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Gender Dysphoria

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Continuing Education Activity

Gender dysphoria (previously gender identity disorder), according to Diagnostic and Statistical Manual of Mental disorders are defined as a "marked incongruence between their experienced or expressed gender and the one they were assigned at birth." People who experience this turmoil cannot correlate to their gender expression when identifying themselves within the traditional, rigid societal binary male or female roles, which may cause cultural stigmatization. This can further result in relationship difficulties with family, peers, friends and lead to interpersonal conflicts, rejection from society, symptoms of depression and anxiety, substance use disorders, a negative sense of well-being and poor self-esteem, and an increased risk of self-harm and suicidality. Patients with this condition should be provided with psychiatric support. Hormonal therapy and surgical therapy are also available depending on the individual case and patient needs. This activity describes the evaluation and management of gender dysphoria and reviews the role of the interprofessional team in improving care for those with this condition.

Objectives:

- Review the etiology of gender dysphoria.
- Describe the presentation of a patient with gender dysphoria.
- Outline the treatment of gender dysphoria.
- Summarize the importance of collaboration and communication among the interprofessional team in creating more awareness about gender dysphoria among health providers and to encourage them to be more forthcoming in providing care for this population.

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Introduction

The origin of the word gender came from the Old French "genre" (now termed "genre") that meant "kind, sort, genus." Generally, children are assigned to their gender at birth based on their anatomy and chromosomes. For most children, this gender assignment corresponds to their gender identity, an innate sense of identifying oneself as male or female. Some children might experience an incongruity and grow into transgender adults.

Gender dysphoria (GD) according to Diagnostic and Statistical Manual of Mental disorders (DSM 5) is defined as a "marked incongruence between their experienced or expressed gender and the one they were assigned at birth." It was previously termed "gender identity disorder."

Children or adolescents who experience this turmoil cannot correlate to their gender expression when identifying themselves within traditional societal binary male or female roles, which may cause cultural stigmatization.

This can further lead to relationship conflicts with family, peers, friends in various aspects of their daily lives and lead to rejection from society, interpersonal conflicts, symptoms of depression and anxiety, substance use disorders, a negative sense of well-being and poor self-esteem, and increased risk of self-harm and suicidality.

More awareness needs to be created to perceive gender expression as a continuum from male to female rather than fixed binary norms. This might help society to understand the population and reduce the burden of mental health problems created by the associated stigma.

The term gender should not be confused with sexual orientation. A transgender man (biological female) may identify himself as heterosexual and still be sexually attracted to women and vice versa.[1]

Etiology

The etiology of gender dysphoria (GD) remains unclear, but it is thought to originate from a complex biopsychosocial link.

Individuals born with congenital adrenal hyperplasia or androgen insensitivity syndrome are usually brought up and socialized as girls, even though they often cross-dress and have an innate sense of belonging to the opposite sex. These changes are more evident around and during puberty. This is one of the well-established biological links.

Associations have also been found with in-utero exposure to phthalates in plastics and polychlorinated biphenyls. They are known to disrupt the regular endocrinology of sex determination before birth. Phthalates can lead to an increase in total fetal testosterone levels, which in turn increases the risk of autism spectrum disorder as well as GD.

GD has been found to have a higher prevalence in people with psychiatric illnesses such as schizophrenia and autism spectrum disorder. The link seems to be neuroanatomical and needs more research. There was a growing evidence that autistic population has a higher risk of GD. However, certain studies seek to disprove this hypothesis.

There is also growing evidence the childhood abuse, neglect, maltreatment, and physical or sexual abuse may be associated with GD. Individuals reporting higher body dissatisfaction and GD have a worse prognosis in terms of mental health. And as mentioned above in epidemiology, individuals with GD are found to have higher rates of depression, suicidal ideations, and substance use.

Neuroanatomical links have been found in certain studies. A major one is faulty neuronal development and differentiation in the hypothalamic links. Functional neuroimaging has shown variations in hemispheric ratios and amygdala connectivity according to gender.

A few case reports have reported some association of GD to maternal toxoplasma infection, although additional data is needed for further evidence.

A genetic association is also identified as one of the causes of GD. Heritability and familiarity of GD have been identified: for instance, higher prevalence in monozygotic twins than dizygotic twins. Some alleles (CYP17 and CYP17 T-34C) have also been found to have an association, although it is difficult to say if it is merely association or causation.[2][3][4]

Epidemiology

According to a sex health study published in 2017, there is a markedly high prevalence ranging from 0.5% to 1.3% for self-reported transgender identity in children, adolescents, and adults. It was traditionally a rare or uncommon diagnosis; however, in the past few decades, the numbers have increased.[5]

According to an analysis of national probability samples in 2016, there were 390 per 100,000 adults who were transgender. However, it also suggested that future surveys will probably observe a higher prevalence.[6]

According to a recent national survey, 1.4 million individuals (0.6%) in the United States identify as transgender. It is also believed that these numbers are underrepresented due to the social stigma. Also, a part of this population might not want to engage in studies; hence, the true prevalence remains higher than what is reported. Nevertheless, an increasing shift is observed in this population seeking health care over the last decade.[7]

Substance use disorders are commonly found in men and women with GD, with some studies showing 28% having reported problems with substance use. In a recent study, about 48.3% of a study population had suicidal ideation, and 23.8% had attempted suicide at least once in their lifetime. Although, they were not able to appreciate any clinically significant difference between male-to-female (MTF) or female-to-male (FTM) groups.[8] Anxiety, depression, and personality disorders are also common comorbidities. One study by Madeddu in 2009 found that personality disorder was comorbid in 52% of cases and the most common was Cluster B personality disorders.[9]

Pathophysiology

Biological Factors

Biological understanding and genetic contribution to gender dysphoria might allow all domains, like social and medical, to have a greater acceptance of gender dysphoria (GD). There have been several hypothetical postulates; however, it is still not well understood. In the 1970s, it was postulated that the development of GD is entirely a learned environmental pathology, and the approach was aimed at adopting conversion and aversion behavior techniques to criticize feminine characteristics in young boys. It is suggested that many genes contribute to make gender identity an inherited, complex multifactorial polygenetic trait. However, it does not necessarily determine complex traits. It is now believed that gender is not dichotomously branched and is actually a spectrum of the “cis-gender” and “transgender” umbrella. Multiple family and twin-based heritability studies have provided evidence for the polygenetic inheritance of GD. Molecular genetic studies to date, have no conclusive evidence of any gene identified for GD.[7]

Gender dysphoria can be present in congenital adrenal hyperplasia or partial androgen insensitivity syndrome, and DSM 5 recognizes this as a specifier.

Psychosocial Factors

The development of gender to its assigned sex in childhood may be influenced by interaction with children’s temperament and parents’ qualities and their dynamic relationship. Young boys are not expected to be effeminate, and young girls are expected to be nurturing, warm and sensitive; these behaviors are also congruent with cultural norms. Children usually start identifying gender between 3 to 5 years of age, although there might be discrepancies. Cross-gender activities are carefully studied in children with GD. They have been increasingly incongruent in the last few decades. Renowned psychoanalyst Sigmund Freud emphasized that gender dysphoria arises in children from oedipal triangle conflicts.

History and Physical

History

Patients with gender dysphoria (GD) can present to their primary care physician, endocrinologist, or mental health provider. Sometimes, it is a primary concern; whereas others might present with compound mental health problems. Also, due to greater exposure, social acceptance, and greater access to care, this population tends to present before puberty whereas, before they might present at adulthood or late adolescence. Necessary referrals should be made according to the patient to provide them with a strong support system.

It is important to obtain a good history from the patient including psychiatric, substance use, social, family, and developmental including any history of trauma. Past psychiatric history would include past suicide attempts, self-injurious behavior, and history of previous inpatient psychiatric condition if they currently have a psychiatrist or a psychotherapist, any past psychiatric treatment.

Social and developmental history includes their childhood, education status, academic performance, social support, history of trauma (mental, physical, sexual), legal history, and if they are currently married or have children.

Family history includes any history of psychiatric illness, completed suicides, or substance use.

Physical Examination

At birth, a thorough genital exam should be carried out. Children born with congenital adrenal hyperplasia or androgen insensitivity syndrome can present as ambiguous genitalia.

Congenital adrenal hyperplasia may present with early signs of dehydration, hyponatremia, and hyperkalemia. In the late-onset subtype, they might present with early signs of virilization and menstrual irregularities in young females. Classic salt-losing type individuals are sicker and need immediate management.

Androgen insensitivity syndrome is when genetic males are insensitive to androgens in the body. They are often raised as girls. They may have hormonal and surgical treatments in early adulthood/adolescence.

Careful and meticulous assessment and genetic testing should be performed on individuals born with ambiguous genitalia.

Evaluation

Diagnosis (in accordance with DSM- V)

Gender dysphoria in children

A. A marked incongruence between one's experience/expressed gender and assigned gender, of at least 6 months' duration, as manifested but at least six of the following (one of which must be criteria A1)

1. A strong desire to be of the other gender or an insistence that he or she is the other gender (or some alternative gender different from one's assigned gender)
2. In boys (assigned gender), a strong preference for cross-dressing or simulating female attire or, in girls (assigned gender), a strong preference for wearing only typical masculine clothing and as strong resistance to the wearing of typical feminine clothing.
3. A strong preference for cross-gender roles in make-believe play or fantasy play.
4. A strong preference for the toys, games, or activities stereotypically used or engaged in by the other gender.
5. A strong preference for playmates of the other gender.
6. In boys (assigned gender), a strong rejection of typically masculine toys, games, activities and a strong avoidance of rough-and-tumble play or, in girls (assigned gender), a strong rejection of typically feminine toys, games, and activities.
7. A strong dislike of one's sexual anatomy.
8. A strong desire for the primary and/or secondary sex characteristics that match one's experienced gender.

B. The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.

Specify if the above criteria are in addition to a disorder of sex development (e.g., a congenital adrenogenital disorder such as congenital adrenal hyperplasia or androgen insensitivity disorder).

Gender dysphoria in adolescents and adults

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:

1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).
2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).
3. A strong desire for the primary and/or secondary sex characteristics of the other gender.
4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

- With a disorder of sex development (e.g., a congenital adrenogenital disorder such as congenital adrenal hyperplasia or androgen insensitivity syndrome).
- *Post-transition*: the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one cross-sex, medical procedure or treatment regimen; namely, regular cross-sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in natal male; mastectomy or phalloplasty in a natal female).

Other specified gender dysphoria

This category applies to presentations in which symptoms characteristic of gender dysphoria that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for gender dysphoria. The "other specified gender dysphoria" category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for gender dysphoria. This is done by recording "other specified gender dysphoria" followed by the specific reason (e.g., "brief" gender dysphoria).

Unspecified gender dysphoria

This category applies to presentations in which symptoms characteristic of gender dysphoria that cause clinically significant distress or impairment in social, occupational or other important areas of functioning predominate but do not meet the full criteria for gender dysphoria. The "unspecified gender dysphoria" category is used in situations in which the clinician chooses not to specify the reason that the criteria are not met for gender dysphoria and includes presentations in which there is insufficient information to make a more specific diagnosis.

Treatment / Management

Patients can present to their primary care providers, endocrinologists, or mental health provider. Sometimes, it is a primary concern, whereas others might present with confounded mental health problems. Also, due to greater exposure, social acceptance, and greater access to care, this population tends to present earlier before puberty, unlike before, when they might present at adulthood or late adolescence. Necessary referrals should be made according to the patient to provide them with a stronger backbone for support.

It should also be specified according to age. Sadock et al. suggest the following. For children, individual, family, and group therapy are important to explore and counsel on gender preference. For adolescents, the added anticipation of puberty is of concern, so hormonal treatment and psychotherapy should be considered simultaneously. For adults, psychotherapy and hormonal and surgical treatments are all available options.

Adequate counseling is necessary for this population before starting treatment:

1. Care team: a comprehensive approach with an endocrinologist and mental health providers should be made available.
2. Expectations: transgender hormonal and surgical treatment options will be helpful in addressing the patient's external appearance to be in congruence with their gender identity. Unrealistic expectations should be addressed adequately. A supportive network of peers, friends, and family is often helpful.
3. Risks and benefits of treatment: for both hormonal and surgical treatments accompany great risks. Venous thromboembolism, bone mineral density, and pubertal suppression.
4. Fertility preservation: before initiating hormonal and surgical treatment, the patient might lose the ability to reproduce. So it is important to discuss the preservation of fertility by freezing the individual's gametes.
5. Sexual health: incidence of sexually transmitted infections and HIV was higher in this population.

Also, the practitioner must understand that even with a standardized protocol in place, the approach needs to be individualized to ensure a good prognosis post-treatment.[10]

The World Professional Association for Transgender Health (WPATH) currently publishes the Standards of Care (SOC) to provide clinical guidelines for the health care of transsexual, transgender, and gender non-conforming persons in order to maximize health and well-being of patients with gender dysphoria. All treatment options should be offered and, depending on an individual's goals and expectations, the most appropriate surgical technique should be performed. The Standards of Care outlined by WPATH recommends against physical interventions before the age of 16. They recommend that surgery only be performed after the age of 18 and after the individual has lived in their desired gender role for at least two years. In order for people to undergo physical (hormonal or surgical) interventions to make their body more in line with their gender identity, they must be assessed by a mental health professional that has special competence in this area, and often recommendations are required from two such mental health professionals.

Hormonal Therapy

The aim is to suppress the internally produced hormones and to administer and maintain cross-sex hormones in their physiological range. There has been a great push to start hormonal therapy in these patients before they hit puberty, but it is still under research, and ethical issues persist.

Criteria for starting treatment:

1. Persistent and well-documented gender dysphoria
2. Capacity to consent for the treatment.

3. Mental or medical underlying issues are in control.[11]

Transgender women (MTF):

Elimination of facial hair, induction of breast formation, and a female body contour are the desired goals. They can be a combination of antiandrogens (spironolactone), progestins, medroxyprogesterone acetate (associated with excess cardiovascular and breast cancer risk in older women taking conjugated estrogen), GnRH agonists (long-acting gonadotropin-releasing hormone-suppresses testosterone), finasteride and estrogen (17-beta-estradiol). The goal of treatment is to avoid supraphysiologic doses or blood levels of estrogen in order to avoid adverse effects. The most common adverse effects of estrogen therapy include thromboembolic disease, liver dysfunction, hypertriglyceridemia, macroprolactinoma (due to the effect on lactotroph), coronary artery disease, cerebrovascular disease, and hypertension.

Counseling should be provided against cigarette smoking, especially to those on estrogens. Estradiol level, testosterone level, blood pressure, cholesterol panel, prolactin, and liver function should be routinely monitored. Clinical and laboratory evaluation every 3 months during the first year of hormone therapy for transgender females and then once or twice yearly is recommended. Speech/Voice therapy can be offered to all transgender females. Different methods can be used including professional techniques for vocal training, speech therapy by trained speech pathologists, or even surgeries. Having voice and speech characteristics be in agreement with one's gender identity is often important to transgender individuals.[12][13]

Transgender men (FTM):

Their primary treatment measure is testosterone injectables, usually scheduled once a week (the oral route is not recommended due to the first pass through the intestines and liver). During the first few months, increased muscle mass, acne, and libido are seen, along with the cessation of menses. Eventually, more permanent changes such as the deepening of the voice and enlarged clitoris occur following 3 to 6 months of therapy. Routine monitoring of hemoglobin, hematocrit, liver function, cholesterol, and screening of diabetes should be done. As per Endocrine society guidelines 2017, hematocrit or hemoglobin needs to be measured at baseline and every 3 months for the first year and then one to two times a year. The goal is to maintain the testosterone levels in the physiologic normal male range and avoid the adverse events resulting from excess testosterone therapy, particularly erythrocytosis, sleep apnea, hypertension, excessive weight gain, salt retention, lipid changes, and excessive or cystic acne. Measuring BMD and screening for osteoporosis is essential especially in patients who are not compliant, or who are at higher risk for bone loss. [14][13]

Providers in this area of care are encouraged to start hormonal therapy before puberty for maximum results and patient satisfaction. However, involving parental consent for children and young adolescents for initiating hormonal therapy still remains controversial. The physician should inform the patients that Testosterone is teratogenic. Contraceptive methods including IUD, etc should be discussed with the patients. [10]

Surgical Therapy

The criterion is needed, in addition to those listed above for initiating hormonal treatment, before opting for surgical treatment. The individual should be on one year of continuous hormone therapy and living in the desired gender role. [11]

This is often the last step of the treatment process. The counseling discussed above should be continued for these patients, and unrealistic expectations should be addressed. Since these are often irreversible procedures, good insight, and counseling along with social support is required to predict a favorable outcome.

These surgeries are often referred to as “top surgery” and “bottom surgery.”

For MTF: breast augmentation is a common top surgery that trans-women desire. Also, gonadectomy includes penectomy and vaginoplasty, is desired to remove the main source of testosterone from the body. Vaginal dilators are also routinely used to maintain anatomy if sexual intercourse is a goal.

For FTM: Metoidioplasty, where the clitoris is released from the ligament it is attached to, and tissue is added to increase the length and the girth. Scrotoplasty (testicular implants) and phalloplasty (penile implant) are also methods; however, due to the expense and expertise required for these surgeries, they are not very common procedures.

In the end, constant and continued support from family, community, and peers predict favorable outcomes, even after seeking medical and mental health treatment. Individual and group therapies should be continued. Confounding substance use problems should be addressed.

Differential Diagnosis

- Autogynephilia
- Body dysmorphic disorder
- Gynandromorphophilia
- Intersex States
- Psychosis
- Paraphilic disorders
- Self-amputation
- Schizophrenia
- Transvestitism

Enhancing Healthcare Team Outcomes

Any mental health illness requires targeting all the three biological, psychological and social aspects of the patient to have the most favorable outcome.

1. To create more awareness about individuals with gender dysphoria and validate the concerns of this vulnerable population we encourage more active parental and peer support. To understand gender as a scale and not as binary forms can help reduce the stigma in seeking timely help to improve prognosis and outcome. Open discussions and mass level education at school and work environment can help achieve this.
2. To create more awareness for gender dysphoria among physicians and other health providers and to encourage providers to be more forthcoming and liberal in providing care and treating for this population. To emphasize an interprofessional team approach that is already in effect. This gives our patients the opportunity to get treatment within the same loop of providers. Also, understand that this population has a higher incidence of psychiatric illnesses, concomitant substance use and personality disorders can be challenging to deal with.
3. Along with this innate sense of rejection and desire to be the opposite sex, these patients need treatment with hormones and therapy. These patients should also be screened for mental health problems like depression, anxiety, safety risk assessments, and substance use during all office visits, including those to primary care providers, psychiatrists, psychologists, social workers, endocrinologists to make necessary referrals in case, patient screens positive.

4. By understanding gender dysphoria as an organic pathology as suggested by available data and not entirely behavioral, as it was previously thought to be, we can try to maximize care and improve outcomes.
5. As discussed above, even after having protocols written to provide care for these patients, the plan should always be individualized.

Review Questions

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