Ovotesticular disorder of sex development (OT-DSD): a case report and literature review

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Introduction: DSDs

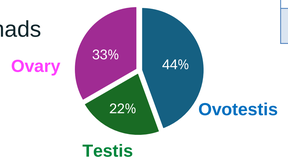
Disorders of sex development (DSDs) represent a diverse group of congenital conditions characterized by atypical development of chromosomal, gonadal, or anatomical sex.

- ❑ DSDs can be associated with variations in genes, developmental programming, and hormones.
- ❑ Incidence: 1 in 2000-4500 live births, varies among ethnic groups
- ❑ Presentations range from ambiguous genitalia at birth to delayed puberty or infertility
- ❑ DSDs are classified into three main groups based on the individual's karyotype:

46, XY DSD	46, XX DSD	Sex chromosomal DSD
Disorders of **gonadal development** • Gonadal dysgenesis, testes regression, ovotesticular DSD, syndromic forms Disorders of **androgen synthesis** • Androgen biosynthesis defects, congenital adrenal hyperplasia, placental insufficiency, syndromic forms Disorders of **androgen action** • Androgen insensitivity **Persistent Müllerian duct syndrome** • Mutations/deficiencies in AMH and AMHR2 **Unclassified** disorders • Hypospadias, epispadias, complex syndromes	Disorders of **gonadal development** • Ovotesticular DSD, monogenic forms of primary ovarian insufficiency, syndromic forms Disorders of **androgen excess** • Aromatase deficiency, congenital adrenal hyperplasia, luteoma, iatrogenic **Unclassified** disorders • Mayer-Rokitansky-Küster-Hauser syndrome (MRKH), Complex syndromes	**45, X0** • Turner syndrome and variants **47, XXY** • Klinefelter syndrome and variants **45,X/46,XY and 46,XX/46XY** • Mixed gonadal dysgenesis, chimerism

Introduction: OT-DSD

- ❑ OT-DSD is a rare form of DSD (3-10% of all cases; 1 in 100,000 births)
- ❑ Characterized by coexistence of **both** ovarian and testicular tissue in the same individual
- ❑ Phenotype: varies from female to normal male
  - XX patients: dependent on Y material translocation and *SRY* gene location
  - Male phenotype <10% of cases
- ❑ Types of gonads



- ❑ Karyotype Distribution

46, XX	60%
Mosaicism	28%
46, XY	12%

- ❑ OT-DSD classification

	Side 1	Side 2
Unilateral	Ovotestis*	Normal gonad
Bilateral	Ovotestis	Ovotestis
Lateral	Ovary**	Testis

*Usually right side
** Usually left side

Case presentation

A 4-week-old infant, delivered at 37 6/7 weeks via cesarean section secondary to maternal preeclampsia, presented with a notable clinical finding of ambiguous genitalia. The infant's weight was appropriate for gestational age, and no abnormal tests or imaging had been detected during the prenatal period. The presence of ambiguous external genitalia prompted a comprehensive medical evaluation to determine the underlying etiology.

Physical exam: Ambiguous genitalia

Virilized external genitalia

- phallic structure in the middle of a bifid scrotum with penoscrotal transposition or rugated labia.
- A single opening at the anterior perineum at the base of the ventral aspect of the phallus.
- The anus was properly aligned with the ischium.
- A palpable gonad was noted in the right inguinal region and a gonad was present in the right labia/hemiscrotum without tenderness.

Genetic analysis

- 46, XX karyotype confirmed by skin biopsy.

Intraoperative examination:

- ✓ Intra-abdominal gonads
- ✓ left hemi-uterus
- ✓ bilateral inguinal hernias,
- ✓ vaginal introitus within the urogenital sinus, as well as a cervix.

Histologic examination of gonads

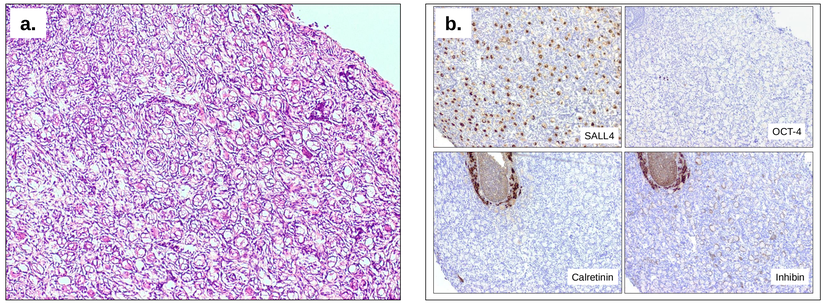


Figure 1. Left gonad: (a) Histologic H&E sections (10X) and (b) and immunohistochemical studies of indicated markers (10X) show ovarian tissue with abundant primary follicles and no significant abnormalities. Immunohistochemistry for SALL4 highlights the primary oocytes in the fragments of ovarian parenchyma, while OCT4 staining is mostly negative, with only a few small groups of positive nuclei, consistent with germ cells with delayed maturation-. Inhibin and calretinin are positive in the ovarian parenchyma highlighting granulosa and theca perifollicular cells.

Case (continued)

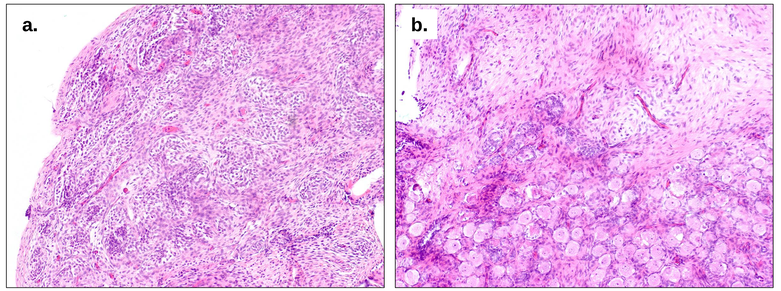


Figure 2. Right gonads: Histologic H&E sections show (a) fragment of tissue with irregular testicular cords featuring a Sertoli-only pattern, no visible germ cells and dense interstitial stroma, surrounded by an irregular fibrous capsule consistent with a poorly collagenized tunica albuginea, characteristic of dysgenetic/dysplastic testicular parenchyma. (b)Also in this gonad, ovarian parenchyma with small irregular tubular structures, possibly representing a distorted rete-ovary.

Discussion and conclusion

- ❖ DSDs involve a complex spectrum of atypical development of chromosomal, gonadal, or anatomical sex.
- ❖ Here we presented the case of a 4-week infant with clinical and pathological findings characteristic of an ovotesticular disorder; with one gonad represented by ovarian parenchyma, while the contralateral gonad featuring both ovarian and testicular parenchyma, thus indicating an ovotestis.
- ❖ The clinical history of ambiguous genitalia and intra-abdominal müllerian structures, is within the spectrum of this difference in sex development.
- ❖ Management of DSDs requires a comprehensive and individualized approach and involves a multidisciplinary team that includes experts in genetic sex, gonadal sex, social and psychological aspects, as well as pediatric endocrinologists, pathologists, urologists and gynecologists. The individual's family/relatives should also be involved.
- ❖ Key factors to consider include in the management plan are the patient's age at diagnosis, the nature and location of the gonads, the development of external genitalia, and the risk of malignant degeneration.

References

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