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An acneiform eruption associated with elexacaftor/tezacaftor/ivacaftor treatment

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To the Editor:

Elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) is a new, highly effective cystic fibrosis (CF) treatment [1]. To our knowledge, acneiform lesions secondary to ELX/TEZ/IVA have not been described in the literature. We report the case of a patient who developed an ELX/TEZ/IVA-induced acneiform eruption that led to medication cessation. Our report highlights this side effect so that clinicians may counsel their patients, place timely referrals, and increase medication adherence.

A 29-year-old man with CF began ELX/TEZ/IVA treatment in April 2019 with marked improvement of his respiratory symptoms. Four months later, he developed papular and comedonal lesions on the extremities, trunk, and face. The lesions evolved, forming cysts and widespread open comedones. In November 2019, the patient decreased the frequency of ELX/TEZ/IVA to every other day to mitigate this side effect. However, his acneiform lesions progressed and he discontinued the medication in January 2021. Inflammatory lesions improved, but his open comedones remained. He had no prior history of acne, abscesses, or hidradenitis suppurativa and had never been seen by a dermatologist.

In April 2021, the patient was hospitalized for CF with liver involvement resulting in ascites, at which time

ELX/TEZ/IVA therapy was re-initiated. His other home medications included empagliflozin, pancrelipase, furosemide, and spironolactone, all of which he had taken for at least one month prior to hospitalization.

Two weeks after re-initiation of ELX/TEZ/IVA, dermatology was consulted to evaluate a nodule under the left breast. The patient reported the nodule started five days prior as a "pimple" which grew into a non-pruritic, mildly tender, cystic lesion. He noted several similar lesions on his back and suprapubic region. He also reported the concurrent onset of aesthetically bothersome "pimples and bumps."

On examination, the patient was found to have hundreds of open comedones and acneiform papules and cysts on the face and trunk (**Figure 1A**). He had several scattered fluctuant nodules and cysts on the trunk and suprapubic region and sparse heme-crusts papules and nodules on the bilateral lower extremities (**Figure 1B**). Basic labs were remarkable for leukopenia, anemia, thrombocytopenia, and elevated alkaline phosphatase secondary to CF. Wound, tissue, acid-fast bacilli, and fungal cultures of a cystic lesion on the left breast were unremarkable. Punch biopsy demonstrated an inflamed epidermoid cyst.

The patient was diagnosed with ELX/TEZ/IVA-induced comedonal and inflammatory acne and

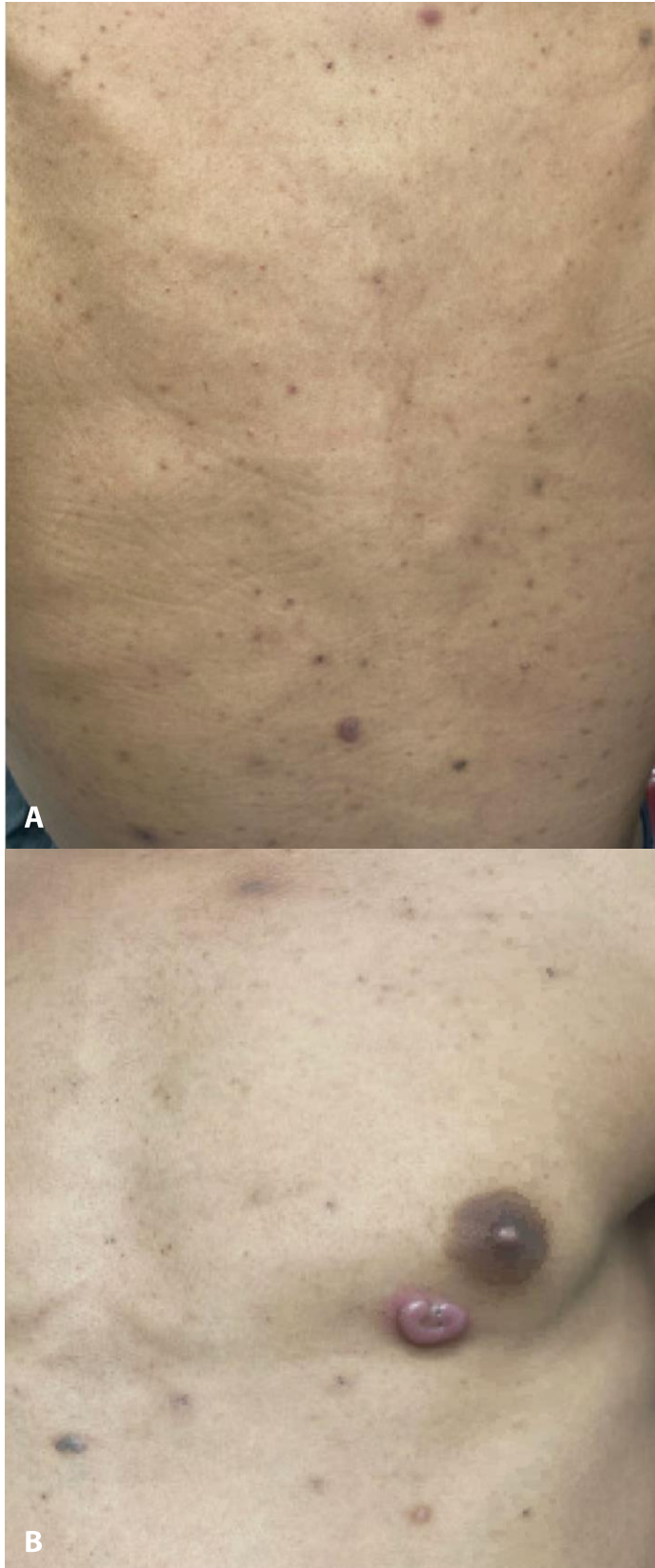


Figure 1. A) Back. Open comedones, acneiform papules, and cysts. **B)** Left breast. An erythematous, fluctuant, irregularly shaped nodule with surrounding open comedones and acneiform papules.

Hurley Stage one hidradenitis suppurativa. He was prescribed clindamycin 1% lotion for tender lesions and advised to follow up in the outpatient dermatology clinic to initiate topical retinoid therapy.

Elexacaftor/TEZ/IVA is generally considered to be safe and well-tolerated [1]. The only cutaneous side effect reported in published studies is a non-specific rash, occurring in about 10% of patients [1]. In addition to rash, the drug package insert for ELX/TEZ/IVA notes acne as an adverse reaction occurring at a frequency of 2-5% [2]. The package insert for ivacaftor, one component of ELX/TEZ/IVA, also reports acne as an adverse reaction in 4-7% of patients [3]. However, this side effect has not been described in the literature for either ELX/TEZ/IVA or ivacaftor.

Although information on acneiform eruptions associated with these medications is lacking in the scientific literature, a quick internet search finds numerous patient reports of new-onset acne with ELX/TEZ/IVA treatment. The mechanism behind this effect is unclear, but there may be an indirect impact on the pilosebaceous unit.

Acne is known to be associated with psychological burden including stress, anxiety, depression, suicidal thoughts/attempts, and stigmatization [4]. As such, development of acneiform eruptions may represent a significant barrier to long-term treatment with ELX/TEZ/IVA. The cutaneous side effects of this drug caused our patient to alter, and ultimately, discontinue his treatment despite noticeable respiratory function improvement. Patients should be counseled regarding this side effect and referred to dermatology for effective treatments to optimize adherence to ELX/TEZ/IVA therapy.

Potential conflicts of interest

The authors declare no conflicts of interest.

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