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A 60-year-old female presented with a three-year history of virilizing symptoms including facial hirsutism and deepening of voice. Her medical history was significant for renal transplantation with immunosuppressive therapy consisting of mycophenolate, cyclosporine, and low-dose prednisone. She was noted to have temporal balding and darkly pigmented terminal hair on the upper lip, cheeks, chin, shoulders, and sternum. Pelvic examination revealed clitoromegaly. Menarche occurred at age 12 with regular menstrual cycles until menopause which occurred at age 50. She had two pregnancies: a miscarriage followed by a successful pregnancy.

Labs revealed an elevated total testosterone of 530 ng/dL (< 60 ng/dL), free testosterone 14.8 ng/dL (<0.87 ng/dL), androstenedione 2140 ng/dL (<200 ng/dL), and 17-hydroxyprogesterone 704 ng/dL (<285 ng/dL). LH, FSH, and estradiol were inappropriately normal in this postmenopausal female. Prolactin, TSH, DHEA-S, IGF-1 were within normal limits. Transvaginal ultrasound found a 2 cm hypoechoic right ovarian mass which was confirmed on MRI. MRI also revealed a 5 mm right adrenal nodule. Tumor markers including CA-125, Inhibin A, Inhibin B, HCG, and AFP were within normal limits. Dexamethasone suppression testing did not lower the testosterone level. 17-hydroxyprogesterone level after cosyntropin stimulation testing was 704 ng/dL (<1000 ng/dL). The patient underwent laparoscopic bilateral oophorectomy and salpingectomy, pelvic washout and omental biopsy. Pathology was consistent with a benign Leydig cell tumor. Following oophorectomy there was complete normalization of the total testosterone level (15 ng/dL, n< 60 ng/dL).

A thorough history and physical exam is vital in determining the cause of hirsutism. Medications, including over-the-counter and herbal formulations should be carefully reviewed. Although cyclosporine has been associated with hirsutism, patients typically present with vellus hair formation in the affected areas rather than darkly pigmented terminal hair. In this case, hirsutism progressively worsened following menopause and physical examination was significant for virilization. Hirsutism in a combination with virilization is typically neoplastic in nature. Endogenous androgen production can originate from either the adrenal glands or ovaries. In our patient, with workup showing both ovarian and adrenal as potential sources of endogenous androgen production, an adrenal cause was excluded due to a normal DHEA-S level at baseline and a lack of suppression of testosterone after dexamethasone suppression testing. As a result, the source was localized to the ovary. While excessive androgen production resulting in virilization is seen with ovarian tumors, Leydig stromal cell tumors are extremely rare and account for less than 0.1% of all ovarian tumors.

Reproductive Endocrinology

TRANSGENDER CARE

"It Wasn't for the Sake of Me and My Mental Health": Transgender People's Perspective on the Role of Mental Health Providers in Initiating Gender-Affirming Hormones - a Qualitative Study

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Introduction: Hormone therapy can be an essential part of medical transition for some transgender people. Despite ongoing debate on the role of mental health providers in the initiation of gender-affirming hormones, little evidence exists to guide the discussion. We seek to elucidate the patient perspective on the feasibility, utility, risks, and benefits of mandatory mental health evaluation (MHE) prior to hormone initiation.

Methods: We conducted semi-structured interviews with individuals who have initiated gender-affirming hormone therapy (n=21). We purposively sampled respondents to include those who indicated that they were required to have mental health evaluation prior to hormone initiation, and those who did not. A transgender advisory board helped develop the semi-structured interview guide. Interviews were transcribed verbatim and coded using emergent and a priori codes.

Results: The majority of respondents saw the requirement for MHE prior to hormone initiation as distinct from, and often discordant with, their mental health care. We identified the following roles of mental health care as seen by patients: 1) General psychosocial support; 2) Identity formation: therapy as a safe space to explore gender and self; and 3) Logistics: assistance navigating the healthcare system. Themes that emerged regarding the MHE requirement included 1) Access: for some, the MHE requirement delayed access to gender-affirming care; 2) "pathologizing my existence": the effects of having one's identity result in a diagnosis of mental disorder; and 3) "auditioning" for care: fear of being denied care if one does not present with a stereotypical transgender narrative. Many participants drew direct connections between the MHE requirement and negative effects on their mental health and the patient/provider relationship, while concurrently identifying mental health care as essential for wellbeing.

Conclusion: While mental health care is appreciated, many transgender people see the universal MHE requirements as having significant negative implications on access, safety, and on even on their mental health. Guidelines should explicitly account for and mitigate the structural barriers preventing transgender individuals from accessing medical and mental health care.

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TRANSGENDER CARE

A Cross Sectional Analysis of the Prevalence of Co-Morbidities in Older Transgender Individuals Receiving Hormone Affirming Therapy in Comparison With the General Population

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Background: Transgender individuals feel an incongruity between the assigned gender at birth and their gender identity. Because the prevalence of cardiovascular risk factors and morbidity associated with cross-sex hormonal therapy is not well established, particularly in the older transgender population, we set out to compare it to that of the general population. **Methods:** Data were collected from medical records of transgender patients treated in the Endocrine Institute at the Tel Aviv-Sourasky Medical Center until October 2018. Data from the Israel National Health Survey INHIS-3 2013-2015 were used as reference. **Results:** 104 (75 transgender women and 29 transgender men) patients over 35 y were identified. The median follow up time was 3 y (1-6.1). Transgender women had a high standardized prevalence rate (SPR) of overweight, smoking and engaging in physical exercise, but not of dyslipidemia compared with cisgender men and women. The SPR for overweight was high in transgender males compared with cisgender men and women. The SPR for smoking and dyslipidemia was high in transgender men compared with cisgender women but not men. Depression and anxiety were markedly increased in transgender women compared with cisgender men [SPR 5.5 (95% CI 3.3-8.5), p<0.001] and women [SPR 2.8 (95% CI 1.7-4.3), p<0.001] in the control population. The SPR of hypertension, diabetes and cerebrovascular disease was not elevated among transgender patients. **Conclusions:** The prevalence of cardiovascular risk factors but not cardiovascular morbidity was higher in the transgender patients compared with the general population. Further studies including a larger population and a longer follow up time are needed to better assess the impact of a high prevalence of risk factors on cardiovascular morbidity on the long run.

Reproductive Endocrinology

TRANSGENDER CARE

A Retrospective Analysis of Progestogen Use in Transgender Women

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Background: Many transgender women seek progestogens as part of their feminizing gender-affirming hormone treatment (GAHT), particularly to address breast development, body composition, mood stabilization, and changes in sexual desire and sleep. However, there are few studies that evaluate the role of progestogen use in feminizing GAHT. Reasons for initiating and continuing progestogen therapy have been mostly anecdotal to date, dependent on patient preference and provider practice style, and data about effects remain scarce.
Objective: To characterize progestogen use patterns in transgender women at one academic center; identify reasons for initiation and continuation of its use; and determine perceived related benefits and adverse events.
Methods: Retrospective analysis of transgender women prescribed feminizing GAHT at Stanford Health Care (SHC) between 2014-2020. Those using either combination estrogen + micronized progesterone or combination estrogen + medroxyprogesterone acetate (MPA) were included in our sample. Twenty-five consecutive charts were reviewed in detail for patterns of progestogen use, reasons for initiation and continuation, and its perceived effects.
Results: 410 transgender women sought care at SHC between 2014-2020. Ninety-six patients (23%) were prescribed micronized progesterone and 15 patients (4%) MPA at some point in their care, in addition to estrogen use. Of the 25 patient charts reviewed in detail (median age 30 years, IQR 25-42), 32% (n = 8) had clear documentation in the medical record of why progestogen was started and 25% (n = 6) included a description of the patient's perceived effects with progestogen therapy. The most common reason to start progestogen was improved breast development (20%, n = 5). Three individuals reported improved nipple/breast growth. Median duration of progestogen use was 34.4 months (IQR 22.3-47.4) with 22 out of 25 patients still on progestogen therapy at time of chart review. Median duration of estrogen use prior to initiation of progestogen use was 14.2 months (IQR 7.1-35.8). No cardiovascular or thromboembolic events were noted in the reviewed patients on progestogen therapy.
Discussion: Over one in four transgender women seeking feminizing GAHT received a form of progestogen therapy as part of their overall GAHT. Most patients on progestogens lack documentation of why it was started or whether the patient seems to benefit from its addition. Given the continued paucity of data supporting or against progestogen use in feminizing GAHT, gender-affirming hormone providers may benefit from further education on how to counsel patients about progestogen use and how to assess for potential progestogen-associated effects over time. Finally, more consistent documentation in the electronic medical record will allow for more definitive conclusions regarding the benefits and risks of progestogen therapy in the future.

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Achieving Physiologic 17-ß-Estradiol Levels in Transgender Females on Estradiol Transdermal Patches and Optimal Dosing

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Purpose: Gender dysphoria is defined as a significant incongruence between an individual's experienced gender and the gender assigned at birth, leading to persistent distress. Hormone therapy and gender affirmation surgery improve gender dysphoria by mitigating or completely removing undesirable primary/secondary sexual characteristics which would better align with one's physical and psychological features. Maintaining cross-sex hormone levels in the physiologic range for the preferred gender is the basis of transgender hormonal therapy. For trans females (MTF), estradiol is most commonly administered orally, and studies have shown this route is often successful in achieving therapeutic hormone levels. However, there is wide individual variability in the dose response to oral estradiol, and approximately 25% of patients will not reach