

Introduction

- Immune checkpoint inhibitors (ICIs), including PD-1 inhibitor **cemiplimab**, have improved outcomes in advanced cutaneous squamous cell carcinoma (cSCC).
- **Hyperprogressive disease (HPD)**: paradoxical rapid tumor growth and clinical decline after ICI initiation.
- Incidence: reported in **4–29%** of ICI-treated patients across cancers.
- Mechanisms: advanced age, genomic alterations, immune dysregulation, tumor-intrinsic factors (e.g., **CCL-20, CXCL-8** overexpression).
- No standardized definition or predictive biomarker → early recognition remains critical.

Case and Clinical Course

- **Patient:** Male, 60's, invasive **acantholytic cSCC** of right temporal region.
- **Presentation:** Progressive facial swelling and ulceration (Figure 1).
- **Initial Imaging:** 6.6 × 2.5 × 5.2 cm lobulated soft-tissue mass involving temporal skin, orbit, and masticator space.
- **Biopsy:** Invasive acantholytic SCC.
- Patient presented with progressive facial swelling, ulceration, and pain from a large temporal cSCC involving the orbit and masticator space.
- After starting cemiplimab, he developed rapid worsening with severe periorbital edema, facial pressure, and pain (Figure 2).
- Workup ruled out infection and orbital complications; MRI showed no intracranial extension.
- The abrupt clinical decline without radiographic progression raised suspicion for HPD.
- A multidisciplinary team recommended salvage therapy with carboplatin/paclitaxel plus cetuximab.
- The patient had rapid improvement in pain, swelling, and eye opening, with further regression of the mass on ongoing outpatient therapy (Figure 3).

Figures



Figure 1: Clinical photograph at presentation showing a large ulcerative temporal mass with associated right facial swelling.

Figure 2: Marked periorbital swelling and facial pressure following initiation of cemiplimab, consistent with suspected hyperprogressive disease.



Figure 3: Improvement in swelling and softening of the ulcerative mass after initiation of carboplatin/paclitaxel plus cetuximab, with restoration of right eye opening.

Discussion

- **Cemiplimab:** Preferred first-line systemic therapy for advanced cSCC (ORR 44–58%).
- **HPD:** Rare but serious complication with poor prognosis.
- In this case, rapid symptomatic worsening with minimal radiographic progression supported HPD diagnosis.
- **Management:** Early discontinuation of ICI + switch to salvage therapy essential.
- **Chemotherapy (carboplatin/paclitaxel) + EGFR inhibitor (cetuximab):** Symptomatic benefit, potential for tumor shrinkage, though typically less durable than ICI.
- **Clinical lessons:**
 - Vigilance for HPD in cSCC.
 - Need for predictive biomarkers (e.g., immune-modulatory gene expression).
 - Importance of **multidisciplinary approach** and willingness to re-introduce cytotoxic/targeted therapies.

References

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