Case Report

Journal Of Clinical & Medical Images Case Reports

Open Access, Volume - 2

Rare Grade 3 Dermatologic Immune-Related Adverse Event: Psoriasis in Patient with Metastatic Lung Cancer, a Case Report

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Received Date : Apr 05, 2022
Accepted Date : Apr 20, 2022
Published Date : May 05, 2022
Archived : www.jcmimagescasereports.org

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Abstract

We report a case of a 62-year-old men with a diagnosis of metastatic squamous lung cancer receiving the anti-PD1 pembrolizumab therapy. After the second maintenance treatment cycle, the patient reported a rare dermatologic immune-related adverse event, characterized by itchy psoriatic manifestations widespread >30% of the body surface. The diagnosis was confirmed by skin biopsy. Patient was treated according to guidelines without significant clinical response.

Keywords: Lung cancer; pembrolizumab; immunotherapy; psoriasiform dermatitis; immune-related adverse event; dermatologic adverse events; skin toxicity.

Abbreviations : ICIs: Immune Checkpoint Inhibitors; NSCLC: Non-Small-Cell Lung Cancer; CTLA-4: Cytotoxic T-Lymphocyte Antigen-4; PD-1: Programmed Cell Death Protein 1; PDL1: Programmed Death Ligand 1; IRADs: Immuno-Related Adverse Events; CT: Computer Tomography; CTCAE: Common Terminology Criteria For Adverse Events.

Introduction

The immune checkpoint inhibitors (ICIs) are now standard of care for several cancers treatment, including non-small-cell lung cancer (NSCLC). Due to their mechanism of action blocking specific targets like Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4) and Programmed cell death protein 1 (PD-1)/ Programmed Death-ligand 1 (Pd-L1) these drugs are associated with a specific toxicity profile. The mechanism of onset immuno-related adverse events (irADs) are not completely understood such as their management are still debated. More than 60% of patients treated with ICIs developed several adverse events, which may involve the gastrointestinal tract, liver, and endocrine glands. Cutaneous toxicities are also among the most common irADs corresponding to a class effect, probably as a trigger of cutaneous autoimmunity [1, 2].

This clinical presentation has a widely spectrum: itch, vitiligo, alopecia areata, erythema nodosum, Sjögren syndrome, maculopapular rashes, pemphigoid, and psoriasis. Psoriasis-like rash represents about 3.8% of skin disorders induced by ICIs. We report a clinical case of a patient with diagnosis of metastatic NSCLC that developed de novo psoriasis during immunotherapy with pembrolizumab, showing a resistance to topical and systemic treatments.

Case presentation

A 62-year-old men with a diagnosis of NSCLC, stage T4N2M1c, PDL1 <1%, was referred to our oncology outpatient in May 2021. In remote pathological history hypertension was reported, he had no history of autoimmune disease. From June to August 2021 the patient underwent 4 courses of carboplatin plus paclitaxel and pembrolizumab (flat dose 200 mg every 3 weeks) resulting in a confirmed partial response at computer tomography (CT) scan. After the 4th cycle, he developed grade 1 pruritus and was treated with topical steroids and H1-antihistamines according to guidelines [3].

In September he started maintenance with pembrolizumab and continued for up to 2 cycles, the treatment was discontinued in November 2021 due to the onset of dermatologic adverse events. The patient developed psoriasis with itchy, multiple, well-marked, and raised, red plaque (**Figure 1**). The skin lesion covered more than 30% of the body surface, these irAE were classified as G3 according to Common Terminology Criteria for Adverse Events, CTCAE v.5 [4]. He was referred to dermatologist and started oral prednisone 1mg/kg/die combined with close monitoring. After 3 weeks of treatment there was an improvement of clinical manifestations, the symptoms pruritus revert to grade 2 while the red plaque were stable.

Citation: Silvia Della Torre, Rare Grade 3 Dermatologic Immune-Related Adverse Event: Psoriasis in Patient with Metastatic Lung Cancer, a Case Report. J Clin Med Img Case Rep. 2022; 2(3): 1135.

Due to the severity and the persistent of psoriasis, following a multidisciplinary discussion of the clinical case, the patient underwent to skin biopsy. Histopathological examination revealed sections of skin showing psoriasiform hyperplasia associated with focal parakeratosis and diffuse acanthosis, ectasic/congested vessels and perivascular and diffuse lymphocytic inflammatory infiltrate were observed; moreover direct and indirect immunofluorescence analyses were negative [5]. The pathologic report was consistent with the diagnosis of psoriasiform dermatitis induced by immunotherapy.

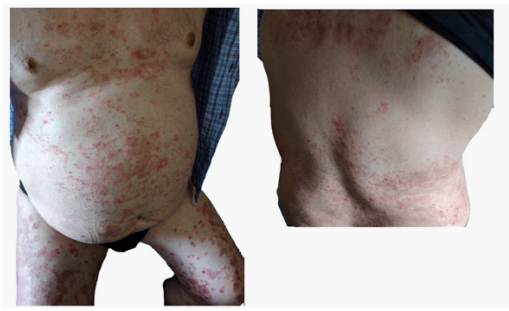

Figure 1: *Presence of multiple red plaque lesions localized to the trunk.*

Two months later, the dermatological evaluation showed a refractory grade 3 skin toxicity, patients continued treatment with oral steroids (prednisone 0.5mg/kg/day), and oral retinoids 10 mg/day (acitretin) ware prescribed with topical agents, mainly topical steroids, and combined treatment with tacalcitol monohydrate and clobetasol propionate [6,7]. Interestingly, the CT scan performed 4 months later the last dose of immunotherapy showed further partial response by immune Response Evaluation Criteria in Solid Tumors (iRECIST) (**Figure 2**). Due to the refractory irADs and the partial response at CT scan the case will be discussed at the multidisciplinary tumor board with the aim to evaluate the opportunity to introduce other biological agents such as immunomodulatory drugs or target therapies.

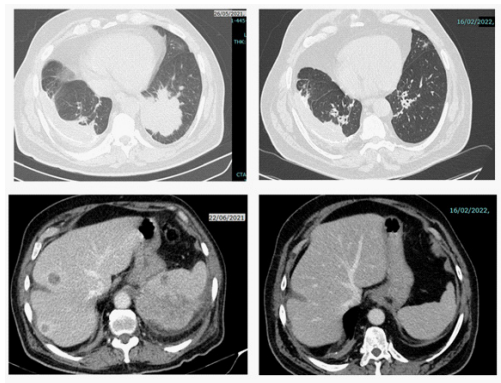

Figure 2: *CT scan, baseline (May 2021 on the left) and 4 months later the last dose of immunotherapy (February 2022 on the right).*

Discussion

Psoriasis is a chronic skin condition caused by a dysregulation of the immune system. Immunotherapy seems induce psoriasis by activation of T-helper cell 17 lymphocyes, increasing levels of interferon-gamma, tumor necrosis factor-alpha (TNF-alpha) and interleukins 2, 6 and 17, even if the mechanism is not still completely clear. According to data from European Medicine Agency (Eudravigilance) reporting system, cutaneous irADs using ICIs are more common with CTLA-4 inhibitor than anti PD-1/PD-L1 inhibitors, like pembrolizumab [8]. Psoriasis-like rash represents about 3.8% of cases, most of them with mild clinical manifestations. Sometimes skin toxicity could have an important effect on Quality of Life and impact on systemic cancer therapy, determining treatment discontinuations. The rate of immunotherapy interruption is 1.9 -5.9% , in about 14% of cases there is a temporarily suspension. Psoriasis is usually a flare of pre-existing personal history. Sometimes, as in our case, it is a new-onset form. Cutaneous lesions appear between two weeks from the beginning of ICIs and several months. Patients with personal or family history of psoriasis may have a shorter interval between the immunotherapy and toxicity compared to patient without associated history (32.8 ± 21.8 days vs 90.5 ± 77.7 days) [9, 10]. Our patient shows classic features of psoriasis after 6 cycles of ICIs.

The management of dermatological irADs includes topical and systemic drugs, according to the grade of skin toxicity, for grade 1 and 2 is recommended the use of corticosteroids therapy, adding narrow bands (NB) UVB phototherapy for grade 2, for grade ≥ 3 is suggested the use of biological agents (e.g. apremilast, infliximab, adalimumab, ustekinumab, guselkumab) [11]. Following the approaches reported by Phillips et al, there is an important reduction in severity or complete resolution of skin toxicity, even if psoriasis has less favorable outcomes. There is no consensus about the use of biological agents in clinical practice. The efficacy is reported in few clinical cases or small case series report, further prospective data are needed with the aim to define the therapeutic algorithm and the impact in terms of efficacy on ICIs and on tumor growth [12, 13].

In conclusion, through our case report, we aims to present a rare case of Psoriasis-like rash, refractory to the recommended treatment options. Moreover, we would like to underline the role of the multidisciplinary teams in the management of diagnosis and timing of treatments, and to define the correct use of biological drug that are not yet recommended by currently guidelines.

Declarations

Consent: Written informed consent has been obtained by the patient.

Conflict of interest statement: The authors declare that there are no conflicts of interest.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments: None.

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