Journal of Pediatric Urology (2025) 21, 1385–1391

Is it possible to separate the testicular and ovarian components of an ovotestis?

Laurence Baskin [a,*], Mei Cao [a], Yi Li [a], Linda Baker [b], Christopher Cooper [c], Gerald Cunha [a]

[a]UCSF, San Francisco, CA, USA

[b]Nationwide, Columbus, OH, USA

[c]Iowa, Iowa City, IA, USA

* Correspondence to: Laurence S. Baskin, Frank Hinman, Jr., MD, Distinguished Professorship in Pediatric Urology Emeritus Chief Pediatric Urology UCSF Benioff Children's Hospitals, University of California, San Francisco, Department of Urology, 550 16th St, 6th Floor, Mission Hall Pediatric Urology San Francisco, CA 94158, USA, Tel.: +1 415 353 2083; fax: +1 415 353 2480
Laurence.baskin@ucsf.edu (L. Baskin)

Keywords
Ovotestis; Ovotesticular syndrome; Differences of sex development

Received 3 January 2025
Revised 27 March 2025
Accepted 3 April 2025
Available online 17 April 2025

Summary

Summary
The presence of an ovotestis is a rare etiology of differences of sex development. Histologically, ovotestis come in two forms: 1) Mixed or 2) Bipolar.

Objective
We hypothesize that it is surgically impossible to cleanly separate and preserve either the testicular or ovarian component of an ovotestis.

Study design
Twenty human gonads with a previous diagnosis of ovotestis were re-sectioned in entirety and re-stained with markers for testicular (SOX9, TSPY, SALL4, DDX4, cP450, AR, α-actin) and ovarian tissue (FOXL2, SALL4, DDX4). Histologic sections were photographed at low power to confirm the presence of the entire cross section of the ovotestis. High power was used to confirm an ovotestis based on the presence of both seminiferous cords (testis) and follicles (ovary).

Results
Six of twenty ovotestis did not meet our criterion for the diagnosis of ovotestis lacking the histologic evidence of both testicular and ovarian tissue (lacking ovarian follicles). The remaining 13 patients in which 14 separate specimens were evaluated, contained ovotestis defined by the presence of both seminiferous cords and ovarian follicles. Seven of these specimens had low power confirmational histologic images that included the entire ovotestis and could be completely evaluated for a potential surgical plane of separation. The other seven specimens were consistent with an ovotestis biopsy without complete borders. For the seven specimens that included the entire ovotestis, 6 of the 7 had ovotesticular cords and 3 had the presence of ovotesticular follicles.

Discussion
None of the seven complete specimens had a clear surgical plane where testicular or ovarian components could be isolated cleanly. Often the ovarian component was composed of a thin layer of follicles, surrounded the testicular component with an in-between, mixed layer of both seminiferous cords and follicles. The remaining seven ovotestis biopsy specimens also did not have a clear plane for surgically isolating either the testicular or ovarian compartment.

Conclusion
Based on the histologic evaluation of the entire ovotestis as well as ovotestis biopsy specimens it does not appear possible to surgically separate the testicular and ovarian component. We have reservations with the concept in both mixed and bipolar ovotestis that it is possible to surgically preserve either the ovarian or testicular component without leaving incongruent tissue. The clinical implications of leaving gonadal tissue inconsistent with the patient's gender identity remains unknown.

https://doi.org/10.1016/j.jpurol.2025.04.009
1477-5131/© 2025 The Author(s). Published by Elsevier Ltd on behalf of Journal of Pediatric Urology Company. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Ovotesticular syndrome is a rare form of disorders of sex development [1]. The incidence has been estimated as to be less than 1/20,000 [2]. The syndrome is characterized the presence of both ovarian and testicular tissue in the same patient. This may take the form of a separate testis and ovary or a gonad that contains both testicular and ovarian tissue, called an ovotestis [3]. Testicular tissue is defined as the present of seminiferous cords/tubules surrounded by smooth muscle cells, Sertoli cells, germ cells, and Leydig cells [4]. Ovarian tissue is defined by the presence of primordial or primary follicles with surrounding granulosa cells [5]. Specific immunohistochemical markers and morphological patterns have been described to accurately define the presence of both testicular and ovarian tissue [6].

Classically, the histology of ovotestis has been described as either mixed or bipolar [3,7,8]. Mixed ovotestis is more common and is characterized by intermingling of testicular and ovarian histology. In contrast, bipolar ovotestis has been described as having a distinct testicular and ovarian component implying the possibility of surgical separation. The concept of separating an ovotestis into components of either viable testicular tissue or ovarian tissue has important clinical implications for patients with ovotesticular syndrome in respect to endocrine function, possible fertility and risk of malignancy in an ovotestis.

Patients with ovotesticular syndrome have variable clinically presentations [7—9]. For example, a classic presentation of ovotesticular syndrome is a neonate with atypical genitalia/severe hypospadias/under virilization with an XX Karyotype and non-palpable gonads. Laparoscopy may reveal two abnormal gonads with biopsy confirmation necessary to prove the presence of both ovarian and testicular tissue. Another less common presentation is a phenotypic male teenager presenting with cyclic testicular pain. Exploration for a presumed diagnosis of torsion reveals a scrotal ovotestis with the pain presumed to be from ovulation in the ovarian component of the scrotal ovotestis. As noted, the diagnosis of an ovotestis is based on the histologic presence of both testicular and ovarian tissue with attempts at biochemical diagnosis based on the levels of FSH and LH during male and female minipuberty being too variable [10].

In both clinical scenarios we have wondered about the ability to accurately separate the testicular and ovarian component of an ovotestis. To address this issue, we retrospectively re-reviewed the histology of ovotestis in patients with ovotesticular syndrome.

Methods

Specimen collection & fixation

This study was performed after approval from the committee on human research at the University of California, San Francisco (UCSF IRB #: 16—19909). MTA transfer agreements were completed with collaborating centers (University of Iowa and Southwestern Medical center). Electronic medical center databases including pathology records were queried for the diagnosis of ovotesticular syndrome and true hermaphrodite (previous descriptor for ovotesticular syndrome) and ovotestis as a pathologic diagnosis.

Hematoxylin & Eosin (H&E) Histochemical and Immunohistochemistry (IHC) staining

Serial sections from each retrieved block were cut at 7 μm, and 4—5 sections were mounted on glass slides (Superfrost Plus, Fisher Scientific, Pittsburgh, PA). Sections were stained with H&E, IHC markers for testicular (SOX9, TSPY, SALL4, DDX4, cP450, AR, α-actin) [4] and ovarian tissue (FOXL2, SALL4, DDX4) [5].

Sections were photographed at 5—40x using a Leica DM 4000B microscope and Leica DFC 500 and DFC 7000T cameras using Leica Application Suite versions 4.1 and 4.13. Low power images were used for overall staining assessment and to determine the presence of an entire ovotestis cross section versus an ovotestis biopsy. Higher power images were used for more precise description of staining and the presence of testicular cords, ovarian follicles, ovotesticular cords and follicles [6].

Results

We reanalyzed 20 gonads with a pathologic diagnosis of ovotestis. 6 of the specimens did not meet our criterion for the diagnosis of ovotestis as they were without histologic evidence of both testicular cords and ovarian follicles. Four had clear evidence of a testicular component but lacked the presence of primordial or primary ovarian follicles, instead containing ill-defined, non-specific "ovarian stroma" or "ovarian like stroma". One had histologic characteristic of a gonadblastoma, and one had characteristics of a streak gonad. Phenotypically all six of these patients had under virilization with presumed failure of gonadal function of the testicular component of the gonad along with retained Mullerian structures.

The remaining 13 patients, from which 14 ovotestis specimens were available for review, each contained ovotestis as defined by the presence of testicular and ovarian tissue. The Table summarizes the characteristics of each ovotestis with location of the ovotestis (when known), karyotype, age at biopsy/removal, biopsy versus removal and type of ovotestis (bipolar or mixed). Note that these specimens span a 38-year window from 1984 to 2022 hence some of the clinical information was not available (NA).

Seven of these specimens had low power confirmational histologic images that included the entire ovotestis and could be completely evaluated for a potential surgical plane of separation. 5 of the 7 were mixed ovotestis and 2 were defined as bipolar. The other seven specimens were consistent with an ovotestis biopsy without complete borders. 6 of 7 of the biopsy specimens were mixed and one bipolar. For the seven specimens that included the entire ovotestis, 6 had ovotesticular cords and 3 had the presence of ovotesticular follicles. None of the seven specimens where the gonad was removed had a clear surgical plane where testicular or ovarian components could be isolated. A common finding noted was the presence of a thin outer layer of ovarian component surrounding the

Table Characteristics of ovotestis.

Patient	Gonad/Location	Karyotype	Age at biopsy/removal	Biopsy versus Gonad Removal	Pathology
1	Left Abdominal	46,XX/47,XXY mosaic	5 months	Gonad removal	Mixed Ovotestis
1	Right Abdominal	46,XX/47,XXY mosaic	1 month	Biopsy	Bipolar ovotestis
2	NA	XY with partial chr 9 deletions	10 months	Gonad removal	Mixed ovotestis
3	Scrotal	46,XX/46,XY mosaic	20.5 years	Biopsy	Mixed ovotestis/Ovarian Stroma
4	Scrotal	46,XX	7 months	Biopsy	Mixed ovotestis
5	Scrotal	46 XX SRY negative	8.4 years	Gonad removal	Bipolar Ovotestis
6	External ring	46,XX/47,XXY. Mosaic	2.1 years	Biopsy	Mixed ovotestis
7	Scrotal	46 XX SRY negative	17.4 years	Gonad removal	Mixed ovotestis
8	Abdominal	46 XX	2-month-old	Gonad removal	Bipolar ovotestis
9	NA	46XX	1 month	Biopsy	Bipolar Ovotestis
10	NA	46 XX	2-year-old	Gonad removal	Mixed ovotestis
11	NA	46 XX	NA	Biopsy	Mixed ovotestis
12	NA	46 XX	NA	Gonad removal	Mixed ovotestis
13	Right Abdominal	46 XY DMRT1 variant	13 months	Biopsy	Mixed ovotestis

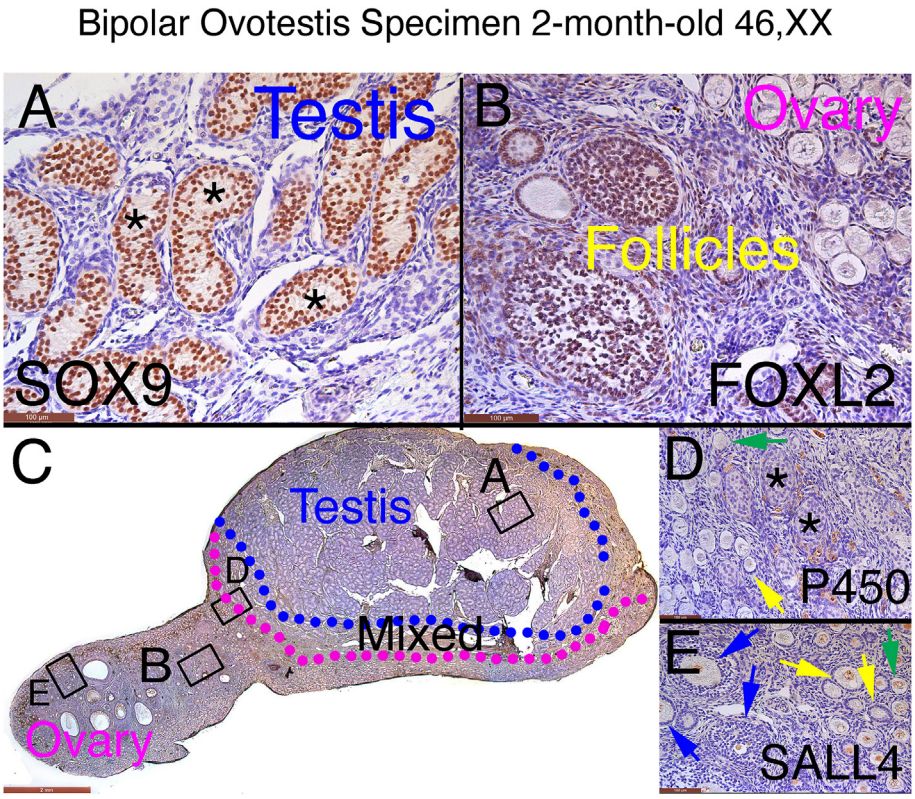

Fig. 1 2-month-old patent with a bipolar ovotestis, XX karyotype. A. Immunohistochemical staining for SOX9 which localizes to Sertoli cells defining testicular cords in the testicular compartment (*). B. FOXL2 staining of the granulosa cells of the primordial, primary and secondary follicles in the ovarian compartment. C. Low power of the entire bipolar ovotestis showing the ovarian (pink), testicular (blue) and the mixed compartments. Note that the ovarian compartment wraps around the testicular compartment making a clean surgical separation difficult. D. Cytochrome P450 staining in the mixed compartment showing the proximity of the testicular cords (*) to the ovarian follicles (yellow arrowhead). E. SALL4 nuclear staining in the ovarian compartment. Note the primordial follicles (green arrows), primary follicles (yellow arrows) and secondary follicles (blue arrows).

testicular component with a mixed layer of both seminiferous cords and follicles, in-between (Figs. 1 and 2).

Another theme was the presence of a testicular compartment surrounded by multiple ovarian compartments with mixed elements in between (Fig. 3).

A third theme was the presence of a distinct testicular and ovarian compartment with mixed layer containing both ovotesticular cords and follicles in between (Fig. 4).

The remaining seven ovotestis biopsy specimens also did not have a clear surgical plane for isolating either the testicular or ovarian compartment.

Discussion

Ovotesticular syndrome is a rare difference of sex development characterized by the presence testicular and ovarian tissue which if in the same gonad is called an ovotestis. The pathophysiological mechanisms that lead to development of an ovotestis is only partially understood at the genetic and cellular level, timing of expression of sex determining factors [11]. Ferrari and colleagues have recently reviewed the genetic basis of 46,XX testicular and ovotesticular DSD, summarizing that 13 autosomal genes and the SRY gene are known to cause testicular differentiation when over or under-expressed in 46,XX individuals [11]. Despite this knowledge, the majority of ovotesticular DSD cases remain unexplained genetically, underscoring the fact that much remains to be discovered. This is important when consideration is given to fertility preservation efforts and the potential impact on offspring.

The presence of both testicular and ovarian tissue in the same patient can lead to incongruent clinical outcome. For example, a patient that identifies as female that has functional testicular tissue can undergo virilization. In a patient that identifies as male the presence of functional ovarian tissue can lead to gynecomastia and uterine function/endometriosis in the presence of retained Mullerian tissue. Thus, these concerns led to the genesis of the clinical concept advocating separation of the discordant tissue in the ovotestis to either testicular or ovarian tissue prior to the onset of puberty.

In a recent review of the histology of patients with ovotestis, we identified two new histologic structures, ovotesticular follicles and ovotesticular cords, that can facilitate the diagnosis of ovotestis [6]. During this investigation we observed that surgical separation of specific components of an ovotestis, with the hope of preserving functional testicular or ovarian tissue would be difficult. In three specimens, we identified a thin rim of ovarian tissue surrounding the testicular component with a mixed layer in between. Shaving off viable ovarian tissue without including either mixed ovotesticular tissue or part of the testicular component did not seem technically possible. To further investigate whether ovotestis can be surgically separated into ovarian and testicular components, we

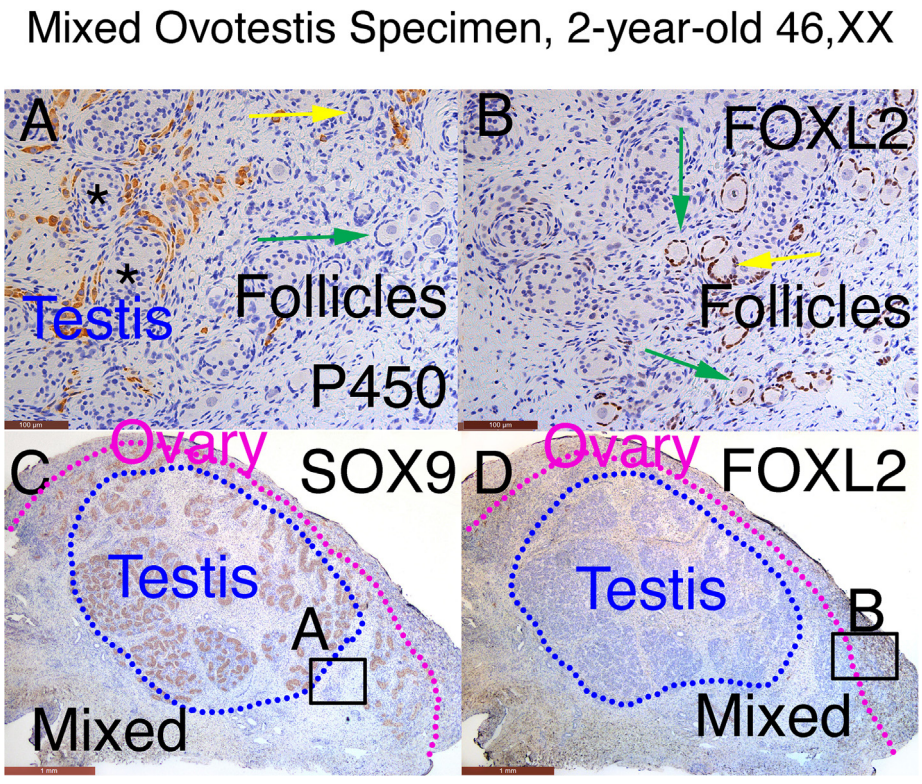

Fig. 2 2-year-old patent with a mixed ovotestis, XX karyotype. A. Immunohistochemical staining for cytochrome P450 showing testicular cords (*) surrounded by P450-positive Leydig cells. B. FOXL2 staining of the granulosa cells of the primordial and primary follicles. Primordial follicles are depicted with green arrows and primary follicles with yellow arrows. (K). Low power of the entire mixed ovotestis stained with SOX9 (C) and FOXL2 (D). Note the thin layer of the ovarian component and surrounding the entire testicular component and the mixed areas containing both testicular and ovarian tissue (A & B) making a clean surgical separation difficult. Adapted from Fig. 4 [6]

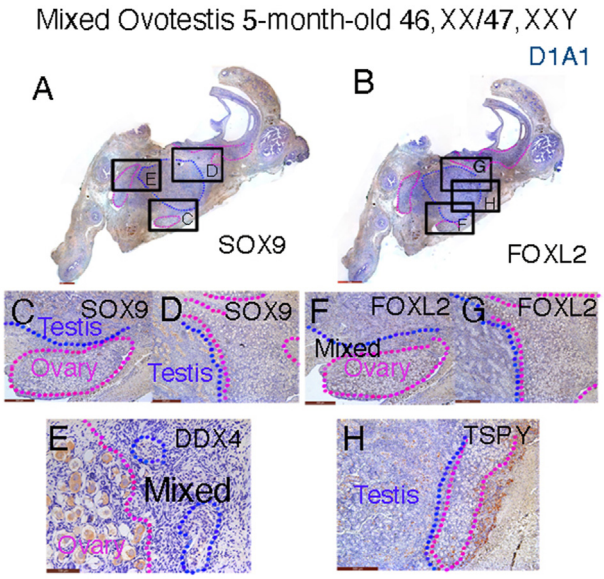

Fig. 3 5-month-old patent with a mixed ovotestis, 46, XX/47XXY karyotype. A & B. Low power immunohistochemical staining for SOX9 and FOXL2 respectively. Note the testicular tissue surrounded by three separate ovarian components making a clean surgical separation difficult. C & D High power from A stained with SOX9 staining defining Sertoli cells in the testicular component. E. DDX4 staining of the ovarian follicles. F & G. High power from B stained with FOXL2 staining defining granulosa cells in the ovarian component. H. TSPY staining of the germ cells in the testicular compartment.

restudied 14 histologic proven cases of ovotestis defined by the presence of both ovarian and testicular tissue. Serial sectioning and histologic evaluation of the entire gonad was possible in 7 of the cases. None of these specimens had a clear surgical plane where testicular or ovarian components could be isolated cleanly. Often the ovarian component was composed of a thin layer of follicles, surrounded the testicular component with a mixed layer of both seminiferous cords and follicles, in-between. The remaining seven ovotestis biopsy specimens also did not have a clear surgical plane for isolating either the testicular or ovarian compartment. In ovotestis that were bipolar (Fig. 1) we observed a thin cap of ovarian tissue that covered the testicular component again making a clean surgical separation difficult. In the majority of specimens, we saw areas of mixed tissue composed of both testicular and ovarian components as well as ovotesticular follicles and ovotesticular cords.

The incidence of cancer in patients with ovotestis has been estimated to be approximately 2.5 %, low when compared to the cancer incidence of 30—40 % in patients with gonadal dysgenesis [12,13]. This is similar to the cancer risk in patients with Complete Androgen Insensitivity and could reflect the known increased cancer that occurs with an intraabdominal testis [14]. The literature documents case reports of cancer in ovotestis such as seminoma presumably arising from the testicular component of an intraabdominal ovotestis [15,16]. A case of Leydig cell tumor in an ovotestis has also been reported, presumably also from the intraabdominal testicular component of the ovotestis [17]. Cancer has also been reported in the ovarian component of an ovotestis with a report of dysgerminoma [18]. Finally, there is also a case report of a sex cord tumor with annular tubules with morphologic features intermediate to those of granulosa cell and Sertoli cell tumors [19]. The one common feature in all these patients is that they tumor occurred in the post pubertal period and in an intraabdominal ovotestis.

The testicular component of ovotestes tends to be dysgenetic compared to the ovarian component [20]. This may explain why fertility is predominantly reported from the ovarian component of patients with ovotesticular syndrome. Gomes reported spontaneous pregnancy in 11 women with ovotesticular syndrome whereas pregnancy reported from a single male patient was achieved by sperm extraction and intracytoplasmic sperm injection [21].

As is being done for pediatric cancer patients, gonadal biopsy and spermatogonia or ovarian oocyte preservation may prove to be beneficial for future fertility in patients with ovotestis [22,23], with the negative caveat of the potential to transfer genetic mutations to the offspring. Given the advances in stem cell therapies for male infertility [24] and in testis organoid development in animal models [25], the future appears bright for individuals with ovotesticular DSD.

The significance of leaving discordant testicular or ovarian tissue, ovotesticular follicles, or ovotesticular cords in a patient with ovotestis remains unknown. In patients with ovotestis, after puberty the ovarian tissue tends to dominate with ovulation occurring in ~25 % of patients and normal menstruation in the majority of patients with retained Mullerian structures [20]. It is known that estrogen production can have deleterious effects on the testis effecting both sperm production and androgen production [26,27]. As noted in patients with ovotesticular syndrome identifying as male the effects of estrogen can manifest itself be causing gynecomastia or menstrual hematuria. In patients identifying as females where testicular function is not suppressed, testosterone can cause virilization/male secondary sexually characteristics.

After attempting surgical separation of an ovotestis, it is theoretically possible to assess for the presence of retained testicular tissue by HCG stimulation and measuring for the presence of testosterone [28]. Alternatively, depending on the age of the patient the presence of Mullerian Inhibiting Substance also suggests retained testicular tissue [28]. To detect the presence of ovarian tissue in a prepubertal patient, both FSH and LH can be given with post stimulation assessment of inhibin and estrogen and sonography documentation of follicular growth in the intraabdominal gonad [29,30].

Based on the histologic evaluation of the entire ovotestis as well as ovotestis biopsy specimens it does not appear possible to cleanly surgically separate the testicular and ovarian component. We have reservations with the concept in both mixed and bipolar ovotestis that it is possible to surgically preserve either the ovarian or testicular component without leaving incongruent tissue when performed traditionally with gross or magnified vision. While bilateral gonadectomy is an option, alternative strategies will need to be developed to attempt clean gonadal dissection. In the

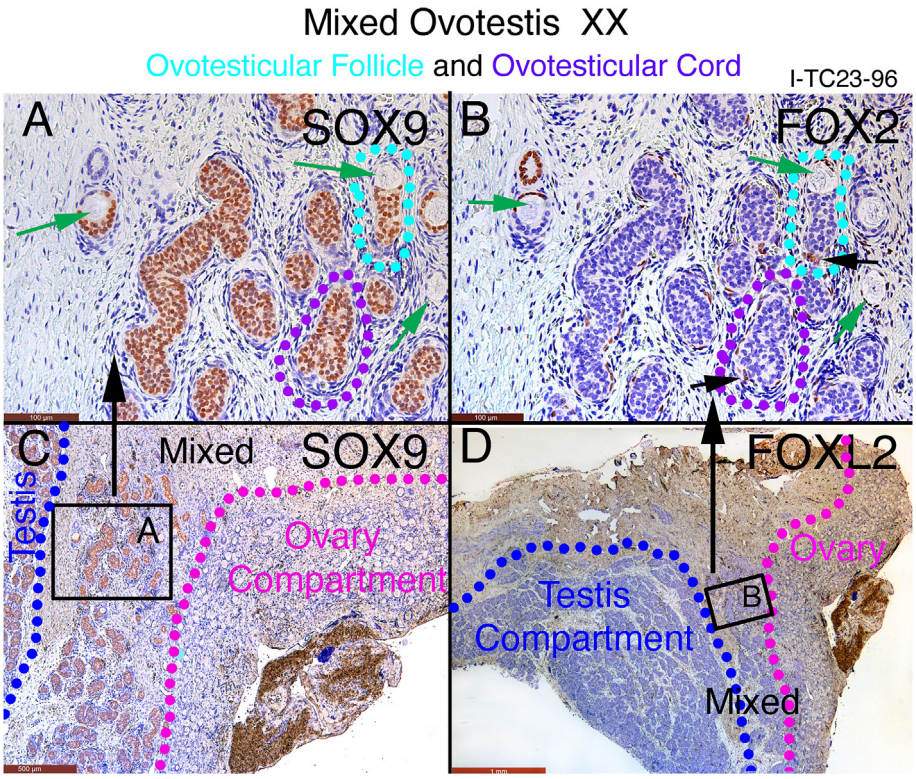

Fig. 4 10-month-old patent with a mixed ovotestis, XX karyotype. A & B. SOX9 and FOXL2 staining respectively in the mixed area highlighting the presence of ovotesticular follicles (light blue) and ovotesticular cords (purple). C & D Low power SOX9 and FOXL2 staining respectively showing the mixed area with the presence of ovotesticular follicles and ovotesticular cords between the testicular and ovarian compartment.

case of complete removal of the ovotestis, cryopreservation of the ovarian component even in pre pubertal children with subsequent reimplantation has proven to be successful for future endocrine function and fertility [31]. Ovarian cryopreservation is standard of care for childhood oncology patients when the ovary is at risk from chemotherapy or radiation [32]. Testicular preservation, however, is presently researched based but may in the future prove to be successful in preserving germ cell function with resultant male fertility. Both, techniques assume that the testicular and ovarian components of the ovotestis can be separated either in vivo or ex-vivo.

While not yet tested, one consideration might be of an intraoperative or ex-vivo resection akin to Mohs micrographic surgery methods for skin cancer [33] to attempt to achieve only one gonadal type at the end of surgery. Otherwise, the clinical implications of leaving gonadal tissue inconsistent with the patients identifying gender identity remains unknown.

Funding

This work was funded by Hinman Foundation UCSF.

References

[1] Yu R, Diamond D. Disorders of sexual development. Campbell - Walsh -Wein urology. 12th ed. Elsevier; 2021. p. 1006.

[2] Hughes IA, Houk C, Ahmed SF, Lee PA, Lawson Wilkins Pediatric Endocrine Society/European Society for Paediatric Endocrinology Consensus G. Consensus statement on management of intersex disorders. J Pediatr Urol 2006;2:148—62. https://doi.org/10.1016/j.jpurol.2006.03.004.

[3] Wiersma R, Ramdial PK. The gonads of 111 South African patients with ovotesticular disorder of sex differentiation. J Pediatr Surg 2009;44:556—60. https://doi.org/10.1016/j.jpedsurg.2008.08.013.

[4] Li Y, Overland M, Derpinghaus A, Aksel S, Cao M, Ladwig N, et al. Development of the human fetal testis: morphology and expression of cellular differentiation markers. Differentiation 2023;129:17—36. https://doi.org/10.1016/j.diff.2022.03.002.

[5] Overland MR, Li Y, Derpinghaus A, Aksel S, Cao M, Ladwig N, et al. Development of the human ovary: fetal through pubertal ovarian morphology, folliculogenesis and expression of cellular differentiation markers. Differentiation 2023;129:37—59. https://doi.org/10.1016/j.diff.2022.10.005.

[6] Baskin LS, Cao M, Li Y, Baker L, Cooper CS, Cunha GR. Ovotesticular cords and ovotesticular follicles: new histologic markers for human ovotesticular syndrome. J Pediatr Urol 2024. https://doi.org/10.1016/j.jpurol.2023.12.016.

[7] Ganie Y, Aldous C, Balakrishna Y, Wiersma R. The spectrum of ovotesticular disorders of sex development in South Africa: a single-centre experience. Horm Res Paediatr 2017;87:307—14. https://doi.org/10.1159/000466693.

[8] Kim HI, Lee I, Kim SH, Lee YS, Han SW, Yun BH. Ovotesticular disorder of sex development in Korean children: a single-center analysis over a 30-Year period. J Pediatr Adolesc Gynecol 2021. https://doi.org/10.1016/j.jpag.2021.02.105.

[9] Aaronson IA. True hermaphroditism. A review of 41 cases with observations on testicular histology and function. Br J Urol

1985;57:775—9. https://doi.org/10.1111/j.1464-410x.1985.tb07052.x.
[10] Lanciotti L, Cofini M, Leonardi A, Penta L, Esposito S. Up-To-Date review about minipuberty and overview on hypothalamic-pituitary-gonadal axis activation in fetal and neonatal life. Front Endocrinol 2018;9:410. https://doi.org/10.3389/fendo.2018.00410.
[11] Ferrari MTM, Silva E, Nishi MY, Batista RL, Mendonca BB, Domenice S. Testicular differentiation in 46,XX DSD: an overview of genetic causes. Front Endocrinol 2024;15:1385901. https://doi.org/10.3389/fendo.2024.1385901.
[12] Pleskacova J, Hersmus R, Oosterhuis JW, Setyawati BA, Faradz SM, Cools M, et al. Tumor risk in disorders of sex development. Sex Dev 2010;4:259—69. https://doi.org/10.1159/000314536.
[13] Cools M, Drop SL, Wolffenbuttel KP, Oosterhuis JW, Looijenga LH. Germ cell tumors in the intersex gonad: old paths, new directions, moving frontiers. Endocr Rev 2006;27:468—84. https://doi.org/10.1210/er.2006-0005.
[14] de la Calle CM, Kim S, Baskin LS. Diagnosis and treatment of the intra-abdominal gonad in the pediatric population: testes, ovaries, dysgenetic gonads, streaks, and ovotestes. J Pediatr Surg 2020;55:2480—91. https://doi.org/10.1016/j.jpedsurg.2020.02.014.
[15] Li Z, Liu J, Peng Y, Chen R, Ge P, Wang J. 46, XX Ovotesticular disorder of sex development (true hermaphroditism) with seminoma: a case report. Medicine (Baltim) 2020;99:e22530. https://doi.org/10.1097/MD.0000000000022530.
[16] Samantray SR, Mohapatra I. Ovotesticular disorder with Seminoma. Cureus 2020;12:e12130. https://doi.org/10.7759/cureus.12130.
[17] Gretser S, Welte MN, Roos F, Kollermann J. Leydig cell Tumor in a patient with 46,XX disorder of sex development (DSD), ovotesticular: a case report and a review of the literature. Case Rep Pathol 2021;2021:5552305. https://doi.org/10.1155/2021/5552305.
[18] Chen CQ, Liu Z, Lu YS, Pan M, Huang H. True hermaphroditism with dysgerminoma: a case report. Medicine (Baltim) 2020;99:e20472. https://doi.org/10.1097/MD.0000000000020472.
[19] Shi S, Tang M, Li W, Wu H, Liu Y, Luo Y, et al. True hermaphroditism with sex cord tumor with annular tubules (SCTAT): a rare case report and review of the literature. BMC Womens Health 2022;22:551. https://doi.org/10.1186/s12905-022-02137-7.
[20] Acien P, Acien M. Disorders of sex development: classification, review, and impact on fertility. J Clin Med 2020;9. https://doi.org/10.3390/jcm9113555.
[21] Sugawara N, Kimura Y, Araki Y. Successful second delivery outcome using refrozen thawed testicular sperm from an infertile male true hermaphrodite with a 46, XX/46, XY karyotype: case report. Hum Cell 2012;25:96—9. https://doi.org/10.1007/s13577-012-0054-3.
[22] Johnson EK, Finlayson C, Finney EL, Harris CJ, Tan SY, Laronda MM, et al. Gonadal tissue cryopreservation for children with differences of sex development. Horm Res Paediatr 2019;92:84—91. https://doi.org/10.1159/000502644.
[23] Van Batavia JP, Kolon TF. Fertility in disorders of sex development: a review. J Pediatr Urol 2016;12:418—25. https://doi.org/10.1016/j.jpurol.2016.09.015.
[24] Modanlou M, Mahdipour M, Mobarak H. Effectiveness of stem cell therapy for male infertility restoration: a systematic review. J Invest Med 2024:10815589241305317. https://doi.org/10.1177/10815589241305317.
[25] Zhang D, Jin W, Cui Y, He Z. Establishment and characterization of testis organoids with proliferation and differentiation of spermatogonial stem cells into spermatocytes and spermatids. Cells 2024;13. https://doi.org/10.3390/cells13191642.
[26] Sapino A, Pagani A, Godano A, Bussolati G. Effects of estrogens on the testis of transsexuals: a pathological and immunocytochemical study. Virchows Arch A Pathol Anat Histopathol 1987;411:409—14. https://doi.org/10.1007/BF00735221.
[27] Li D, Ping H, Li K, Lin J, Jiang X, Zhang X. Environmental oestrogens disrupt testicular descent and damage male reproductive health: mechanistic insight. J Cell Mol Med 2023;27:2095—102. https://doi.org/10.1111/jcmm.17837.
[28] Lucas-Herald AK, Kyriakou A, Alimussina M, Guaragna-Filho G, Diver LA, McGowan R, et al. Serum anti-mullerian hormone in the prediction of response to hCG stimulation in children with DSD. J Clin Endocrinol Metab 2020;105:1608—16. https://doi.org/10.1210/clinem/dgaa052.
[29] Steinmetz L, Rocha MN, Longui CA, Damiani D, Dichtchekenian V, Setian N, et al. Inhibin A production after gonadotropin stimulus: a new method to detect ovarian tissue in ovotesticular disorder of sex development. Horm Res 2009;71:94—9. https://doi.org/10.1159/000183898.
[30] French S, Rodriguez L, Schlesinger A, McCullough L, Dietrich J, Hicks J, et al. FSH injections and ultrasonography determine presence of ovarian components in the evaluation of ovotesticular disorders of sex development. Int J Pediatr Endocrinol 2009;2009:507964. https://doi.org/10.1155/2009/507964.
[31] Affdal AO, Salama M, Ravitsky V. Ethical, legal, social, and policy issues of ovarian tissue cryopreservation in prepubertal girls: a critical interpretive review. J Assist Reprod Genet 2024;41:999—1026. https://doi.org/10.1007/s10815-024-03059-z.
[32] Errasti T, Asadi-Azarbaijani B, Guell F, Calleja-Agius J. Review paper on fertility preservation in children and prepubertal adolescents with gynaecological cancer. Eur J Surg Oncol 2024:109483. https://doi.org/10.1016/j.ejso.2024.109483.
[33] Trost LB, Bailin PL. History of mohs surgery. Dermatol Clin 2011;29:135—9. vii. https://doi.org/10.1016/j.det.2011.01.010.