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# Differences of sex development (DSD) in 46XY, 5-alpha-reductase-2 deficiency patient for vaginoplasty: A case report

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## ABSTRACT

Male pseudohermaphroditism, a syndrome defined by inadequate differentiation of male genitalia in 46, XY patients, is caused by steroid 5-alpha-reductase 2 deficiencies, an uncommon ailment. Here, we discuss the case of a 13-year-old from Wardha, Maharashtra, who was identified as female by relatives and who displayed primary amenorrhea, ambiguous genitalia, and absence of breast development. Every serum hormone profile showed testosterone levels of 460ng/dl (normal), dihydrotestosterone levels of 16ng/dl (decreased), and an elevated T/DHT ratio. Chromosome analysis identified a 46, XY karyotype. A Phallus reduction and Mcindode vaginoplasty were carried out, along with clitoroplasty, orchiopexy, and gonadoplasty, and estrogen-based hormone replacement therapy was initiated. In conclusion, babies with unclear genitalia or adolescents or young adults with the recognizable phenotypic and blood hormone profiles may have 5-alpha-reductase 2 deficiencies. However, the psychological aspects put more of an emphasis on the patient's quality of life as it relates to their health, as well as their family's adjustment and their psycho-social and psycho-sexual development.

**Keywords:** DSD, 46XY, ambiguous genitalia, multifactorial approach, gender assignment

## 1. INTRODUCTION

DSD is a group of congenital anomalies in which development of chromosomal, gonadal and anatomic sex is atypical. Analysis of clinical management strategies focuses on accurate diagnosis and delivering appropriate surgical treatment, gender assignment, desirability of the family and timing of genital reconstruction surgery (Lee et al., 2006). But on the contrary, the psychological aspect focuses on patient's health-related quality of life and adaptation of family and patient, psycho-socially and psycho-sexually. 1 in 20,000 births among persons with 46, XY are predicted as incidence rate to be affected by a DSD. Ovotesticular DSDs have been

estimated to occur in 1 of 100,000 live births. The frequency of testicular or mixed gonadal dysgenesis is estimated at 1:10,000 (Pasterski et al., 2010). The worldwide incidence of 46, XX DSD, consisting primarily of CAH - mostly 21-hydroxylase deficiency, has been estimated to be 1 in 14,000-15,000 live births, but it varies by regions because of ethnic differences in gene mutation frequency. CAH and mixed gonadal dysgenesis constitute about half of all DSD patients presenting with genital ambiguity (Lin-Su et al., 2015).

When all congenital genital anomalies are considered, including cryptorchidism and hypospadias, the rate may be as high as 1:200 to 1:300 (Blackless et al., 2000). Among patients with hypospadias and cryptorchidism, currently the diagnosis of specific DSD conditions is generally limited to those with proximal hypospadias with cryptorchidism. The overall incidence estimations also include those with Klinefelter syndrome (estimated in 1:500 to 1:1000 live births) and Turner syndrome (about 1:2,500 live births). These known estimates hopefully provide a useful perspective (Nistal et al., 2015).

## 2. HISTORY

A 13 year patient, identified as female child by family members since birth (Figure 1) and voiding through urethral opening in perineum. Patient presented in OBGY opd, AVBRH wardha with husky voice and amenorrhoea/ breast development at puberty with secondary sex characteristics of female.

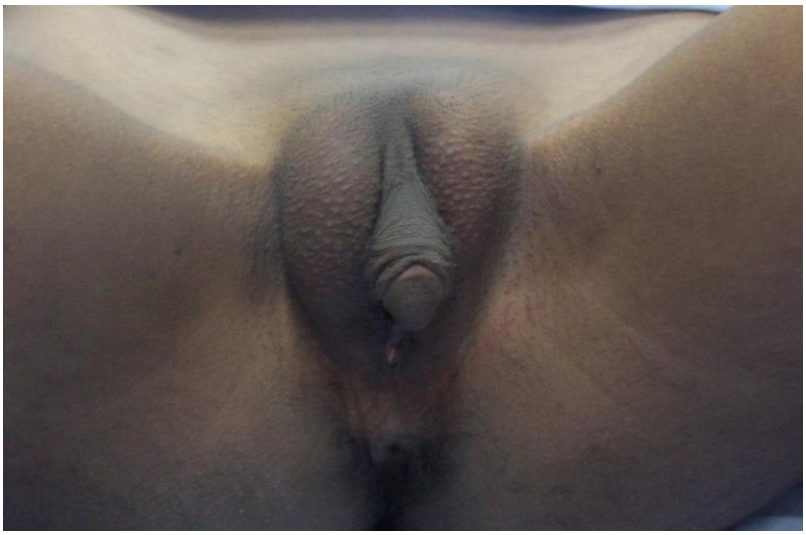

**Figure 1** 46 XY Identified as female by relatives

**External findings**

Undifferentiated phallus, urethral opening through perineum, non-fused labioscrotal folds containing both testis were seen (Figure 2).

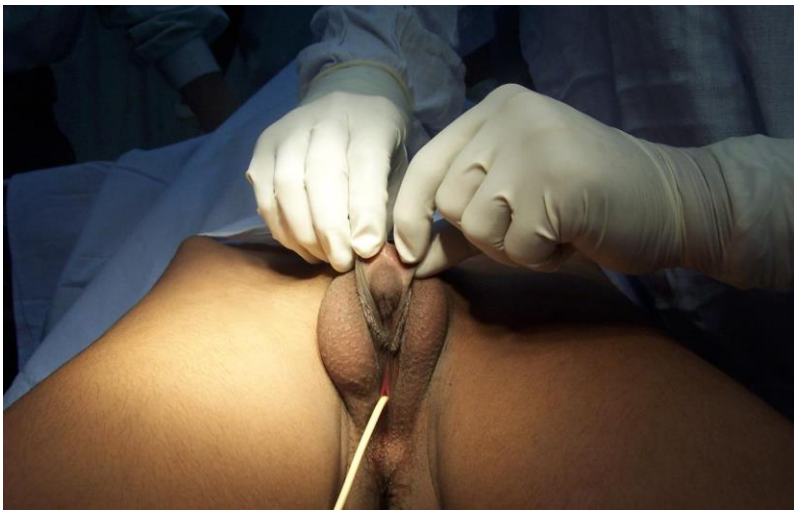

**Figure 2** Undifferentiated phallus, urethral opening through perineum, non-fused labioscrotal folds

**Investigations**

Chromosomal structure on karyotyping: 46XY

Laboratory findings: 460ng/dl testosterone (normal), dihydrotestosterone 16ng/dl (decreased); increased T/DHT ratio.

Abdominopelvic - USG: no internal female structures. Urethrocystoscopy: male urethra poorly developed prostate, blind-ending vagina.

**Diagnosis**

5-alpha-reductase-2 deficiency; under-virilised male-ambiguity of genitalia

**Aim**

To restore external genitalia closest to being non-ambiguous, retaining full sensation and sexual satisfaction.

**Preoperative workup**

Family and patient's wish was to remain a female so were provided with psychological counselling for 4 months with disclosure that she can experience masculinization shortly if not intervened. Prognosis (gender identity outcome, fertility and sexual function) with risks and benefits for proposed procedures were explained.

**Surgery**

1. Phallus reduction and bilateral gonadectomy (Figure 3)
2. Mcindode Vaginoplasty at age 21 (6 months before marriage) (Figure 4)

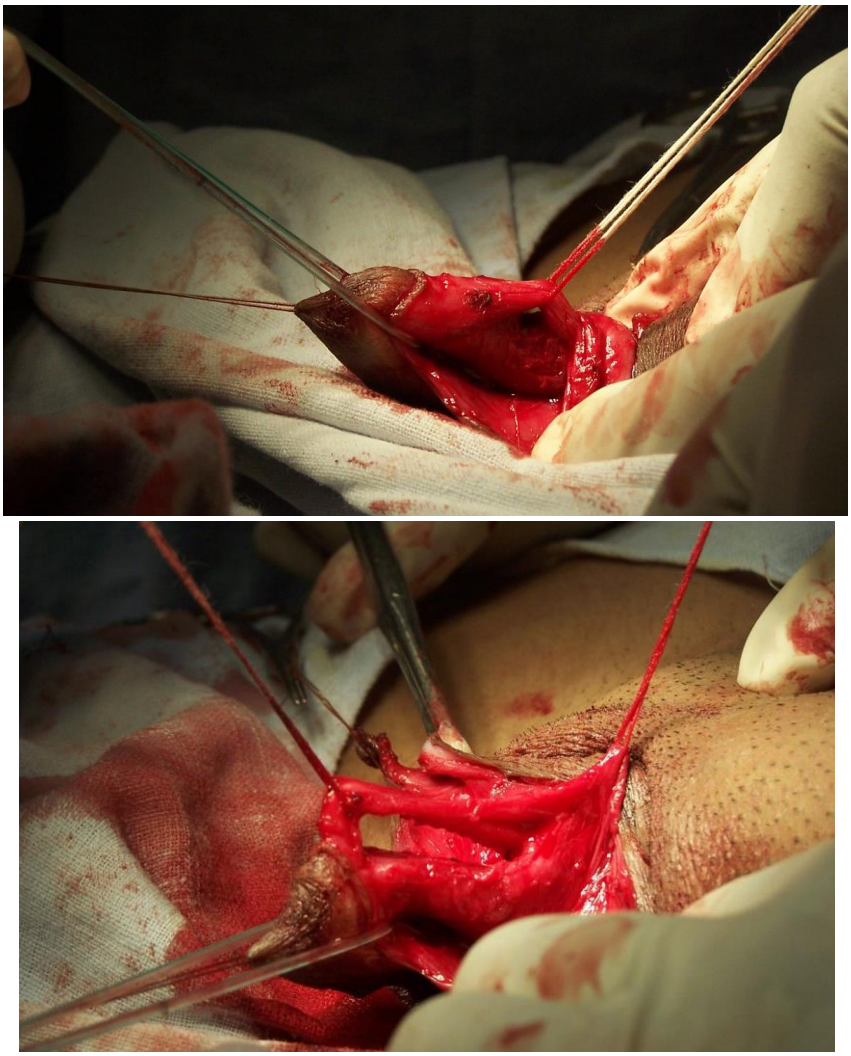

**Figure 3** Phallus reduction and Mcindode Vaginoplasty

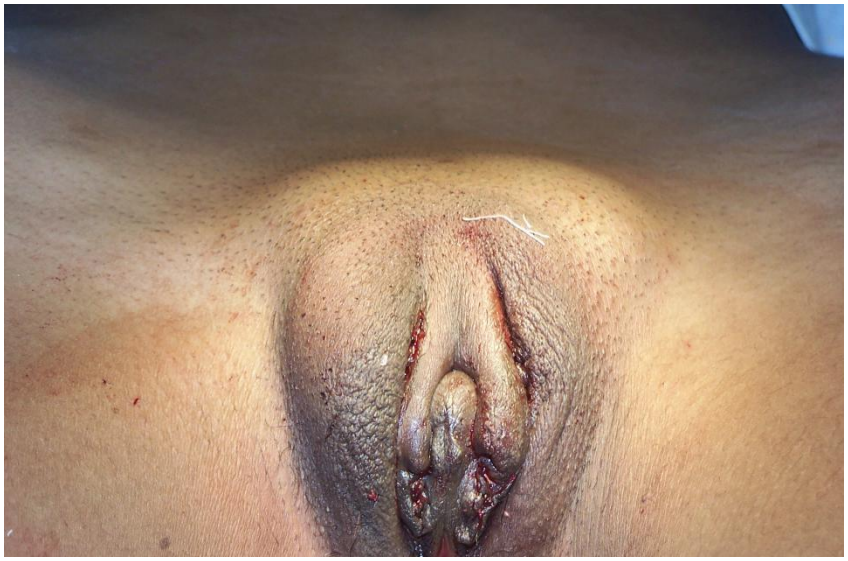

**Figure 4** Vaginoplasty done

DSD surgery includes 4 main components: (1) surgery of the genital tubercle which can be reduced in size (clitoroplasty) or reconstructed (hypospadias repair or phalloplasty) (2) the management of the Müllerian structures (vagina, uterus) which includes the connection of a vaginal cavity to the pelvic floor, vaginal substitution, dilatation of a vaginal cupule or removal of Müllerian remnants; (3) surgery of the gonads involves descent (orchiopexy), removal (tumor risk/late virilization) or biopsy for pathology or the preservation for reproduction, and (4) refashioning of the perineum (perineoplasty) (Figure 4), (5) Lifelong estrogen supplement with reasonably developed breasts. Considerations for each of these procedures involve indications, timing, technical aspects, possible complications and long-term outcome.

## 3. DISCUSSION

The 2006 Consensus Statement was a landmark for providers caring for individuals with DSDs and the larger community. Increasingly collaborative relationships are occurring in care settings and at national peer support group (PSG) meetings, reflecting growing prioritization of patient perspectives focusing on health and well-being outcomes (Skakkebaek et al., 2001). Community priorities for improvement have been identified, while disagreements regarding mutual goals for patient-centered research and care persist.

Overall contributors to be evaluated for male or female gender assignment included probable adult gender identity is most important factor but tentative, anticipated quality of sexual function, surgical options/indications/risks, fertility potential, evidence of fetal CNS exposure to androgens, gonadal malignancy risk and psychosocial factors (Thyen et al., 2006). While most difficult to predict, the anticipated quality of sexual function is a key factor.

**Multifactorial approach**

The initial physical examination must to be thorough, well-planned, and leisurely. Along with vital signs, anthropometric characteristics should be evaluated. Dysmorphic characteristics should be thoroughly inspected in the facies, limbs, and fingers. Despite medical interventions, psychologically informed research with adults using a variety of methods has identified specific challenges, such as dissatisfaction with binary gender, dissatisfaction with the DSD terminology, fear of devaluation, negative body image, social isolation, non-entitlement to relationships, preoccupation with heterosexual intercourse, functional sexual difficulties, barriers to communication with significant others, and experiencing narcissistic traits.

Since the effects of a diagnosis on well-being depend on a wide range of intrinsic and extrinsic factors over time, including physical health, age, social values, and access to resources like work, education, supportive relationships, and health-care experiences, psychological factors with any causal link between a diagnosis and a single psychometric measure are flawed (Nordenvall et al., 2014). Assigning newborns with ovotesticular syndrome to male or female genders is independent of karyotype highlights bias in gender determinations and the urgent need for evidence-based consensus. The assignment in the past was

affected by the placement of the urethral meatus and the attendant surgical difficulties, by testicular tissue with dysgenetic characteristics, and by the presence of a uterus and normal ovarian tissue.

Case studies describe patients who experienced gender dysphoria or who underwent patient-initiated gender transitions. Only systematic large long-term gender outcome and quality of life questionnare data will provide a sound empirical foundation for identifying the key variables influencing assignment decisions for this condition and others.

Factors to be evaluated before deciding further management of DSD patient (Figure 5): Clinical evaluation, Biochemical evaluation, Psychosocial and Psychosexual well being, Genotype, Hormonal treatment of patients, Assignment of male or female genitalia, Risks of tumour development, Possibility of fertility, Ethical, legal and cultural issues.

**Limitation**

Parents are responsible for consenting to interventions believed on the basis of available evidence to be in the best interests of their child, their right to consent to non-medically necessary irreversible procedures that may adversely affect the child's future sexual function and/or reproductive capacity has been questioned.

## 5. CONCLUSION

After diagnosis, male gender assignment is ideal due to prenatal androgen imprint on brain and masculinization at puberty; causing less chances of gender dysphoria with fertility, but phallus disfigurement, sexual dissatisfaction to partner and voiding difficulties are drawbacks. While female gender assignment considering psychological effect of retaining the gender identified at birth by family, plays a dominant social factor in deciding genital reconstruction with better functions but no fertility. This study emphasizes above two aspects of DSD surgery.

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**Informed Consent**

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

**Author's contribution**

All the authors contributed equally to the case report.

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**Conflicts of interest**

The authors declare that there are no conflicts of interests.

**Data and materials availability**

All data associated with this study are present in the paper.

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