



Female urogenital reconstruction in a case of sexual development disorder (46, XY) with cloacal exstrophy associated with diphallia

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ABSTRACT

Disorders (or differences) of Sex Development (DSD) comprise a state of genetic, gonadal and genital variation. Among the conditions associated with DSD is cloacal exstrophy, a rare congenital malformation part of the exstrophy-epispadias malformation complex. Thus, the case of a patient with rare involvement of DSD 46, XY cloacal exstrophy associated with diphallia who underwent surgical treatment for female urogenital reconstruction is reported. The patient's electronic medical record was reviewed after presenting and accepting the Informed Consent. Sociodemographic and clinical-epidemiological variables and pre- and postoperative data were analyzed. The patient was 20 years old, white and raised considering to be female. She was born with cloacal exstrophy, with severe morphological changes in the external genitalia, and submitted to terminal ileostomy, cystoplasty, and rudimentary large bowel colectomy during the neonatal period. At 13 years of age, the patient reported discomfort with the appearance of her external genitalia and the need for constant use of diapers due to urinary incontinence. The patient underwent reconstruction of the urinary and genital tracts during adolescence besides a genitoplasty followed by regular vaginal dilation. At age 17, she reported feeling satisfied with the surgical result, denied discomfort with the current aspect of her genitalia and mentioned identifying herself with the female and male genders, with increased adherence to typically female behaviors. A supposedly favorable outcome in the late adolescence of a DSD 46, XY cloacal exstrophy subject who underwent surgical adaptation for sexual definition after a multidisciplinary approach was reported. The patient revealed a non-binary gender identity, absence of gender dysphoria, satisfaction with her own body and androphilic sexual orientation.

Reconstrução urogenital feminina em um caso de transtorno do desenvolvimento sexual (46, XY) com extrofia de cloaca associada a difalia

RESUMO

Os distúrbios (ou diferenças) do desenvolvimento sexual (DDS) compreendem um estado de variação genética, gonadal e genital. Entre as condições associadas à DDS está a extrofia cloacal, uma malformação congênita rara que faz parte do complexo de malformação extrofia-epispádia. Assim, relata-se o caso de uma paciente com raro acometimento de extrofia cloacal DDS 46, XY associada a difália que foi submetida a tratamento cirúrgico para reconstrução urogenital feminina. O prontuário eletrônico da paciente foi revisado após a apresentação e aceitação do Termo de Consentimento Livre e Esclarecido. Foram analisadas variáveis sociodemográficas e clínico-epidemiológicas, bem como dados pré e pós-operatórios. A paciente tinha 20 anos, era branca e criada considerando-se do sexo feminino. Nasceu com extrofia cloacal, com graves alterações morfológicas na genitália externa e foi submetida durante o período neonatal (em 2000) a ileostomia terminal, cistoplastia e colectomia rudimentar de intestino grosso. Aos 13 anos a paciente relatou desconforto com a aparência da sua genitália externa e necessidade de uso constante de fraldas devido à incontinência urinária. A paciente foi submetida à reconstrução do trato urinário e genital na adolescência, além de genitoplastia seguida de dilatação vaginal regular. Aos 17 anos relatou sentir-se satisfeita com o resultado cirúrgico, negou desconforto com o aspecto atual da genitália e referiu identificar-se com os gêneros feminino e masculino, com maior adesão a comportamentos tipicamente femininos. Foi relatado um resultado supostamente favorável no final da adolescência de um sujeito de extrofia cloacal DDS 46, XY que passou por adaptação cirúrgica para definição sexual após uma abordagem multidisciplinar. A paciente revelou identidade de gênero não binária, ausência de disforia de gênero, satisfação com o próprio corpo e orientação sexual andrófila.

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1. Introduction

Disorders (or differences) of Sex Development (DSD) comprise a state of genetic, gonadal and genital variation. These disorders present an estimated incidence of 1:4,500 live births, encompassing a heterogeneous group of phenotypic manifestations with different etiologies and broad variability of presentation, even within the same etiological group (1).

Among the conditions associated with DSD is cloacal exstrophy, a rare congenital malformation with an estimated incidence between 1:400,000 and 1:200,000 live births, which is part of the exstrophy-epispadias malformation complex, characterized by impairment of the urinary, genital and digestive systems. These alterations in the embryonic formation are related to DSD due to the involvement of the external genital, which results, at birth, in a mistaken interpretation of the presumed embryogenesis, which may present an outcome with an atypical gender designation (1).

Scenarios involving DSD are challenging to healthcare teams and patients' families, imposing interdisciplinary and intensive work to coordinate medical, social, cultural and legal issues. Among the main challenges is the definition of the patient's gender, whose study requires the explanation of concepts related to psychosexual development (1). Gender identity is defined by the individual's self-characterization, which can be identified as male, female, both, or neither (2). The characterization of gender involves behaviors, attitudes, and personality traits that in a given culture or society, in a specific period, are typically considered female or male genders (2). Among the factors usually considered for evaluation in previous studies is the preference for toys that involve movement or violence or toys that involve care and rest, choices for sports, and preferences for typically female or typically male clothing (3).

Usually, the sexual phenotypic definition regarding this development is binary (typically with male or female genital), creating the expectation that the gender identity and its role develop in correspondence to the observed genital. DSD-related phenotypic sex determination is generally neither binary nor immediate, with some degree of genital ambiguity. Gender identity and the role of gender in cases of DSD can also present themselves in a complex way, being challenging to elucidate in advance, with consequences for the global development of the affected child (3).

In this context, we aim to report the case of a patient with rare involvement of DSD 46, XY cloacal exstrophy associated with diphallia, who underwent surgical treatment for female urogenital reconstruction. Furthermore, a retrospective assessment of the psychosocial and functional results was carried out using a qualitative approach, with a review of concepts of psychosexual identity and a discussion of the main paradigms in surgical management related to the sexual definition in cases of DSD. All procedures performed in the study were in accordance with ethical standards and approved by the Ethics Committee of Hospital Infantil Joana de Gusmão under registration 80487617.2.0000.5361 - 2.533.979.

2. Case report

This report was conducted following the electronic medical record review of a patient diagnosed with DSD 46, XY cloacal exstrophy associated with diphallia and hospitalized for surgical treatment of female urogenital reconstruction after presentation and acceptance of the Informed Consent. The following sociodemographic and clinical-epidemiological variables were analyzed: sexual identity, religious beliefs, socialization and interpersonal relationships; diagnosis, classification, treatment and complications

related to DSD, psychological or psychiatric evaluations, quality of life and psychosexual development. The images were obtained from the medical records and collection of the Pediatric Surgery Service of the Hospital Infantil Joana de Gusmão, Florianópolis, Brazil. No new records were made to preserve the participant's anonymity, confidentiality, privacy and dignity.

The bibliographic search was carried out using the PubMed and Virtual Health Library (BVS-CAPES) databases with the following keywords: disorders of sexual development, DSD, cloacal exstrophy, quality of life, gender, psychosexual development, sexual identity, and gender identity. The articles cited in this study were selected considering their relevance in the field and date of publication, prioritizing the most recent.

The patient was 20 years old, white, raised as female, born and resident in Joinville (SC). According to the medical report, the patient was born with cloacal exstrophy with severe morphological changes in the external genitalia and submitted during the neonatal period (in 2000) to terminal ileostomy, cystoplasty and rudimentary large bowel colectomy. Later, she was discharged by the maternity hospital for registration in the female sex. On occasion, the child's parents were informed that there would be no conditions for the surgical construction of male external genitalia. Therefore, the immediate designation of the female gender and family raising were considered appropriate.

At three years of age, the child began follow-up at the Joana de Gusmão Children's Hospital in Florianópolis (SC) for gender definition but lost follow-up in 2004. The initial endocrinological investigation revealed a basal testosterone dosage of less than 20 ng/mL and a basal DHT of 3.3 pg/mL, with post-stimulus testosterone of 133 ng/mL and a post-stimulus DHT of 147 pg/mL, showing responsiveness to the stimulus and, therefore, the presence of functioning testicular tissue. Genetic analysis revealed the genotype 46, XY. In the initial consultations, the genetic, endocrinological and morphological aspects of the diagnosis were explained to the child and parents to inform them about the complex dimensions of the disorder (psychosexual and morphological). Emphasis was given to the multifactorial character of the evaluation before gender determination, making them aware of the importance of factors such as genotype, gonad evaluation, response to androgenic stimulus, and secondary significance of the external genitalia aspect.

The patient resumed follow-up in 2007, when there was a conflict between the parents regarding the gender in which the child should be raised. In 2009, the child was reassessed in an outpatient clinic, opting for the definition of the female gender and starting then hormone replacement therapy with estrogens. There was another loss to follow-up in 2009, returning in 2013. Until that moment, the patient had been socialized as a girl. At the time, at 13 years of age, the patient reported discomfort with the appearance of her external genitalia and the need for constant use of diapers due to urinary incontinence. When asked about gender behavior, she described engaging in sports-oriented games and outdoor activities, contacting male peers predominantly, but preference for "feminine" clothes.

She was ectomorphic, thin, with evident musculature and without breast development on physical examination. Pulmonary and cardiac auscultations were unaltered, the abdomen with terminal ileostomy in the right iliac fossa, perineum with imperforate anus, impalpable gonads, presence of two hemiphalli, with well-formed glans (the right one with partially tubularized urethral plate, pervius up to 1 cm and the left one with a partially tubularized urethral plate, pervius up to 2.5 cm), open bladder neck pervius to a digital pulp.

Abdominal ultrasound and magnetic resonance examinations showed ectopic kidneys located bilaterally in the pelvis, left kidney without alterations, right kidney with reduced

dimensions, lithiasis, atrophic and moderately hydronephrotic. Müllerian structures were not visualized. Static renal DMSA scan showed functional exclusion on the right. In November 2013, a urinary endoscopy showed a bladder with small capacity and thickened walls without visualization of the ureteral ostium. Due to an opened bladder neck, no cystography or cystoscintigraphy was performed.

In June 2014, the patient underwent reconstruction of the urinary and genital tracts. A right nephrectomy was performed, besides a continent urinary diversion for Monti-type bladder catheterization (Mitrofanoff principle), Politano-type left ureteral reimplantation, bladder neck disconnection, bilateral gonadectomy, ileal vaginoplasty, feminizing genitoplasty and ileostomy. Hydronephrosis was observed in the remaining kidney during postoperative follow-up (grade III on the left, according to the Society for Fetal Urology grading system), requiring bladder enlargement. The procedure was carried out in March 2016, with good evolution. In July 2016, the patient underwent surgical repairs of the genitoplasty, with good evolution, followed by regular vaginal dilation (Figures 1-3).

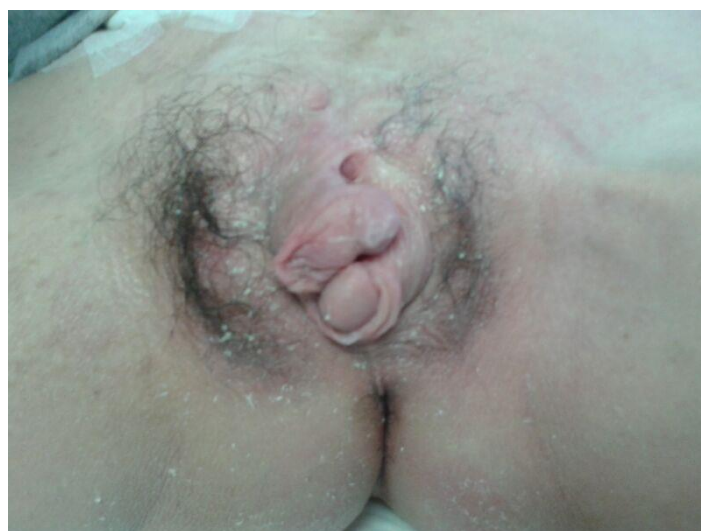


Figure 1 – Preoperative perineal aspect.



Figure 2 – Preoperative perineal aspect with the expression of the tubularized urethral plate on the right and an open bladder neck.



Figure 3 – Preoperative perineal aspect (1st and 2nd upper frames) and immediate postoperative appearance after corrective genitoplasty in July 2016 (remaining frames).

In the most recent follow-up, at age 17, the patient reported feeling satisfied with the surgical result. She denied discomfort with the current aspect of her genitalia and mentioned identifying herself with the female and male genders. However, the patient stated a progressive increase in adherence to typically female behaviors, such as makeup and greater interest in clothes considered feminine. Both the patient and her family members were retrospectively satisfied with the degree of information and dialogue established during the process of defining gender and sexuality and the genital surgical intervention. The patient reported that the surgical interventions positively impacted her daily life. The procedures provide urinary continence, eliminating the need to wear diapers and allowing her to feel more comfortable with her own body, improving her self-care. Also, she reported an exclusive romantic interest in male peers, without sexual activity so far. She denied worrying or feeling impaired by the lack of reproductive capacity. In addition, she expressed the desire to obtain tools that would allow her a less limited experience of leisure and socialization activities.

Cloacal exstrophy in individuals with XY karyotype may represent a complex malformation, considering the critical change in the urogenital anatomy. This factor often favors, due to technical issues, the performance of feminizing genitoplasty instead of penile reconstruction or phalloplasty (3). Another relevant factor is the growing number of gender identity problems in this group of patients. Thus, it has been proposed to postpone the surgical sexual designation until older ages (4).

Importantly, older practices of gender definition were exclusively oriented by the individual's karyotype, without considering the external or internal genital morphology. This approach was replaced in the 1960s by the optimal gender approach, considering the possibility of fertility, traditional sexual practices and genital surgical reconstruction (5).

Although there is an urgency in the sex determination in children with DSD, the negative influence of early surgical procedures on the quality of life of these patients when they reach adulthood has been shown. Currently, there is a tendency to postpone non-urgent

surgical interventions to encourage the participation of patients and their families in the decision-making process for their treatment.

Research carried out in the USA in 2011 with pediatric urologists identified that 79% of them agreed with the male determination for DSD 46, XY cloacal exstrophy. Among the main reasons listed for the decision is the possibility of testosterone imprinting (and its possible influence on favoring masculine identity and behavior). On the other hand, the arguments of physicians who preferred the female designation are mainly justified due to the greater ease of successful surgical reconstruction and the difficulty or uncertainty regarding phalloplasty results (6).

The mentioned imprinting effect seems uncertain in cases of cloacal exstrophy. Mirheydar et al. reported in 2009 the case of an XY DSD patient with cloacal exstrophy and female designation at birth, with female self-identification, who underwent feminizing genitoplasty (and, it was believed, bilateral orchiectomy) in childhood, who began masculinization at age 17 following elevated serum testosterone levels. The patient was previously unaware of being genotypically male, previously being informed that female gonads had been removed shortly after birth. After an imaging study, a remaining pelvic structure was identified, resected and identified as immature testicular tissue. The patient showed discomfort with masculinization, choosing to remove the hormone source. Afterward, she continued to identify herself as female, even though she was exposed to testosterone imprinting during childhood and its elevation at puberty (7).

The uncertainty of sex designation in cases of DSD is further evidenced through studies comparing its outcomes with those of other causes of DSD. Kreukels et al. reported 1,040 subjects who participated in the DSD-LIFE (multicenter study with 6 European countries), all affected by six groups of DSD (including cloacal exstrophy). An occurrence of 5% of gender transition initially attributed to the group as a whole was observed, with 1% of the group changing gender after puberty (or 3% if individuals affected by Turner or Klinefelter are excluded - conditions in which the identity of gender is not of great concern) (8). These data represent rates higher than expected for the general population, in which 0.2% to 0.7% of dysphoria or gender incongruity are estimated.

Although most gender transitions occurred during early childhood - often without the possibility of obtaining consent from the patient or guardians - the patient's desire for a new gender change in adolescence or adulthood was rare. Following the Chicago Consensus (2006), it is not possible to establish an age limit for impositions of gender change to be implemented without impairing child's gender identity development. According to previous data, a higher occurrence of gender change was observed in DSD 46, XY subjects exposed to androgens raised as females (8.6%) than in males (2.6%), as well as a higher incidence of change in patients with DSD than in the general population, but at not very high rates (7). Also, the desire for gender change can be alleviated in societies where "other gender" or "non-binary" gender options are accepted, with a greater possibility of accepting non-female, non-male, or intermediate gender identities. Mirheydar et al. showed self-reported identification with a gender nonconformity in 2.6% of subjects.

Patients with non-binary gender identification comprise a population of clinical interest due to the search for medical treatment for gender affirmation, contrasting with the lack of knowledge and protocols. To adequately address gender issues, it is essential to consider that not all patients identify with typical female or male social roles. Recognizing that gender is a non-binary phenomenon could facilitate an individual's satisfaction with their gender, regardless of their place on the gender spectrum (7).

However, it is noteworthy that the "gender role" differs from the "gender identity". Such differentiation is well exemplified in the literature in cases of DSD XX Congenital

Adrenal Hyperplasia, in which there is, in general, a more significant role for males than for females, although they maintain, for the most part, the female gender identity. Cases of cloacal exstrophy in XY karyotype subjects also illustrate the variability of the hormonal influence on psychosexual development, as it is common to maintain male gender identity even with severe genital alteration and variable exposure to testosterone (8).

It was observed in the present report that the patient had a gender profile with mixed characteristics and the presence of suggestive factors of "behavioral masculinization", which could be related to testosterone exposure. The patient preferred to remain female, agreeing with the feminizing genitoplasty. She identified herself as equally feminine and masculine (a "non-binary" identity), which can be unexpected for an XY cloacal exstrophy case.

Variations in psychosexual outcomes related to the supposed predictability that would result from exposure to androgens are relevant, as they show the potential for flaws in the decision-making of sexual, social and surgical determination based on this factor as determinant. Given the rarity of DSD 46, XY cloacal exstrophy, the lower predictability of outcomes and the presumed embryogenesis, the reporting of individuals who reach adulthood gains great importance.

3. Conclusion

The present report shows a supposedly favorable outcome in the late adolescence of a DSD 46, XY cloacal exstrophy patient who underwent surgical adaptation for sexual definition after multidisciplinary follow-up in a reference service. The patient revealed a non-binary gender identity, absence of gender dysphoria, satisfaction with her own body, and androphilic sexual orientation in the follow-up.

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