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Dermatologic conditions in transgender populations

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Synopsis

Transgender persons face unique burdens of dermatologic conditions related to cutaneous effects of gender-affirming hormone therapy and procedures. Skin diseases in transgender patients often underdiagnosed and underrecognized despite potential for significant impairments quality of life and mental health from skin diseases. We discuss basic pathophysiology, diagnosis and treatment of common skin diseases in the transgender populations. For transmasculine patients, common conditions include acne vulgaris and male pattern hair loss. For transfeminine patients, common conditions include hirsutism, pseudofolliculitis barbae, and melasma. Post-procedural keloids and other cutaneous complications are discussed. Unique aspects of skin health in transgender persons should be considered in the context of multidisciplinary gender-affirming care.

Keywords

Transgender; Dermatology; Acne; Hair loss; Hirsutism; Keloid; Gender Affirmation

Introduction

Transgender persons, particularly those receiving gender-affirming hormone and/or surgical treatments, may face specific dermatologic concerns. Hormone therapies and gender-affirming procedures can affect the skin and change the prevalence and presentation of routine skin conditions. Transgender patients with dermatologic disease may face body image dissatisfaction, which is closely tied to levels of gender dysphoria, anxiety, depression, and other secondary health problems.[1] Transgender patients also face greater barriers to care and often benefit from a comprehensive approach to care from providers they do see.[2] Therefore, it is important for clinicians caring for transgender persons should recognize and address common dermatologic conditions relevant to gender-affirming

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treatments. We will review the clinical presentations, diagnosis, and treatment of skin conditions common in transgender patients, particularly for transmasculine and transfeminine patients undergoing gender-affirming endocrine or surgical therapies, as well as indications for dermatology referral.

Hormone therapy

Gender-affirming hormone therapy for transmasculine persons consists of testosterone to develop secondary male sex characteristics.[3] In the skin, testosterone increases sebum production, increases facial and body hair growth, decreases scalp hair, and redistributes body fat (Table 1).[3] Gender-affirming hormone therapy for transfeminine persons consists of estrogen and/or antiandrogens such as spironolactone in the USA and cyproterone in most of Europe and GnRH agonists in the UK.[4] In the skin, estrogen decreases skin sebum production, reduces facial and body hair growth, promotes epidermal thickness, stimulates melanocytes, and changes sweat and odor pattern.[3,5] Masculinizing and feminizing effects in the skin may be observed within one month of hormone therapy initiation but may not reach maximum effect until a few years later.[3]

Common Transmasculine Skin Conditions

Acne vulgaris

Acne vulgaris is a common and chronic skin disease characterized by the formation of comedones (blackheads and whiteheads), papules, pustules, nodules, and cysts.[6] Clogged hair follicles, increased skin sebum production, and the inflammatory response incited by *Propionibacterium acnes* contribute to the development of acne.[7] Acne is frequently driven by androgens.[8-10] Other risk factors may include chest binding, diet, stress, and medications – such as corticosteroids and lithium.[8,11]

Acne often impacts the psychosocial health of affected individuals.[12] Conspicuous acne lesions, secondary post-inflammatory hyperpigmentation and scars can be disfiguring and stigmatizing (Figure 1). Patients with acne experience higher rates of low self-esteem, depression, and withdrawal from social activities and relationships.[13] A survey of 3,775 18-19 year-old young adults found those with significant acne were more likely to have suicidal ideation and mental health problems as compared with those without acne.[14] Sexual minority patients with acne were shown to also have increased risks of suicidal ideation and antidepressant use as compared with sexual minority patients without acne.[15]

This is particularly relevant due to high rates of acne with testosterone therapy.[11] For example, one study of 21 transmasculine adults found 94% had facial acne and 88% back acne after four months of testosterone therapy, an increase from pre-treatment rates of 29% and 17%, respectively.[16] While the natural history of hormone therapy-induced acne remains poorly understood, small studies suggest that acne severity often peaks in the first six months of testosterone therapy and may gradually improve over 1-2 years.[17-19] The psychosocial effects of acne may compound gender dysphoria and high pre-existing rates of psychiatric comorbidity in transgender patients.[20,21] Since clinicians often underestimate the patients' negative experience and impact from acne, signs and symptoms of acne should be

inquired and addressed, and treated if symptomatic, even if considered mild based on the clinician's initial impression.[21]

Acne severity should direct initial therapy (Figure 2).[22] The Investigator Global Assessment severity scale (Table 2) is a commonly used tool to classify acne as clear, almost clear, mild, moderate, or severe. Acne with cysts, nodules, or significant scarring is often treated as severe.[22] First-line therapy for mild acne is a topical retinoid, topical benzoyl peroxide, or a combination of the two.[7] Topical retinoids, such as tretinoin, adapalene, and tazarotene, are comedolytic and anti-inflammatory agents that serve as the core of acne therapy.[7] They help resolve precursor microcomedone lesions and improve secondary scarring and hyperpigmentation.[23] Topical adapalene 0.1% gel is now available over-the-counter and may be considered for patients whose insurance plans do not cover topical retinoids. Common side effects of topical retinoids include photosensitivity, skin dryness, peeling, erythema, and irritation. Side effects are minimized by slow up-titration and typically peak in the first 2-4 weeks of use, improving over time. Anticipatory guidance is crucial to improve adherence and prevent premature treatment discontinuation.[23] Patients should be counseled to apply a small pea-size amount every 2-3 nights, then gradually increase frequency to nightly over 2-4 weeks as tolerated, with concurrent daily moisturizer and sunscreen use.[7] Benzoyl peroxide (BP, available over the counter in 2.5%-10% washes, creams, or gels) is effective for mild to moderate inflammatory acne. It can be used as monotherapy or in combination with various concentrations of topical clindamycin or erythromycin and/or topical retinoids. Notably, current guidelines do not recommend topical antibiotic monotherapy without BP due to emerging bacterial resistance. For moderate acne, combination topical therapy with BP +/− topical antibiotics +/− topical retinoids should be initially used. Systemic antibiotics – most commonly oral doxycycline or minocycyline – should also be considered for moderate to severe acne. Oral antibiotics should be limited to the shortest possible duration (<3 months). Concurrent topical therapy is crucial to sustain acne improvement following antibiotic tapering. Patients with moderate to severe acne, as well as those with significant postinflammatory hyperpigmentation or scarring, should be referred to dermatology for aggressive treatment to prevent further scarring or disfiguration.

Oral isotretinoin has been effective at treating severe, refractory, or nodulocystic hormone-induced acne in transgender patients without interfering with testosterone dosing.[18] Isotretinoin is a potent teratogen and all U.S. patients are required to registered in the iPLEDGE system by the U.S. Food and Drug Administration. Isotretinoin patients with reproductive potential must concurrently use 2 forms of effective contraception and undergo monthly pregnancy tests and counseling with their isotretinoin prescriber. Unfortunately, iPLEDGE currently enforces a gender-binary patient classification system requiring patients to be registered and provided contraception management based on sex assigned at birth rather than focusing on anatomic inventory and sexual behaviors with reproductive potential.[24] Gender-neutral reform of the iPLEDGE system has been advocated. Notably, isotretinoin may be associated with increased risks of depression and suicidality, as well as delayed surgical wound healing for up to 6-12 months after isotretinoin completion. Multidisciplinary care coordination among dermatologists, mental health providers, gynecologists, endocrinologists, and/or surgeons is crucial.

Male Pattern Hair Loss / Androgenetic alopecia

Male pattern hair loss (MPHL), also known as androgenetic or androgenic alopecia, is the most common cause of progressive hair loss. The multifactorial causes include age, androgens, and genetic predisposition.[25] In cisgender men, MPHL is associated with anxiety, depression, and sexual dysfunction.[26]

MPHL is characterized by hair loss in the temporal scalp, midfrontal scalp, or vertex area of the scalp in a “horseshoe” pattern. The mid-occipital region is mostly unaffected.[27] Circulating 5α-dihydroxytestosterone (DHT), converted from testosterone by 5α-reductase, interacts with androgen receptors in hair follicles. DHT miniaturizes scalp hair follicles and shortens the anagen stage that is the primary growth stage of hair, resulting in progressively decreasing hair coverage of the scalp.[28] Concomitant nail pitting, scalp itch, or focal hair loss beyond the scalp vertex may warrant dermatology referral.[28]

Hormone-induced MPHL presents similarly in transmasculine patients as in cisgender men. It often begins a few years after initiation of testosterone.[17,29] A cross-sectional study of 50 transmasculine patients showed mild to severe hair-loss in 62% of the participants on long-term testosterone; only one transmasculine person acquired MPHL within the first year of therapy.[17] MPHL may be a desirable masculine feature for some TM patients, but unwanted by others.[30]

Topical minoxidil and oral finasteride are first-line therapies for MPHL.[29] Topical minoxidil (brand name Rogaine), a potent vasodilator, is available over-the-counter for men as a 5% solution or foam. It is safe for long-term use and improves hair survival, increases the duration of the anagen growth phase, revitalizes hair-keratin proteins, and decreases inflammatory signals on the scalp.[31-33] In one study, 51% of patients noted benefit from 5% minoxidil compared to 26% with placebo and significantly higher hair count was noted in the minoxidil group.[34] Side effects may include scalp irritation, dryness, itching, and redness. Patients with MPHL refractory to minoxidil should be referred to a dermatologist for more extensive treatment. Oral finasteride, an FDA-approved treatment for MPHL, is a competitive inhibitor of type II 5α-reductase enzyme on hair follicles to inhibit conversion of testosterone to DHT. It improves scalp coverage in cis-men, one meta-analysis suggested a 25% increase in hair counts.[26,35,36] It does not interfere with serum testosterone level in transmasculine patients but effects on secondary sex characteristics are still unclear.[30,37] Some have suggested that finasteride should be delayed until all desired gender-affirming changes secondary to hormone therapy are complete (usually after two years of testosterone therapy).[30] Finasteride was safe and effective in one study of 10 transmasculine patients.[37] Side effects of finasteride may include teratogenicity, sexual dysfunction, depression, breast enlargement, and the potential to mask elevations in PSA.[25]

Common Transfeminine Dermatologic Conditions

Hirsutism / Pseudofolliculitis barbae

Estrogen and antiandrogen treatments generally do not cause cessation of facial hair growth.[38] Facial hair is visually prominent and common male secondary sex characteristic that is associated with body image dissatisfaction in transfeminine persons.[39] Facial hirsutism in

transfeminine persons can be disfiguring and contribute to gender dysphoria. Hair removal is considered medically necessary for transfeminine persons suffering from associated gender dysphoria[40]. Additionally, hair removal is important prior to genital gender-affirming surgeries. Hair follicles on surgically inverted skin flaps can lead to postoperative intra-vaginal or intra-urethral hair growth and serve as a nidus for irritation and infection.[30] Mild hirsutism can be treated with shaving, plucking, threading, waxing, or topical eflornithine (brand name Vaniqa), which is FDA-approved to treat hirsutism in women. More permanent treatment options for facial hair and for preoperative skin flap hair removal include electrolysis and laser hair removal (LHR).

The frequent shaving or trimming of facial hair in transfeminine patients with hirsutism can lead to pseudofolliculitis barbae (PFB), also known as razor bumps. PFB is a common condition of the bearded area, axilla, pubic region, and legs.[41] It is a chronic inflammatory disorder that primarily affects individuals with curled hair. Prevalence rates reach 80% in African-American and Hispanic cisgender men and cisgender women with facial hirsutism or hypertrichosis.[42,43] Curved hair can grow back into the skin after being shaved or trimmed, causing inflammation and a foreign body reaction.[43] This presents as painful, itchy papules with erythema and hyperpigmentation. Post-inflammatory hyperpigmentation or keloid scarring may develop. Patients often find the disorder distressing and it may exacerbate gender dysphoria.[43] Discontinuation of shaving is typically curative for PFB, but this is generally inappropriate for transfeminine persons. It can be alleviated with proper shaving techniques or use of topical depilatories. Pre-shave preparation with mild soap and warm water is recommended before applying shaving cream, followed by shaving in non-overlapping and unidirectional strokes.[43] More likely, medical therapy will be needed (Figure 3). Topical retinoids and low-potency topical corticosteroid may be used as first-line therapy.[42] Combination BP and topical clindamycin may also reduce inflammation and lesion count.[44] Eflornithine may be added to reduce hair growth.[42] Destruction of hair follicles through LHR has become the gold standard for a permanent treatment option, although electrolysis can also be used.[45] PFB can be difficult to treat and early referral to dermatology should be considered to prevent post inflammatory hyperpigmentation and scarring.[29,46]

Dermal Fillers and Facial/Body Contouring

Facial feminization and body contouring procedures are common for transfeminine persons. Neuromodulators such as botulinum toxin A injections and dermal fillers yield immediate and long-lasting contouring and feminizing effect. Transgender individuals often face barriers to care and are affected by the high-cost of these procedures, and are at risk to engage in unsafe practices such as receiving fillers from unlicensed personnel.[47,48] Injections of illicit “filler” material by non-licensed persons are often toxic with complications including foreign-body granulomas; bacterial, fungal or mycobacterial infections; bleeding; pain; scarring and keloid formation; ulceration and necrosis; gross disfiguration; silicone embolism; and death (Figure 4).[47,48] Prevalence estimates of unlicensed silicone injections in the transfeminine population have ranged from 25-32%, this is of particular concern given the high complication rate of silicone injections.[49,50] Commonly used FDA-approved materials include collagen, hyaluronic acid, calcium

hydroxylapatite, poly-L-lactic acid, and polymethylmethacrylate.[51] Physicians should refer patients to licensed physicians, such as board-certified dermatologists and plastic surgeons, for dermal fillers, and to treat dermal complications from illicit filler use.[51]

Keloids and Hypertrophic scars

Keloids and hypertrophic scars are fibrous proliferation initially caused by dermal injury.[52] Hypertrophic scars and keloids present as firm and elevated flesh-colored papules and nodules.[53] Hypertrophic scars remain within the borders of the original scar, while keloids extend beyond the original scar. They are occasionally pruritic or painful. The appearance and physical discomfort can significantly impact a patient's quality of life and can lead to depression and social withdrawal.[54]

Like all individuals undergoing surgery, transgender patients undergoing gender-affirming surgery are at risk for hypertrophic scar and keloid development, especially if they have a darker-skin type, a family or personal history of keloids, or undergo surgery at high-tension skin areas such as the chest.[55] Keloid scarring can hinder a transgender patient's ability to "pass" as their identified gender.[30] Keloids and hypertrophic scars usually develop over a period of weeks or months. Surgical scar prevention and management should be discussed in at-risk patients. These patients should be carefully monitored even several months after surgery.

The first-line therapy for both treatment and prevention of keloid and hypertrophic scars is intralesional corticosteroid injections.[53] Repeated triamcinolone injections yield moderate reduction of the scar with 50% reoccurrence rate a few years after injection.[56] Surgical excision is an option for treatment-resistant keloids, but there is a high risk of reoccurrence without both post-operative and follow-up injections of intralesional corticosteroids.[53] Dermatology referral is warranted given the often refractory or recurrent nature of keloids.

Melasma

Melasma, also known as chloasma, is a skin pigmentary disorder that affects 8% to 40% of the population and is the one of the most frequent dermatologic complaint worldwide.[57] Melasma affects over 5 million Americans of all skin types and ethnic groups. Higher prevalence is observed in population in intertropical areas where there is greater exposure to UV, such as Washington, DC and Texas, and those of skin types III-V.[58] Melasma can be disfiguring and impactful to the patient's social life and emotional well-being.[59]

Melasma presents as symmetrical hyperpigmented brown to blueish-gray macules and patches on the sun-exposed skin, especially the face. Darker skin types, UV exposure, and hormones, particularly estrogen, are risk factors for melasma.[60] There is no pain or other associated symptoms. Transfeminine patients undergoing estrogen hormone therapy are at risk of developing melasma. Melasma management includes prevention of further hyperpigmentation and lightening of affected skin. Strict use of sunscreen and photoprotection is required. Hydroquinone 2-4% cream is the first-line skin lightening agent and can be combined with topical retinoids or corticosteroids.[60] Dermatology referral is warranted for treatment of refractory melasma with additional treatment options such as chemical peels and lasers.

Miscellaneous Dermatologic Conditions

Other dermatological conditions described in transgender persons is lichen sclerosus. Lichen sclerosus presents as crinkled or thickened patches of skin with pruritus and tenderness at the anogenital area.[61] LS has been reported in transfeminine patients and ought to be treated and monitored.[62,63] Complications of lichen sclerosus may include scarring, pruritus, pain, obliteration of external genitalia, as well as squamous cell carcinoma.

HPV infection and HPV-related skin diseases has also occurred in the neovagina of transfeminine patients. These include condylomas, which can be treated with topical application of trichloroacetic acid, cryotherapy, or surgical excision. Low-risk dysplasia, high-risk dysplasia, and HPV-related squamous cell carcinoma have also all been reported.[64,65]

The transgender population has increased prevalence of HIV rates and is subsequently at risk for HIV-associated dermatologic conditions.[66] HIV patients with normal CD4 T-cell levels can develop psoriasis, folliculitis, condylomas, seborrheic dermatitis, and dry skin. Lower T-cell levels can predispose patients to basal cell carcinoma, squamous cell carcinoma, Kaposi sarcoma, resistant herpes simplex, molluscum contagiousm, fungal infection, etc.[67]

Conclusion

Transgender persons face unique burdens of dermatologic conditions related to cutaneous effects of gender-affirming hormone therapy and procedures. Skin diseases in transgender patients often underdiagnosed and underrecognized despite potential for significant impairments quality of life and mental health from skin diseases. For transmasculine patients, common conditions include acne vulgaris and male pattern hair loss. For transfeminine patients, common conditions include hirsutism, pseudofolliculitis barbae, and melasma. Post-procedural keloids and complications of filler injections should be considered. Unique aspects of skin health in transgender persons should be considered in the context of multidisciplinary gender-affirming care. Greater recognition and implementation of dermatologic care will improve overall clinical outcomes of gender-affirming care in transgender patients.

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Key Points:

1. Skin conditions are often underdiagnosed and undertreated in transgender patients despite potential for significant impairments quality of life and mental health from skin diseases.
2. Hormone therapy affects the skin and changes the prevalence and severity of many dermatologic conditions, including acne, male-pattern hair loss, hirsutism and pseudofolliculitis barbae, and more.
3. Clinicians caring for transgender persons should recognize and address common dermatologic conditions relevant to gender-affirming treatments.

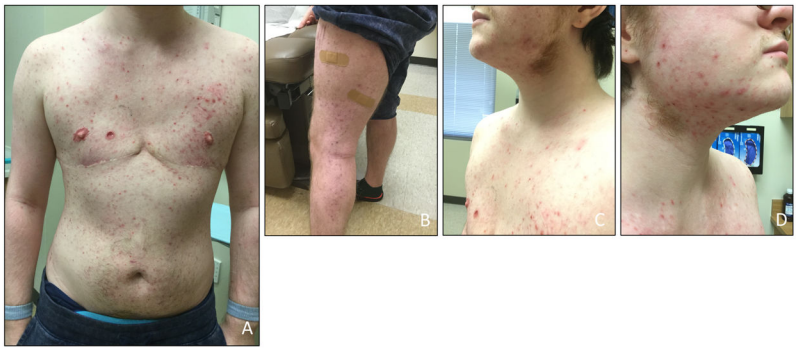

Figure 1.

Acne excoriee and pseudofolliculitis barbae in transmasculine patient on testosterone. (A) Demonstrates widespread erythema, comedones, and a large excoriated lesion on the R breast. (B) Demonstrates further comedones on the L leg, as well as excoriations. (C) and (D) Demonstrate comedones on the chest, and pseudofolliculitis barbae on the face.

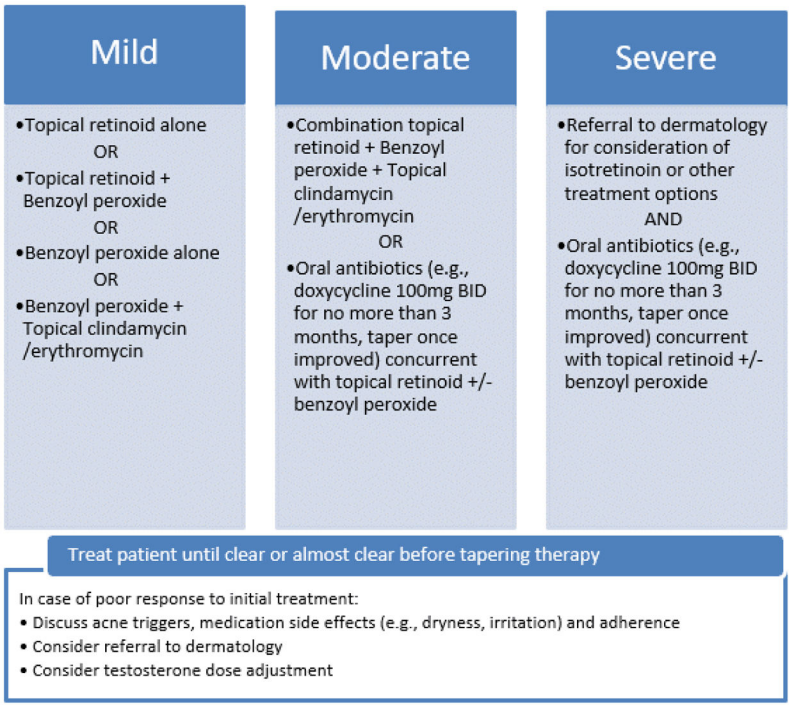

Figure 2:

Initial treatment options for mild, moderate, and severe acne as adapted from the American Academy of Dermatology acne guidelines

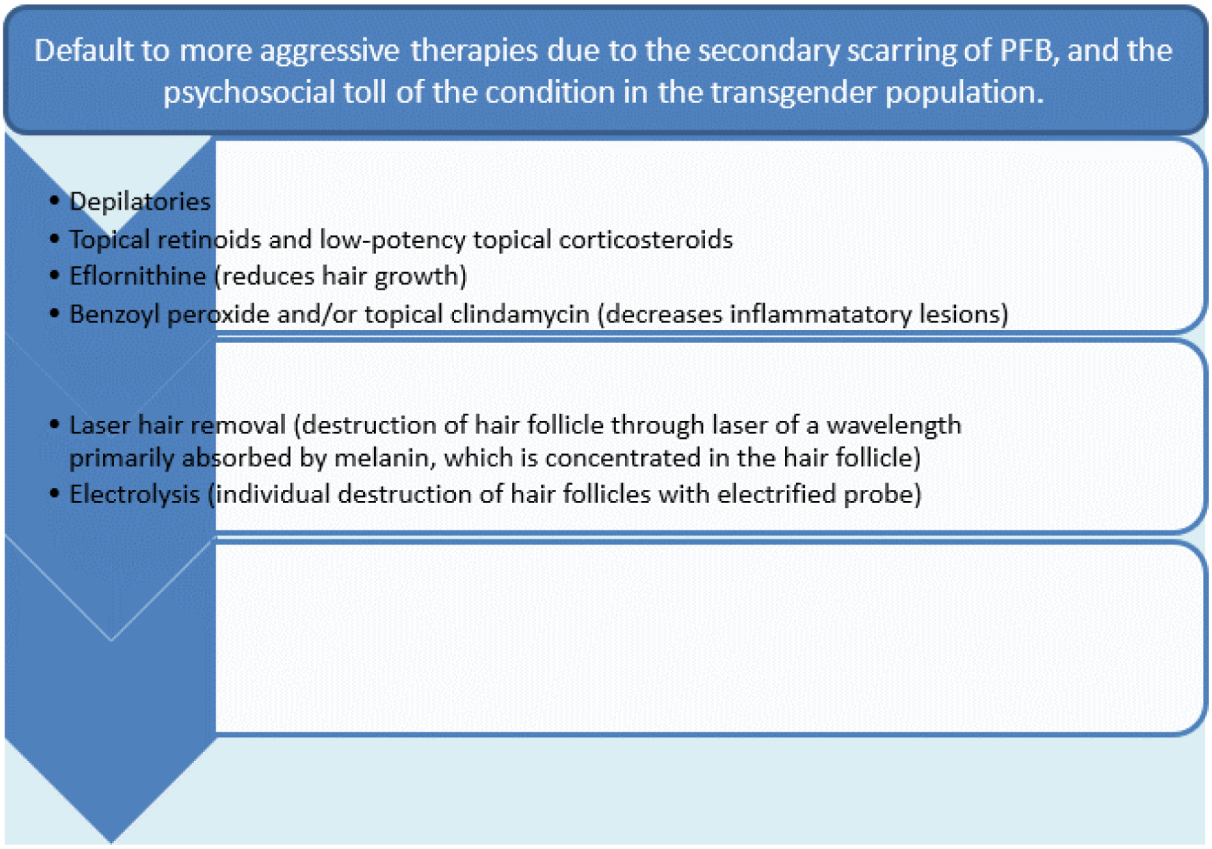

Figure 3:
Summary of treatment options for pseudofolliculitis barbae

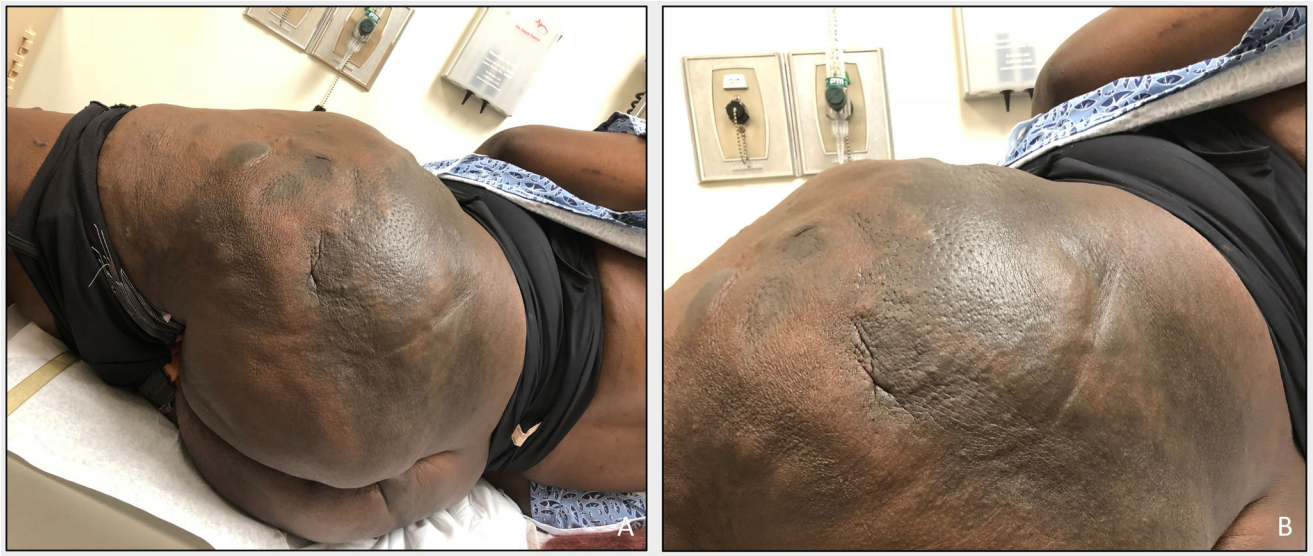

Figure 4.

(A) and (B) display a transfeminine patient with a painful silicon granuloma on the L buttocks.

Table 1:

Dermatologic effect of hormones

Androgens
• ↑ sebaceous gland sebum production
• ↑ facial and body hair growth
• ↓ scalp hair
• redistributed body fats
Estrogen
• ↓ sebaceous gland sebum production
• ↓ facial and body hair growth
• ↑ epidermal thickness
• ↑ melanocyte stimulation
• changed sweat and odor patterns

Table 2:

Investigator Global Assessment Scale for Acne

Grade	Clinical Description
0 (Clear)	No comedones (blackheads/whiteheads) or inflammatory papules/pustules
1 (Almost clear)	Rare comedones with 1 to a few inflammatory papules/pustules
2 (Mild)	Some comedones with no more than a few inflammatory papules/pustules; no nodules
3 (Moderate)	Many comedones with some inflammatory papules/pustules; up to 1 small nodule
4 (Severe)	Many comedones and inflammatory papules/pusules; more than 1 nodule

Data from *Acne Vulgaris: Establishing Effectiveness of Drugs Intended for Treatment- Guidance for Industry.* fda.gov/downloads/drugs/guidances: Food and Drug Administration, Center for Drug Evaluation and Research;2018.