ISSN 2640-9615 | Volume 8

Journal of Clinical and Medical Images

Case Report Open Access

Cutaneous Immune-Related Adverse Events as Predictors of Pembrolizumab Efficacy: A Case Report of Complete Response in Metastatic Urothelial Cancer

Ali Fuat Gurbuz*, Tuba Karaçelik, Oguzhan Yıldız, Omer Genc, Melek Karakurt Eryılmaz, Murat Araz and Mehmet Artac

Department of Medical Oncology, Necmettin Erbakan University, Konya, Turkey

***Corresponding Author:**
Ali Fuat Gurbuz, Department of Medical Oncology, Necmettin Erbakan University, Konya, Turkey

Received: 30 Mar 2025
Accepted: 09 Apr 2025
Published: 15 Apr 2025
J Short Name: JCMI

Keywords: Pembrolizumab; UrothelialCarcinoma; Immune-RelatedAdverse Events; Skin Lesions; Immunotherapy Response

Citation: AF Gurbuz. Cutaneous Immune-Related Adverse Events as Predictors of Pembrolizumab Efficacy: A Case Report of Complete Response in Metastatic Urothelial Cancer. J Clin Med Img. 2025; V8 (7): 1-3

1. Abstract

Pembrolizumab is a PD-1 inhibitor widely used in various cancers, including urothelial carcinoma. While immune-related adverse events (irAEs) are known to indicate better response in some cancers, the role of skin lesions in predicting pembrolizumab efficacy remains unclear.We present a 58-year-old male with metastatic urothelial carcinoma who developed a remarkable complete response to pembrolizumab after the development of immune-related skin lesions. The patient developed pruritic, bullous lesions were observed on the lower lip, the dorsum of both hands, and around the ankle after the 27th cycle. Follow-up imaging showed significant tumor regression. The skin lesions regressed after topical steroid treatment, while the tumor response continued. Following the attainment of a complete response total 35 cycle, the patient was transitioned to drug-free follow-up.This case highlights the potential role of cutaneous irAEs as predictive biomarkers for immune checkpoint inhibitor response. Further prospective studies are needed to establish their clinical significance.

2. Introduction

Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment. Pembrolizumab, a PD-1 inhibitor, has shown promising results in patients with advanced urothelial carcinoma (UC). Immune-related adverse events (irAEs), especially skin toxicities, are among the most common side effects and may correlate with treatment efficacy. However, clinical interpretation of these findings remains a challenge [1].In melanoma and nonsmall cell lung cancer (NSCLC), some studies have reported that skin reactions are associated with clinical efficacy [2]; however, little is known about this association in UC. Additionally, immune-related pruritus is a frequent adverse event among patients with cancer that is associated with lower quality of life (QOL) [3]. Therefore, it is important to identify the predictors of skin reactions. In our case, the association between the development of skin reactions and clinical benefit, and the predictive markers of skin reaction in patients with metastatic UC who were treated with pembrolizumab monotherapy.

3. Case Presentation

A 58-year-old male patient was admitted to the urology clinic with a complaint of haematuria for a period of approximately three months. Abdominal ultrasonography revealed a 23*14 mm mass on the left posterolateral wall of the bladder. The patient was diagnosed with invasive high-grade papillary UC, invading the deep muscular layer, as a result of transurethral bladder cancer. Preoperative staging revealed a mass extending from the left posterior wall of the bladder to the trigone, with no distant metastasis. Radical cystoprostatectomy was performed, resulting in a diagnosis of invasive high-grade papillary UC, with two metastatic lymph nodes removed. The pathological result was t3n2m0, stage 3. The preoperative PSA value was 3 ng/dl, and the postoperative value decreased to 0.003 ng/dl.Following the administration of four cycles of adjuvant gemcitabine and cisplatin, multiple metastatic lymph node metastases, the largest of which measured 13 mm, were detected in the abdomen approximately one year later (Figure 1). Following a multidisciplinary tumour council meeting, a decision was made to proceed with immunotherapy for the patient, as radiotherapy was deemed unsuitable due to the size of the tumour bed. The patient was administered 200 mg of Pembrolizumab every three weeks. Prior to the commencement of treatment, the patient exhibited a creatinine level of 1.64 mg/dL. Following the administration of four cycles of Pembrolizumab, a partial response was observed on positron emission tomography-computed tomography (PET-CT). The treatment was continued, and subsequent PET-CT scans revealed that the right common iliac lymph node had regressed to 8 mm (SUVmax: 4.95) (Figure 2). There was no toxicity, and the creatinine value had decreased to 1.29. Subsequently, stereotactic body radiation therapy was applied to the right common iliac lymph node in the radiation oncology clinic. However, at the 27th cycle, pruritic, bullous lesions were observed on the lower lip, the dorsum of both hands and around the ankle (Figure 3). A dermatological consultation was initiated as a result.A skin biopsy revealed the presence of eosinophils beneath the epithelium, which was reported as supporting a drug reaction. Following the administration of oral and topical steroids, as well as antihistamines, the lesions underwent complete regression. The patient received a total of 35 cycles of Pembrolizumab. No fluorodeoxyglucose -retaining lesion was detected in the last two PET-CT scans. Following the attainment of a complete response, the patient was transitioned to drug-free follow-up. The most recent creatinine value within normal limits, measuring 0.94mg/dl.

4. Discussion

ICIs such as pembrolizumab have reshaped the treatment landscape for various malignancies, including UC. Among irAEs, dermatologic toxicities are both common and often among the earliest observed. Recent evidence suggests a potential correlation between cutaneous irAEs and favorable treatment outcomes, possibly reflecting heightened systemic immune activity [1].A broad spectrum of skin-related irAEs has been reported, ranging from mild rashes and pruritus to severe bullous disorders and autoimmune-like dermatoses, such as bullous pemphigoid, lichenoid dermatitis, or vitiligo. These reactions are not merely collateral effects but may reflect the degree of immune activation against both tumor and normal tissues. The pathophysiology involves aberrant activation of autoreactive T cells and cross-reactivity between tumor antigens and skin components, although the exact mechanisms remain under investigation [2,3].The correlation between skin irAEs and improved outcomes has been most robustly demonstrated in melanoma and NSCLC. In these cancers, cutaneous events-particularly vitiligo-have

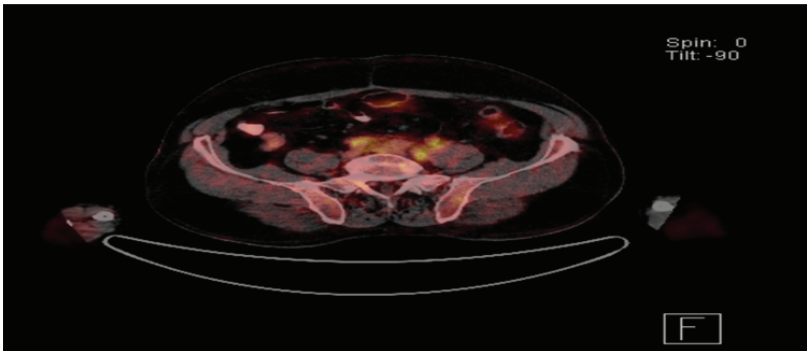

Figure 1: Pretreatment PET-Ct.

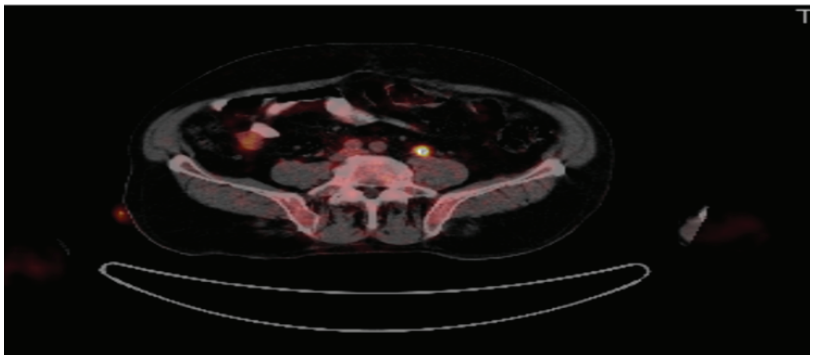

Figure 2: Postreatment PET-CT.

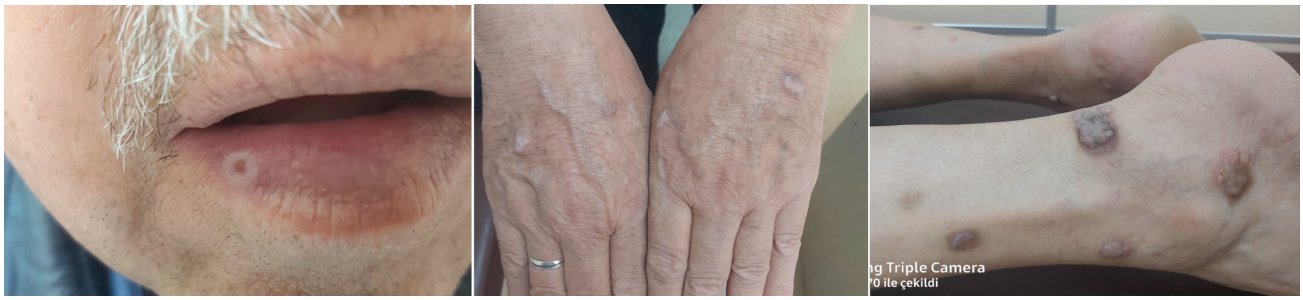

Figure 3: Lesions were observed on the lower lip, the dorsum of both hands, and around the ankle.

been consistently associated with higher objective response rates (ORR), longer progression-free survival (PFS), and overall survival (OS) [4-6]. However, such associations in urothelial carcinoma are underexplored.In our patient, the development of bullous and pruritic skin lesions occurred relatively late in the treatment course (after 27 cycles), yet coincided with continued tumor regression. This temporal association reinforces the hypothesis that cutaneous irAEs could be surrogate markers of immune engagement and ongoing tumor response—even in the late phases of treatment. Notably, the patient achieved a complete response (CR) after 35 cycles of pembrolizumab, suggesting that the appearance of skin toxicity did not necessitate treatment discontinuation, and instead may have paralleled the treatment's durable efficacy.Interestingly, while most literature emphasizes early-onset irAEs as predictive markers, our case shows that even late-onset dermatologic toxicity might retain prognostic value. This may reflect an evolving immune-tumor interaction over time or delayed immune priming. It also prompts reconsideration of the timing and implications of irAE emergence as dynamic, rather than fixed phenomena.Furthermore, the histopathological finding of eosinophilic infiltration in the skin biopsy supports a type IV hypersensitivity pattern, commonly seen in immunotherapy-associated reactions [7]. This finding, along with the clinical resolution after topical corticosteroids, reflects the immune-mediated nature of the skin toxicity and also demonstrates the feasibility of managing such irAEs without compromising anti-tumor efficacy. Although causality cannot be firmly established based on a single case, this report supports the notion that cutaneous irAEs might serve not merely as side effects but as potential biomarkers of therapeutic benefit in UC. Identifying such clinical markers is of high value in real-world settings where tissue biomarkers such as PD-L1 or tumor mutational burden may be unavailable or insufficiently predictive. Future studies should aim to stratify patients with UC receiving ICIs based on the development, timing, and severity of irAEs, to better understand their prognostic and predictive implications. Incorporating dermatologic monitoring into treatment algorithms and exploring immunologic signatures associated with skin toxicity may further refine personalized immunotherapy approaches.

5. Conclusion

This case suggests that skin-related immune adverse effects might serve as indicators of response to pembrolizumab in metastatic UC. Prospective studies and biomarker validation efforts are required to support clinical decision-making based on these observations..

References

1. Nakamura Y. Correlation between cutaneous immune-related adverse events and efficacy of nivolumab in melanoma patients. J Dermatol. 2017;44(10):1171-1174.
2. Shi VJ. Dermatologic toxicities associated with anti-PD-1 therapy. JAMA Dermatol. 2016;152(10):1195-1201.
3. Hwang SJ. Cutaneous adverse events of immune checkpoint inhibitors: a review on pathogenesis and management. Am J Clin Dermatol. 2019;20(5):653-664.
4. Freeman-Keller M. Nivolumab in resected and unresectable metastatic melanoma: characteristics of immune-related adverse events and association with outcomes. Clin Cancer Res. 2016;22(4):886-894.
5. Teraoka S. Impact of immune-related adverse events on prognosis in patients with non-small cell lung cancer treated with nivolumab. PLoS One. 2017;12(11):e0187352.
6. Rogiers A. Clinical impact of immune-related adverse events in patients with metastatic melanoma treated with immune checkpoint inhibitors. Oncologist. 2019;24(9):e962-e970.
7. Radonjic-Hoesli S, Brüggen MC, Feldmeyer L, Simon HU, Simon D.Eosinophils inskin diseases. Semin Immunopathol. 2021;43(3):393-409.