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EDITORIAL

The ESPU/SPU standpoint on the surgical management of Disorders of Sex Development (DSD)

DSD management and more specifically surgical management of DSD has been the target for much criticism coming from various sources including a recent UN report on torture (!) and a Swiss ethical committee. Specialists involved in DSD management are primarily represented by paediatric urologists as well as paediatric endocrinologists who are aware of the dissatisfaction expressed by some DSD patients who feel that the treatment they received, several (sometimes more) more than 30 years ago, did not result in the anticipated outcome. Multidisciplinary DSD teams including surgeons acknowledge these difficult situations and the questions raised. They also understand and respect the suffering expressed by some patients. It is with great humility that several DSD surgeons-on behalf of several scientific societies - would like to make the following comments to dissipate some inappropriate and biased statements and try to clarify our perspective.

Who are we talking about?

DSD is a generic term introduced in 2005 (Chicago consensus conference) that applies to different congenital conditions many of which are characterized by the unusual appearance of external genitalia and/or atypically developed gonads with potential negative consequences on psychosexual development, fertility and cancer risk. The same consensus meeting tried classifying these complex conditions according to their underlying chromosomal profiles. Although this new classification is not ideal, it has the advantage of avoiding previous terms which were both confusing and considered pejorative by some patients and patient support groups.

DSD is currently classified into four main groups:

1) The **46,XX DSD** patients are individuals who are genetically female, most commonly due to Congenital Adrenal Hyperplasia (CAH), and presenting with an overdeveloped genital tubercle (clitoris), no vaginal connection to the perineum and enlarged and merged genital folds. The internal genitalia are female and usually normal.
2) The **46,XY DSD** patients are genetically male and constitute a more heterogeneous group representing a spectrum from normal appearing females to males with hypospadias and infertility. These patients may have underdevelopment of the genital tubercle (hypospadias and/or micropenis) with or without undescended gonads, with or without feminine remnants (mullerian structures). Within this group are patients with dysfunctional gonads (gonadal dysgenesis), impaired steroidogenesis (17 beta hydroxysteroid dehydrogenase deficit…), dysfunctional central hormonal control, and dysfunctional target tissues (androgen insensitivity; 5 alpha reductase deficiency).
3) The **chromosomal abnormalities** or mosaicisms are mostly represented by the 45,X0/46,XY individuals (mixed gonadal dysgenesis).
4) The rarest group is the ovo-testicular DSD. These two last groups (3 and 4) of patients bear both female and male genetic and anatomic elements. They typically have asymmetric genitalia with one side more masculine and the other side more feminine. The gonads can be testis, ovary or both, or dysgenetic gonads with a high risk for gonadal tumour development later in life.

We will not mention here other genetic or chromosomal disorders such as Klinefelter syndrome or Turner syndrome where the external genitalia are usually normally developed.

This quick overview of the different forms of DSD demonstrates the extraordinary complexity of each of these conditions which cannot be grouped under one broad title misguidedly done in some of the statements referred to above. Additionally, even within each of these categories is

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a spectrum of anomalies, adding to the difficulty in generalizations regarding management and outcomes.

Diagnostic context

The context of DSD diagnosis can be described in three periods of life:

Prenatally, discordance between the ultrasound appearance of the foetus's genitalia and the karyotype can suggest a possible DSD.

A common presentation is at birth with a child born with unusual genitalia. In some complex cases, assignment of the child's gender can be delayed by the medical team until the diagnostic process is completed. Assigning a gender based upon anatomical (phenotype) and biological criteria without certainty of the individual's ultimate gender identity is a major challenge which is at the core of some of the criticisms directed at the medical team.

The diagnosis can occur later in life, as in an individual raised as female who undergoes surgery for an inguinal hernia in which testis are found in whom primary amenorrhea is diagnosed (complete androgen insensitivity syndrome) or a girl who presents signs of virilization at puberty (5 alpha reductase; 17 beta hydroxysteroid reductase…). Alternatively, an individual raised as male may present with gynecomastia or infertility. In this group of patients, the gender identity is usually well established.

What are the possible consequences of these situations?

Atypically developed genitalia can affect not only physical appearance and body image, but also function of the urinary tract, kidneys, gonads, and the psychological and psychosexual development of the individual. Therapeutic management of these patients is, therefore, not limited to "cosmetic" surgery as stated in some reports but has a direct impact on:

Assignment of gender in rare and complex conditions.

Connection of the genital cavities to the perineum which may lead to fluid retention early in life and dysmenorrhoea and sexual dysfunction later.

Poor penile development and its consequences on sexuality in the adult male.

Enlargement of the clitoris which can alter body image and be associated with painful erections in the female.

Fertility in both males and females.

The risk of gonadal cancers early and later in life.

The risk of urological symptoms such as incontinence and the development of urinary tract infection.

Development of an individual's gender identity and gender role, a multifactorial process in which anatomical appearance likely plays a role.

What are the aims of medical and surgical management?

Avoiding potential health hazards related to the altered anatomy and function of the urogenital tracts, meeting parents' expectations and helping the individual to achieve future satisfactory sexual function, consistent with their gender identity are the three main objectives of the DSD team management. It is clearly a great challenge which can best be fulfilled if an experienced multidisciplinary team is available to advise the patient and his/her family. This suggests that specific DSD centres should be identified to provide the most appropriate care to these children and their families.

What does surgery entail?

Feminization procedures include the opening of the vaginal cavity to the perineum as in CAH or, androgen insensitivity syndromes, steroidogenesis deficits, enlargement or creation of a vagina either by dilatation or by substitution (bowel, peritoneum), the possible reduction of the genital tubercle for clitoral hypertrophy with nerve preservation, and reconstruction of the perineum.

Masculinization procedures include hypospadias surgery or, in rare cases, phalloplasty.

Ovaries are usually preserved unless associated with dysgenetic testicular tissue which may carry a risk of malignancy.

Testes are either brought down in boys or removed if dysgenetic with tumour risk or in complete androgen insensitivity syndrome or 5 alpha reductase deficiency. Testicular prostheses can be inserted at puberty at the patient's request.

Mullerian remnants can also be removed in boys if they cause urological (infection, dysuria) or gynaecological (menstruation) symptoms.

The current dilemma in 2013

Recent controversies regarding DSD management have involved:

The long-term outcomes of early reconstructive genital surgery with reportedly poor cosmetic and functional results.

The irreversibility of the reconstruction.

The absence of consent from the young patient in a major decision for his or her future.

Secrecy or incomplete disclosure of relevant medical information to patients.

It is critical to understand that the outcomes which one evaluates today result from surgery performed 20 or more years ago with techniques which are now considered obsolete. It does not guarantee superior results from modern techniques but one will have to wait another 15 years to evaluate current procedures. Current techniques are designed to preserve important function and anatomical structures, particularly the nerves leading to the clitoris.

The few publications available on long-term outcomes of feminization procedures are all retrospective and uncontrolled, reporting short and heterogeneous series. Some of them are quite positive, others very critical, regarding the impact on sexual function and particularly clitoral sensitivity primarily in the CAH group. There is also heterogeneity of DSD management between centres, which contributes to the confusion of analysing outcomes.

Some DSD patients who were gender assigned early in life developed gender dysphoria (divorce between the assigned and the individual's own gender identity) at a later age. This has been recognized with 5 alpha reductase deficiency, where it has been reported that 60% initially raised as female decided to choose a male gender after puberty and 46,XY DSD raised as female (cloacal exstrophy). These conflicting situations are at the origin of a plea by social scientists and support groups to avoid irreversible surgery at an early age when the concerned individual has no voice, and must rely on a surrogate (parent) to decide.

One critical issue is, therefore, the timing of genital reconstruction with some supporting a later procedure when the individual is able to express his/her views on the situation, whereas others favour early surgery to restore more normal visible anatomy, and avoid ambiguity which is often the parents' wish.

Supporters of the latter option claim that surgery is technically easier early with possibly less psychological impact than genital surgery at adolescence, which bears a much higher morbidity risk as the magnitude of the procedure is even more significant with very few surgeons experienced in this field. It is of interest that opponents of early surgery have no evidence that late surgery is better.

What are the alternatives?

There is an ongoing debate on the indications and timing of genital surgery in DSD. Each patient and each situation is different and it is the role of the multidisciplinary team to individualize the treatment to the patient and family. The therapeutic approaches to the multitude of DSD's vary widely and it would be an oversimplification to generalize their management, as has unfortunately been done in several recent reports.

The Chicago consensus meeting of 2005 was in favour of early gender assignment to allow a "social visibility" essential for the child and the family. Indications and timing of surgery were not detailed.

It is perfectly reasonable to delay gonadal surgery as long as the tumour risk is evaluated and the gonadal follow-up secured. The critical issue is the irreversibility of early surgery versus untried and unevaluated major reconstructive surgery at adolescence a highly stressful period of psychological development.

We are reminded by transgender patients (with normal chromosomes, gonads and anatomy but the sense that they are the incorrect gender) of the difficulty in predicting gender identity when structures are ambiguous. And unfortunately, there are situations for which any decision may lead to dissatisfaction.

Where do we go from here?

A discussion on these complex issues is essential. We strive for a more prospective scientific approach to each specific DSD condition with the contribution of all parties with an emphasis on proper outcomes research. Participation in databases should be strongly encouraged. It is the desire of all DSD surgeons to promote this discussion and avoid the biased and counterproductive reports whose lack of evidence does not further our understanding of the issues nor serve the interests of our patients. Although we lack all answers to these questions today, we do know that it is essential that treatment be individualized and attempts to develop broad management policies for such a disparate spectrum of anomalies would be ill-conceived and disregarding of a multidisciplinary knowledge base that has accrued over the last generation of scientists in this field.

This statement was reviewed, edited and approved by the leadership of the European Society for Paediatric Urology and the Society of Pediatric Urology of the United States.

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