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DSD in Ukraine: our experience

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Background

The term “disorder of sex development” (DSD) includes congenital conditions in which development of chromosomal, gonadal or anatomic sex is atypical.

Methods

A retrospective analysis of the 75 medical cards of patients with DSD since 2000 up to 2017 years was done. Our database was created based on the self referring and does not cover all children with DSD in Ukraine. The criterion for including patients to the database was ambiguous genitalia and/or a discrepancy between the chromosomal and gonadal/genital sex.
At the time of examination the number of patients aged < 1 month was 17%, 1 month-up to 1 y.o. - 25%, 1-12 y.o. - 37%, >12 y.o. - 21%. The results of clinical data, laboratory tests and instrumental examination were analyzed. All patients (from birth to 18 y.o.) carried out a cytogenetic test, and, if necessary, fluorescence in situ hybridization (FISH). Molecular genetic testing was done in selected group of patients with 46,XY DSD in Ukraine (n=2) and in Institute Pasteur, France (n=19), using whole exome sequencing.

Results

Table 1. In a group of patients with 46,XY DSD at first visit we suspected following clinical diagnoses:

Androgen insufficiency syndrome (CAIS/PAIS)	3/18
Perineal hypospadias	7
Complete gonadal dysgenesis	6
Bilateral anorchism	5
Androgen biosynthesis defect	4
Partial Gonadal dysgenesis	3
Ovotesticular DSD	2

Figure 1. Structure of DSD in Ukraine

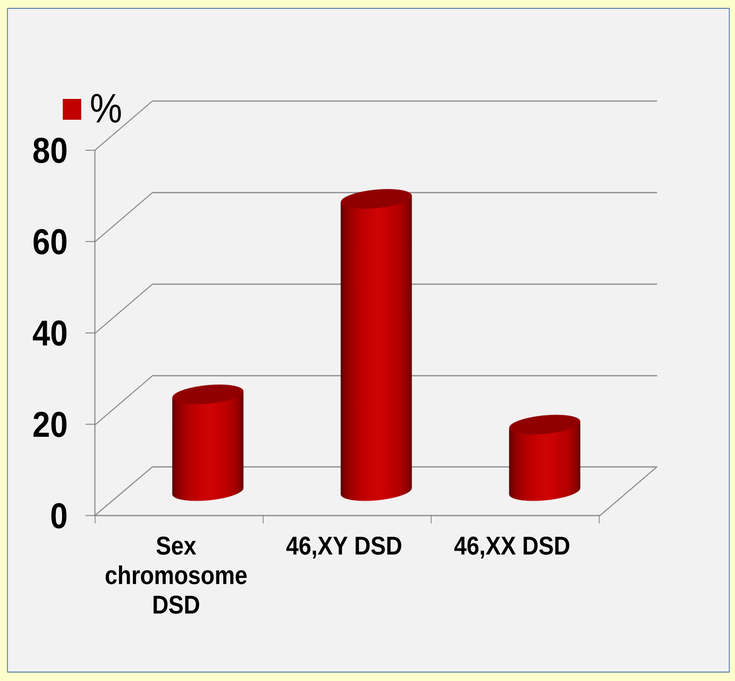

Table 2. Genetic findings in 46,XY DSD (n=21)

Disorders of gonadal (testicular) development	
CBX-2	1
WT1	1
NR5A1	3
Disorders in androgen synthesis or action	
AR	5
SRD5A2	1
HSD17B3	1
AMHR2	1
	13 (62%)

In a group of patients with 46,XX DSD we diagnosed: testicular 46,XX DSD (n=5), 21-hydroxylase deficiency with virilization IV-V degree by Prader (n=4), 46,XX gonadal dysgenesis (n=1) and DSD in VACTER-association (n=1).

Genetic testing in 46,XY DSD group was done in 21 (44%) cases.
In 4 patients (19%) genes we found were not consistent with phenotype and their causality should be proven in further studies. In 4 (19%) patients no mutations were found.
In the entire cohort 6/75 (8%) cases the gender registration of the civil sex was changed during the first 2 years of life.
A multi-disciplinary team has been created for gender assignment in DSD newborns and to improve the tactics of further management, including the time of gonadectomy.

Conclusions

Further studies to identify novel genes causing DSD are required.

References

1. Y.Shcherbak, N.Zelinska. Case report 46, XY disorder of sex development *NR5A1*-related. ESPE 2017.
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