46,XY disorder of sex development due to 5 alpha reductase deficiency: analysis of a clinical case and updated review.

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Summary

Introduction: Disorders of sex development (DSDs) constitute a group of congenital conditions characterized by a discrepancy between chromosomal, gonadal, and phenotypic sexes. The objective of this study is to describe a clinical case of ambiguous genitalia in adulthood associated with a 5-alpha-reductase deficiency and to contextualize its management from an updated clinical, diagnostic, and psychosocial perspective.

Case report: We describe the case of a female patient with a history of primary amenorrhea who was diagnosed in late adolescence with male pseudohermaphroditism due to 5-alpha-reductase deficiency. A review of recent literature on this disorder is presented.

Diagnostic workshop: The patient presented with ambiguous genitalia, a 46,XY karyotype, and hormonal studies consistent with 5α-reductase deficiency. The diagnosis was confirmed, and a multidisciplinary approach focused on sex reassignment and surgical correction was initiated.

Conclusion: 5α-Reductase deficiency is a rare but well-characterized cause of male pseudohermaphroditism. Early diagnosis and comprehensive management are essential for patients' well-being, preventing premature interventions and promoting autonomy in making decisions about their body and identity.

Keywords:

Male pseudohermaphroditism, genital ambiguity, 5 alpha reductases, disorders of sexual development, sex reassignment.

Abbreviations

DSD: Disorder of sexual development.

Supplementary information

No supplementary materials are declared.

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Authors' contributions

Ramon Miguel Vargas Vera, conceptualization, research, original draft writing, resources, software, supervision.

Martha Verónica Placencia Ibadango Methodology, Data Curation, Formal Analysis, Fundraising, Project Management, Validation, Visualization, Writing, Review and Editing.

Ingrid Mariela Toapanta-Rea, conceptualization, research, original draft writing, resources, software, supervision.

Melanie Nicole Lino Mejía, conceptualization, research, original draft writing, resources, software, supervision.

Julio César Pacheco-García, conceptualization, research, original draft writing, resources, software, supervision.

María Yamileth Varela-Palma, conceptualization, research, original draft writing, resources, software, supervision.

All the authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and analyzed during this study are available to the corresponding author upon reasonable request.

Introduction

Disorders of sex development (DSDs) constitute a group of congenital conditions characterized by a discrepancy between chromosomal, gonadal, and phenotypic sexes. Among these conditions is male pseudohermaphroditism, which is defined as the presence of a 46,XY karyotype with testicular gonads but with incomplete or ambiguous development of the external genitalia. The etiology includes mutations that affect the synthesis or action of androgens, including a deficiency of the enzyme 5α-reductase type 2 [1].

This enzyme converts testosterone into dihydrotestosterone (DHT), a hormone essential for the masculinization of the external genitalia during the fetal period. Mutations in the SRD5A2 gene, which encodes this enzyme, result in incomplete virilization [2], with a variable phenotype that can range from female genitalia to ambiguous genitalia.

The diagnosis and management of these cases involve not only biomedical aspects but also psychological, social, and ethical considerations. The decision regarding sex assignment and the timing of possible interventions should be made within the framework of a multidisciplinary, patient-centered approach.

Case report

Medical records

This is a 19-year-old patient born by an uncomplicated cesarean section to consanguineous parents (first cousins). He was raised as a woman and consulted for primary amenorrhea. Physical examination revealed androgenic habits, scant breast development, pubic hair in a male pattern, clitoromegaly of 4 cm, prominent labia majora, palpable gonads, and a urogenital orifice at the base of the clitoris (Figures 1 and 2).

Diagnostic workshop

Hormonal studies revealed normal levels of LH, FSH, and total testosterone at the lower limit of the male range. Estradiol and prolactin levels were within the expected values for males. Abdominopelvic ultrasound revealed the absence of internal female genitalia and the presence of testicular tissue in the labia majora. Transrectal ultrasound revealed a smaller prostate gland and seminal vesicles. The karyotype was 46,XY (Figure 3).

Evolution

Based on these findings, a diagnosis of male pseudohermaphroditism due to 5α-reductase deficiency was established. Psychological support and genetic counseling were initiated. The patient was identified as male; therefore, surgical intervention and complementary hormone therapy were planned.

Figure 1. Clinical case 1.

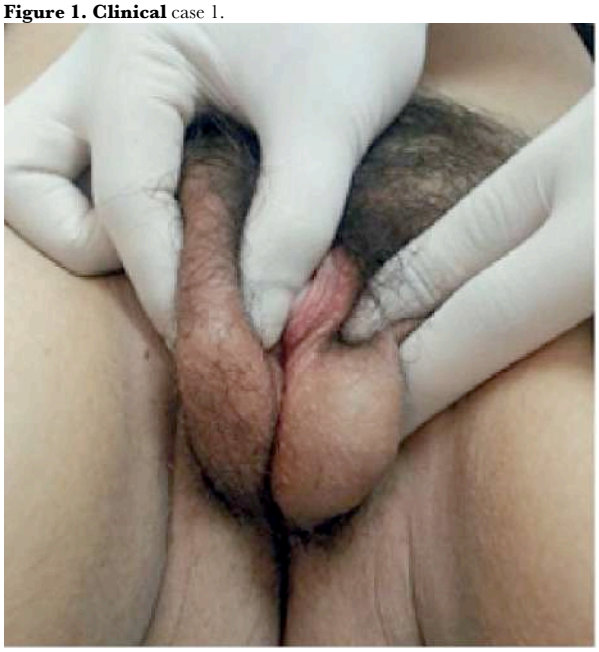

Figure 2. Clinical case 1.

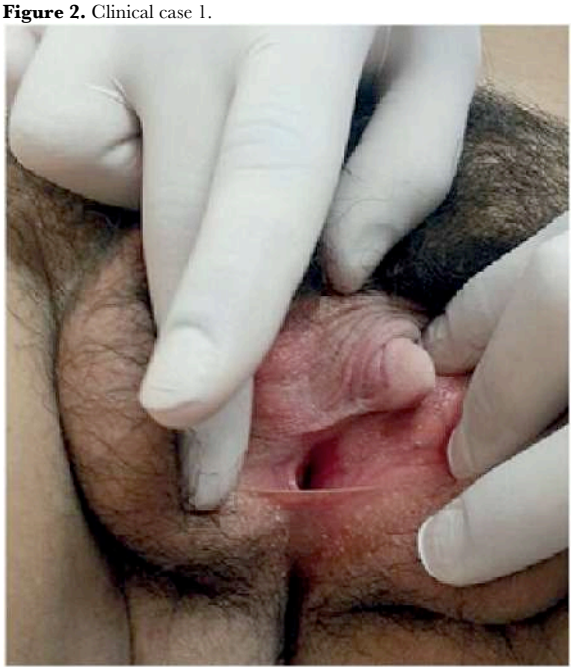

Fig. 2 Clitoromegaly with perineoscrotal hypospadias.

Figure 3. Karyotype.

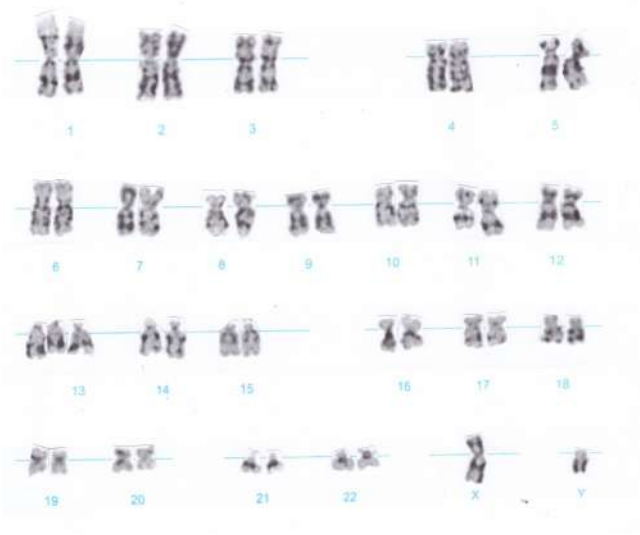

Fig. 3 Karyotype 46,XY.

Discussion

Type 2 5α-reductase deficiency is a rare condition associated with 46,XY sex development disorders. Its phenotypic expression can be heterogeneous, depending on the type of mutation and residual tissue sensitivity to androgens. Many of these patients are initially female but may undergo spontaneous virilization during puberty [3].

Diagnostic confirmation requires genetic testing (SRD5A2 gene sequencing) and hormonal evaluation. Management should be individualized and involve specialists in endocrinology, urology, gynecology, genetics, psychology, and social work. The avoidance of irreversible surgeries in childhood is recommended until the individual can participate in decision-making [4].

Recent studies emphasize the need to consider gender identity [5-8], future sexual function, reproductive desire, and mental health as fundamental aspects of treatment. Respect for the autonomy of patients and their environment is crucial.

The following is a comparative table of the central disorders of sexual development in 46,XY to contextualize the differential diagnosis of 5-alpha-reductase deficiency [9]:

Feature	5α-Reductase Deficiency	Partial Androgen Insensitivity	Gonadal dysgenesis
Karyotype	46,XY	46,XY	46,XY
affected gene	SRD5A2	AR (Androgen receptor)	Several
Enzyme/Receptor	5α-Reductase type 2	Androgen receptor	Gonadals
External genitalia	Ambiguous/pseudofeminine	Ambiguous	Female
Testicles	Palpable on scrotal lips	Cryptorchidism or inguinal canal	Absent or dysgenetic
Testosterone production	Normal	Normal	Low or absent
Dihydrotestosterone (DHT)	Decreased	Normal	Decreased
Virilization in puberty	Partial or significant	Scarce	Absent
Common gender identity	Male	Feminine or ambiguous	Female

Conclusions

Male pseudohermaphroditism due to 5α-reductase deficiency should be considered in patients with ambiguous genitalia and a 46,XY karyotype. Timely diagnosis and comprehensive management improve the prognosis for physical and mental health. This case highlights a multidisciplinary, patient-centered approach that encompasses not only biomedical implications but also ethical, social, and psychological aspects.

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Abstract

Introduction: Disorders of sex development (DSDs) are a group of congenital conditions characterized by a discrepancy between chromosomal, gonadal, and phenotypic sexes. This study aims to describe a clinical case of genital ambiguity in adulthood associated with 5-alpha-reductase deficiency and to contextualize its approach from an updated clinical, diagnostic, and psychosocial perspective.

Case report: We describe the case of a patient raised as a woman with a history of primary amenorrhea who was diagnosed in late adolescence with male pseudohermaphroditism due to 5-alpha-reductase deficiency. A review of the recent literature on this DSD is conducted.

Diagnostic workshop: The patient presented with clinical symptoms of genital ambiguity, a 46 XY karyotype, and hormonal studies compatible with 5α-reductase deficiency. The diagnosis was confirmed, and a multidisciplinary approach aimed at sexual reassignment and surgical correction was initiated.

Conclusion: 5α-Reductase deficiency is a rare but well-characterized cause of male pseudohermaphroditism. Early diagnosis and a comprehensive approach are essential for patients' well-being, avoiding premature interventions and fostering autonomy in decision-making about their bodies and identities.

Keywords: Male pseudohermaphroditism, genital ambiguity, 5-alpha reductase, disorders of sex development, sex reassignment.

Statements

Ethics committee approval and consent to participate

This method is not required for clinical cases.

Publication consent

The authors obtained the patients' written consent for the publication of images, radiographs, and specific studies.

Conflicts of interest

The research has no financial interests or conflicts of interest.

Use of generative AI

The authors declare that they did not use generative AI.

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