Disorder of Sexual Development- A Medical Issue of Social Importance

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Abstract

Disorder of sexual development-formally known as ambiguous genitalia is not only a medical condition of importance, but is also a social emergency. A through workup is needed of the condition as sex assignment to this baby is very important. The article will focus on how to approach these cases along with their management.

Keywords: Congenital adrenal hyperplasia (CAH), Disorder of sexual development (DSD), Gonads.

Introduction

A social emergency-Disorder of sexual development (DSD) is basically is the ambiguity between the genetic, gonadal and phenotypic sex. A thorough assessment is the need of the hour as internal anatomy, karyotype and sex assessment cannot be only done from the baby's external appearance and also it should be expedited because of the life threatening conditions (e.g.: salt wasting CAH) within the first few days of life. Sex assignment to the baby is essential for the parents, but it should not be done rapidly to draw premature conclusions as the sex assignment basically depends on the anatomy, functional pre and post natal hormonal milieu, and the potential for sexual functioning and fertility, which may be independent of the genetic sex. DSD in a neonate can present with the following presentations (Table 1):

Table 1: Different presentations of DSD

a.	Bilaterally non-palpable testis with a phallus
b.	Unilateral cryptorchidism with hypospadias
c.	Bilateral descended testis with peno or perineoscrotal hypospadias
d.	Asymmetrical labioscrotal folds(with or without cryptorchidism)
e.	Discordance of prenatal karyotyping and external genitalia
f.	Overtly abnormal genital development (eg.cloacalexstrophy)
g.	Apparently female appearance with inguinal hernia or enlarged clitoris

Evaluation of a neonate with suspected DSD: The complete evaluation of a neonate with suspected DSD involves a through history, physical examination and laboratory evaluation.

History

The following points in history are to be considered in detail:

History of early neonatal death: Death of a male sibling from dehydration in early infancy (suspicion of CAH).

Drug exposure during pregnancy: Exposure to androgens, anti-androgens, estrogens, progestins or antiepileptics during pregnancy is to be considered.

Maternal virilisation during pregnancy: Due to maternal CAH per se, virilising ovarian or androgenic tumours or placental aromatase deficiency.

Ante natal examination findings: Oligohydroamnios, genitourinary malformations are to be taken into due consideration.

Family history: Family history of consanguinity, hypospadias, cryptorchidism, infertility, delayed puberty, corrective genital surgery, genetic syndromes, CAH etc. needs to be thoroughly taken.

Examination

A. **External genitalia:** The following things are to be examined:
   1. Stretched penile length
   2. Corporal width and engorgement
   3. Chordee if present
   4. Position of urethral orifice
   5. Presence of vaginal opening
   6. Symmetry and pigmentation of the scrotum or labiscrotal folds 2.5 cm is the normal stretched penile length of a term male neonate whereas clitoris is <1 cm in length in a normal term female.

B. **Gonadal examination:** Gonadal size, position and descent are to be seen. Abnormal genital

development with clitoromegaly, or a well formed phallus with an empty scrotum should raise an alarm that it is a case of female virilisation by CAH.

C. **Examination for mullerian structure:** A bimanual rectal examination can reveal the mullerian structures.

D. **Associated anomalies:** This should be carefully noted. Dysmorphism suggests a generalised disorder and so syndromes should be looked for.

Investigative Approaches

Laboratory Tests:

a. **1st line investigations:** Serum electrolytes, blood urea nitrogen, creatinine, karyotyping, 17 OHP, testosterone.

b. **2nd line investigations:** Plasma rennin activity, LH, FSH.

c. **Others:** Fluorescent in situ hybridisation.

Radiological examination: Sonography of the pelvis to localise cryptic testis, to see for mullerian structure and moving further to MRI if sonography is inconclusive. Radiological examination of the kidneys, ureters and bladder should also be done.

Voiding cystourethrogram or genitogram: It may reveal connections between genital and urinary tracts, a vagina with a cervix at its apex or a mullerian duct remnant.

Treatment: A dedicated multi-speciality involvement is needed in a case of DSD which should include along with a pediatrician, a pediatric endocrinologist, an urologist, a reconstructive surgeon, a medical gene cist and a psychiatrist. The treatment options are:

1. **Reconstructive surgery:** The main goal in this therapy is cosmetic so that the genitalia look natural and also restoration of sexual functions. Repeat surgeries may be required to achieve the above goal. Some surgeries are successful when performed after birth whereas on the other hand some are performed at puberty.
   Sexual function of organs is often not compromised despite any ambiguous appearance for female babies. It should also be kept in the mind that testis are to be removed soon after birth if female sex of rearing has been decided.
2. **Hormone therapy:** Hormone therapy alone may be enough to correct the initial hormonal imbalance, but this depends on the severity of the condition. An important factor in sex assignment is-the ability of the gonads to produce appropriate hormones for sex of rearing. Henceforth it is useful to retain a gonad appropriate to the assigned sex if it is likely to function adequately. Ovaries of the virilised genetic females can be assumed to be normal functioning. Even in the case of true hermaphrodites, the ovaries may also produce adequate levels of estrogen. On the other hand, the testes of true hermaphrodites and those of infants with mixed gonadal dysgenesis may initially show good function but it declines during childhood, so testosterone supplements may be necessary for pubertal establishment.

Needless to say, long term studies are still needed which need to be unbiased in this aspect of gender identity and sexual functioning for those born with DSD, so that our understanding into this difficult task of gender assignment is increased.

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