Down Syndrome and disorders of sex development – only coincidence or more?

Instituto da Criança, University of São Paulo, Brazil.

Pupo JB, Santos TJ, Steinmetz L, Cominato L, Manna TD, Menezes Filho HC, Kuperman H, Dichtchekenian V, Setian N, Damiani D

INTRODUCTION

Disorders of sex development (DSDs) are congenital conditions in which development of the chromosomal, gonadal, or anatomic sex is atypical and may affect up to 1:4000 individuals in the population. The prevalence of Down syndrome (DS) is 1:1000 and its association with DSDs is quite rare.

CASE REPORT

We report four DS patients with DSD (clinical characteristics are summarized in **table 1**)

Patient 1 – 22 days old, undefined sex, with a 2.5cm phallus, non-palpable gonads, and perineal urethra. Testosterone (T) was 332 ηg/dL (at 1 month) and uterus was found on pelvic ultrasound, 47,XY+21 karyotype. It was assigned the female gender of rearing. A gonadoblastoma on the left gonad and a streak on the right was diagnosed at 11 months old, consistent with a DSD Mixed Gonadal Dysgenesis.

Patient 2 – 7.1-year-old male, with a 3.0 cm phallus, non-palpable gonads and proximal hypospadia. There was no response of T under hCG, 46,XY+t(21q 21q) karyotype. Histopathological examination was consistent with a DSD 46,XY dysgenetic.

Patient 3 – 1.1-year-old male, with a 2.5 cm phalus, palpable gonads, and topic urethra. T under hCG was 250.5 ηg/dL and no müllerian remnants were found on pelvic ultrasound. 47,XX+21 karyotype and positive SRY. Histopathological examination revealed bilateral testes, consistent with DSD testicular.

Patient 4 – 5.1-year-old male, with a 1cm phallus, palpable gonads (prior orchidopexy) and topic urethra. There was no T response to hCG and 47,XYqh+21 karyotype. The clinical diagnosis was consistent with DSD 47,XY dysgenetic.

CONCLUSION

The mean survival of DS patients has increased. Although rare, they may present DSD and it is important to look for the diagnosis, since it will change the future approach regarding rearing sex. Moreover, dysgenetic and undescended testes are the major risk factors for testicular cancer, a more common malignancy for DS patients.

Table 1: Clinical Characteristics

	Age	Gender of rearing	Phalus (cm)	Palpable gonads	Gonads found	T-response under hCG (ηg/dL)	Karyotype	DSD
1	22 days	female	2.5	no	Streak/testis	332	47,XY+21	Mixed gonadal Dysgenesis
2	7.1yr	male	3.0	no	Dysgenetic testes	125	46,XY+t(21q21q)	Disgenetic
3	1.1yr	male	2.5	yes	testes	250.5	47,XX+21	Testicular
4	5.1yr	male	1.0	orchidopexy	Biopsy not performed	<11	47,XYqh+21	Disgenetic

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