International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Pemphigus Foliaceus following Tirzepatide Use

Saba Suleman[1], Ramlah Khan[2], Cerin Tomson[3], Ahmed Abdelmonem[3]

[1]Baylor Scott & White All Saints, USA

[2]Texas A&M University, USA

[3]Baylor University Medical Center, USA

Citation: *Saba Suleman, Ramlah Khan, Cerin Tomson, Ahmed Abdelmonem. Pemphigus Foliaceus following Tirzepatide Use. Int Clinc Med Case Rep Jour. 2023;2(15):1-5.*

Received Date: 30 August, 2023**; Accepted Date:** 02 September, 2023**; Published Date:** 04 September, 2023

***Corresponding author:** Saba Suleman, Baylor Scott & White All Saints, USA

Copyright: © Saba Suleman, Open Access 2023. This article, published in Int Clinc Med Case Rep Jour (ICMCRJ) (Attribution 4.0 International), as described by http:// creativecommons.org/licenses/by/4.0/.

ABSTRACT

Pemphigus foliaceus, a rare autoimmune condition, is one among several entities that make up a group of life threatening blistering disorders called pemphigus. It is distinguished by isolated cutaneous involvement and subcorneal acantholytic blisters. Considering the risks associated with a delayed diagnosis or misdiagnosis and the potential for overlap in clinical features and treatment, evaluation for suspected pemphigus disease often requires thorough clinical assessment an laboratory testing. Diagnosis is focused on individual biopsies for histopathology and direct immunofluorescence.

Drugs are the most common trigger of pemphigus. Tirzepatide is a relatively new drug that is FDA approved for glycemic control in adults with Type II Diabetes Mellitus. Here, we present a 63 year old female who presented with arthralgias and diffuse, blistering ulceration 1-2 days after initiating tirzepatide for her Type II diabetes. These lesions spread down both of her arms, legs, and feet with satellite lesions below her breasts. Upon another dose of tirzepatide, she noticed worsening of her symptoms and experienced mild fever, chills, and appetite changes. She presented to the hospital with cellulitis of her wounds and was treated with three weeks of vancomycin and cefepime. Biopsy results and clinical presentation led to a diagnosis of pemphigus foliaceus. Tirzepatide was stopped and she was treated with a prednisone taper course. She had significant improvement of her lesions upon initiation of antibiotics and steroids and was stable for discharge.

INTRODUCTION

Pemphigus is a group of immunobullous disorders that are clinically significant because, if left untreated, can lead to high morbidity and mortality. Diagnosis of pemphigus is often delayed.[1] Their pathophysiology is largely driven by an autoimmune process, and therefore, antibody testing is the basis of diagnosis and treatment strategies.[1,2] The target antigens are Desmoglein (Dsg)-1 and Dsg-3, which are key components of desmosomes that hold

keratinocytes together in the epithelia. Loss of function of the desmosome results in keratinocytes splitting from one another and leading to the formation of blisters.[1]

In pemphigus foliaceus, there is a high level of blister formation in the subcorneal region of the epidermis, and hence, the blisters are more fragile than those seen in pemphigus vulgaris. Diagnosis of pemphigus foliaceus is based on histology and direct immunofluorescence of a well-sampled tissue biopsy in combination with clinical findings. Histology illustrates subcorneal blistering in pemphigus foliaceus, though is often reported as nonspecific due to the superficial blister that may have its thin roof detached, indicating a relatively normal looking epidermis.[2]

The distribution of skin lesions is clinically similar for both pemphigus vulgaris and foliaceous. However, a key differentiation is the absence of desmoglein (Dsg)-3 in pemphigus foliaceus, and therefore, mucosal surfaces are not affected.[1]

Pemphigus foliaceus is caused by antibodies directed at Dsg-1 and presents with scattered superficial blisters and cutaneous erosions on an erythematous base.[1,2] It also commonly presents with scaly or crusty, erythematous patches similar to exfoliative dermatitis.[1]

Here, we report a patient who presented with new-onset pemphigus foliaceus upon initiation and continued use of tirzepatide. This case provides supportive evidence for the potential association of pemphigus foliaceus with tirzepatide and highlights the clinical importance of screening for drug-induced pemphigus when suspicious lesions arise after starting a new therapy.

CASE REPORT

A 63-year-old Caucasian female, with a past medical history of type II diabetes mellitus, arthritis, skin cancer, and uterine cancer, presented with arthralgias and diffuse, blistering ulceration 1-2 days after initiating oral tirzepatide for her type II diabetes. Her symptoms began with severe joint pain in her right carpometacarpal joint, which then migrated to her left index finger distal interphalangeal joint. She then noticed small, white lesions on her elbows that developed into white, flaccid blisters within a couple days (Figure 1). These lesions spread down both of her arms, legs, and feet (Figure 2). She also had 2-3 remote lesions below her breast.

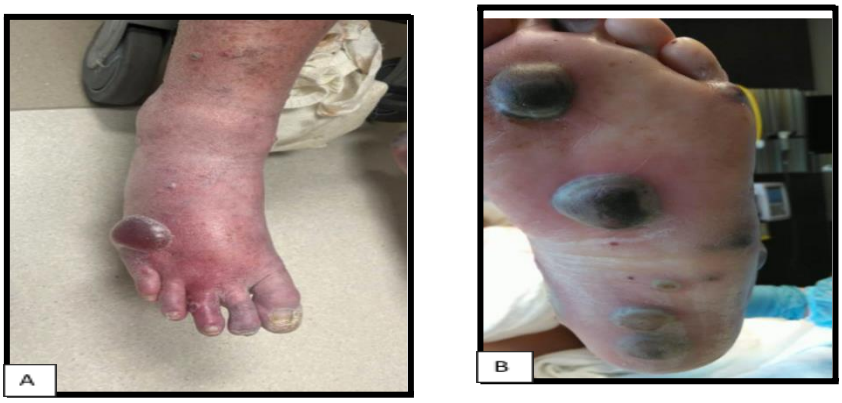

Figure 1: Flaccid bullae over the lateral right foot (A) and plantar surface of the left foot (B).

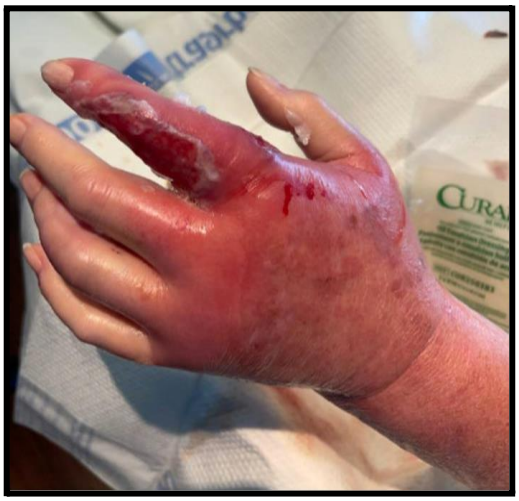

Figure 2: Deep eroded papules and plaques on the left hand.

The patient took tirzepatide again, a week after the initial dose, and noticed a worsening of her symptoms. She had associated mild fever, chills, and appetite changes. She presented to the hospital and was found to have overlying cellulitis of her wounds. Infectious disease and hand surgery were consulted, and the patient underwent a 3 week course of vancomycin and cefepime and debridement of her left hand. Wound care was also consulted, and the patient's lesions were popped daily followed by wound care with silver alginate. Dermatology was consulted, and differentials considered included bullous impetigo lesions, pemphigus, diabetic bullae, and drug eruption. On day 9 of admission, biopsies of the lesions obtained for Hematoxylin and Eosin (H&E) and direct immunofluorescence (DIF) staining from the left fourth finger and H&E from the left dorsal foot identified superficial acantholysis. DIF was negative. Serologic study was positive for anti-Desmoglein-1 IgG. Given the biopsy results and clinical presentation, the patient was diagnosed with pemphigus foliaceus. Tirzepatide was stopped and added to the patient's allergies list. The patient was treated with oral 40mg prednisone and tapering over 12 days. She experienced significant improvement of her lesions upon initiation of antibiotics and steroids. She was stable for discharge to a skilled nursing facility with instructions to follow up with wound care, infectious disease, and dermatology.

DISCUSSION

Tirzepatide (Mounjaro™) is a once-weekly subcutaneous injectable that works on both glucose dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. This drug stimulates insulin secretion and decreases glucagon secretion to delay gastric emptying, increase satiety, and suppress appetite.[3,4]

Tirzepatide was approved by the Food and Drug Administration in May 2022 for patients with Type II Diabetes to improve glycemic control. Similar to other incretin-based therapies, tirzepatide's most frequently reported side effects includes transient gastrointestinal events, especially when starting treatment.[3]

In this case, the patient was prescribed oral tirzepatide. Tirzepatide is a relatively new drug with no known case reports of associated pemphigus foliaceus. A review of the literature indicates that drugs are the most common triggers of pemphigus.[5] Most common causes of drug-induced pemphigus involve exposure to thiol drugs.[2,5] Other diabetes drugs such as Dipeptidyl peptidase 4 (DDP-4) inhibitors have been associated with pemphigus in prior case reports.[6] Drug-induced pemphigus is four times more likely to present as pemphigus foliaceus than pemphigus vulgaris.[2]

Pemphigus foliaceus clinically presents with painful blisters and erosions without involvement of mucosal surfaces.[2,7] It primarily involves seborrheic areas, including the scalp, face, and trunk. On H&E, pemphigus foliaceus demonstrates acantholysis within the upper epidermis, adjacent or within the granular layer, leading to a subcorneal cleft.[7] Drug-induced pemphigus should be considered if there are significant eosinophils present. Negative DIF studies can be found in drug-induced pemphigus. In pemphigus foliaceus, indirect immunofluorescence shows intercellular deposition of IgG antibodies, and serology indicates the presence of antibodies against Dsg-1 only.[2] In this case, the combination of the patient's clinical presentation, superficial acantholysis on H&E, negative DIF, and antibodies to only Dsg-1 is highly indicative of pemphigus foliaceus. Given the temporal relationship of starting tirzepatide with the onset of lesions, and worsening of symptoms upon repeat injection of the drug suggests an association between tirzepatide and pemphigus foliaceus.

CONCLUSION

This case demonstrates a possible relationship between the drug tirzepatide and pemphigus foliaceus. Tirzepatide has not been associated with pemphigus foliaceus in previous studies. Given the temporal relationship between starting tirzepatide with the onset of lesions and worsening of symptoms with repeat administration of the drug, this case could be the first to suggest an association between tirzepatide and pemphigus foliaceus. First-line treatments for mild pemphigus foliaceus typically include topical steroids, systemic steroids, dapsone, and rituximab. Our patient's wound improved upon receiving antibiotics and a prednisone taper, which augmented healing.

The mechanism by which tirzepatide induces pemphigus is obscure. The majority of agents that directly or indirectly lead to stimulation of the immune system can lead to adverse events in susceptible individuals. This response can be due to hormonal alteration, disease, drugs, diet, emotional stress, or other environmental factors.

The family of pemphigus diseases can have a profound mobidity for patients if left untreated or there are delays in treatment. Thus, clinicians should be aware of the possible side effects of tirzepitide and monitor patients for skin conditions like pemphigus foliaceus when initiating patients on tirzepitide.

DECLARATION OF INTEREST

The authors report no conflicts of interest.

REFERENCES

1. V Melchionda, KE Harman. Pemphigus vulgaris and pemphigus foliaceus: an overview of the clinical presentation, investigations and management. Clin Exp Dermatol . 2019;44(7):740-746.
2. Ali M Malik, Sarah Tupchong, Simo Huang, Abhirup Are, Sylvia Hsu, Kiran Motaparthi. An Updated Review of Pemphigus Diseases. Medicina (Kaunas). 2021;57(10):1080.
3. Syed YY. Tirzepatide: First Approval. Drugs. 2022;82(11):1213-1220.
4. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide once weekly for the treatment of obesity. New England Journal of Medicine. 2022;387(3):205–216.
5. Tavakolpour S. Pemphigus trigger factors: special focus on pemphigus vulgaris and pemphigus foliaceus. Arch Dermatol Res. 2018;310(2):95-106.
6. Efi Pasmatzi, Alexandra Monastirli, John Habeos, Sophia Georgiou, Dionysios Tsambaos. Dipeptidyl peptidase-4 inhibitors cause bullous pemphigoid in diabetic patients: Report of two cases. Diabetes Care . 2011;34(8):e133.
7. Liu L, Deng J, Cibull T, Pesce CE. Invasive breast cancer found in a patient with new-onset pemphigus foliaceus. JAAD Case Rep. 2021;18:67-70.