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Topic: Adverse drug reactions, TEN

When Antidiabetic Therapy Affects the Skin – case report and literature review.

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Introduction

Bullous reactions represent rare but clinically significant cutaneous adverse effects of antidiabetic therapies. The literature reports an association between dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins) and autoimmune bullous diseases, particularly bullous pemphigoid, while only isolated cases have been described in relation to sodium-glucose co-transporter 2 (SGLT2) inhibitors (flozins). The underlying mechanisms remain incompletely understood; however, immune dysregulation and potential cross-reactivity with basement membrane zone antigens have been reported.

A 60-year-old male patient with a history of psoriasis and type 2 diabetes presented to the Dermatology Department with blisters and purpuric lesions (petechiae) on the hands and feet that had developed over several weeks. Additionally, he reported a three-month history of pruritic papules and erosions on the trunk. One year prior to presentation, empagliflozin had been added to his long-term metformin therapy. Initial dermatological management included systemic antihistamines and topical triamcinolone combined with tetracycline spray. Owing to the lack of clinical improvement, serological testing was performed to exclude autoimmune bullous disorders, with negative results. A referral to a diabetologist was therefore recommended to reassess and modify the antidiabetic treatment.

At the two-month follow-up visit, the patient reported that empagliflozin had been switched to dapagliflozin. Clinical examination revealed partial remission, with resolution of lesions on the hands, post-inflammatory desquamation on the feet, and persistence of a few erosive lesions and scattered papules on the trunk and lower legs. Patch testing demonstrated positive reactions to gallates and sulfur compounds. At a subsequent visit, the patient reported that dapagliflozin had also been discontinued due to the development of balanitis. The patient was maintained on metformin monotherapy. At that time, complete resolution of all cutaneous lesions was observed.

Materials and Methods

N/A

Results

In 1835, phlorizin, a dihydrochalcone isolated from apple tree bark, was identified as the first naturally occurring compound with sodium–glucose cotransporter 2 (SGLT2) inhibitor activity [1]. SGLT2 inhibitors represent a relatively novel class of oral hypoglycemic agents used in the treatment of type 2 diabetes mellitus (T2DM) [2]. This drug class includes canagliflozin, dapagliflozin, empagliflozin, ipragliflozin, luseogliflozin, and tofogliflozin [3]. SGLT1 and SGLT2 transporters, located in the proximal convoluted tubule of the kidneys, are responsible for the reabsorption of glucose and sodium from the glomerular filtrate. In patients with T2DM, upregulation of SGLT2 contributes to persistent hyperglycemia via an insulin-independent mechanism [4]. Beyond glycemic control, SGLT2 inhibitors demonstrate cardioprotective effects, including blood pressure reduction through glycosuria and natriuresis, weight loss, and a decreased risk of cardiovascular events [5]. The most commonly reported adverse effects include hypotension, genital and urinary tract infections, and diabetic ketoacidosis [6]. Dermatological adverse events associated with SGLT2 inhibitor therapy are uncommon but have been reported, including Fournier's gangrene (necrotising fasciitis), fixed drug eruptions, pruritus, Sweet syndrome, bullous pemphigoid, psoriasis, and psoriasiform vulvitis [7].

Conclusions

In the present case, blistering lesions developed after more than one year of empagliflozin therapy and showed partial remission following drug substitution and complete resolution after discontinuation of SGLT2 inhibitor treatment , suggesting a possible association with a non-autoimmune bullous reaction. This observation highlights the importance of considering SGLT2 inhibitors (flozins) in the in the differential diagnosis of bullous or blistering skin eruptions in patients with type 2 diabetes mellitus.