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Rare Diseases Congress-2018: Rare diagnosis in disorders/differences of sex development - Yolanda van Bever - Erasmus Medical Centre

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DSD- Disorders/Differences of Sex Development comprise a rare collection of diseases and abnormalities that can current on different ages and have very mutable presenting symptoms. Prenatally discrepancy between genotypic sex and ultrasound phenotype or an abnormal genital as seen by ultrasound. Neonatal or Pediatric symptoms can be a genuine ambiguous genital, inguinal (ovotestes) in a girl detected during inguinal hernia surgery, Disorders of sexual development (DSD) encompass a group of congenital conditions associated with atypical development of internal and external genital structures. These conditions can be associated with variations in genes, developmental programming, and hormones. Affected individuals may be recognized at birth due to ambiguity of the external genitalia. Others may present later with postnatal virilisation, delayed/absent puberty, or infertility. The estimated frequency of genital ambiguity is reported to be in the range of 1:2000-1:4500 [1]. According to the Danish Cytogenetic Central Registry, the prevalence of XY females is 6.4 per 100,000 live born females. In this registry, the prevalence of androgen insensitivity was 4.1 per 100,000 live born with median age at diagnosis of 7.5 years. The prevalence of XY gonadal digenesis was 1.5 per 100,000 live born females with median age at diagnosis of 17 years [2]. The incidence of DSD varies among ethnic groups with the highest incidence in the southern African population. Small stature in a 45, X/46 XY girl etc. It is important to note that sex does not indicate gender; sex refers to the biology of the internal and external genital structures that is traditionally considered to be a binary categorization. Gender identity is the self-defined experience of one's gender. Tales from Greco-Roman cultures, e.g. Hermaphrodite and Daphne, have documented and celebrated transformations and fluidity in sex and gender identity others are only detected at puberty or when trying to get pregnant. There is consensus that patients should be evaluated by multidisciplinary teams and that it is important to involve patients or caretakers in the process of diagnosis and management. Psychological, socio-cultural and economic-organizational aspects play an important role. Patients with anorectic malformation and upper limb anomalies: genetic evaluation is warranted within the group of diagnosis that fall under the term DSD, there are well-known syndromes as Turner syndrome and variants, CAH, or proximal hypospadias, which can have many causes and can present as ambiguous genitalia. Halim D, Hofstra RM, Signorile L, Verdijk RM, van der Werf CS, Sribudiani Y, Brouwer RW, van IJcken WF Other causes are very rare and may not be easily recognized. Some of these will be presented here. Copy number variations in 375 patients with oesophageal atresia and/or fistula .The experience and organization of our team and DSD When presented with a child with ambiguous genitalia, unique decision-making challenges can occur regarding sex of rearing, parent and patient education, and medical management care in the Netherlands and the place and timing of NGS based diagnostics will be discussed. For the future it is important to realize the importance of choosing the right words to communicate about the condition, especially also for professionals who have little or no involvement with DSD but who are often the first to see the patient. Transition from prenatal care to postpartum professionals, from a peripheral clinic to a particular clinic or from adolescent to adult experts often offers room for improvement. We should not negligence that in these exhilarating times of rising diagnostic possibilities.

Recent Publications:

1. Van Bever Y, Wolffenbuttel KP, Brüggenwirth HT, Blom E, de Klein A, Eussen BHJ, van der Windt F, Hannema SE, Dessens AB, Dorssers LCJ, Biermann K, Hersmus R, de Rijke YB, Looijenga LHJ. Multipara meter Study of a 46, XX/46,XY Tetragametic Chimeric Phenotypical Male Patient with Bilateral Scrotal Ovotestes and Ovulatory Activity. Sex Dev. 2018; 12(1-3):145-154. 2. Hermes R, van Bever Y, Wolffenbuttel KP, Biermann K, Cools M, Looijenga LH. The biology of germ cell tumors disorders of sex development. Clin Genet. 2017 Feb; 91(2):292-301. 3. Brosens E, Marsch F, de Jong EM, Zaveri HP, Hilger AC, Choinitzki VG, Hölscher A, Hoffmann P, Herms S, Boemers TM, Ure BM, Lacher M, Ludwig M, Eussen BH, van der Helm RM, Douben H, Van Opstal D, Wijnen RM, Beverloo HB, van Bever Y, Brooks AS, IJsselstijn H, Scott DA, Schumacher J, Tibboel D, Reutter H, de Klein A. Eur J Hum Genet. 2016 Dec; 24(12):1715-1723. 4. Halim D, Hofstra RM, Signorile L, Verdijk RM, van der Werf CS, Sribudiani Y, Brouwer RW, van IJcken WF, Dahl N, Verheij JB, Baumann C, Kerner J, van Bever Y, Galjart N, Wijnen RM, Tibboel D, Burns AJ, Muller F, Brooks AS, Alves MM. ACTG2 variants impair actin polymerization in sporadic Megacystis Microcolon Intestinal Hypoperistalsis Syndrome. Hum Mol Genet. 2016 Feb 1; 25(3):571-83. 5. van den Hondel D, Wijers CH, van Bever Y, de Klein A, Marcelis CL, de Blaauw I, Sloots CE, IJsselstijn H. Eur J Pediatr. 2016 Apr; 175(4):48997.

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