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Complete Pathologic Response to Cemiplimab in a Patient With Fungating Cutaneous Squamous Cell Carcinoma of the Forehead: A Case Report

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Abstract

Cutaneous squamous cell carcinoma (cSCC) is typically managed successfully with surgical excision, yet a subset of tumors exhibit aggressive behavior with regional and distant metastases. Until recently, systemic treatment options for advanced disease were limited. The introduction of immune checkpoint inhibitors has significantly expanded treatment options for unresectable and metastatic cSCC.

We report the case of a man with rapidly progressive cSCC of the forehead with cervical lymph node involvement who demonstrated significant clinical and radiographic improvement following treatment with cemiplimab, a programmed cell death-1 (PD-1) inhibitor. Treatment was initiated for unresectable disease and resulted in marked tumor regression, allowing for subsequent surgical resection. Final pathology demonstrated no residual carcinoma, consistent with a complete pathologic response. This case highlights the potential role of PD-1 inhibition in downstaging advanced cSCC and enabling definitive surgical management.

Categories: Pathology, Dermatology
Keywords: cemiplimab, immunotherapy, metastasis, pd-1 inhibitor, squamous cell carcinoma

Introduction

Cutaneous squamous cell carcinoma (cSCC) is the second most common nonmelanoma skin cancer [1]. While the majority of tumors are successfully treated with surgery, a subset demonstrates aggressive behavior with lymph node involvement and distant metastases [2]. Advanced cSCC is associated with worse clinical outcomes, particularly in high-stage tumors with an increased risk of regional nodal involvement [2]. Surgical excision with clear margins remains the standard of care for treatment of localized disease when feasible [3].

Immune checkpoint inhibitors have shown substantial efficacy in the treatment of locally advanced and metastatic cSCC not amenable to curative surgery or radiotherapy [4]. Cemiplimab, a monoclonal antibody targeting the programmed cell death one (PD-1) receptor, was the first therapy approved specifically for locally advanced or metastatic cSCC [5]. Clinical trials have demonstrated substantial and durable responses to immune checkpoint inhibition in patients with advanced cSCC [5,6]. For example, in a Phase II study, cemiplimab demonstrated response rates of 47% in patients with metastatic cSCC [6]. These advances have established systemic immunotherapy as an important treatment option for patients with advanced cSCC, particularly when disease progression limits the effectiveness of local treatment alone.

This report describes a patient with cSCC of the right forehead who was treated with cemiplimab due to the unresectable nature of his disease.

Case Presentation

A 64-year-old man with a history of non-melanoma skin cancer presented for evaluation of a lesion on the right forehead that had been present for several months and had progressively enlarged. Over time, the lesion began to bleed intermittently and became painful.

On physical examination, there was a large, ulcerated, fungating mass involving the right frontal scalp, with surrounding erythema, crusting, and friable tissue, measuring 6.0 x 5.0 cm (Figure *1*).

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FIGURE 1: Large ulcerated, exophytic lesion of the right forehead measuring approximately 6.0 × 5.0 cm with surrounding erythema and crusting.

Bilateral periauricular and occipital lymphadenopathy was noted. Biopsy of the forehead lesion in October 2024 confirmed cSCC (Figures *2*-*3*).

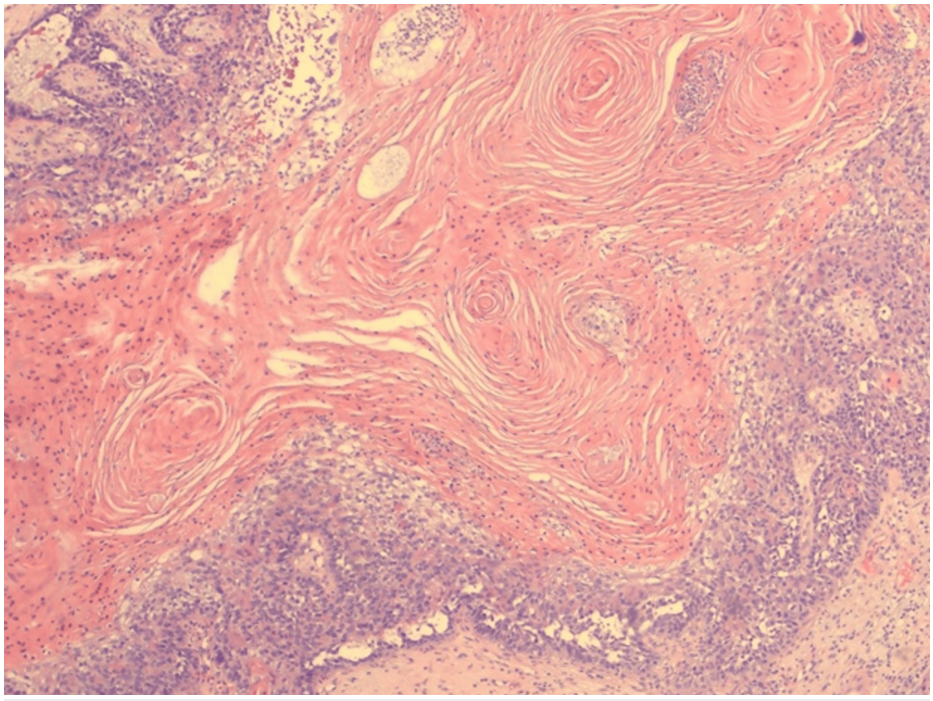


FIGURE 2: Skin biopsy of the right forehead demonstrating invasive squamous cell carcinoma with atypical keratinocytes and keratin pearl formation (hematoxylin and eosin (H&E)).

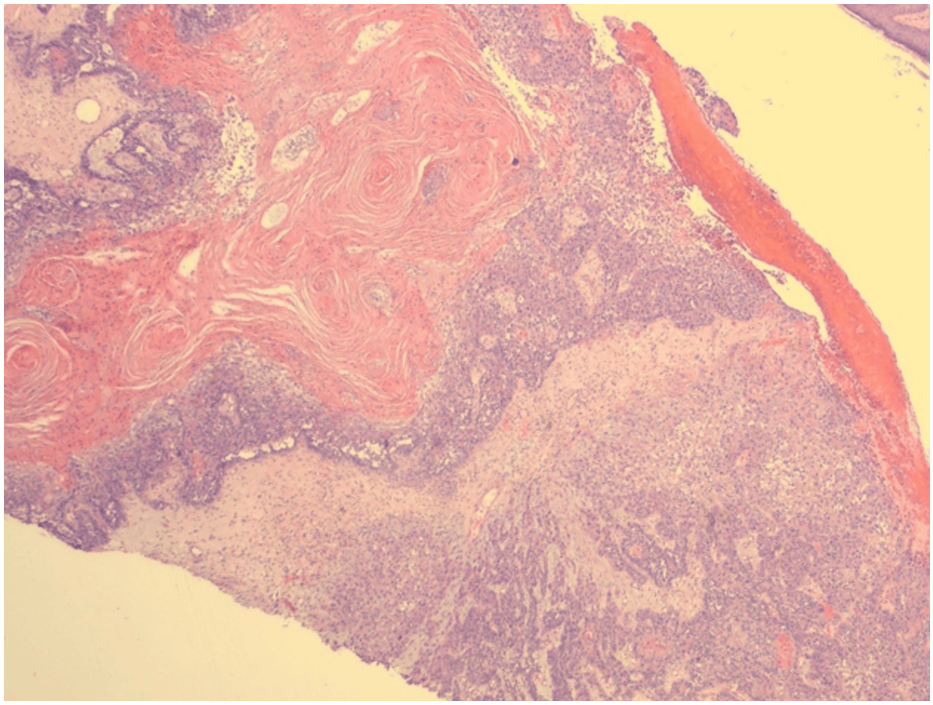


FIGURE 3: Squamous cell carcinoma demonstrating keratinization (hematoxylin and eosin (H&E) stain).

Computed tomography (CT) of the head performed in January 2025 demonstrated the primary scalp lesion and associated cervical lymphadenopathy. Subsequent positron emission tomography (PET) and CT imaging in January 2025 revealed increased fluorodeoxyglucose (FDG) uptake in the scalp lesion and cervical lymph nodes, raising concern for regional nodal metastasis.

Given the extent of disease and its initially unresectable nature, systemic therapy with the PD-1 inhibitor cemiplimab was initiated in January 2025. Cemiplimab was administered at 350 mg intravenously every three weeks for a total of nine cycles. Treatment was well tolerated without clinically significant immune-related adverse effects.

Follow-up PET/CT imaging performed in August 2025 demonstrated a decrease in the size and FDG avidity of the scalp lesion, as well as a reduction in the size of the cervical lymph nodes, consistent with treatment response. Serial clinical examinations demonstrated a marked reduction in tumor bulk and improvement in ulceration and associated lymphadenopathy following initiation of cemiplimab (Figure *4*).

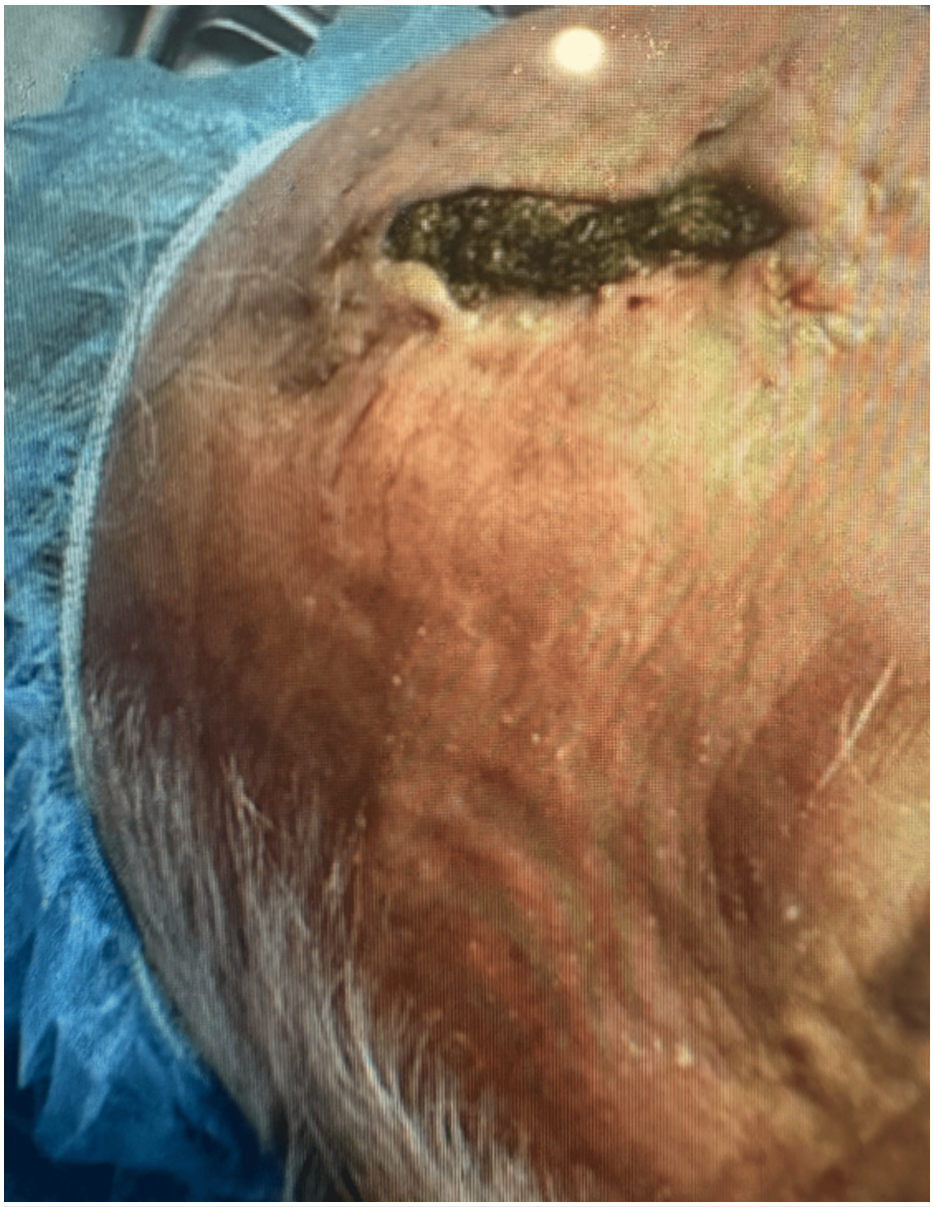


FIGURE 4: Clinical response following cemiplimab therapy demonstrating marked reduction in tumor burden and improvement in ulceration prior to surgical resection.

The patient received nine cycles of cemiplimab, demonstrating a marked clinical and radiographic response, with mild fatigue as the only reported adverse event, which did not affect quality of life or daily activities. The patient underwent radical surgical resection of the primary lesion in November 2025 to address the possibility of residual disease. Final surgical pathology demonstrated negative margins and no residual carcinoma at the primary tumor site. Histopathologic examination revealed a healing biopsy site with a foreign body-type giant cell reaction, reactive inflammatory changes, and regenerative changes, consistent with a complete pathologic response at the primary site. Postoperative recovery was uncomplicated. Postoperative examination demonstrated a well-healed surgical site without clinical evidence of residual

tumor (Figure 5). The clinical timeline is summarized in Figure 6.



FIGURE 5: Postoperative appearance following surgical resection demonstrating complete removal of the lesion with a well-healed surgical site and no clinical evidence of residual tumor.

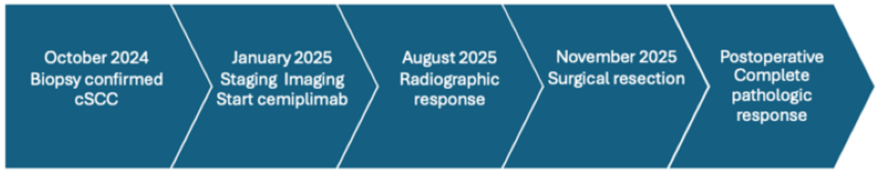


FIGURE 6: Clinical timeline demonstrating diagnosis, staging, initiation of cemiplimab therapy, radiographic response, surgical resection, and complete pathologic response.

Discussion

Cemiplimab is a monoclonal antibody immunotherapy that promotes antitumor immune activity through blockade of the PD-1 receptor [5]. In the phase II EMPOWER-cSCC 1 trial, cemiplimab demonstrated clinically significant responses in patients with locally advanced or metastatic cSCC, with objective response rates of 40%-50% across study groups [5,6]. Follow-up studies have confirmed prolonged duration of responses [1].

High-stage cSCC carries a risk of nodal metastasis [2]. The high mutational burden of cSCC associated with chronic ultraviolet exposure, together with the increased incidence of cSCC in immunosuppressed patients [6], highlights the importance of the immune system in tumor recognition and control. The high mutational burden may contribute to the responsiveness of cSCC to PD-1 inhibitors, providing a rationale for immune

checkpoint inhibition.

The present case highlights the clinical utility of cemiplimab in a patient with aggressive, locally advanced cSCC with suspected regional nodal involvement. Staging CT and PET/CT imaging demonstrated a scalp lesion with increased FDG uptake and associated cervical lymphadenopathy suspicious for regional nodal metastasis, supporting the decision to initiate systemic immunotherapy. Cemiplimab was initiated due to the initially unresectable nature of the disease, with the goal of reducing tumor burden before surgical intervention. Following treatment, the patient demonstrated both clinical and radiographic improvement with a marked reduction in tumor burden. Surgical resection was subsequently performed to assess for residual disease despite the clinical response.

Immune checkpoint inhibitors can induce antitumor immune responses but may also cause immune-related adverse events [7]. The patient in this report experienced only mild fatigue despite nine cycles of therapy, demonstrating a favorable clinical response with minimal treatment-related toxicity.

The foreign body-type giant cell reaction observed in the patient's surgical pathology may reflect a local tissue response to tumor destruction. Similar reactions have been described in the setting of rapid tumor necrosis, where macrophage activation and multinucleated giant cell formation facilitate clearance of dying tumor cells [8].

Interval PET/CT imaging demonstrated a reduction in tumor burden prior to surgical intervention. Subsequent surgical resection demonstrated negative margins and no residual viable tumor at the primary tumor site, consistent with a complete pathologic response.

This case illustrates the role of immune checkpoint inhibition in the management of advanced cSCC, particularly in patients with unresectable disease. While surgical excision remains the standard of care for localized cSCC, systemic immunotherapy is an important treatment option for advanced disease that is unresectable or not amenable to curative local therapy [2,3]. Ongoing follow-up remains critical to evaluate durability of response and to guide the timing and integration of additional local therapies when appropriate.

Conclusions

This case highlights the potential for PD-1 inhibition to induce complete pathologic response in advanced cSCC. In this patient with initially unresectable disease, systemic immunotherapy resulted in significant tumor regression, allowing for subsequent surgical resection with no residual carcinoma on final pathology. The degree of response observed in this case suggests that selected patients may achieve meaningful tumor clearance with immunotherapy prior to surgery. These findings support the role of immune checkpoint inhibitors not only as a treatment for advanced disease but also as a strategy for downstaging advanced disease in a neoadjuvant setting to enable definitive surgical management.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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