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CASE REPORT

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Novel reaction to new cystic fibrosis medication Trikafta

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Abstract

We present a novel case of an urticaria multiforme-type drug reaction to the new cystic fibrosis medication Trikafta (elexacaftor + tezacaftor + ivacaftor). Equipped with this information, clinicians may be more prepared to counsel and treat patients if they experience similar symptoms after beginning Trikafta.

KEYWORDS

cystic fibrosis, drug rash, Trikafta, urticaria, urticaria multiforme

1 | CASE

A 24-year-old white woman with a history of cystic fibrosis (CF) presented to our clinic 2 weeks after starting Trikafta (elexacaftor + tezacaftor + ivacaftor) with a 1-week history of a pruritic rash that began on her extremities spreading to her trunk. The patient reported swelling of the hands and feet, facial swelling, and a low-grade fever without lymphadenopathy, chills, or other constitutional symptoms. She denied mucosal involvement, urinary symptoms, shortness of breath, joint pain, or significant cutaneous pain associated with the rash. No other new medications had been started in the past year and she had no known new infections in the past month. On exam, the patient was non-toxic. On the trunk and bilateral extremities, there were diffuse erythematous, annular, urticarial thin plaques with dusky, gray-hued centers (Figures 1 and 2). No bullae were noted. Nikolsky and Asboe-Hansen signs were both negative. Mucosal surfaces were noninflamed. A punch biopsy taken from a representative lesion on the right anterior thigh was read as hypersensitivity dermatitis with urticarial features (Figures 3 and 4).

2 | DISCUSSION

Urticaria multiforme is a benign cutaneous hypersensitivity reaction typically seen in pediatric patients. It characteristically presents with blanching, annular, pruritic plaques with dusky centers, and swelling in the hands, feet, and face. Urticaria is nonlife-threatening but can be mistaken for erythema multiforme (EM), despite distinct differences in presentation. While usually unnecessary, biopsy can be used to differentiate between the two.[1] Urticaria multiforme histologically demonstrates classic urticarial features such as superficial dermal edema, vasodilation, scant perivascular, and interstitial infiltrate predominantly composed of neutrophils.[2]

Trikafta (elexacaftor + tezacaftor + ivacaftor) is a new combination medication approved for use in CF patients 12 years and older.[3] As it is a combination drug, the mechanism of action for Trikafta is multifaceted. Elexacaftor and tezacaftor function to improve CFTR protein processing and trafficking, while ivacaftor augments channel gating.[4] Of note, skin manifestations related to the initiation of Trikafta were noted in approximately 10% of patients

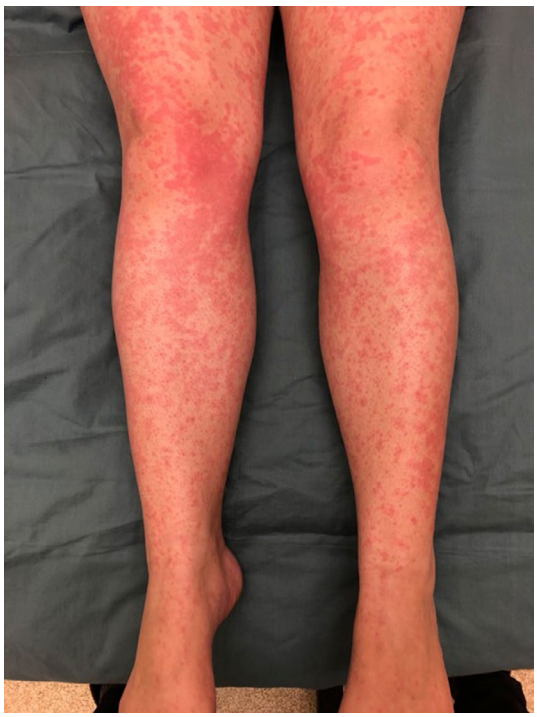

FIGURE 1 Bilateral legs of patient upon presentation to dermatology

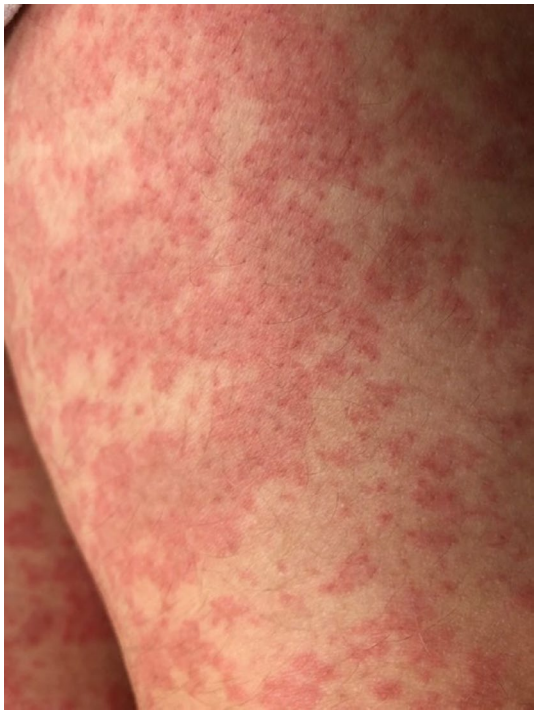

FIGURE 2 Close-up image of urticaria multiforme on patient's left leg

during clinical trials, although morphology was not specified.[5] Factors known to cause urticaria multiforme eruption to include antecedent viral infection, bacterial infection,

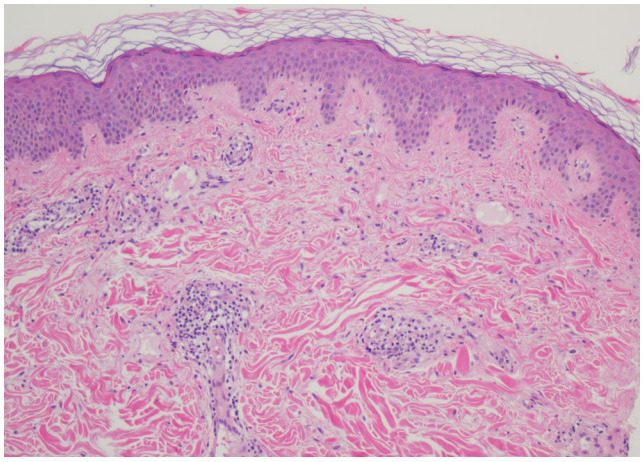

FIGURE 3 Spongiotic epidermis with a mild superficial perivascular and periadnexal lymphocyte-predominant infiltrate (H&E, 10×)

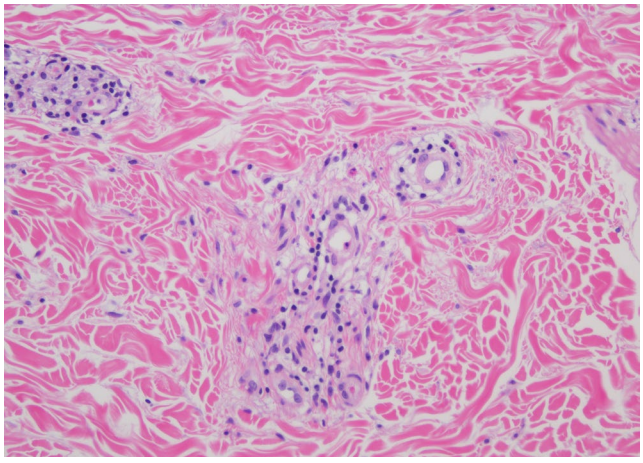

FIGURE 4 Dermal vascular plexuses with superficial perivascular and interstitial lymphocytic infiltrates, occasional dermal eosinophils, and rare mast cells (H&E, 20×)

antibiotics (eg, amoxicillin, cephalosporins, macrolides), or antipyretics (eg, aspirin, acetaminophen).[1] As noted above, the patient had not had any recent infections and had not recently started any other new medications. The timing of the start of Trikafta fits well with the timing of clinical presentation. The patient subsequently cleared within 1 week of discontinuation of Trikafta, further suggesting the diagnosis of urticaria multiforme secondary to Trikafta.

We feel it is important that clinicians are aware of the possible urticaria multiforme-like reaction associated with Trikafta described in our case. Trikafta is approved for CF patients 12 years and older, making it relevant to a wide patient population. Given this information, we hope that providers will be more prepared to counsel, diagnose, and treat patients if they experience a similar reaction after starting Trikafta.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

JS: wrote the initial draft of this manuscript. PC: contributed to further edits and revisions of the drafts. VM: provided figures and image captions. BZ: provided editorial support and reviewed the final manuscript. All authors: approved the final content. This case has not been published previously.

ETHICAL APPROVAL

Hereby, I, Julian Stashower consciously assure that the following are true:

1. This material is the authors' own original work, which has not been previously published elsewhere.
2. The paper is not currently being considered for publication elsewhere.
3. The paper reflects the authors' own research and analysis in a truthful and complete manner.
4. The paper properly credits the meaningful contributions of co-authors and co-researchers.
5. The results are appropriately placed in the context of prior and existing research.
6. All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
7. All authors have been personally and actively involved in substantial work leading to the paper and will take public responsibility for its content.

INFORMED CONSENT

Pictures are not identifiable and patient provided verbal consent.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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REFERENCES

1. Shah KN, Honig PJ, Yan AC. "Urticaria multiforme": a case series and review of acute annular urticarial hypersensitivity syndromes in children. *Pediatrics*. 2007;119(5):e1177-e1183.
2. Emer JJ, Bernardo SG, Kovalerchik O, Ahmad M. Urticaria multiforme. *J Clin Aesthet Dermatol*. 2013;6(3):34-39.
3. Hoy SM. Elexacaftor/ivacaftor/tezacaftor: first approval. *Drugs*. 2019;79(18):2001-2007.
4. Keating D, Marigowda G, Burr L, et al. VX-445–tezacaftor–ivacaftor in patients with cystic fibrosis and one or two Phe508del alleles. *N Engl J Med*. 2018;379(17):1612-1620.
5. Middleton PG, Mall MA, Dřevínek P, et al. Elexacaftor–tezacaftor–ivacaftor for cystic fibrosis with a single Phe508del allele. *N Engl J Med*. 2019;381(19):1809-1819.

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