46, XY COMPLETE GONADAL DYSGENESIS WITH LATE DIAGNOSIS

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BACKGROUND

46, XY Complete Gonadal Dysgenesis (Swyer Syndrome) is a rare cause for DSD with incidence around 1:80000. It was first reported by G. I. M. Swyer in *British Medical Journal* in 1955.The syndrome is characterised by defective formation of the gonads as a result of structural anomalies in the sex chromosomes or mutations in specific genes. In 20 % of the patients deletion/mutation in SRY can be found. Mutations, deletions or duplications in other genes (NRD5A1, DHH, DAX1, WNT4, DMRT, etc.) are also reported. The phenotype is completely female and the diagnosis is usually made at puberty because of primary amenorrhoea. Early diagnosis is important because of increased tumor risk in the dysgenetic gonads.

THE PATINET

History:

- Uneventful pregnancy and delivery in non consanguineous family;
- Uneventful premorbid history;
- At the age of 16 evaluated by a gynecologist for absence of breast

development and primary amenorrhoea, treatment with OCP started;

- At the age of 18 because of poor treatment results consulted by another

gynecologist and a karyotyping was performed;

- Karyotype - 46, XY with no significant chromosomal rearrangements;
- Referred to the multidisciplinary DSD team at our institution.

Physical examination:

- Lean, tall girl, W 51.2 kg, H 174.2 cm, BMI 16.87 kg/m^2,

Arm span 178 cm;

- Normal physical examination;
- Puberty – B1,P3,A2, M (-);
- Normal female external genitalia, no clitoromegaly, no palpable gonads in labia majora, EMS 0/12.

Hormonal analyses:

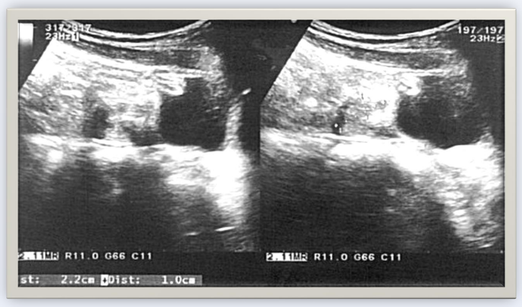
LH	FSH	E2	T	AMH	InhB
31.5mIU/ml	119 mIU/ml	103 pmol/l	0,707 nmol/l	< 0.03 pg/l	< 10 ng/ml
1.1-11.6	2.8-11.3	101-905	< 2.8	1.7-9.5	10-200

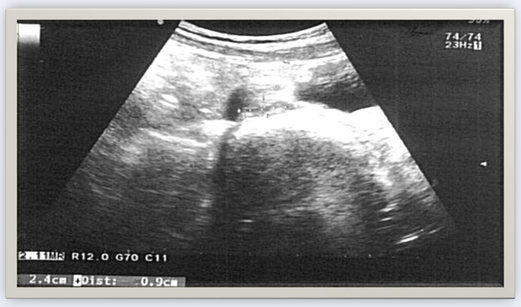
Genetic investigations:

- Presence of Y-chromosome confirmed by QF-PCR analysis.
- No mutations of the coding regions and exon/intron boundaries in *SRY* and *NR5A1* genes detected.
- Next, MLPA tests planned (for deletion/duplication screening in *DMRT1*, *WNT4,* etc.).

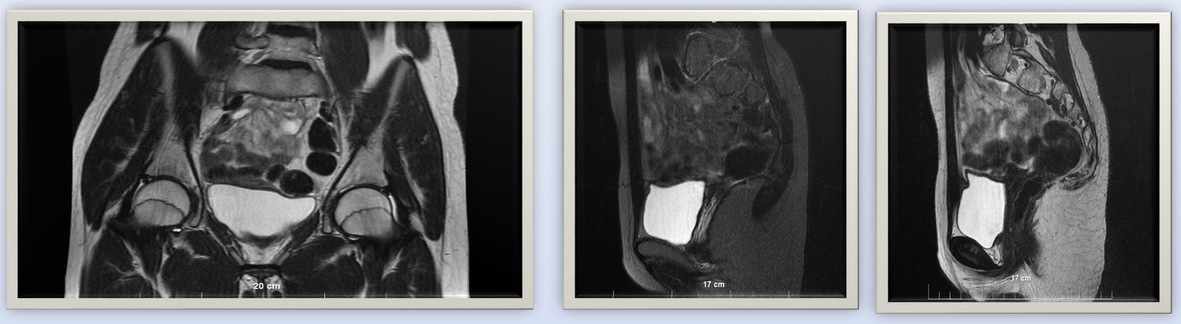
Imaging:

US: Uterus with tubular structure and thin mucous layer. Ovaries - not visualized.



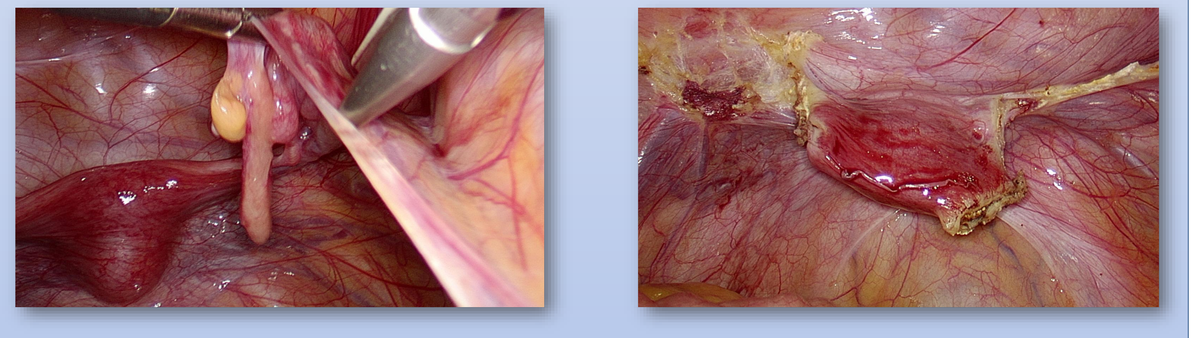


MRI: To the upper pole of the bladder - adjacent a tubular structure with dimensions 23/6 mm and hyperintense central linear zone. Ovaries - not visualized bilaterally.



Treatment:

- hormone replacement therapy with estrogen initiated;
- Laparoscopic gonadectomy performed.



Histology: Both gonads - fibrous tissue, groups of Leydig cells and tubules with immature Sertoli cells, ovarian parenchyma with primordial follicles.

CONCLUSIONS

Management of patients with DSD should be performed in centres with adequate diagnostic and therapeutic potential. Exact genetic diagnosis is not always feasible and new techniques like whole exome sequencing analysis could be considered for clarifying the genetic basis in such cases

DISCLOSURE STATEMENT

The authors have nothing to disclose.

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