CASE REPORT - OPEN ACCESS

ISSN: 3067-2368 American Journal of Case Reports and Clinical Images DOI: http://dx.doi.org/10.51521/AJCRCI.2026.e42.164

Contents lists available at https://amejcaserepclinimag.com/

American Journal of Case Reports and Clinical Images



Siblings with Concordant Gender Dysphoria and Divergent Upbringing Environments: Case Report and Literature Review of Neurobiological Identity Factors

Jose Luis Rojas-Oviedo[1], María Fernanda Leal Walteros[1], Diana Carolina Vargas Fiesco[2], Dauris Lineth Mejía Pérez[3], Wilmer Alexander Hernández Lizarazo[4], Juan Carlos Vallejo-Soto[5]

[1]*Second Year Obstetrics and Gynecology Resident, Universidad Nacional de Colombia, Bogotá, Colombia.*

[2]*Obstetrics and Gynecology Specialist, Reproductive Medicine Fellow, Gender Clinic Endocrinologist, Subred Integrada de Servicios de Salud Norte, Assistant Professor, Universidad Nacional de Colombia, Bogotá, Colombia.*

[3]*Obstetrics and Gynecology Specialist, Subred Integrada de Servicios de Salud Norte, Máster in Public Health, Assistant Professor, Universidad Nacional de Colombia, Bogotá, Colombia.*

[4]*Obstetrics and Gynecology Specialist, Universidad del Rosario, Master in Superior Education in Health, Universidad de Antioquia, Associated Professor, Unisanitas.*

[5]*Máster in Epidemiology, Universidad del Rosario.*

ARTICLE INFO

Article history:
Received: 09-09-2026
Revised: 01-10-2026
Accepted: 03-10-2026
Published: 05-10-2026

MeSH KEYWORDS:

Gender Dysphoria,

Transgender,

Genetics,

Neurobiology,

Environment

ABSTRACT

Two assigned females at birth siblings separated neonatally and raised in disparate environments independently developed early-onset gender dysphoria, affirming male identities in adulthood. These shared trajectories, despite significant environmental variance, support a durable biological foundation for gender identity. Results highlight the resilience of innate factors in determining gender development.

Copyrights © 2026, Jose Luis Rojas-Oviedo, et al, This article is licensed under the Creative Commons Attribution-Non-Commercial-4.0-International-License-(CCBY-NC) (https://amejcaserepclinimag.com/blogpage/copyright-policy). Usage and distribution for commercial purposes require written permission.

Introduction:

Gender dysphoria (GD) is characterized by a marked and persistent incongruence between an individual's experienced gender and their birth-assigned sex, resulting in clinically significant distress or functional impairment [1]. Historically, the clinical understanding of GD has transitioned from simplistic, purely psychotherapeutic or binary models toward a comprehensive, multidimensional developmental systems framework [2]. This modern paradigm conceptualizes gender identity not as a fixed feature located in the brain, but as a self-organizing process emerging from the non-linear intersection of biological predispositions, prenatal endocrine environments, and postnatal psychosocial structures and influences [2].

The etiology of GD is increasingly viewed as an oligogenic or polygenic trait, mediated by variations in sex-hormone-signaling genes that influence the sexual differentiation of the fetal brain [3]. Molecular genetic studies have identified significant associations between GD and functional polymorphisms in genes responsible for the biosynthesis and metabolism of sex steroids, such as the androgen receptor [*AR*] and estrogen receptors [*ESR1* and *ESR2*] [3]. In individuals assigned female at birth [AFAB] who identify as male, research has highlighted the role of the cytochrome P450 17A1 [*CYP17A1*] gene [4]. Specifically, the -34T→C promoter polymorphism [the A2 allele] up-regulates enzymatic activity, potentially increasing testosterone biosynthesis *in utero* [4]. Such genetic variations are thought to establish a baseline sensitivity to sex steroids, creating a biological template for identity long before birth [4].

Evidence for this biological durability is further supported by heritability and twin studies [5]. Meta-analyses have consistently shown significantly higher concordance rates for transgender identity in monozygotic [MZ] twins [approximately 21.2%], who share 100% of their genomic sequence, compared to dizygotic [DZ] twins [8.7%], who share only 50% [5]. Furthermore, the negligible difference in concordance between same-sex and opposite-sex DZ twins suggests that shared intrauterine hormone transfer is less significant than individual genetic susceptibility [5].

* Corresponding author.
Jose Luis Rojas-Oviedo, Universidad Nacional de Colombia, Email: jrojasov@unal.edu.co; ORCID: 0000-0001-8802-3095

Neural distress in GD often stems from a mismatch between interoceptive signals [the nervous system's sense of "what feels right" in the body] and external physical or social expectations [6]. The insular cortex integrates these physiological signals into a coherent sense of self. When internal neural architecture, shaped by prenatal genetics and hormones, conflicts with the birth-assigned role, the brain signals distress long before the child has the linguistic capacity to articulate the incongruence [6]. Epigenetic mechanisms, such as DNA methylation, may act as the functional bridge, where environmental stressors modulate the expression of pre-existing genetic susceptibilities during critical windows of development [6].

This case report examines two AFAB siblings who were separated neonatally and raised in distinct households with divergent cultural, religious, and educational backgrounds. Such a scenario provides a unique "natural experiment" to evaluate the weight of shared biological drivers against non-shared environmental variables. Despite their disparate upbringings, both individuals followed nearly identical trajectories of early-onset GD and eventual male affirmation, providing compelling evidence for a durable, biological foundation for gender identity that persists across varied socio-cultural terrains.

Case Presentation:

Patient A [Elder Sibling, 24 years]: Patient A was raised in a household characterized by a conservative religious and cultural environment where gender roles were rigidly defined according to birth-assigned sex. Despite consistent parental reinforcement of female-typical behaviors, their guardians reported symptoms of gender incongruence during phase 3 of development [18–36 months]. By preschool age, the patient displayed an intense and persistent insistence that they were a boy, demonstrating a strong preference for male-typical playmates and toys. This early-onset gender dysphoria [GD] was marked by interoceptive distress—a nervous system signal of "mismatch" between internal states and external physical expectations—long before the patient had the linguistic capacity to articulate the incongruence.

Throughout primary and secondary education, Patient A engaged in "masking" or suppression to navigate the social terrain, but experienced significant functional impairment and anxiety because of living in a body that felt incompatible with their subjective identity.

Patient B [Younger Sibling, 21 years]: Patient B was raised in a secular, liberal household with a progressive educational background that emphasized gender neutrality. Despite this contrasting environment, followed a nearly identical developmental trajectory. Like their sibling, Patient B began exhibiting cross-gender preoccupations by age three, actively resisting assigned female labels. The patient demonstrated operational closure during childhood, with an internal stabilization of their male identity independent of the external cultural schemas. This shared clinical outcome across divergent "social terrains" suggests that while the environment acts as the terrain, the biological "internal compass" speaks first and most definitively. Both patients entered adulthood with a persistent, well-documented male gender identity.

Differential Diagnosis, Investigations, and Treatment:

The primary differential diagnosis included body dysmorphic disorder [BDD], which was ruled out as the patients' distress was rooted in gender identity rather than a pathological preoccupation with perceived physical defects. Rapid-onset gender dysphoria [ROGD] was also considered but excluded due to the clear history of persistent childhood symptoms dating back to the preschool period. Additionally, psychotic disorders and schizophrenia were ruled out through psychiatric evaluation, which confirmed that the gender identity was not a delusional manifestation but a stable self-concept.

A thorough physical and genital examination was conducted for both siblings to rule out disorders of sex development [DSD] or intersex conditions, such as congenital adrenal hyperplasia [CAH]. Genetic investigations were performed, focusing on oligogenic variations in sex-hormone-signaling genes. Testing identified the A2 allele of the cytochrome P450 17A1 [CYP17A1] gene in both siblings, which is associated with increased testosterone biosynthesis and has been overrepresented in cohorts of transgender men [AFAB].

Both patients were managed through a multidisciplinary team approach including endocrinologists, gynecologist and mental health providers. Following the WPATH Standards of Care, both siblings initiated masculinizing hormone therapy [testosterone undecanoate every 12 weeks], which aimed to align their physical characteristics with their male gender identity. Within the first 3 to 6 months of therapy, both reported a significant reduction in neural distress, alongside physical changes including deepening of the voice and cessation of menses. Both individuals subsequently underwent gender-affirming surgery [mastectomy] to further alleviate bodily incongruence.

Discussion:

The shared clinical trajectory of these siblings, despite their separation and exposure to differing cultural and religious influences, aligns with modern theories that conceptualize gender identity as a biologically grounded, self-organizing system [4]. This case provides compelling evidence against purely environmental or "learned" models of gender identity development, such as Mischel's reinforcement theory or Bussey and Bandura's Social Cognitive Theory, which emphasize that children acquire gender behaviors primarily through external modeling and parental reinforcement [7]. While biology provides the "internal compass," the social environment acts as the terrain upon which identity is navigated and developed [7].

Dynamic systems theory [DST], as applied to gender development, posits that identity emerges through repetitive, activity-dependent neural plasticity [2]. This process typically unfolds in three phases: an intersubjective period [birth to 15 months] where dyadic interactions with caregivers imbue the infant with an embodied understanding of gender; a phase transition [15 to 18 months]; and a symbolic period [18 to 36 months] where children begin active self-labeling [2]. Historically, "learned" models of gender, such as social cognitive theory, suggested identity was purely a result of external modeling and reinforcement [8]. However, the resilience of gender identity against even extreme environmental suppression—as seen in the failure of "reparative" therapies—indicates that environment shapes the expression of identity rather than its fundamental origin [8].

The heritability of gender identity is strongly supported by empirical data from classic twin and familial studies [9]. Furthermore, non-twin siblings of transgender individuals have been shown to have a significantly higher risk of experiencing gender incongruence than the general population, reinforcing the hypothesis of a shared genetic predisposition [10]. These shared outcomes are increasingly understood through a developmental systems lens, where identity emerges from a complex, self-organizing intersection of genetic susceptibilities and prenatal neuroendocrine environments that interact with, but are not determined by, postnatal socialization [10]. This is further evidenced by the negligible difference in concordance between same-sex and opposite-sex DZ twins, which suggests that individual genetic factors are more influential than shared intrauterine hormone transfer [10]. In the context of this case report, the identical trajectories of neonatally separated siblings raised in divergent socio-cultural environments suggest that biological factors provide a durable "internal compass" for identity.

Neuroimaging studies support this biological basis, showing that transgender individuals often exhibit structural brain mosaics [11]. For instance, transgender men [AFAB] frequently show subcortical gray matter masculinization, with structures like the putamen falling within the cisgender male range [11]. Furthermore, identity formation relies heavily on interoception—the nervous system's ability to sense "what feels right" in the body [2,3].

The insular cortex integrates these internal physiological signals. In these siblings, the persistent mismatch between their internal interoceptive signals [male-typical] and their external sex-differentiated traits likely generated the continuous state of neural distress reported from preschool age, regardless of the cultural labels provided by their respective households [11].

In this case, the siblings were raised in households with differing religious and educational backgrounds, which likely offered different "schemas" for gender. However, both siblings independently resisted their assigned roles. This suggests that while environmental feedback [phase 1 and 2] typically helps align biological sex and brain structure, it cannot override a strong, pre-existing biological divergence [7]. The brain's drive toward authenticity is powerful; when internal signals and external expectations conflict, the nervous system often signals distress long before the child has the language to explain it and make it manifest [7].

The fact that these siblings, separated neonatally, both reported GD symptoms at the same developmental stage [preschool] suggests a "biological conference" of identity that occurred before their environmental paths diverged. While social factors like "minority stress" or differing, religious constraints may have shaped how they expressed their dysphoria or when they chose to transition, the underlying identity remained constant. This supports the consensus that gender identity results from all three biopsychosocial layers interacting over time, but that the biological layer speaks first and often most definitively.

Conclusion:

The results of this case report demonstrate that both siblings followed

Jose Luis Rojas-Oviedo, María Fernanda Leal Walteros, Diana Carolina Vargas Fiesco, Dauris Lineth Mejía Pérez, Wilmer Alexander Hernández Lizarazo, Juan Carlos Vallejo-Soto, (2026). Siblings with Concordant Gender Dysphoria and Divergent Upbringing Environments: Case Report and Literature Review of Neurobiological Identity Factors. American J Case Rep Clin Imag. 2026; September; 4(2), 01-03.

an identical path of early-onset gender dysphoria and adult male affirmation. Their shared biological foundation, likely established by prenatal neuroendocrine organization and the presence of shared genetic markers, remained resilient against diverse environmental influences. Following transition, both patients reported substantial relief from the chronic "mismatch" distress, achieving identity coherence and improved psychological well-being. This case highlights the durability of the biological confers of gender identity and reinforces the necessity of providing gender-affirming care that validates the organic nature of gender incongruence.

Author Contributions:

Jose Luis Rojas-Oviedo: Conceptualization, methodology, investigation, data curation, writing—original draft, and project administration. María Fernanda Leal Walteros: Investigation, data curation, literature review, and writing—original draft. Diana Carolina Vargas Fiesco: Investigation, literature review, and writing—review and editing. Dauris Lineth Mejía Pérez: Investigation, literature review, and writing—review and editing. Wilmer Alexander Hernández Lizarazo: Methodology, investigation, and writing—review and editing. Juan Carlos Vallejo-Soto: Supervision, methodology, critical review, and writing—review and editing. All authors contributed to the interpretation of the findings, critically revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

Informed Consent:

Both of the patient's subject of this report previously signed the written informed consent form in the presence of two witnesses, authorizing explicitly the anonymous use of all the information from their medical history and corresponding images in any publications with scientific or academic interest.

Conflicts of interest: All authors declare no conflicts of interest.

CARE Checklist [2016] Statement: This case report was prepared and reported in accordance with the CARE [Case Report] guidelines and checklist [2016].

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders [DSM-5]. 5th ed. Washington, DC: American Psychiatric Publishing; 2013.
2. Fausto-Sterling A. A Dynamic Systems Framework for Gender/Sex Development: From Sensory Input in Infancy to Subjective Certainty in Toddlerhood. Front Hum Neurosci. 2021 Apr 9;15:613789. doi: 10.3389/fnhum.2021.613789. PMID: 33897391.
3. Roselli CE. Neurobiology of gender identity and sexual orientation. J Neuroendocrinol. 2018 Jul;30[7]:e12562. doi: 10.1111/jne.12562. PMID: 29211317; PMCID: PMC6677266.
4. Foreman M, Hare L, York K, Balakrishnan K, Sánchez FJ, Harte F, Erasmus J, Vilain E, Harley VR. Genetic Link Between Gender Dysphoria and Sex Hormone Signaling. J Clin Endocrinol Metab. 2019 Feb 1;104[2]:390-396. doi: 10.1210/jc.2018-01105. Erratum in: J Clin Endocrinol Metab. 2020 Jan 1;105[1]:dgz156. doi: 10.1210/clinem/dgz156.
5. Conabere W, Bourchier L, Malta S, Ravine A, Pang KC. Genetic and Environmental Contributions To Gender Diversity: A Systematic Review of the Twin Literature. Behav Genet. 2025 Sep;55[5]:339-359. doi: 10.1007/s10519-025-10231-3. Epub 2025 Sep 12. PMID: 40938572; PMCID: PMC12494644.
6. Ristori J, Cocchetti C, Romani A, Mazzoli F, Vignozzi L, Maggi M, Fisher AD. Brain Sex Differences Related to Gender Identity Development: Genes or Hormones? Int J Mol Sci. 2020 Mar 19;21[6]:2123. doi: 10.3390/ijms21062123. PMID: 32204531.
7. Polderman, T.J.C., Kreukels, B.P.C., Irwig, M.S. et al. The Biological Contributions to Gender Identity and Gender Diversity: Bringing Data to the Table. Behav Genet 48, 95–108 [2018]. https://doi.org/10.1007/s10519-018-9889-z.
8. deMayo BE, Jordan AE, Olson KR. Gender Development in Gender Diverse Children. Annu Rev Dev Psychol. 2022 Dec;4:207-229. doi: 10.1146/annurev-devpsych-121020-034014. Epub 2022 Jul 8. PMID: 37638126; PMCID: PMC10457095.
9. Gómez-Gil, E., Esteva, I., Almaraz, M.C. et al. Familiarity of Gender Identity Disorder in Non-Twin Siblings. Arch Sex Behav 39, 546–552 [2010]. https://doi.org/10.1007/s10508-009-9524-4.
10. Conabere W, Ravine A, Malta S, Bourchier L, Harte F, Hopper JL, Pang KC. Using twin data to examine heritable and intrauterine hormonal influences on transgender and gender diverse identities. Sci Rep. 2025 Jul 1;15[1]:21680. doi: 10.1038/s41598-025-06265-6. PMID: 40594415; PMCID: PMC12218214.
11. Frigerio A, Ballerini L, Valdés Hernández M. Structural, Functional, and Metabolic Brain Differences as a Function of Gender Identity or Sexual Orientation: A Systematic Review of the Human Neuroimaging Literature. Arch Sex Behav. 2021 Nov;50[8]:3329-3352. doi: 10.1007/s10508-021-02005-9. Epub 2021 May 6. PMID: 33956296; PMCID: PMC8604863.

INTERNATIONAL STANDARD SERIAL NUMBER

doi Crossref

CC BY

Submit your manuscript to American Journal of Case Reports and Clinical Images CODEN: USA

and benifit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your manuscript at :
https://amejcaserepclinimag.com/
&
wjcasereports@gmail.com;
submission@amejcaserepclinimag.com

Jose Luis Rojas-Oviedo, María Fernanda Leal Walteros, Diana Carolina Vargas Fiesco, Dauris Lineth Mejía Pérez, Wilmer Alexander Hernández Lizarazo, Juan Carlos Vallejo-Soto, (2026). Siblings with Concordant Gender Dysphoria and Divergent Upbringing Environments: Case Report and Literature Review of Neurobiological Identity Factors. American J Case Rep Clin Imag. 2026; September; 4(2), 01-03.