Acne fulminans in a transgender boy after an increase in testosterone dosage

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INTRODUCTION

Acne fulminans (AF) is a rare, severe variant of inflammatory acne that is characterized by painful erosions and hemorrhagic crusts that heal with severe, disfiguring scars. It can be associated with systemic symptoms such as fever, malaise, leukocytosis, thrombocytosis, polyarthralgia, hepatomegaly, and high levels of inflammatory markers and transaminases.[1,2] The pathogenesis of AF is unknown, although alterations in innate immunity, autoimmunity, adaptive immunity, and autoinflammation have been proposed. There are 4 subtypes of AF: AF with systemic symptoms, AF without systemic symptoms, isotretinoin-induced AF with systemic symptoms, and isotretinoin-induced AF without systemic symptoms, which is the most common form.[3] AF is most frequently seen in Caucasian adolescents between the ages of 13 and 22 who were assigned male at birth. Other risk factors include genetics, increased testosterone levels, use of anabolic steroids, and higher initial doses of isotretinoin. In this report, we discuss an unusual case of AF developing in a transgender adolescent who was taking testosterone.

Abbreviations used:

AF: acne fulminans
GAHT: gender-affirming hormone therapy

CASE REPORT

A 16-year-old transgender male (assigned female at birth) with no significant medical history was started on 0.125 mg of subcutaneous testosterone weekly for gender-affirming hormone therapy (GAHT). At his 6-month follow-up visit, he was noted to have more acne than at baseline and was given benzoyl peroxide and tretinoin, which had minimal effect. His testosterone dose was increased according to his provider's GAHT protocol, and within a few weeks of the dose increase, he presented with a painful cyst with hemorrhagic crust on his right side of the jawline (Fig 1). He was seen at urgent care and prescribed doxycycline for a presumed facial abscess, which he was unable to tolerate. At his first dermatology visit 1 week later, his acne had rapidly progressed on his face and bilateral shoulders with numerous open and closed comedones and many pink, follicular-based acneiform papules, pustules, and nodules (Fig 2). He was afebrile and denied malaise or arthralgias. White blood cell count and transaminases were normal. He was diagnosed with AF without systemic features in the setting of increased exogenous testosterone. He was started on a 1-month prednisone taper beginning at 40 mg daily, with continued tretinoin and benzoyl peroxide, and was registered in the iPLEDGE system with his first pregnancy test. At his follow-up visit in 1 month, he was started on low-dose isotretinoin based on the *Journal of the American Academy of Dermatology*'s evidence-based recommendations of 0.1 mg/kg/day.[3] His weight was 68.5 kg at the time, and therefore an initial dose of 10 mg daily for 30 days was prescribed. Concurrently, he was covered with another 1-month prednisone taper. He was continued on low-dose isotretinoin (10 mg daily for 4 months, then 20 mg

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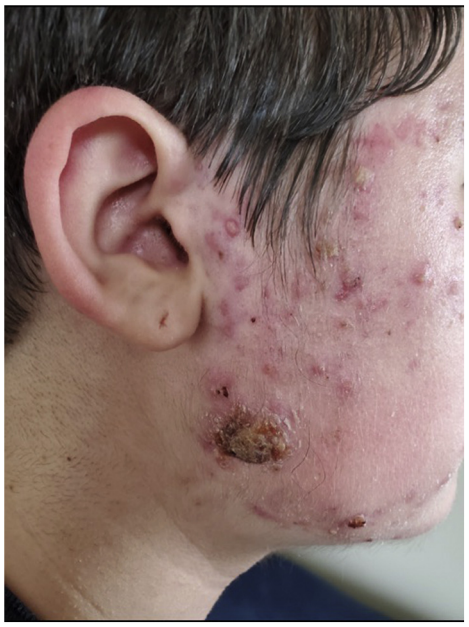

Fig 1. Photograph provided by the patient showing cyst with hemorrhagic crust on his right side of the jawline.

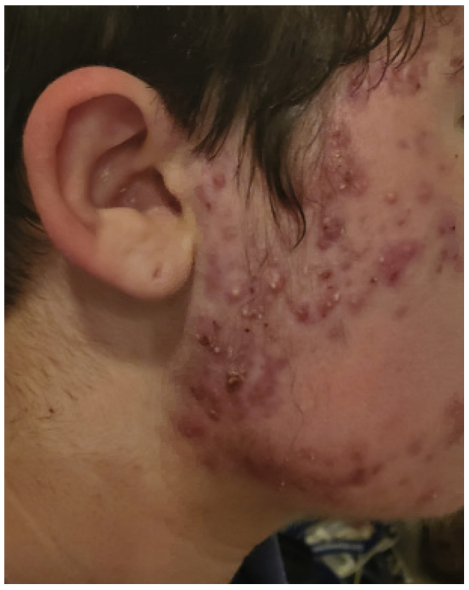

Fig 2. Clinical examination revealed numerous open and closed comedones and many pink, follicular-based acneiform papules, pustules, and nodulocystic lesions, most notably on the right cheek.

daily for 3 months) and has seen a gradual improvement in his acne, although significant scarring is noted (Fig 3). With his stable course, his isotretinoin dose was increased to 40 mg daily for 1 month. He is currently receiving the recommended standard dose of 1 mg/kg (80 mg) daily and has been clinically stable and asymptomatic.

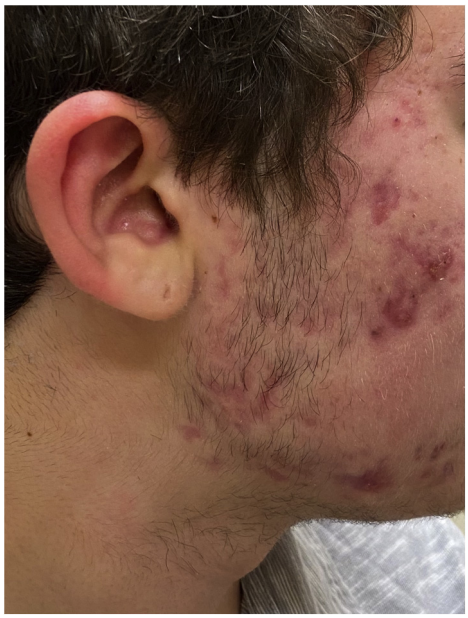

Fig 3. Clinical examination at the most recent follow-up visit revealed resolving erythematous nodulocystic acne lesions on a background of fading erythema with interspersed icepick scarring on the right cheek.

DISCUSSION

Transgender men and boys along with genderqueer or nonbinary individuals have increasing access to GAHT; they may choose to use testosterone therapy to induce virilization, such as male-pattern hair growth, voice deepening, and increased muscle bulk.[4,5] Access to GAHT for transgender people is a critical part of treatment for gender dysphoria and is an important step forward in creating health equity for this historically disenfranchised community.[6] One adverse effect of testosterone therapy can be the development or worsening of acne, which is typically mild and peaks within the first 6 months of therapy. Gradual improvement is noted within the first year, although the acne can be persistent and last for years after the initiation of testosterone therapy.[5,7] A study by Wierckx et al[5] evaluating the short- and long-term clinical effects of testosterone on the skin showed that most participants had little to no acne after long-term treatment and that the severity of acne was not correlated with individual serum testosterone levels. However, our patient presented with AF 8 months into his testosterone treatment, and his presentation was correlated with a standard increase in his testosterone dose. Although there is a theoretically increased risk of AF with testosterone treatment, there are few documented cases, particularly in transgender individuals.[3,8] Treatment of AF in the setting of GAHT typically starts with a combination of oral steroids and low-dose isotretinoin

rather than topical retinoids or tetracycline antibiotics.[1,3]

The requirement for iPLEDGE enrollment is worth discussing explicitly. This Food and Drug Administration program refers to transgender men as "female patients who are or may become pregnant." It enforces mandatory counseling and e-learning on contraception as well as confirmation of either abstinence or 2 forms of approved contraception. Additionally, it requires monthly pregnancy tests. After initial registration, patients in this category must be using 2 forms of contraception or practicing abstinence for 30 days, regardless of their sexual behavior, before they can be prescribed isotretinoin. For individuals with AF assigned female at birth who would benefit from rapid initiation of isotretinoin, this step acts as a barrier. Dermatologists enrolling transgender men and genderqueer or nonbinary individuals into this program must also recognize 3 population-specific ramifications of iPLEDGE. First, enrollment and participation in this program occur within the health care setting, a system in which transgender patients have historically experienced discrimination and mistreatment.[9] Second, the required contraceptive counseling must be tailored to the patient; traditional estrogen-progesterone contraceptive methods may be anathema for people using GAHT for masculinization. Finally, the required monthly pregnancy test is not benign. For transmasculine individuals, in-office or laboratory pregnancy testing may trigger gender dysphoria and may lead to actual or perceived "outings," which can raise serious safety concerns.[10] The Food and Drug Administration recently announced changes to the iPLEDGE program based on advocacy efforts from the American Academy of Dermatology Association to address these concerns. Since December 13, 2021, the patient risk categories have been reduced from 3 options to 2: patients who can get pregnant and patients who cannot get pregnant. The gender category has been removed, and the terminology has been changed to be more inclusive of transgender individuals. We acknowledge that this process is only one step toward addressing the population-specific concerns raised above.

A key takeaway from cases of AF in transgender people who are taking testosterone is patient-centered discussion of the risks and benefits of isotretinoin and oral steroids, rather than immediate discussion of stopping testosterone therapy. Patients should be aware that their acne is likely worsened by taking testosterone, but given the critical role that GAHT can play in the mental health and quality of life of transgender people,[6] clinicians should actively work with patients to maintain GAHT despite the rare complication of AF. Our patient's unusual presentation suggests that clinicians should be on the lookout for AF with increases in testosterone dose and counsel patients appropriately about returning to care immediately if they have an extreme acne flare. Although rare, AF during testosterone therapy should be anticipated and, if it occurs, treated aggressively with steroids and isotretinoin to reduce the potential for disfiguring scarring. Any discussions of reducing or stopping GAHT should be autonomy-supportive for patients and contextualized within the larger role that hormone therapy plays in gender affirmation and the patients' holistic wellness.

Conflicts of interest

Dr. Greenberg is a paid trainer for the Food and Drug Administration-required Nexplanon insertion training. Authors Lee, Ferri-Huerta, and Somers have no conflicts of interest to declare.

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