CASE REPORT

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ACUTE "ASTEATOTIC" DERMATITIS INDUCED BY PAZOPANIB AND NIVOLUMAB IN A PATIENT WITH CLEAR CELL RENAL CELL CARCINOMA

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Abstract. Introduction: *Scientific research on cancer biology in the past few decades has enabled the development of multiple different types of new anticancer drugs. These therapeutic agents include tyrosine kinase inhibitors, monoclonal antibodies, and immunotherapies. They are significantly more precise than classical chemotherapies, but frequently induce adverse effects. Cutaneous side effects are the most frequently observed ones, and when they are severe or prolonged in time, they eventually lead to morbidity, dose modification or drug discontinuation. They significantly affect the quality of life in patients, medication adherence, elevate infection risk, resulting in high economic burden and many hospital visits for cancer patients.* ***Case Presentation:*** *We report a case of severe acute asteatotic dermatitis in a 54-year-old male patient induced by pazopanib and nivolumab for the treatment of clear cell renal cell carcinoma. After treatment, the erythema faded, desquamation and xerosis were significantly reduced. Systemic oncology therapy was switched to M-TOR inhibitor everolimus. The patient maintains mild generalized skin xerosis, but is using topical emollient cream daily and topical corticosteroids occasionally for maintenance. The patient is being followed up.* ***Conclusion:*** *The use of tyrosine kinase inhibitors and immunotherapy is constantly increasing, and dermatologists care for a growing number of cancer patients with cutaneous adverse events with different pathogenesis and complexity in comparison to the classical dermatoses. This leads to the need for a collaboration between dermatologists and oncologists.*

Key words: *clear cell renal cell carcinoma, pazopanib, nivolumab, adverse events, asteatotic dermatitis*

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INTRODUCTION

The scientific research on cancer biology in the past three decades has led to a better understanding of carcinogenesis, neoangiogenesis, tumor microenviroment, proliferation and invasion of cancer cells, signaling pathways and immune response. All these findings enabled the development of multiple different types of new drugs. These therapeutic agents include tyrosine kinase inhibitors (TKI), monoclonal antibodies and immunotherapies. They have been designed to be significantly more precise than classical chemotherapies, but frequently induce adverse effects (AEs). Cutaneous AEs are the most frequently observed side effects and when they are severe or prolonged in time, eventually lead to morbidity, dose modification, or drug discontinuation [1]. These AEs can significantly affect the quality of life in patients, medication adherence, and elevate infection risk, resulting in higher economic burden and many hospital visits for cancer patients [2]. For the reporting standards and stratification of side effects for cancer patients accordingly a Common Terminology Criteria for Adverse Events (CTCAE) was presented and in 2025 a 6th version of it is expected [3]. It determines the cutaneous toxicity as follows: grade 1 rash covering <10% of the body surface area (BSA) with or without symptoms; grade 2 rash covering 10–30% of BSA with or without symptoms affecting daily living or >30% of BSA; grade 3 rash covering >30% of BSA with moderate or severe symptoms; grade 4 rash – life-threatening consequences requiring urgent intervention.

CASE PRESENTATION

We present a 54-year-old male patient who was diagnosed with clear cell renal cell carcinoma of the right kidney in November 2022 and underwent nephrectomy. A follow-up PET/CT was performed and discovered metastases in lungs, peritoneum, paraaortic lymph nodes and right adrenal gland.

In January 2023 the patient initiated therapy with pazopanib tabl. 200 mg (800 mg daily). Two weeks later a mild xerotic and pruritic rash on scalp, thorax and arms appeared. The rash was treated with topical emollient cream and topical mild corticosteroid successfully.

In September 2023, a follow-up PET/CT found progression of the disease with new metastatic lesions in the lungs, liver, and peritoneum.

The therapy was switched to immunotherapy with nivolumab 480 mg i.v. every 21 days. Ten days after the first administration, the patient presented with worsening of the skin condition. The pathological skin changes involved the scalp, face, neck, chest and upper extremities. They were presented with generalized xerosis and fine desquamation, hypopigmented macules, and erosions in the scalp and face. In the presternal area, an extensive erosive plaque without infiltrate covered with yellow-brownish crusts was found. There were multiple erosions on the abdomen and upper limbs. The patient complained of severe itch and pain (Fig. 1).

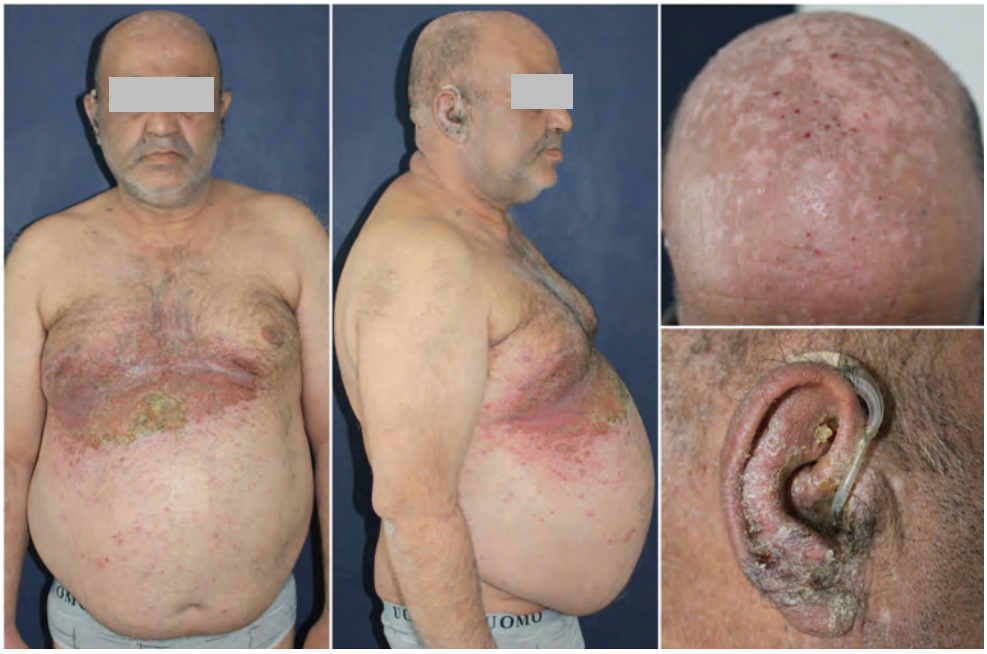

Fig. 1. Generalized xerosis and fine desquamation, hypopigmented macules and erosions in the scalp and face. Presternal area – an extensive erosive plaque without infiltrate, covered with yellow-brownish crusts. Multiple erosions on abdomen and upper limbs. Severe itch and pain

The results from complete blood count and biochemistry found low hematocrit and lymphocyte levels, high C-reactive protein level and leukocytosis. Microbiological examination revealed Staphylococcus aureus wound infection. The histopathological examination revealed irregular acanthosis and parakeratosis, mild spongiosis with focal spongiotic vesiculation, and perivascular lymphohistiocytic inflammatory infiltrate (Fig. 2).

Based on medical history, dermatological status, histopathological and instrumental investigations, the patient was diagnosed with acute dermatitis induced by pazopanib and aggravated by nivolumab.

Intravenous treatment with ceftriaxon, methylprednisolone, chloropyramine hydrochloride and local therapy with potassium permanganate baths, emolients, flumetasone pivalate/clioquinol unguentum for the scalp and gentamycin cream for the wound on the chest for 10 days, were administered.

The erythema faded, desquamation and xerosis were significantly reduced (Fig. 3). Systemic oncology therapy was switched to M-TOR inhibitor everolimus. The patient maintains mild generalized skin xerosis, but is using topical emollient cream daily and

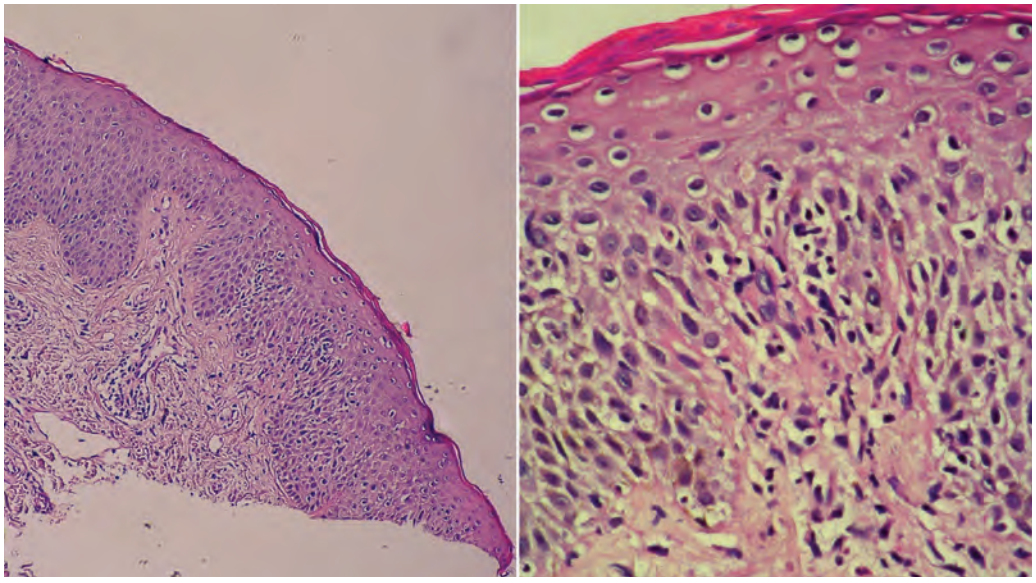

Fig. 2. The histopathological examination: irregular acanthosis and parakeratosis, mild spongiosis with focal spongiotic vesiculation and perivascular lymphohistiocytic inflammatory infiltrate

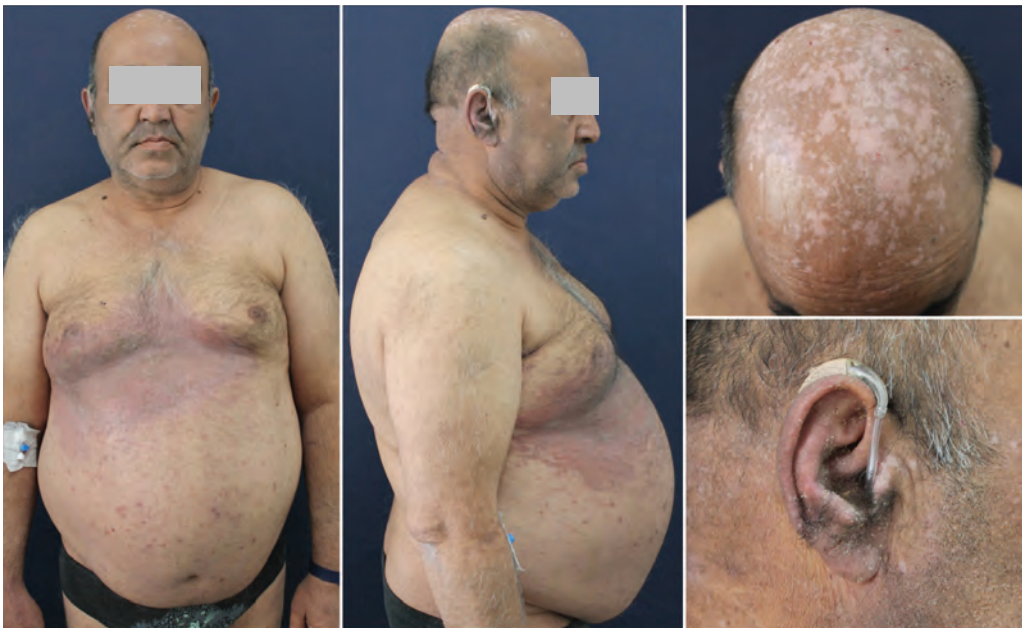

Fig. 3. Erythema faded, desquamation and xerosis were significantly reduced

topical corticosteroids occasionally for maintenance. The patient is being followed up.

DISCUSSION

Renal cell carcinoma (RCC) presents almost 90% of all kidney tumors. Clear cell carcinoma is the most common histological subtype of the disease, affecting 80%-90% of the patients [4]. The leading potentially modifiable etiological factors for RCC development are hypertensive disease, obesity, and cigarette smoking, as in the case presented in the paper [5]. Epidemiologically, around 295,000 new cases are diagnosed annually [6]. In the United States, 65,340 new cases were recorded for 2018, with 14,970 deaths [7]. The male-to-female ratio is close to 2 to 1 [8].

Asteatotic dermatitis, also known as "eczema craquelé", is a common type of pruritic dermatitis. It is characterized by erythematous, inflamed, xerotic skin with fissures and desquamation. The disease usually begins as generalized xerosis, and as it becomes more severe, the skin can crack and cause fissures, a result of epidermal water loss. Asteatotic dermatitis is often associated with severe pruritus and can be correlated with malignancy, hypothyroidism, and malnutrition or with drugs such as diuretics, retinoids, TKIs, and immunotherapy [9, 10].

Pazopanib is a multikinase TKI that limits tumor growth by targeting angiogenesis. It inhibits multiple enzymes, including vascular endothelial growth factor receptor 1-3 (VEGFR 1-3), platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor 1 and 3 (FGFR 1, 3), proto-oncogene c-*Kit*, and others.

Boers-Doets et al. report skin toxicity in up to 90% of the patients under treatment with pazopanib [11]. The most common cutaneous AEs are xerosis, pruritus, papulo-pustular rash, erythema exudativum multiforme, hand-foot skin reaction, and hyper- and hypopigmentation of the skin.

Nivolumab is a high-affinity, human, IgG4 monoclonal antibody that blocks the interaction of PD-1 (programmed cell death protein 1) with PD-ligand 1 between T-lymphocytes and tumor cells. This action leads to suppression of tumor cell differentiation and proliferation and activation of anti-tumor immune response. Hwang et al. describe skin side effects in up to 49% of the patients treated with nivolumab [12]. The most commonly described cutaneous AEs are erythematous papular rash, pruritus, vitiligo, lichenoid reaction, eczema/dermatitis/asteatotic dermatitis, like in our case, and vesiculobullous reaction, such as bullous pemphigoid, Stevens-Johnson syndrome, and Toxic epidermal necrolysis.

The prevention and treatment of these cutaneous AEs allows patients to stick to the therapy regime and obtain maximum clinical benefit from it.

The treatment of asteatotic dermatitis is primarily by skin hydration. Lotions with high oil content are better for these patients and high water lotions can worsen the cutaneous xerosis [13]. Alpha-hydroxyl acid emollients are also beneficial after warm water soaks or steroid ointment treatment [14].

Topical steroids should always be used in conjunction with emollients. Patients with moderate or severe disease should use medium or high-potency corticosteroids. These include fluocinolone, triamcinolone, and betamethasone.

Other topical agents, like pimecrolimus 1% have been shown to be effective for pruritus control, as well [15].

CONCLUSION

The use of TKIs and immunotherapy is constantly increasing, and dermatologists care for a growing number of cancer patients with cutaneous AEs with different pathogenesis and complexity in comparison to the classical dermatoses. This leads to the need for a collaboration between dermatologists and oncologists.

Xerosis of the skin is one of the most common AEs in oncological patients treated with TKIs and immunotherapy, but the development of acute asteatotic dermatitis is observed rarely.

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Consent for publication: *Consent form for publication was signed by the patient and collected.*

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