Pembrolizumab-Induced Grover's Disease in a Patient with Merkel Cell Carcinoma

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Introduction

- Immune checkpoint inhibitors (ICIs) have transformed the treatment of various cancers, including Merkel cell carcinoma (MCC)[1].
- These agents restore T-cell activity against tumor cells by blocking inhibitory pathways, most notably programmed cell death 1 (PD-1), programmed cell death ligand 1 (PD-L1), and Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4)[1].
- Despite their efficacy, ICIs are also associated with immune-related adverse events (irAEs)[1].
- Dermatologic irAEs occur in 30–40% of patients receiving PD-1 inhibitors such as pembrolizumab and in up to 50% of those treated with ipilimumab[1].
- Common presentations are maculopapular, lichenoid, psoriasiform, or eczematous eruptions, while rare cases involve Grover's disease (GD), a condition increasingly reported in oncologic patients[2].
- GD, also termed transient acantholytic dermatosis, typically presents as a pruritic papulovesicular eruption on the trunk, with histopathology showing suprabasal acantholysis and dyskeratosis[3].
- The true incidence is difficult to obtain, as it can be misdiagnosed as folliculitis, miliaria, or drug eruption[3].
- Reported triggers of Grover's disease include heat, sweating, prolonged immobility, and xerosis[2,4].
- In oncology patients, both malignancy and therapy (chemotherapy, radiation, immunotherapy) are implicated as risk factors[2,4].
- Systematic reviews show immunotherapy was the most frequently observed oncologic treatment associated with GD[2].
- Although ICI-associated GD is rare, cases have been documented with ipilimumab[5,6,7], nivolumab[8,9], and pembrolizumab[10].
- Pembrolizumab-induced GD remains rarely reported.
- This case expands the literature by describing GD in a patient with MCC.

Case Presentation

- A male with MCC of the left nasal ala underwent Mohs surgery in March 2024, followed by radiation.
- Metastatic disease was detected in mid-2024, prompting initiation of pembrolizumab therapy.
- The patient achieved remission but presented in January 2025 with an itchy eruption involving the left clavicular skin and right upper chest. Examination revealed erythematous papules confined to those regions.
- Initial management included emollients, wet dressings, triamcinolone cream, and use of antihistamines and Sarna lotion for pruritis.
- By March 2025, the eruption extended to the right inferior upper back and right medial chest.
- Clobetasol 0.05% cream and a methylprednisolone dose pack were added to his regimen.
- In April 2025, the eruption generalized with pruritic pink papules distributed along the trunk and arms.
- Differential diagnosis included unspecified dermatitis, generalized drug eruption secondary to pembrolizumab, pityrosporum folliculitis, bacterial folliculitis, and GD.
- Biopsies from the xiphoid and chest revealed acantholytic dyskeratosis with suprabasal clefts and superficial perivascular lymphocytic infiltrates, confirming GD.
- Pembrolizumab was discontinued, and at follow-up, the eruption remained stable.

Clinical and Histopathological Images

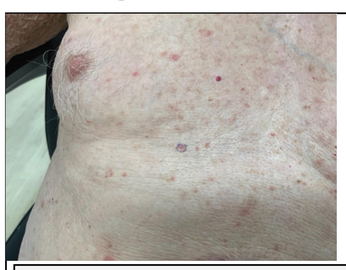

Figure 1: Erythematous papules located on the xiphoid region corresponding to biopsy site.

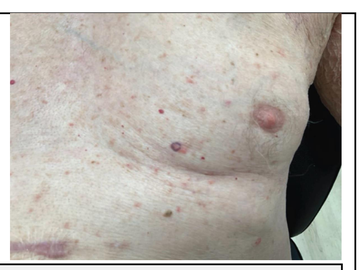

Figure 2: Erythematous papules located on left medial inferior chest corresponding to biopsy site.

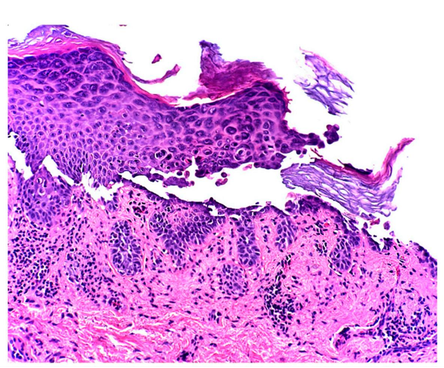

Figure 3: Suprabasal acantholysis and dyskeratosis with superficial lymphohistiocytic infiltrate and eosinophils (H&E, 200x)[11].

Discussion

- This case highlights pembrolizumab-induced Grover's disease in a patient treated for MCC, expanding the spectrum of immune checkpoint inhibitor-associated cutaneous irAEs.
- In a systematic review of 31 oncologic GD cases, immunotherapy was the most frequently associated oncologic treatment[2].
- Our patient's presentation of pruritic papules localized to the trunk and histology showing acantholysis and dyskeratosis was consistent with classic GD features[3].
- Recognition of GD often requires biopsy, as it is often misclassified as a nonspecific drug eruption without histological confirmation[1].
- The pathogenesis remains unclear but likely reflects immune dysregulation, with evidence of CD4+/CD8+ infiltrates, Th1/Th17 skewing, and possible epitope spreading, pointing to multifactorial immune activation in GD[7,8,9].
- Management is supportive, with topical or systemic corticosteroids achieving remission in most cases. Some patients may continue ICIs with improvement, while others require discontinuation for control.
- As ICIs gain wider oncologic use, clinicians should recognize GD as a rare, benign, and treatable irAE to ensure accurate diagnosis, minimize unnecessary discontinuation of therapy, and optimize patient outcomes.

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