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Gender Dysphoria in Turner Syndrome

Disforia de Género en el Síndrome de Turner

Disforia de gênero em Síndromde de Turner

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Abstract

Objectives: To report a case of a patient with Turner Syndrome (TS) experiencing gender dysphoria (GD), which refers to the psychological distress (lasting at least six months) that may result from an incongruence between the given and the experienced gender. **Case Details:** At sixteen, the patient realized she wanted to belong to the opposite gender, wishing to eliminate female secondary sexual characteristics. The patient developed a fleeting consideration of suicide and engaged in non-suicidal self-injury. Her mood symptoms worsened at nineteen, and she became more socially isolated as her academic performance declined. At 21, she did not present GD and did not want to transition gender anymore. **Final Considerations:** To the best of our knowledge, this is the first report of GD in a patient with the syndrome. It aligns with the understanding that gender identity is not only a social process but also a unique, individual construction. This case report highlights the importance of caution in transitional procedures since patients may need time to build their gender identity.

Keywords: Turner Syndrome; Gender Dysphoria; Gender Identity; Chromosomal Abnormalities**.**

Resumen

Objetivos: Reportar un caso de un paciente con Síndrome de Turner (ST) que experimenta disforia de género (DG), que se refiere al malestar psicológico (que dura al menos seis meses) que puede resultar de una incongruencia entre el género dado y el experimentado. **Detalles del caso**: A los dieciséis años, la paciente se dio cuenta de que quería pertenecer al sexo opuesto, deseando eliminar los caracteres sexuales secundarios femeninos. El paciente desarrolló una fugaz consideración del suicidio y se autolesionó de forma no suicida. Sus síntomas anímicos empeoraron a los diecinueve años y se aisló socialmente más a medida que su rendimiento académico declinaba. A los 21 años no presentó DG y ya no quería hacer la transición de género. **Consideraciones finales**: Hasta donde sabemos, este es el primer informe de EG en un paciente con este síndrome. Se alinea con la comprensión de que la identidad de género no es sólo un proceso social sino también una construcción individual y única. Este informe de caso destaca la importancia de tener

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precaución en los procedimientos de transición, ya que los pacientes pueden necesitar tiempo para construir su identidad de género.

Palabras clave: Síndrome de Turner; Disforia de género; Identidad de género; Anomalías cromosómicas.

Resumo

Objetivos: Relatar o caso de uma paciente com Síndrome de Turner (ST) apresentando disforia de gênero (DG), que se refere ao sofrimento psíquico (com duração mínima de seis meses) que pode resultar de uma incongruência entre o gênero determinado e o vivenciado. **Detalhes do caso**: Aos dezesseis anos, a paciente percebeu que queria pertencer ao sexo oposto, desejando eliminar as características sexuais secundárias femininas. A paciente desenvolveu uma ideia fugaz de suicídio e se envolveu em automutilação não suicida. Seus sintomas de humor pioraram aos dezenove anos e ela ficou mais isolada socialmente à medida que seu desempenho acadêmico diminuía. Aos 21 anos, não apresentava DG e já não queria fazer transição de gênero. **Considerações Finais**: Até onde sabemos, este é o primeiro relato de DG em um paciente com a síndrome. Alinha-se com a compreensão de que a identidade de género não é apenas um processo social, mas também uma construção única e individual. Este relato de caso destaca a importância da cautela nos procedimentos de transição, uma vez que os pacientes podem precisar de tempo para construir a sua identidade de género.

Palavras-chave: Síndrome de Turner; Disforia de Gênero; Identidade de gênero; Anormalidades cromossômicas.

INTRODUCTION

A fundamental aspect of the sense of identity is the individual's internal experience of gender. The 21st-century paradigmatic shift acknowledges gender identities existing beyond the binary (FURLONG Y e JANCA A 2022), considering gender diversity a normal human expression variation. Gender-diverse identities are not conditions of mental illness; classifying them as such can cause enormous stigma (PERLSON JE et al., 2021). Transgender people form a broad group, many living without adequate healthcare access. The search for medical and psychological issues resolution varies from searching for indirect information and advice on health to searching for specialized clinics (WINTER et al., 2016).

As a rising number of people with gender incongruence (GI) and gender dysphoria (GD) search the healthcare system, medical professionals debate how to approach gender identity-related issues (PERLSON JE et al., 2021). The 11th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-11) separates mental distress from GI. ICD-11 defines it as a marked and persistent incongruence between an individual's experienced gender and the assigned sex, often leading to a desire to align their body with the experienced gender (WORLD HEALTH ORGANIZATION, 2019).

Several surgical and non-surgical approaches may be considered for the transition process when people with GI decide to change their natal sex characteristics to one that corresponds to their internal gender identity. GI is not synonymous with psychological suffering or dysfunction. Nevertheless, some people may go through a stage where developing gender identity causes psychological suffering. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines GD as psychological distress (lasting at least six months) that may result from an incongruence between the given and the experienced gender (AMERICAN PSYCHIATRIC ASSOCIATION, 2013). The clinical importance of identifying GD lies in the need to approach the person experiencing psychological suffering differently according to their necessities.

There is a high prevalence of behavioral health diagnoses among people with GD, including higher rates of depressive symptoms, anxiety, and self-harm behavior (NUNES-MORENO M et al., 2022). Factors including decreased self-esteem (WATSON RJ et al., 2017), resilience (DELOZIER AM, 2020), and support from the family (DURWOOD L et al., 2017) may be significantly impaired in some patients and correlate with the

development of future illness during adulthood. The approach to GD, especially in its beginning (often in early adolescence), includes multidisciplinary therapy, supporting emotional well-being, and family communication (EDWARDS-LEEPER L e SPACK NP, 2012). The use of gonadotrophin-releasing hormone (Gn-RH) as puberty suppression and gender-affirming hormones are also tools used as there is continuous patient monitoring (HEMBREE WC et al., 2017). Surgical procedures such as mastectomy or genital surgeries are interventions used in specialized centers (KYRIAKOU A et al., 2020) during the clinical follow-up.

People with disorders of sexual development may have different exposure to hormones during their growth than most of the population, which leads to visible changes in sexual characteristics identified during early life and, possibly, to gender-related issues. This fact raises the question of whether this population may suffer more frequently from GD illnesses than the general population (KREUKELS et al., 2018).

It is important to note that chromosomal abnormalities such as Turner syndrome (TS) or Klinefelter syndrome are rare diseases, making it difficult to carry out long-term studies and monitor psychiatric manifestations (KREUKELS et al., 2018). TS is not associated with genital ambiguity during birth and may lead to a different gender identity construction than natal genital abnormalities directly related to enzymatic or hormonal changes.

TS is the phenotypic females' most common chromosomal disorder abnormality, affecting one in 2500 liveborn females with one intact X chromosome and complete or partial absence of the second sex chromosome associated with one or more clinical manifestations (ELSHEIKH M et al., 2002).

The objective of this article is to describe the case of a 21-year-old female patient with TS and attention deficit hyperactivity disorder (ADHD), who was regularly monitored at the endocrinology service, experiencing GD in her first years of life. Seven years of joint monitoring with the psychiatric service demonstrated the importance of a global understanding of this particular case. There are reports of atypical psychosocial traits in patients with TS (REIMANN GE et al., 2020), but this is the first report of GD in a patient with the syndrome.

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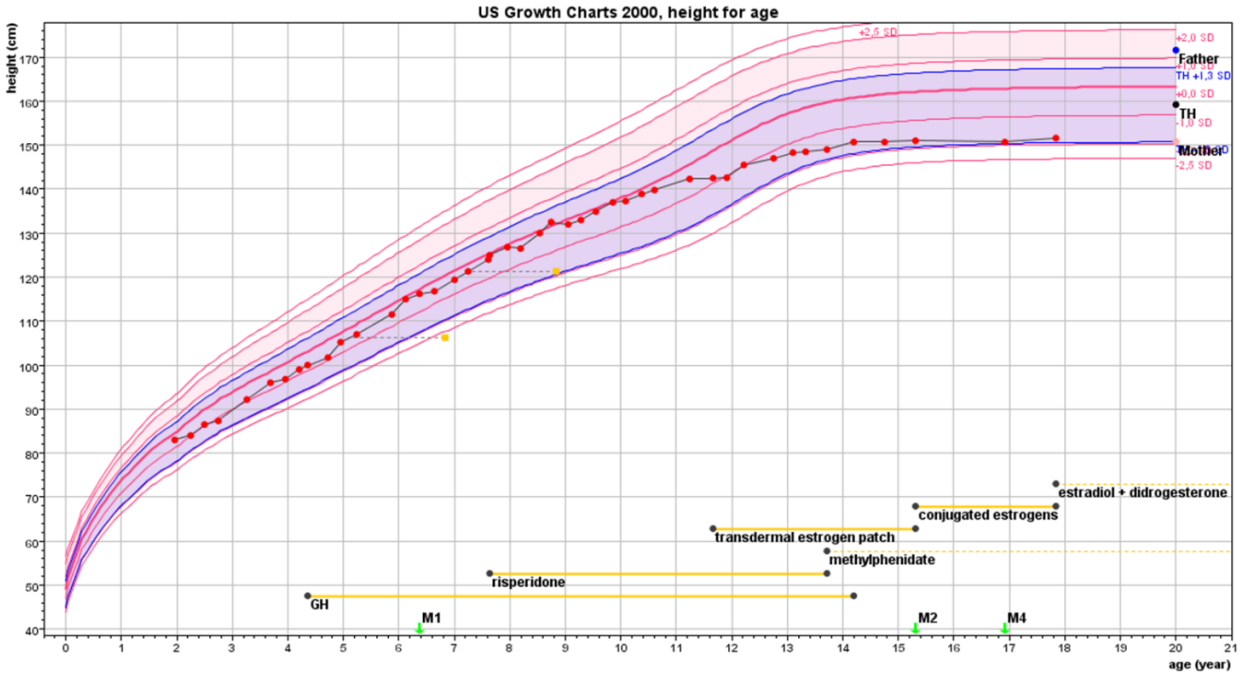
CASE REPORT

The patient is a twenty-one-year-old, M5P5 Tanner stage, female high school student with TS diagnosed at birth whose 20-cell karyotype was 45,X[20]. Testis-specific Protein Y-linked (TSPY) gene quantification was performed using the quantitative real-time PCR (qPCR) assay and showed amplification of the TSPY gene fragment located on chromosome Yp11.2 in the 31.93 ($\pm$ 0.96) quantification cycle.

She has a webbed neck, epicanthus, hands, and feet edema, cubitus valgus, a high-arched palate, low posterior hair implantation, short stature, and typically feminine genitalia. The patient received somatropin treatment from four to fourteen years old. Her puberty was induced with transdermal estrogen starting at twelve years old. Estrogen use was irregular due to the high cost for her family income status, and at fourteen years of age, she started treatment with conjugated estrogens (Premarin, 0.625 mg orally). The first transvaginal bleeding occurred at age sixteen and nine months. She was on combined cyclic estrogen and progesterone replacement, but use was irregular and was discontinued at age seventeen to undergo valve replacement surgery. A pelvic ultrasound performed when she was eighteen demonstrated a uterus of 16 cm^3, endometrium thickness of 3.9 mm, a right ovary partially characterized, and a left ovary with a size of 8.2 cm^3 without dominant follicles. There were no genitourinary tract anatomical anomalies.

The patient reached a height of 150.7cm (target adult height: 154cm). She had a bicuspid aortic valve and aortic stenosis diagnosed in the first year of life. Therefore, she underwent commissurotomy in her first year of life, balloon valvuloplasty at fifteen, and metal valve replacement at seventeen. Since then, daily use of warfarin 10mg and hormone replacement therapy has continued without pause. The patient has mild hearing loss due to recurrent episodes of acute otitis media. Figure 1 shows the evolution of the patient's height, bone age, and puberty in response to treatment throughout the follow-up.

Figure 1. Timeline for patient's growth and pharmacological interventions.



The patient was born full-term, via vaginal birth, after an uneventful pregnancy. Her parents divorced when she was a baby. During childhood, she had a good relationship with her mother, whom she describes as a caring mother. Her father suffered from alcohol use disorder. By age six, she was referred to a neuropediatrician due to agitation, aggressivity, inattention, and learning difficulties. She was diagnosed with ADHD at seven. Using risperidone improved her school performance and reduced her hyperkinetic and aggressive symptoms. Nevertheless, she did not use risperidone regularly, showing worsening. Taking methylphenidate improved her school performance, but the use was irregular, and the patient ended up suspending treatment for ADHD.

She reports that, since childhood, she has preferred male clothes, toys, and games. In addition, she remembers being physically attracted to people of the same sex. At thirteen, her father told her he wished she was a boy so that "she would be more helpful." At fifteen, she told her mother about her sexuality, but her family condemned it. The patient started experiencing sadness, anhedonia, initial insomnia, and more difficulty concentrating.

At sixteen, she realized she wanted to belong to the opposite gender, wishing to eliminate female secondary sexual characteristics, such as breasts, and develop male secondary sexual characteristics, such as a beard. Her previous psychiatric symptoms worsened, and she started feeling empty and anxious. She developed a fleeting consideration of suicide without a detailed plan or suicide attempts and engaged in non-suicidal self-injury to alleviate her emotional pain. Suicidal ideation subsided spontaneously within days, while self-injury persisted for a few months.

During adolescence, disagreements with her mother started. She does not have a close relationship with her stepfather. She complains about his and her mother's comparisons between the patient and her healthy and younger half-sister. She admits that she is constantly trying to please everyone. The patient reports feelings of resentment toward her emotionally distant father. She has lived with her grandmother since the age of ten.

She was on irregular estrogen use from seventeen to nineteen, with breast growth arrest. At seventeen, the patient started to cut her lengthy hair, adopted a male haircut, bound her breasts, and wore masculine clothing. Her family did not accept the changes. When asked whether she would like to change the characteristic physical features of the TS, the patient replied that what she disliked about her body was having female features. However, the patient never mentioned wanting to use testosterone as a gender-affirming hormonal regimen. She did not change the social name but preferred a genderless abbreviation of her name.

Her mood symptoms worsened at nineteen, she became more socially isolated, and her academic performance declined. She started psychiatric follow-up, was initially diagnosed with depressive disorder and ADHD, and started taking citalopram 20mg/day. The patient responded well to drug treatment, achieving complete remission of mood symptoms. During the follow-up, the marked incongruence between her experienced/expressed gender and assigned gender became evident, leading to the diagnosis of GD according to the DSM-5.

The patient has been under regular endocrinological monitoring since childhood and had a good relationship with the medical team. Nevertheless, during a psychiatric assessment, she first mentioned the incongruence between her experienced gender and the assigned gender at nineteen. The patient described a strong preference for games or activities stereotypically used or engaged in by the other gender and a strong preference for cross-dressing since childhood. Although the clinical team had difficulty identifying early signs of GD, the condition manifested when the patient was sixteen. She continued psychiatric treatment for a year. The psychiatrist referred her to psychotherapy, but the patient did not attend regularly. Additionally, she stopped taking citalopram on her own at twenty years of age.

At 21, the patient appeared very happy with her gender identity. She kept her interest in same-sex partners but did not want to transition gender anymore. Her visual appearance changed remarkably. She had make-up on and was wearing hoop earrings, a low-cut dress, and a purse. The patient was very comfortable and at ease. She followed a musical career, recorded a CD, and worked singing. Her self-esteem increased as she became recognized for her talent. She uses hormone replacement (17 beta-estradiol and Dydrogesterone 5 mg) and has regular cycles.

DISCUSSION

Here, we present the case of a patient with a complete loss of one sex chromosome, short stature, hypogonadism, and a typical TS phenotype. She experienced psychological distress due to gender incongruence since she was sixteen, supporting the diagnosis of GD. The most recent follow-up (at age 21) revealed no desire to transition and, most importantly, no psychological distress.

Studies in adolescents without TS have shown that body awareness and idealization during physical intimacy impair sexual behavior and that body dissatisfaction increases depressive symptoms (ALMEIDA S et al., 2012; ROUSSEAU A et al., 2017). Dissatisfaction with the physical characteristics of TS may have contributed to the depressed mood and gender conflict of our patient. Carel and colleagues found that self-esteem, social adjustment, and the onset of sexual activity are disturbed when puberty does not occur at a physiologically appropriate age in patients with TS (i.e., before 15 years) (CAREL JC et al., 2006). Puberty was induced in our patient by twelve, which is considered appropriate.

Loss of ovarian function in TS begins prenatally, resulting in estrogen and androgen deficiency (KNICKMEYER RC e DAVENPORT M, 2011). Although there is a biological contribution to developing an individual's gender identity and sexual orientation (ROSELLI CE, 2018), we can only speculate about a different brain activation in our patient. A cross-sectional study in fourteen European centers did not find any case of GD in patients with TS, in contrast to the 5,1% found in patients with other disorders of sexual development (Klinefelter syndrome, congenital adrenal hyperplasia, etc.). Notably, the study found that patients with disorders of sexual development and GD had lower self-esteem and were more anxious and depressed than participants without GD (KREUKELS BPC et al., 2018).

Our patient received the diagnosis of ADHD at the age of seven. Patients with TS are at increased risk for neurodevelopmental conditions that are more common in males than in typical females (e.g., autism and ADHD) (KNICKMEYER RC e DAVENPORT M, 2011). Previous studies have shown that patients with ADHD are 6.64 times more likely to have gender variance (STRANG JF et al., 2014). This neurodevelopmental disorder may have contributed to GD development in our patient.

There is a great deal of misinformation among parents of patients with TS (FILIBELI BE et al., 2020), and the physical characteristics of patients with TS influence their relationship with their parents (especially their fathers). Moreover, parental behavior is especially likely to encourage infantilization when a child's size or appearance is unusually immature for a prolonged period (SKUSE D, 1987). Another psychological factor is that the patient clearly remembers when her father expressed his wish that she was a boy. The patient admitted that she wanted to be emotionally closer to her father. Patients with GD may feel disconnected from their family and community, mainly due to stigmatization; paternal contact may have supported the patient.

Social influences and maladaptive coping mechanisms may be the origin of GD (LITTMAN L, 2018). Besides GD, the patient also had depressive symptoms and body image dissatisfaction, which caused emotional discomfort. Suicidal ideation tends to have a higher frequency in people with GD than in general (HOSHIAI M et al., 2010). Children with GD show an increased rate of self-harm/suicidality as they age (AITKEN M et al., 2016), and suicidal thoughts in patients with GD usually begin around 19 years old (GARCÍA-VEGA E et al., 2018). Our patient considered suicide earlier, at the age of 16. Monitoring for depressive symptoms may reduce suicidal ideation and prevent its associated attempts.

At 21, our patient did not want to transition gender anymore. Realizing that GD relates to issues other than GI (70%) is the most common reason for ceasing a transgender identification (VANDENBUSSCHE E, 2022). Natal females usually detransition at a young age (around 23 years old) (KREUKELS BPC et al., 2018). In most cases, patients feel they did not receive an adequate evaluation from a mental health professional. Other reasons for detransition include medical complications, the absence of mental health improvement after the transition, or dissatisfaction with results (LITTMAN L, 2021). This case report highlights the importance of caution in transitional procedures since patients may need time to build gender identity. In our patient, the desire to transition turned out not to be permanent, reinforcing the idea that gender identity is not only a social (ZUCKER KJ, 2017) but also a unique, individual construction.

Future studies may explore the interaction between psychological, social, hormonal, genetic, and epigenetic factors in developing gender identity in patients with TS. It is necessary to approach patients with sexual development disorders regarding their needs when GD is suspected and to manage complications associated with emotional distress. Medical teams must consider social and behavioral aspects to optimize clinical management for each situation during patient development.

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