INTRODUCTION

Differences/disorders of sex development (DSD) comprise a group of congenital conditions, affecting human sex determination and/or differentiation. Patients with DSD are classified in: sex chromosome DSD; 46,XY DSD and 46,XX DSD. 46,XY DSD include defects in androgen synthesis or action, or disorders of gonadal development with complete (CGD)/partial (PGD) gonadal dysgenesis.

RESULTS

• Medical records of 140 patients (P) followed at the Endocrinology Department because of 46,XY DSD were reviewed. DNA samples were obtained in 87/140.

Subjects were divided into 3 groups (G1, G2, G3) based on clinical characteristics, hormonal measurements, gonad histology and ultrasound/laparoscopic findings: G1: defects in androgen synthesis (n=8), G2: defects in androgen action (n=39) and G3: disorders of gonadal development CGD/PGD (n=40).

Whole genome CGH

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<thead>
<tr>
<th>Candidate gene sequencing</th>
<th>Targeted gene panel</th>
<th>Whole exome sequencing</th>
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<tbody>
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<td>G1 (n=40)</td>
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<td>G2 (n=39)</td>
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<td>G3 (n=40)</td>
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Note: For every clinically significant variant was confirmed by Sanger sequencing in proband and parents to elucidate inheritance pattern.

CONCLUSIONS

• In this cohort, excluding enzymatic defects, molecular characterization was reached in approximately 63% (50/79).

• Diagnosis in 46,XY DSD can be challenging due to overlapping clinical characteristics or poor genotype/phenotype correlation. Thus, candidate gene sequencing strategy might not be adequate in all cases.

• NGS can be a better approach to reach an etiologic diagnosis reducing time and medical interventions.

• Other etiologies should be considered: non coding genomic regions, oligo/multigenic inheritance, epigenetic pathways or environmental factors.