A RARE CASE REPORT OF OVOTESTICULAR DISORDER OF SEXUAL DIFFERENTIATION WITH LATE PRESENTATION

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ABSTRACT

BACKGROUND

Disorder of Sex Development (DSD) is a condition where there is a misalignment of gonads or chromosomes with the genitalia. One of the rarest forms of DSD is Ovotesticular DSD (OT-DSD), which is characterized by the presence of both ovarian and testicular tissues in the same individual and a diverse range of phenotypes with various penetrations.

CASE SUMMARY

A 16-year-old patient who was raised as a female presented with ambiguous genitalia and regular menstrual cycles. Ultrasound examination revealed a normal-sized uterus and three gonads. Cy-togenetic analysis showed a mosaic karyotype, and PCR testing for the SRY gene was positive. Postoperative histology indicated the presence of two ovaries and one ovotestis gonad.

CONCLUSION

In low-resource healthcare settings, caregivers should remain vigilant for ambiguous genitalia and ensure timely referral for accurate diagnosis and counseling before sex assignment. This case highlights the importance of maintaining a high level of suspicion for DSD in adolescents dis-playing abnormal pubertal development or atypical genital findings.

KEYWORDS: Ovotesticular DSD, SRY gene, true hermaphrodite

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INTRODUCTION

Disorders of sex differentiation (DSD) are medical and psychosocial emergencies that require an expert multidisciplinary team for proper management and favorable long-term outcomes.[1,2] The incidence of DSD ranges between 1:4500 and 1:5000 live births, with ovotesticular DSD (OT-DSD) (true hermaphroditism) accounting for 4% to 10% of all DSD cases.[3] The condition ap-pears to be more common in African countries such as Kenya, South Africa, and Sudan.[4,5] Pa-tients with OT-DSD usually present as under-virilized males with female karyotypes (46,XX).[4]

The diagnosis of OT-DSD involves a series of costly tests, such as chromosomal and molecular genetic analysis, hormone testing, ultrasound or MRI, and gonadal biopsy. Access to these tests and their high cost pose significant challenges, particularly in low-income countries, resulting in delays in diagnosis. Additionally, even in developed countries, addressing this condition requires a multidisciplinary approach due to its diverse presentation, potential impact on fertility, risk of gender dysphoria, gonadal malignancy, and implications for gender assignment.[6]

The disease is commonly identified in neonates based on genital abnormalities or in adolescents who present with abnormal sexual development at puberty. The management of OT-DSD re-quires a multidisciplinary approach, including pediatric endocrinology, pediatric surgery or urol-ogy, radiology, genetics, psychology or child psychiatry, and pediatrics.[7] This approach is necessary to address potential sexual function, genitourinary function, future fertility issues, gender dys-phoria, and long-term follow-up for potential surgical complications and functional outcomes.[8] Psychological assessment and counseling for both the family and the patient are critical when making shared decisions about treatment, including sex assignment, hormonal therapy, and sur-gical intervention.[4,7] Herein, we report a late presentation of a unique case of OT-DSD, with three gonads and a functioning Mullerian structure.

Case Presentation

A 16-year-old, single female, reared as a female, presented to the Elite Center for Genetics Di-agnosis, Khartoum, Sudan, complaining of an abnormal external genitalia shape (Figure 1). Her regular cycle started at 14 years old, and she denied any familial history of genital ambiguity. She had no other complaints.

Clinical examination showed stable vital signs, a female phenotype with Tanner stage 3 breasts, and female axillary and pubic hair distribution. External genitalia examination revealed a 5 cm penis with a urethral opening on the tip of the glans, absent labia majora, and atrophied labia minora (Figure 1). She had a normal-looking vagina with an intact hymen and a left palpable inguinal structure. Per rectal examination revealed an intact sphincter and an impalpable pros-tate gland. Examination of other systems was unremarkable.

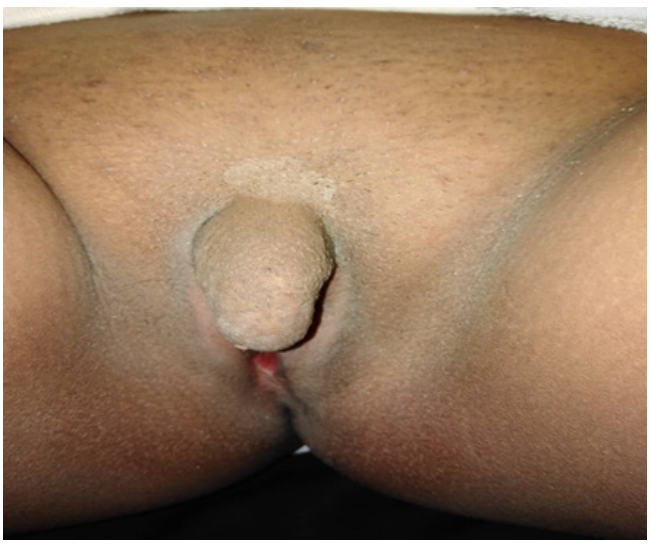

Figure 1: Patient's external genitalia

An ultrasound scan revealed a normal-sized uterus, bilateral ovaries, and a left inguinal testicular-like structure. Chromosomal analysis revealed mosaic karyotype (46,XX/46,XY) (Figure 2).

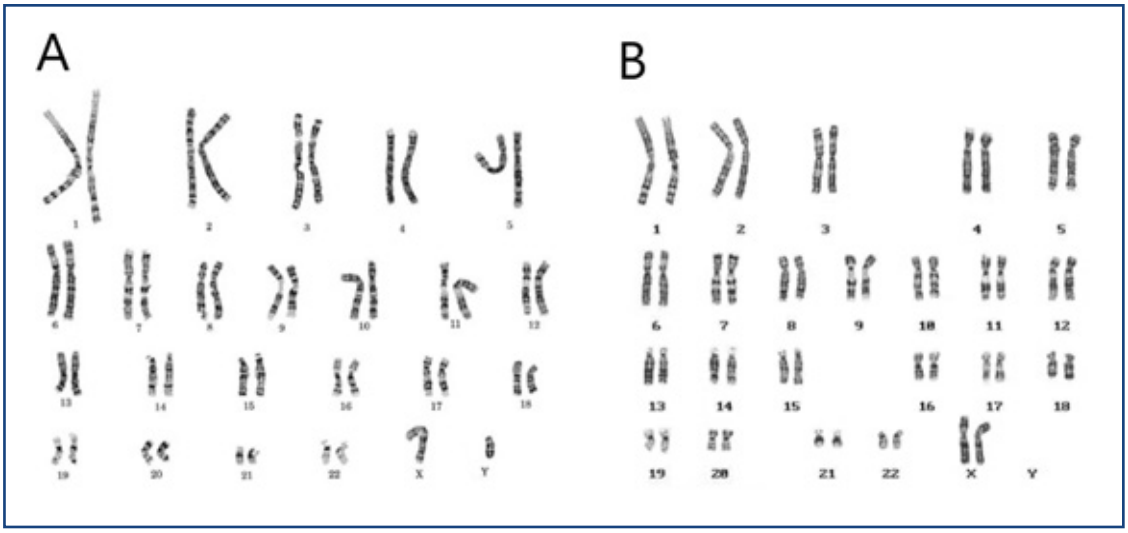

Figure 2: Mosaic karyotype of the patient showing (A) 46,XY and (B) 46,XX

Molecular study using PCR analysis for the SRY gene revealed the presence of the SRY gene sequence (Figure 3).

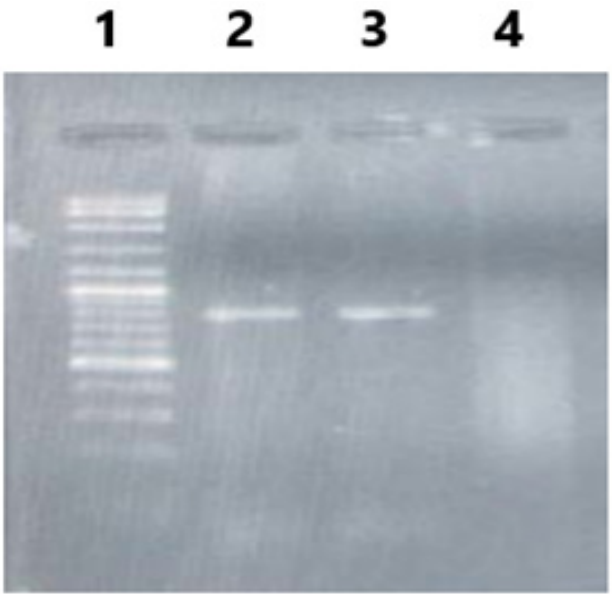

Figure 3 PCR amplification of the SRY gene: (lane 1) 100 bp ladder; (lane 2) +ve control (fer-tile female); (lane 3) patient, (lane 4) -ve control (fertile male).

A sexual orientation study using the Minnesota Multiphasic Personality Inventory (MMPI) showed a strong female personality.

The diagnosis of OT-DSD was reached, and following several counseling sessions by the Sudanese Intersex Working Group (SIWG), the patient and her family agreed that the patient should continue being reared as a female. Left orchiectomy and phallus reduction were per-formed with an uneventful post-operative course.

Post-operative histopathology revealed spindle cell stroma supporting degenerative tubules, suggesting ovotestis for the first spacemen. In contrast, the second specimen showed stratified squamous epithelium. The fibrovascular stroma indicates penile tissue.

The case report received ethical approval from the ethical committee of Al Neelain Stem Cell Center, Al Neelain University. The data were anonymized and informed consent was obtained from the parents of the patients.

DISCUSSION

Sudan, as a vast nation with diverse cultures and deeply ingrained belief systems, faces a high prevalence of illiteracy, particularly in rural areas. Within this societal context, individuals affected by DSD are often perceived as having either a spiritual gift, a curse, or a social stigma, leading to parental reluctance in seeking medical advice or Western treatment.[10] Families who pursue medical assistance for their DSD-affected children may face social isolation, rejection, job loss, and may even need to relocate.[11] The substantial psychological burden on patients and their families often results in concealing the condition, contributing to delayed diagnoses seen in developing countries compared to developed nations.[12]

Most DSD cases in Sudan, including our patient, are delivered at home (64.8%) and assigned a gender by non-trained personnel. This practice leads to delayed diagnosis in 40% of patients, with early diagnosis occurring in only 4.9% of cases.[7] Incorrect sex assignment can result in lifelong consequences, especially for XY DSD individuals wrongly assigned as female, who may undergo female genital mutilation (FGM). This practice leads to irreversible damage to the genital organs and greatly impacts reassignment decisions.[4,7] Fortunately, our patient avoided FGM, allowing for reconstructive surgery limited to reducing the phallus size and ensuring a potential for a normal sexual life.

A recent 5-year study in Sudan observed that OT-DSD accounted for 6.7% of XY DSD cases and 3.2% of XX DSD cases.[13] Patients with OT-DSD typically presented in three patterns: lateral (20%) with a testis on one side and an ovary on the other, bilateral (30%) with both testicular and ovarian tissue bilaterally, often as ovotestis, and unilateral (50%) with an ovotestis on one side and an ovary or testis on the other. The ovary was more frequently on the left side, while the testis was more commonly on the right in lateral OT-DSD cases. [7,13]

Notable findings in our case include the presence of three gonads (two ovaries and one ovotestis) and fully developed functioning Mullerian structures, resulting in a normal-sized uterus and regular menstrual cycles.[14] The patient sought medical attention solely due to ambiguous genitalia (a large phallus, later identified as a penis). She was treated by the Sudanese Intersex Working Group (SIWG), a multidisciplinary team established 20 years ago and based in Khartoum, that includes a psychiatrist, obstetrician, urologist, pediatric surgeon, pediatrician, and clinical geneticist to elevate the diagnosis and management of DSD cases in Sudan.[8] However, as the team is based in Khartoum, only patients able to travel to the capital can receive their care. Despite this limitation, SIWG's media campaign has encouraged rural populations to seek assistance, expanding its role to include social support and providing free investigations and genetic workup for financially disadvantaged patients.

CONCLUSION

In low-resource healthcare settings, it is essential for caregivers to remain vigilant for ambiguous genitalia and to facilitate timely referrals for accurate diagnosis and counseling before sex assignment. Given the heterogeneity and complexity of DSD, a multidisciplinary approach is crucial in providing optimal care. This case emphasizes the importance of maintaining a high index of suspicion for DSD in adolescents presenting with abnormal pubertal development or atypical genital findings.

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