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Case Report

Nivolumab-induced immune mediated eczematous dermatitis in patient with carcinoma of buccal mucosa

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ABSTRACT

An elderly man undergoing treatment for carcinoma of left buccal mucosa experienced the appearance of skin lesions on his chest, both upper limbs, and both lower limbs after receiving the first cycle of nivolumab therapy. A biopsy report confirmed that the patient had eczematous dermatitis, which was believed to be induced by nivolumab. Patient received symptomatic treatment with Prednisolone, Clobetasol propionate and Fusidic acid. The Skin lesions improved, and subsequently Framycetin cream was recommended, resulting in no further recurrence of lesion. Clinicians should remain vigilant about development of T-cell activation-related skin disorders when administrating immune checkpoint inhibitors, such as nivolumab.

Keywords: Nivolumab, Eczematous dermatitis, Immune-related adverse event

INTRODUCTION

The discovery of T cell receptor and costimulatory signal pathways identified the necessary conditions for activating T-cells during antigen presentation. Recently, a novel class of cancer treatments called immune checkpoint inhibitors *like* Pembrolizumab, Nivolumab, and Cemiplimab has emerged.[1] These inhibitors promote antitumor immune responses by targeting various molecules such as programmed cell death protein-1 (PD-1), programmed death ligand-1 (PD-L1), and cytotoxic T-lymphocyte associated protein-4 (CTLA-4).[2] However, immunotherapy can cause a distinct set of immune reactions known as immune related adverse events.

Drug induced eczematous dermatitis is a type of eczema that is caused by an allergic reaction to medication. It can occur when a person's immune system overreacts to a drug and triggers an inflammatory response in the skin. Drugs that can induce eczematous dermatitis, include antibacterial agents, anti-inflammatory drugs, antifungal medications and anticancer agents and manifest with reactions like red, itchy, and scaly skin as well as blistering and swelling. Roughly one-third of individuals who undergo immunotherapy treatment experience dermatological toxicities; PD-1/PD-L1-induced dermatitis has recently emerged as a potential dermatologic toxicity.[3]

RESULTS

A 67-year-old male patient visiting the department of oncology in a tertiary care centre, Bangalore was diagnosed as carcinoma left buccal mucosa, staging T4N2M0. Patient is a known case of type 2 diabetes mellitus, hypertension, coronary artery disease and also has undergone percutaneous transluminal coronary angioplasty. He was on tab Aspirin 75 mg once daily, tab Olmesartan medoxomil + Amlodipine 40/5 mg once daily, tab Rosuvastatin 10 mg once daily and tab Metoprolol 50 mg twice daily for the management of comorbid condition.

For the management of carcinoma left buccal mucosa, six cycle neoadjuvant weekly Paclitaxel + Carboplatin was administered from November 2022 to January 2023 After

three weeks of the above chemotherapy, Nivolumab therapy + oral Metronomic chemotherapy was planned. In the last week of January 2023, Nivolumab 100 mg in 100 ml normal saline intravenous infusion was administered over 2 hours. Following which patient complained of skin lesions over chest, both upper and lower limbs (Figure 1). Biopsy taken from lesion and report showed eczematous dermatitis and was treated symptomatically with T. Prednisolone, Clobetasol Propionate and Fusidic acid cream for one week and after the lesions have dried up, was advised to apply glycerin cream for the next two weeks. After two weeks in the following visit, skin lesions showed improvement (Figure 2) and patient was advised to apply Framycetin cream for another 10 days.

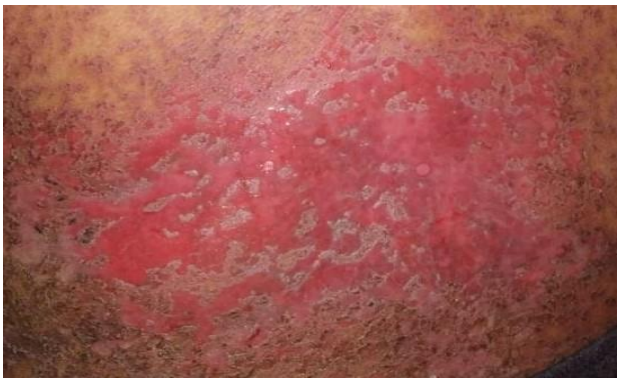

Figure 1: Erythematous patches with areas of erosions noted.

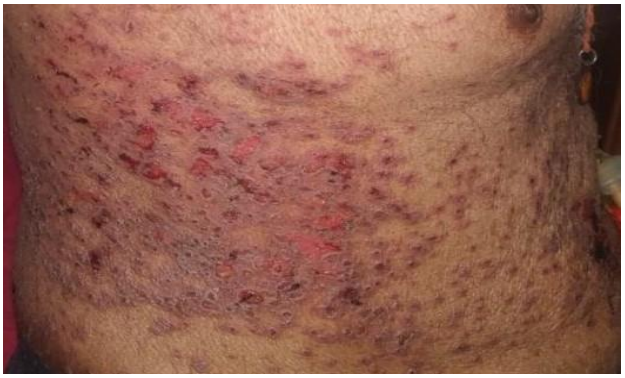

Figure 2: Erythematous plaques with haemorrhagic crusts.

DISCUSSION

This case report emphasizes the significance of monitoring immune-related adverse events in patients receiving immune checkpoint inhibitors. We encountered a case of eczematous dermatitis that developed following administration of Nivolumab for carcinoma of buccal mucosa. Skin toxicities are known to be common immune-related adverse events associated with immune checkpoint inhibitors, with reported frequencies ranging from 35% to 50%.[4,5] These skin toxicities manifest as various types of rashes, including maculopapular rash, pruritus, lichenoid reactions, psoriasis, acneiform rashes, vitiligo-like lesions, and autoimmune skin diseases.[4] However, no previous reports have described a skin eruption diagnosed specifically as eczematous dermatitis attributed to nivolumab treatment. To the best of our knowledge, this is the first documented case of eczematous dermatitis suspected to be caused by nivolumab therapy in India.

Study conducted at a single institution, involving 82 patients receiving single-agent anti-PD-1 therapy for metastatic melanoma, reported that 14 patients developed lichenoid reactions. Among these patients, 17% experienced lichenoid reactions, 17% developed eczema, and 15% developed vitiligo.[6]

In this case, patient developed eczematous dermatitis type of allergic dermatitis; but the most frequently occurring adverse effects for nivolumab were rash, itching, and vitiligo. However, the occurrence of mild and severe side effects seems to be low for both pembrolizumab and nivolumab. It's worth noting that pembrolizumab, a humanized monoclonal antibody, may have a slightly higher likelihood of triggering an immune response compared to nivolumab, which is a fully human monoclonal antibody.[7]

CONCLUSION

This is unique case of eczematous dermatitis that developed after nivolumab treatment in a patient with buccal mucosa carcinoma. Skin disorders are relatively common among patients undergoing immune checkpoint inhibitor treatment, so close monitoring for immune-related adverse events is crucial, particularly for those receiving nivolumab. Additional research is needed to gain a deeper understanding of the immunological mechanisms involved in the dermatological toxicity induced by nivolumab.

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