.	2022	Metastatic lung adenocarcinoma	75	Male	Death after 3 weeks (autopsy: pCR)	Thyroiditis, hepatitis, myositis, myocarditis, pneumonitis, myasthenia gravis
4	14	Ahdi et al.	2023	Metastatic renal cell carcinoma	58	Male	Not reported	Dermatitis, hepatitis, myositis, myocarditis, myasthenia gravis, thrombocytopenia
5	15	Martinez-Calle et al.	2018	Multiple myeloma	67	Female	Death within 10 days	Fulminant myocarditis
6	16	Watanabe et al.	2022	Recurrent LCNEC of lung	68	Male	4 years	Interstitial pneumonitis
7	17	Kato et al.	2021	Advanced lung adenocarcinoma with OP history	88	Male	≥18 months	Relapse of organizing pneumonia
8	18	Tokuyasu et al.	2019	Pulmonary pleomorphic carcinoma	73	Male	17 months	Grade 1 pneumonitis
9	19	Matsumura et al.	2025	Stage IIB squamous cell lung cancer	61	Male	19 months	Grade 2 pneumonitis
10	20	Shen et al.	2021	Metastatic thymoma	39	Female	9 months	Myocarditis, liver & kidney dysfunction, hypothyroidism
11	21	Jin et al.	2020	Unresectable locally advanced gastric cancer (MSI-H, PD-L1+)	66	Male	pCR after 1 dose	Not reported

Figures

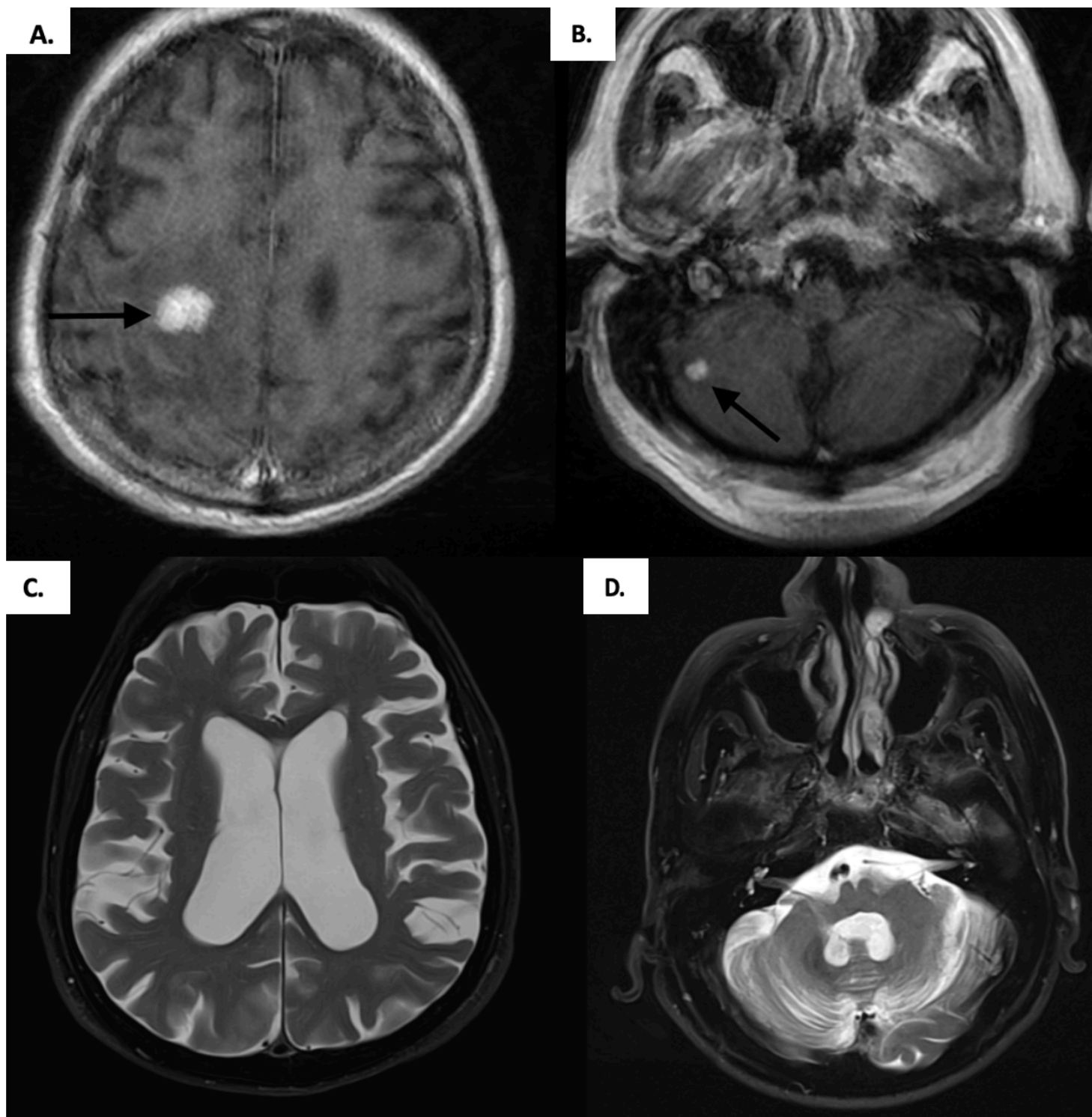


Figure 1

Contrast-enhanced cranial MRI.

(A) Paracentral mass in the right cerebral hemisphere before treatment.

(B) Metastatic lesion in the right cerebellar hemisphere before treatment.

(C–D) Follow-up MRI showing complete resolution of intracranial lesions after treatment.

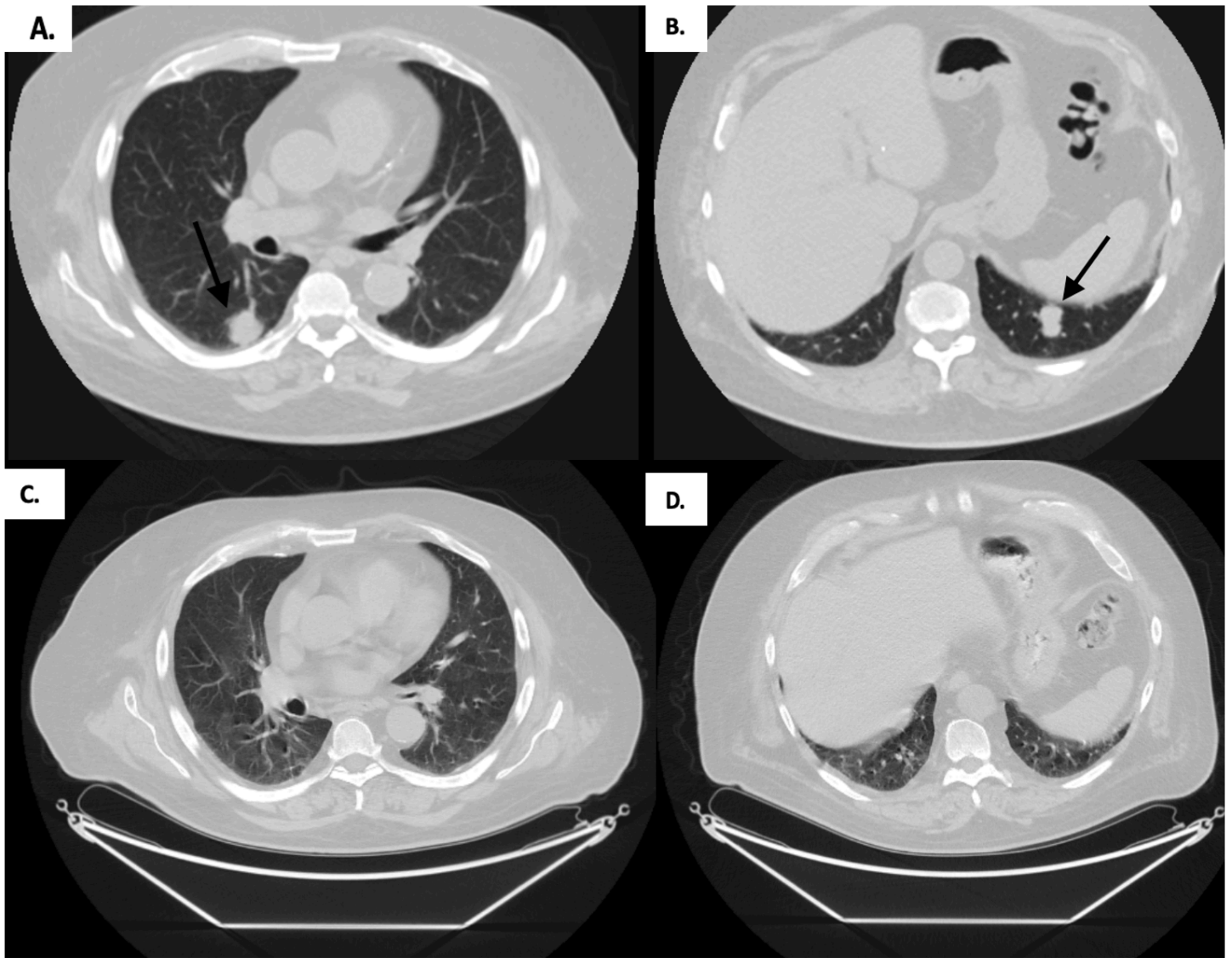


Figure 2

Thoracic CT scans.

(A–B) Lobulated solid lesions in both lungs before treatment.

(C–D) Follow-up CT demonstrating complete resolution of pulmonary lesions after treatment.

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Figure 3

Maculopapular skin rash observed after pembrolizumab administration, consistent with grade 1 immune-related skin toxicity.