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Transition from pediatric to adult surgery care for patients with disorders of sexual development

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ABSTRACT

Disorders of sexual development (DSDs) are relatively rare congenital conditions in which the development of the chromosomal, gonadal, or anatomic sex is atypical. Some conditions may not manifest until puberty or adulthood. The examination and workup of either an infant or an older patient with suspected DSD should be directed and performed systematically by a multidisciplinary team. Ideally, the team will include those with not only an interest in DSD but also experience with this group of patients. This article will briefly orient the reader to the conditions and decisions that may have been made during infancy, childhood, and adolescence and then focus on the challenges that may accompany transitioning the care of DSD patients from pediatric to adult surgeons and specialists to enable appropriate decisions and care. The actual transition will optimally involve a well-developed action plan that will take place gradually over a number of years as the person becomes educated about their condition and empowered to participate knowingly and actively in their own care.

Introduction

Disorders of sexual development (DSDs) are relatively rare congenital conditions in which the development of the chromosomal, gonadal, or anatomic sex is atypical. A person may be born with reproductive or sexual anatomy that does not seem to fit the typical definitions of female or male, but some persons will have external genitalia that appear normal, and a DSD will not initially be suspected. The general diagnosis of a DSD is often made soon after birth, although the precise diagnosis may be dependent on a host of diagnostic tests. Some conditions may not manifest until puberty or adulthood. Taking care of persons with DSD is not a "one-size-fits-all" process. Perhaps the ideal approach is to consider each patient and family as a unique unit and work within the constraints of their environment to provide optimal care and empathy. This article will briefly orient the reader to the conditions and decisions that may have been made during infancy and childhood and then focus on the challenges that may accompany transitioning the care of persons with DSDs from pediatric to adult specialists and surgeons to enable an appropriate decisions and care.

Categories of disorders of sexual development

DSDs may be categorized into 3 main groups: genetically female with phenotypic masculinization (female DSD or 46,XX DSD), genetically male with phenotypic feminization (male DSD or 46,XY DSD), and gonadal ambiguities or absence resulting from chromosomal abnormalities or syndromes. Table 1 provides examples of conditions in each category.

There are somewhat limited data on the prevalence and incidence of DSDs, although the reported incidence seems to be increasing. The incidence of the conditions that comprise DSD is estimated to be somewhere between 1:5500[1] and 1:2000 globally.[2] Congenital adrenal hyperplasia (CAH) is the most common recognized cause of infant DSD with a global incidence estimated at 1:15,000, and mixed gonadal dysgenesis is considered the second most common cause with an incidence of 1:10,000.[1] The reported incidence of DSDs in individuals with hypospadias and cryptorchidism ranges between 17% and 50%.[3] Not all conditions classified as a DSD result in abnormalities of the external genitalia. For example, Turner syndrome (45,XO) and Complete Androgen Insensitivity

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Table 1
Disorders of sexual development categories

Female DSD 46,XX DSD	Male DSD 46,XY DSD	Gonadal ambiguities or absence
Congenital adrenal hyperplasia 21-Hydroxylase deficiency 11-Hydroxylase deficiency 3β-Hydroxysteroid deficiency	Androgen insensitivity syndrome Partial AIS Complete AIS	Mixed gonadal dysgenesis (45,X/46,XY)
Aromatase deficiency	Insufficient testosterone production P450scc defect P450c11 defect P450c17 defect P450c21 defect	Pure gonadal dysgenesis (46,XY) Ovotesticular DSD Developmental disorder or syndrome Cloacal abnormalities Bladder exstrophy Caudal regression syndrome VACTERL syndrome
	Inability to convert testosterone to dihydrotestosterone 3β-Hydroxysteroid dehydrogenase 17-Ketosteroid reductase 5α-Reductase deficiency	
	Persistent Mullerian duct syndrome	

Adapted from Fallat et al.[6]

Syndrome (CAIS) both have a normal female phenotype, and Klinefelter syndrome (47,XXY) has a normal male phenotype.[4]

Diagnosis

The examination and workup of either an infant or an older patient with suspected DSD should be directed and performed systematically by a multidisciplinary team. Ideally, the team will include those with not only an interest in DSD but also experience with this group of patients. The team may consist of surgeons, gynecologists, urologists, endocrinologists, neonatologists, pediatricians, psychiatrists or psychologists, nursing staff, and social workers depending on the age of the patient at presentation. Initial evaluation will include some or all of the following: a careful history and physical examination, karyotype, electrolytes, serum hormone analyses, and cytogenetic and molecular studies. Radiologic studies may include ultrasound examination, magnetic resonance imaging, and contrast study (retrograde genitogram or voiding cystourethrogram).[4,5] In some cases, cystoscopy, endoscopy, and laparoscopy are performed. Given the spectrum of findings and diagnoses, no single evaluation algorithm or protocol is recommended for all circumstances, and more detailed descriptions of the indications for specific tests are available elsewhere.[6]

Management

Once a DSD is identified, the management of the patient becomes paramount. The central issues to consider include the following: the DSD categorical diagnosis of the patient, gender assignment if the patient is a newborn infant, endocrine medical treatment, indications for and timing of surgical procedures, and disclosure of medical information to the patient and family. Simple definitions that may be pertinent during evaluation of an age-appropriate person with a DSD include “Gender Identity” or the conscious and unconscious feelings of belonging to one sex or the other, “Gender Role” or what a person does or says to communicate his or her status to others, and “Gender Dysphoria” or feeling that one’s gender identity may be incorrect. Research on gender identity has shown that children can accurately label their sex at 24–36 months, although there is variability in this ability. Children differentiate male/female sex by physical and behavioral characteristics of others using activities, dress, hairstyle, behavior, and anatomy. A “Gender Identity Disorder” (GID) may arise at any age when there is incongruity of genetically determined sex, somatic phenotype, and gender identity.

While this article will not cover the details of medical treatment of DSD patients, it is crucial that this aspect of care is not overlooked. If not already done, DSD patients should establish care with an endocrinologist who is familiar with the spectrum of DSD diagnoses and respective medical management. Age-appropriate patients may alternatively find it valuable to discuss hormonal management, sexual function, and/or fertility considerations with a gynecologist, urologist, andrologist, or reproductive endocrinologist (Table 2).

What is the role of the pediatric surgical specialty team?

The pediatric surgery specialty team may include pediatric surgeons, pediatric urologists, and pediatric gynecologists and may not be the same in all medical centers. Surgery for patients with DSD is typically performed for one of the following reasons: (1) to treat or prevent a medical complication such as trapping urine in the vagina in a patient with a urogenital sinus, (2) to remove potentially dysgenetic gonads in a patient with mixed gonadal dysgenesis (MGD) or androgen insensitivity syndrome (AIS), (3) to improve the cosmetic appearance of the genitalia, (4) to enable a patient to participate in vaginal–penile intercourse, and/or (5) to achieve a sex-typical manner of urination.[7] The timing of surgical procedures, which procedures offer the best outcome, and whether surgery should be performed at all may be controversial in individual cases, and care may need to be individualized based on patient and family circumstances.

In the past 15 years, there has been a paradigm shift in the surgical management of DSD conditions. Historically, there was more aggressive surgical correction soon after diagnosis aligned with the sex of rearing, and this has been replaced with focused surgical correction directed by medically appropriate indications until such time as the individual can participate in the decision-making process.[8–13] One of the difficulties that ensues with this approach is the social stigma and developmental challenges that may await both the family and the developing person who must cope with looking and possibly feeling different until such time as gender is more definitively established or decisions are felt to be warranted or can be made. There is some knowledge that has been gained by understanding the natural history of gender orientation in individuals whose brain has or has not been influenced by the hormonal effects of androgen. For example, persons who have conditions such as CAIS where androgen receptor absence results in a complete lack of androgen effect despite a Y chromosome have a complete sex reversal and female orientation. Men with 5α-reductase deficiency, those with XY cloacal exstrophy, and severely