Treatement of acne and acne-related scarring with fixed combination clindamycin phosphate and benzoyl peroxide gel (1.2%/3.75%) and tretinoin gel microsphere 0.06% in an Asian American transgender female

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Abstract
Acne vulgaris is one of the most common skin diseases in the United States and can affect any gender or ethnic group. Post-inflammatory hyperpigmentation (PIH) and scarring from acne can have a negative psychosocial impact on patients. Skin of color patients are particularly prone to PIH, as the dark marks left from acne may take several months to resolve, far after the acne has cleared. Here, we report a case of moderate acne with associated scarring in a transgender, Asian American female who was successfully treated with fixed combination topical therapy with clindamycin phosphate and benzoyl peroxide gel 1.2%/3.75% and tretinoin gel microsphere 0.06%.

Keywords
Acne vulgaris, skin of color, hyperpigmentation, acne-related scarring, tretinoin, clindamycin, benzoyl peroxide, transgender dermatology, hormone therapy, estrogens

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Introduction
Acne vulgaris (AV) is one of the most common inflammatory skin diseases, affecting people of all genders and ethnic groups. AV lesions and their sequelae including scarring and post-inflammatory hyperpigmentation (PIH) can have a significant psychosocial impact, resulting in depression, suicidal ideation and negative body image issues. This effect may be magnified in lesion, gay, bisexual, transgender, questioning + other (LGBTQ+) patients, who are already at increased risk for psychological distress, depression, self-harm and suicide. The effect may be magnified in these patients.

Acne is a well-documented side-effect of exogenous androgen therapy used to either manage gender dysphoria or promote the development of masculine secondary sexual characteristics in female-to-male transgender patients. One study of 20 transgender men showed the prevalence of facial acne increased from 35% to 82%, 6 months after starting testosterone therapy. Acne has not, however, been previously reported in male-to-female transgender patients undergoing hormone therapy with estrogens and anti-androgens to induce breast formation, reduce male pattern hair growth, and change fat distribution. Conversely, these medications have been used to effectively clear acne in women when used alone or in combination. Although acne affects all ethnic groups, differences exist in the presentation, sequelae of, and therapy for, acne in certain skin types. Indeed, Hayashi et al. reported that 90.8% of Japanese patient’s with acne had some degree of acne scarring. Because of its relatively increased level of melanin pigmentation, Asian skin has also been observed to be more prone to develop PIH when inflamed or injured. In addition, Asian skin has been found to have the least skin barrier strength, the lowest degree of maturation, and consequently, the highest degree of skin sensitivity making it more prone to irritation to certain topical agents. Effective treatment

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can prevent future risk. Topical therapies for acne such as clindamycin, benzoyl peroxide (BP) and tretinoin remain the most common and often effective treatment options for mild-to-moderate acne and may also reduce severe acne. In addition, tretinoin has anti-inflammatory and bleaching properties which are important factors for reversing acne scarring and PIH.

Here, we present a case of acne and acne-related scarring in an Asian American transgender woman that was successfully treated with a fixed combination topical therapy of clindamycin phosphate and BP and tretinoin 0.06% gel microsphere.

Case
A 29-year-old Asian American transgender female presented with a 15-year history of recurrent red facial acne and scarring (Figure 1). Based on clinical assessment, she was given an acne Evaluator’s Global Severity Score (EGSS) of 3 (moderate) and a global acne scar severity grading scale of 3 (moderate). She had tried a generic tretinoin 0.025% topical cream a few years prior to presentation, but discontinued use due to cutaneous side-effects including burning, itching and dryness.

Past medical history was otherwise unremarkable, aside from severe depression. As a transgender woman, she had been assigned male gender at birth, but identified as female and had begun hormonal transition 2 years prior, with estrogen and the 5α-reductase inhibitor finasteride. An endocrine analysis was not performed as her hormonal status was already being managed by her transgender health care team and interpretation of laboratory results in the male to female transgender population is notoriously difficult.

In accordance with the American Academy of Dermatology guidelines for moderate acne which recommend a first-line combination of benzoyl peroxide, topical retinoid and a topical antibiotic (erythromycin or clindamycin), she was prescribed the topical combination therapy: tretinoin gel 0.06% microsphere (Retin-A-Micro, Ortho Dermatologics; Bridgewater, NJ) nightly as tolerated and clindamycin phosphate and benzoyl peroxide gel, 1.2%/3.75% (Onexton, Ortho Dermatologics; Bridgewater, NJ) daily, as these products have demonstrated cutaneous tolerability in clinical studies. She was advised to avoid sun exposure or use SPF 15+ and cover treated areas with protective clothing if in the sun.

At her 2-month follow-up appointment, her acne had decreased to an EGSS of 1 (almost clear) and acne scaring to a severity grading scale of 2 (mild) (Figure 2). No treatment-related side-effects were reported. The patient stated that this was the first time since puberty that her acne was under control, and she finally felt confident about her appearance.

Discussion
To our knowledge, this is the first reported case of persistent acne in a male to female transgender adult. The effects of acne frequently go beyond cutaneous sequela. Acne frequently places a heavy emotional and psychological burden on patients that may be far worse than its physical impact, often independent of its severity. In transgender persons, in particular those receiving gender-affirming hormones, acne can increase psychosocial distress.

In Asian patients, acne-associated PIH and scarring can be equally or more distressing than acne. It is therefore unsurprising that this patient, with her 15-year history of acne and scarring, also had a long history of depression. Acne had begun in puberty and may have been associated with rising hormone (androgen) levels, had persisted through adult life and had not improved despite high-dose estrogen therapy used to inhibit testosterone and induce feminizing effects as part of her male-to-female transition. This is surprising as estrogen is known to both suppress sebum production and through its metabolism in the liver, it increases sex hormone-binding globulin (SHBG). SHBG has a high affinity for testosterone and will bind to it preferentially over estrogen. As testosterone
is the primary androgen involved in acne, increased SHBG should lead to improvement in acne.

Although hormone therapy had not controlled this patient’s acne and she had failed on topical tretinoin cream in the past, fixed combination topical therapy with clindamycin phosphate and benzoyl peroxide gel 1.2%/3.75% and tretinoin 0.06% gel microsphere resulted in significant improvements in both acne and acne-associated scarring.

Tretinoin has been shown to decrease the synthesis of matrix metalloproteinases and increase dermal procollagen and collagen synthesis, which may improve and prevent acne scarring. Adverse effects of topical tretinoin can include local skin irritation, erythema, blistering, dryness and peeling, although these appear mitigated with microsphere technology.

Benzoyl peroxide has known bactericidal, keratolytic, and mild anti-inflammatory effects. Clindamycin is an antibiotic that works by targeting the 50s subunit of bacterial ribosomes and interfering with protein synthesis, thereby exerting antibacterial effects; it also has anti-inflammatory properties. Theoretically, because of the differences in mechanism of action, when used in combination, these products may result in better clinical improvement than when used individually.

**Conclusion**

The stigma of facial acne can only be understood by those afflicted. When acne is accompanied by scarring the perceived disfigurement often results in significant psychosocial distress. This can be further magnified in LGBTQ+ patients who already have an elevated risk of depression and suicide. In transfeminine patients with acne recalcitrant to hormone therapy, endocrine evaluation may be considered to titrate feminizing hormone doses and to rule out underlying hyperandrogenic states.

First-line treatment recommendations for moderate acne include a combination of benzoyl peroxide, topical and/or oral antibiotic, and a topical retinoid. Timely selection of agents that are formulated to be effective against both inflammatory and non-inflammatory acne enhance matrix repair and reduce scarring, while minimizing local adverse events may enhance both physical and psychological patient outcomes.

**Author note**
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