



Medical dermatologic conditions in transgender women

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ABSTRACT

Many previous reviews and studies on transgender dermatology have highlighted the expected dermatologic manifestations of hormone affirmation therapy in transgender patients. Others have highlighted attitudes and practices of both transgender patients and medical professionals taking care of these patients. This review compiles data from other, lesser known aspects of transgender dermatology, including neovaginal concerns, neoplastic concerns (both neovaginal and cutaneous), autoimmune conditions, and the sequelae of injectable substances that have not been approved by the U.S. Food and Drug Administration. This review, like others, will be a stepping-stone and serve as an impetus for future research in transgender dermatology.

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Introduction

Transgender health is an emerging field of medicine that continues to gain momentum, especially in the context of increasing public awareness. Despite this attention, transgender people continue to face barriers to adequate care, such as lower insurance rates, low levels of physician comfort and knowledge of transgender medical issues, and persistent discrimination and prejudice (Gardner and Safer, 2013). Nonetheless, medical professionals have made strides in some areas of transgender care, such as the management of hormone therapy, surgical affirmation surgery, psychological counseling, and general health maintenance (Gardner and Safer, 2013). The field of dermatology is particularly critical because optimizing the external aspect of one's physical being is important in affirming transgender patients' gender identities.

Previous studies and observations have detailed the effects of hormones on hair and skin changes in transgender individuals. For those who undergo hormone treatment, male-to-female (MTF) transgender women have changes in distribution and reduced rates of hair growth on certain parts of their bodies, such as the face and chest; improved androgenic alopecia; and reduced rates of acne (Adenuga et al., 2012; Conrad and Paus, 2004; Gardner and Safer, 2013; Stevenson

et al., 2016). In contrast, female-to-male transgender men have increased rates of terminal hair growth on the face and axillary regions, increased susceptibility to androgenic alopecia, and increased rates of acne (Gardner and Safer, 2013; Harper, 2006; Maheux et al., 1994; Randall, 2008; Sauerbronn et al., 2000; Thornton, 2013; Wierckx et al., 2014).

Herein, we address neovaginal conditions, such as postsurgical complications and microflora. We also explore neoplastic disease both of the neovagina and elsewhere, autoimmune disease in transgender patients, and the cutaneous and systemic consequences of injectable substance use that have not been approved by the U.S. Food and Drug Administration. We have included a table that outlines the transgender medicine terminology we use in this article (Table 1). This review will increase the visibility of dermatologic issues in the transgender population and highlight areas for future investigation.

Neovaginal postsurgical complications

Neovaginas are surgically-constructed vulvo-vaginal tissues in transgender women that are designed to resemble the vaginas of cisgender women. Surgical techniques include using tissue from non-genital skin grafts, penile tissue, scrotal tissue, or intestinal tissue to create neovaginas (Bizic et al., 2014). The esthetic and functional utility of neovaginas are important for patients; thus, complications after transition surgery should be monitored closely.

One meta-analysis found that the most common complication was stenosis or stricture of the neo-urethra (14.4%), which could

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affect urinary function or predispose patients to urinary tract infections. One in 10 patients developed stenosis of the neovagina, which could affect sexual functioning.

Another significant complication of surgery is the development of intravaginal hairballs or the development of hair growth in the intravaginal area or introitus, which can be accompanied by pain and increased discharge. This can result from neovaginas created using tissue with hair follicles, such as the scrotum. This complication can be avoided by performing electrolysis or laser hair removal in these areas prior to surgery or by using nongenital skin grafts (Bizic et al., 2014; Suchak et al., 2015).

Other less common, but still significant, complications include wound infection (3.2%), neo-vaginal prolapse (1.6%), and recto-vaginal fistulas (1.0%; Dreher et al., 2018). The relatively common overall occurrence of complications should warrant the close monitoring of patients who have recently undergone surgery.

Neovaginal microbiology

Not much is known about the microbiome of the neovagina. One study found that five patients developed symptomatic neovaginal candidiasis after penile inversion vaginoplasty. All patients presented with discharge, unpleasant odor, and severe itch, and the symptoms resolved with topical treatment (de Haseth et al., 2018).

One study mapped the microflora of 50 transgender patients and found that most patients had mixed microflora of aerobic and anaerobic species that are native to the skin and intestinal tract. Similarities with microflora that are found in association with bacterial vaginosis were observed (Weyers et al., 2009). A study on whether this flora differs significantly from that of cisgender women and whether microflora differences correlate with the activity of any vulvovaginal disease would be worthwhile.

Neovaginal cancer risk

MTF patients with neovaginas could be at risk for certain types of vulvovaginal cancer. A case report showed the development of human papilloma virus (HPV)-associated squamous cell carcinoma in a neovagina that was created from scrotal tissue. This suggests

that the chronic inflammation from surgical incisions could increase the risk for the development of such cancer (Bollo et al., 2018).

Another report showed the development of a mucinous adenocarcinoma in a neovagina that was constructed from the colon (Kita et al., 2015). One study showed that the cytology of neovaginas resembles normal cervical cytology in only a minority of cases and concluded that patients with neovaginas should undergo routine cancer screening. This study also found that 5% to 10% of patients carried low- or high-risk HPV strains in their tissues (Grosse et al., 2017).

One case demonstrated the development of poorly controlled lichen sclerosis in the anal and neovaginal regions of a transgender patient (McMurray et al., 2017). Further studies should investigate whether transgender patients are more susceptible to chronic inflammatory conditions, such as lichen sclerosus, in the setting of surgical interventions. Although squamous cell carcinoma of the vagina is rare, chronic inflammation (particularly in the setting of lichen sclerosus) can predispose patients to the development of cancer.

Despite these suggestions for a possible increased risk of certain types of cancer, there is no strong evidence for increased screening of these patients. Furthermore, there are not enough data for the predicted incidence of developing cancer in this population, and there is no known timeline from surgery to cancer for these patients. Reports have found cancer development at a wide range of times postsurgery.

Until more data and/or guidelines exist, we recommend following the cervical cancer screening recommendations in terms of frequency of Papanicolaou tests on neovaginal tissue (U.S. Preventive Services Task Force, 2012). Similar to the recommendations for anal Papanicolaou tests, if factors exist that place a patient at a higher risk for HPV-related cancer (HIV positive-status, history of condyloma, or other genital HPV-related conditions), we suggest more frequent screenings (Kreuter et al., 2015; Liszewski et al., 2014). If an area of tissue is chronically inflamed, such as from lichen sclerosis, then the patient should be followed closely, similar to cisgender women with these conditions.

Benign neovaginal disease

A few benign conditions have also been reported in the neovaginas of transgender women. Several studies have demonstrated the presence of condyloma acuminata in transgender women, mainly in neovaginas constructed from penile and scrotal tissues (Brown et al., 2015; Galea et al., 2015; Nureña et al., 2013; van der Sluis et al., 2016). These lesions can present with coital pain and bleeding (van der Sluis et al., 2016). Although the incidence is not known, it is suggested that the high rate of HIV in this population predisposes patients to having a high rate of HPV infection (Nureña et al., 2013). Treatment options are similar to those in cisgender patients, including topical podophyllotoxin, excision, or laser evaporation (van der Sluis et al., 2016). There was also one reported case of condyloma gigantea in neovaginal tissue that was constructed from the prepuce and scrotum, which was treated with laser and repeated liquid nitrogen (Yang et al., 2009).

A case report also exists on a transgender woman with lichen sclerosus et atrophicus, which presented with several years of vulvar pruritis and burning. The patient was found to have involvement of the labia, clitoral hood, and perianal area. Multiple topical treatments, such as triamcinolone, camphor, menthol, and lidocaine, were attempted without success, and the patient received only some relief of pain and itch with oral gabapentin. Biopsy test results revealed lichen sclerosis with superimposed contact dermatitis. The patient's vaginal involvement could be explained by the construction of her neovagina with penile and scrotal tissue, but her perianal involvement was unusual because cisgender men usually do not have perianal involvement (McMurray et al., 2017). This presentation

Table 1
Transgender medicine terminology

Term	Definition
Female-to-male, FTM, transman, transgender man	Assigned female sex at birth with female anatomical reproductive organs, has gender identity of man
Male-to-female, MTF, transwoman, transgender woman	Assigned male sex at birth with male anatomical reproductive organs, has gender identity of woman
Surgical affirmation therapy	Any surgical intervention that aids transgender persons achieve anatomical concordance with identified gender (e.g., facial feminization surgery, breast implantation, and neovaginal construction in transgender women)
Hormone affirmation therapy	Hormone treatment that helps transgender persons achieve levels to those of identified gender (e.g., oral estrogen and spironolactone for transgender women)
Neovagina	Surgically constructed vulvo-vaginal area in transgender women meant to resemble vaginas in cis-gendered women; usually constructed from penile, scrotal, and/or colonic tissue; also refers to construction of vaginas in congenital abnormalities, vaginal malignancies, and intersex disorders

could be unique to transgender women in the context of their hormone use, chronic irritation, and trauma/scarring from surgery (Bjekić et al., 2011; Friedrich and Kalra, 1984).

Skin cancer risk

Estrogen is a known contributor to the growth of breast, ovarian, and endometrial cancer. Although the association between estrogen and melanoma is less clear, melanoma is known to rarely occur before puberty and rapid growth of melanoma occurs during pregnancy, which could imply that melanoma growth is estrogen dependent; however, this link is tenuous (Sato et al., 2008; Schmidt et al., 2006).

Estrogen receptor-beta is one of two estrogen receptors found in the skin and has been shown to be associated with dysplastic and malignant melanocytic lesions. Estrogen receptor-beta expression is dense in dysplastic nevi with severe atypia and lentigo malignas, which suggests estrogen involvement in the development of atypical and neoplastic pigmented lesions (Chaudhuri et al., 1980; Schmidt et al., 2006). Future studies elucidating whether a link exists between estrogen and melanoma need to be performed.

Additionally, there is currently no evidence of a higher risk of melanoma in transgender women compared with cisgender women, which also leaves room for future studies to investigate. Due to these findings and lack of data, there are no screening recommendations for skin cancer in patients who take estrogen replacement, and there is not enough evidence to make any suggestions to patients that estrogen replacement confers an elevated risk of skin cancer.

Autoimmune diseases

Systemic lupus erythematosus (SLE) is an autoimmune condition with a predilection for women of childbearing age. This gender predilection has been thought to be due to the autoimmunity-enhancing effects of estrogen and prolactin via their effects on B-cell maturation, selection, and activation (Cohen-Solal et al., 2006).

Short-term hormone replacement in postmenopausal women has not been shown to increase the incidence of autoimmune disease. However, there are case reports of transgender women with no known predisposing autoimmune factors who developed SLE with cardiorespiratory and renal involvement after long-term estrogen therapy (Chan and Mok, 2013; Santos-Ocampo, 2007).

Disease severity may be greater in this population because biological men have been shown to exhibit more severe systemic manifestations of SLE during flare-ups (Agrawaal and Dhakal, 2014). One case report described significant improvement of cutaneous lupus in a transgender woman after initiating testosterone treatment, which possibly indicates a protective role of androgens in lupus (Ocon et al., 2018). Additionally, a case series highlighted the development of systemic sclerosis, which is another female-predominant autoimmune disease, in three MTF patients after initiating hormone therapy (Campochiaro et al., 2018).

Black market injectables

"Pumping" is the illegal use of black market injectables by transgender patients. For many reasons, including the high cost of gender-affirmation procedures, limited access to health care, discrimination by medical professionals, and community norms, some transgender people choose illicit materials as a method to alter their bodies (Murariu et al., 2015; Wilson et al., 2014). Injectables mainly include testosterone, estrogen, and silicone. Testosterone and estrogen are usually injected in the abdomen as a form of hormone affirmation therapy. Silicone is used for body contouring purposes, typically in the buttocks, breasts, and face. However, the use

of these materials can lead to complications resulting from the use of dirty needles or impure substances or because the injected compound was not the advertised product.

Reports have shown cases of cellulitis or other skin infections due to these injections. Multiple reports exist on chronic skin ulcers or granulomas in the skin of transgender patients at the site of silicone or hormone injections (Carella et al., 2013; Ohnona et al., 2016; Rothman et al., 2016). Other cutaneous complications include lymphatic and vascular compromise and angioedema/pseudo-angioedema, possibly due to the massive volume of the injections or an inflammatory reaction in the area (Deutsch, 2016; Hage et al., 2001; Styperek et al., 2013).

A few cases have shown the development of hypercalcemia secondary to granuloma formation in patients who injected silicone for body contouring purposes (Agrawal et al., 2013; Visnyei et al., 2014). One case report documented the development of pulmonary hemorrhage after the injection of silicone into the breast tissue of a patient (Macedo et al., 2013). Of note, death occurred in some patients due to complications from illegal/black market injectables, which should serve as an impetus to provide better counseling and care for this population (Wilson et al., 2014).

Conclusions

Due to the concerted efforts of physicians in the field of endocrinology, clear guidelines exist for the supplemental hormone treatment for transgender individuals. However, not much is known about the dermatologic effects of hormones on these patients beyond changes in acne and hair distribution, or the cutaneous consequences of gender-affirming surgery. Neovaginal postsurgical complications, cutaneous infections, HPV and non-HPV related neoplasia, autoimmune disease, and the use of black-market injectables have been reported. Larger-scale studies are needed to more closely examine dermatological issues in transgender patients.

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