Case Reports in Dermatology

Case Rep Dermatol 2024;16:42–46
DOI: 10.1159/000535168
Received: April 16, 2023
Accepted: November 8, 2023
Published online: February 21, 2024

Single Case

Atezolizumab-Induced Acrodermatitis and Pustular Psoriasis in a Patient with Non-Small Cell Lung Cancer: A Rare Case Report

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Keywords

Immune checkpoint inhibitors · Immune-related adverse events · Autoimmune disease · Psoriasis · Acrodermatitis · Pustular psoriasis · Atezolizumab · Case report · Immunotherapy · Malignancy · Psoriasiform lesions

Abstract

Introduction: Immune checkpoint inhibitors are new drugs approved for the treatment of many types of malignancies. Despite their wide use and unquestionable clinical benefits, these agents have also been associated with a unique spectrum of side effects known as immune-related adverse events. In this study, we report the first case of atezolizumab-induced pustular psoriasis and acrodermatitis. ***Case Presentation:*** A 61-year-old woman presented to our department with erythematous-desquamative and pustular lesions involving all hands and feet fingers, inguinal region, and trunk, associated to severe psoriatic onychodystrophy. She was affected by non-small-cell lung carcinoma from 12 years, and 7 months before admission, she started a treatment with atezolizumab. ***Conclusion:*** Immune checkpoint inhibitors such as atezolizumab are linked to a plethora of adverse events. Identifying and treating certain adverse skin events, particularly in cancer patients, can be a challenge, leading oncologists to discontinue immunotherapy. Our case shows how it is necessary to have a shared therapeutic algorithm in order to manage serious skin reactions in cancer patients and avoid disruption of the oncotherapy.

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DOI: 10.1159/000535168

Introduction

Immune checkpoint inhibitors (ICIs) are an emerging type of biological drugs, characterised by a unique pattern of action that aims to enhance the host's immune response against cancer cells. Particularly, three different types of molecules are widely used in oncotherapy: anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) such as ipilimumab; anti-programmed cell death protein-1 (PD-1) antibodies such as pembrolizumab, nivolumab, and cemiplimab; and anti-programmed death-ligand 1 (PD-L1) inhibitors such as atezolizumab, avelumab, and durvalumab. Their mechanism of action leads to cytotoxic T-cell activation and subsequent elimination of cancer cells [1].

Although they are associated with favourable oncological outcomes, these agents are linked to a plethora of adverse events, known as immune-related adverse events (irAEs). Cutaneous irAEs are the most frequent toxicities. These irAEs should be always reported and studied since they may also predict response to immunotherapy [2].

Cutaneous irAEs are observed in more than one-third of patients. They mainly include maculopapular rash and pruritus, but a wide range of other AEs, such as lichenoid eruptions, acneiform eruptions, vitiligo-like lesions, autoimmune skin diseases (e.g., bullous pemphigoid, dermatomyositis, alopecia areata, psoriasis), sarcoidosis, and nail and oral mucosal changes can also occur [3, 4]. In this study, we report the first case of pustular psoriasis and acrodermatitis in a cancer patient induced by atezolizumab.

Case Presentation

A 61-year-old woman affected by non-small-cell lung carcinoma from 12 years presented to our department with pustules, erythema, and desquamation of all hands and feet fingers, psoriatic onychodystrophy, and erythematous-desquamative plaques with pustular lesions in the inguinal region and trunk. Moreover, she presented multiple raised well-demarcated red plaques with a white scaly surface on the lower limbs and on the sub-mammary sulcus. She complained of intense itching and huge impairment of the quality of life, especially for the destructive nail alterations (Fig. 1, 2). Seven months before admission, she started a treatment with atezolizumab at the dosage of 1,200 mg every 3 weeks. The patient had no personal and familiar history of any skin diseases, but she suffered from hypercholesterolaemia, hypothyroidism, and chronic kidney disease. A skin biopsy specimen, taken from a new lesion, revealed epidermal hyperplasia, hypogranulosis, and the presence of tortuous papillary blood vessels with an inflammatory infiltrate in the dermis characterised by T lymphocytes, some macrophages, and prevalence of neutrophils, some of them within the epidermis. A diagnosis of atezolizumab-induced pustular psoriasis was performed. Therefore, the patient started treatment with salicylic acid in 20% cream, topical fusidic acid, and betamethasone every day. Two weeks later, the patient showed a slight benefit only. The patient's oncologists did not allow to begin a treatment with biologics, methotrexate, cyclosporine, and apremilast due to the patient's renal failure, so we decided to initiate a treatment with acitretin 10 mg per os every day.

Discussion

Atezolizumab is a monoclonal antibody that specifically blocks PD-L1, and it is a treatment option in monotherapy for non-small-cell lung carcinoma with high PD-L1 expression [5]. The PD-1 signalling pathway acts as a mechanism for tumours to evade

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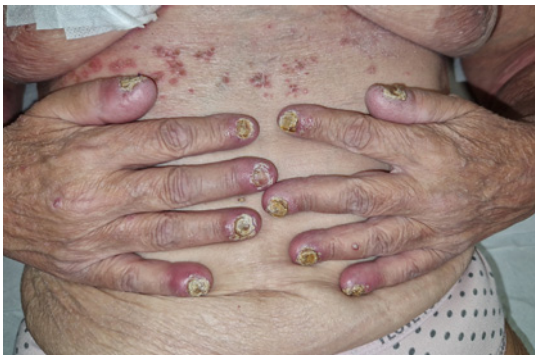

Fig. 1. Severe acrodermatitis. Distal phalanges are edematous, erythematous, scaly, and some pustular lesions are visible. Crumbling, hyperkeratosis and leukonychia are visible on the nails.

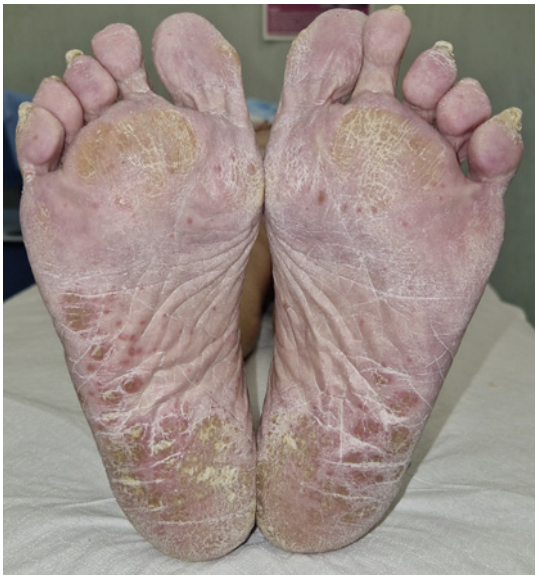

Fig. 2. Erythematous scaly plaques and pustular lesions on the soles of the feet. Nails are hyperkeratosic and dystrophic.

T-cell-mediated immune response and blockade of PD-L1 that resulted in enhanced T-cell activation and subsequently inhibition of tumour development [5].

It is still described in the literature the possibility of developing psoriasis with ICIs like atezolizumab, even though detailed data on its prevalence and incidence are still lacking. Most cases show a psoriasis eruption in patients with pre-existing disease, but several cases of new-onset psoriasis are also reported [6, 7].

Psoriasis is a chronic, immune-mediated systemic disorder which can have considerable negative effects on the patient's quality of life. It is characterised by a cell-mediated immune response, in which dendritic cells activate naive T cells and promote selection of Th1-type $CD4^+$ T cells that produces high levels of IFN-γ and TNF-α. This leads to the activation of (Th) 17 and 22 cells with production of IL-17, IL-22. Those cytokines activate cascades of inflammatory responses by promoting keratinocyte proliferation and recruitment of neutrophils to sites of inflammation [8]. Psoriasis can be induced by many triggering factors such as infections, physical trauma to the skin (the Koebner phenomenon), exposure to emotional stress, and also exposure to drugs [8, 9]. However, the pathogenesis behind the development of psoriasis in patients treated with immunotherapy is still unknown. An explanation could be the enhancing of T-cell activation caused by the blockade of PD-L1. Indeed, there is evidence that the inhibition of the PD-1 pathway may lead to an upregulation of Th17 lymphocytes with

secondary overexpression of proinflammatory cytokines (IL-17, IL-23, IL-1, TNF-α) [10]. So, the Th17 upregulation could be the key link of psoriasis development or worsening during the anti-PD-1 therapy.

The development of pustular psoriasis and acrodermatitis during immunotherapy is occasional, and prevalence data are lacking in the literature. Treatment options for this condition are currently topical corticosteroids; vitamin D analogues; ultraviolet-based phototherapy; and systemic treatments such as methotrexate, cyclosporine, acitretin, and apremilast [11]. According to a recent study, some biological drugs (anti-TNF-α agents, anti-interleukin 23, 12/23, or 17 agents) may represent a valuable therapeutic weapon against anti-PD-1-induced psoriasis [12]. Despite their effectiveness in treating psoriasis, these agents are associated with important adverse reactions and loss of antitumor efficacy [12].

Conclusions

In patients with active malignancy and severe comorbidities, as in our case, the only treatment possibility is often represented by acitretin or topical drugs, and sometimes, oncologists are obliged to discontinue therapy with ICIs. Therefore, we believe that innovative drugs should be found in cancer patients to treat severe skin adverse reactions such as psoriasis. Further studies are necessary to elucidate the underlying pathogenetic mechanisms so that we can highlight new, safer, and more specific therapeutic targets. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000535168).

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors received no funding for this work.

Author Contributions

Davide Fattore and Gianluca Esposito: conceptualisation, validation, visualisation, and writing – original draft preparation, review, and editing. Ludovica Carangelo: conceptualisation, visualisation, and writing – original draft preparation. Maria Antonietta Luciano: data curation, investigation, and methodology. Matteo Megna: writing – original draft preparation, review, and editing.

Data Availability Statement

All data generated or analysed during this study are included in this study and its online supplementary material. Further enquiries can be directed to the corresponding author. All the authors read and approved the final version of the manuscript.

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