Journal of Pediatric Nursing (2014) **29**, e23–e34

Understanding Disorders of Sexual Development

Amy C. Rothkopf RN, MS, CPNP, MPH*, Rita Marie John EdD, DNP, CPNP, PMHS

Columbia University School of Nursing, New York, NY

Received 19 January 2014; revised 3 April 2014; accepted 7 April 2014

Key words:
Disorders of sexual development;
DSD;
Intersex

Abstract Studies estimate that the incidence of genital anomalies could be as high as 1 in 300 births. While it is rare for an infant to present with truly ambiguous genitalia, it is plausible that the pediatric nurse will encounter a patient with disorders of sexual development in his or her career. Cases of disorders of sexual development are challenging due to complexities of diagnosis, gender assignment, uncertain outcomes, treatment options, and psychosocial stressors. This article discusses the evaluation and management of children with disorders of sexual development and the nurse's role as child advocate and family educator.

A FAMILY ARRIVES in the office with a 5-day-old infant for a newborn visit. When reviewing the chart, you notice that the parents were told that their baby would be female based on prenatal ultrasound results. However, amniocentesis revealed a karyotype of 46, XY. Therefore the parents had expected a son, but the delivery room genital exam revealed a micropenis with penoscrotal hypospadias and partially fused labia majora. No labia minora are present, no testes are palpable, and an anatomically correct anus is normally placed. How will you educate this parent about their child's disorder? How will you help them decide on what treatment, if any, to pursue? How will you answer their questions about their child's future gender identity, sexuality, and fertility? This article will discuss the management of disorders of sexual development (DSD) to inform the integrated primary care and management of the child with DSD. It is the role of the nurse to provide education about diagnosis, complications, and treatment options, explain specialty findings, help the patient and family through psychological and social stressors, and ensure holistic care for the child with DSD.

Overview

DSD encompasses congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical (Lee, Houk, Ahmed, & Hughes, 2006). Studies estimate that the incidence of true genital ambiguity in DSD is 1 in 5000 to 1 in 4500 births (Thyen, Lanz, Holterhus, & Hiort, 2006; Ahmed & Rodie, 2010). It is estimated that the presence of genital anomalies, however, could be as high as 1 in 300 births (Ahmed & Rodie, 2010). While it is rare for an infant to present with truly ambiguous genitalia, it is plausible that the primary care pediatric nurse will encounter a patient with some form of DSD in his or her career. Cases of DSD can be challenging due to complexities of diagnosis, gender assignment, treatment options, and psychosocial stressors. Tables 1 and 2 provide a list of acronyms and terms used throughout the paper.

* Corresponding author: Amy C. Rothkopf, RN, MS, CPNP, MPH.
E-mail address: acr2151@columbia.edu.

http://dx.doi.org/10.1016/j.pedn.2014.04.002
0882-5963/

Etiology

DSD were categorized into three distinct groups (Table 3) by the Lawson Wilkins Pediatric Endocrine Society (LWPES) in 2006: sex chromosome DSD, 46, XY DSD, and 46, XX DSD, with some overlap between these groups (Figure 1) (Lee et al., 2006). A revised nomenclature was also proposed by this group in 2006 (Table 4). Normal sexual development follows a complex pathway of genetics and gonadal, ductal and genital development (Murphy, Allen, & Jamieson, 2011). Therefore, there are multiple steps in which interference or interruption of normal physiology will result in atypical genitalia at birth (Figure 2).

Sex chromosome DSD is associated with a numerical sex chromosome abnormality, which leads to abnormal gonadal development. Sex chromosome DSD includes gonadal dysgenesis and ovotesticular DSD. Patients with 46, XY DSD have one of three underlying DSD etiologies: defects in androgen synthesis and metabolism, resistance to androgens, or malformation syndromes. The etiology of 46, XX DSD is either exposure to excess androgens in utero or malformation disorders. While significant progress has been made in determining the genetic etiology of DSD, molecular and genetic diagnosis is determined in only 20% of DSD cases (Lee et al., 2006). Table 3 summarizes the classification, definition, and etiology of DSD, in addition to providing examples of each disorder.

Clinical Presentation

Diagnosis of the child with DSD is often a complicated, multi-step process involving multidisciplinary input from endocrinology, surgery, urology, social work and/or psychology, genetics, and often a fetal specialist. An understanding of how the diagnosis was reached is crucial to explaining treatment guidelines and reducing parental uncertainty through education of sexual functionality and fertility possibilities. It is also important that the nurse recognizes the psychological trauma that may be associated with multiple physical exams, blood draws, and imaging.

Table 1 Acronyms used in this paper.

Term	Definition
11-OH	11β-hydroxylase
17-OH	17-hydroxylase
21-OH	21-hydroxylase
5-ARD	5α-Reductase deficiency
CAH	Congenital adrenal hyperplasia
CAIS	Complete androgen insensitivity syndrome
CGD	Complete gonadal dysgenesis
DHEA	Dehydroepiandrosterone
DHT	Dihydrotestosterone
DSD	Disorders of sexual development
MGD	Mixed gonadal dysgenesis
PAIS	Partial androgen insensitivity syndrome
PCOS	Polycystic ovary syndrome
PGD	Partial gonadal dysgenesis
SOX 9	SRY-Box 9 transcription factor
SRY	Sex determining region Y gene
TSPY	Testis-specific protein Y-encoded

Table 2 Terms used in this paper.

Mosaic	Two or more populations of cells with different genotypes that have all developed from single fertilized egg (zygote), resulting from recombination or mutation in mitosis or meiosis. For example, in mosaic Turner syndrome, one X chromosome is missing in some cells but not others.
Chimeric	Two or more genotypes arise from the fusion of more than one fertilized egg (zygote) in the early stages of embryonic development. For example, in ovotesticular DSD, a 46, XX and 46, XY zygotes have fused.
Streak gonad	An incompletely formed ovary
Dysgenetic testis	An incompletely formed testis
Urogenital sinus	Confluence of vagina and urethra which exit as a common channel.

History

The first step in care should always be a thorough family and prenatal history. This should include family history of consanguinity, infertility, gonadal and urogenital malformations, and known familial occurrences of DSD, such as congenital adrenal hyperplasia (CAH) or complete androgen insensitivity syndrome (CAIS). Many parents are not aware of any family history of DSD, as it may have been hidden to protect the family member from stigma. A thorough investigation and family interview is therefore warranted. A comprehensive maternal and pregnancy history should include antenatal drug use and maternal symptoms of androgen excess, such as hirsutism or virilization. There is no evidence that assistive reproductive technologies are associated with DSD prevalence (Hughes, Morel, McElreavey, & Rogol, 2012). Whenever possible, prenatal ultrasound and karyotype reports should be obtained. Any evidence of ambiguous genitalia or discordinance between prenatal karyotype and ultrasound assessment of genitalia should be duly noted.

Physical Exam

A general physical exam should then be conducted with attention to dysmorphic features and genital anatomy.