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Case report

Ovotesticular disorders of sex development with dysgerminoma in a 46, XX/46, XY female: A case report

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ABSTRACT

The diagnosis of ovotesticular disorders of sex development can only be confirmed when both testicular and ovarian tissues are present simultaneously in the same individual, regardless of the patient's karyotype. This report aims to discuss the diagnosis and treatment of a rare case of ovotesticular disorders of sex development complicated by dysgerminoma. The patient, a 24-year-old female, was admitted to hospital due to clitoral hypertrophy. Chromosomal analysis revealed a chimeric karyotype of 46, XX/46, XY. Biopsies of both ovaries indicated the presence of dysgerminoma in the right ovarian tissue. Postoperative pathology confirmed true hermaphroditism with dysgerminoma. Surgical intervention included the removal of the right ovary and plastic surgery of the external genitalia. Adult ovotesticular disorders of sex development combined with dysgerminoma is exceptionally rare, particularly with a chimeric karyotype. Comprehensive analysis of clinical manifestations, cytogenetic examination, histomorphology, and immunophenotype is crucial for accurate diagnosis and treatment. Early intervention and surgical management are essential to prevent disease progression.

1. Introduction

True hermaphroditism, now classified as ovotesticular disorder of sexual development (OT-DSD), is an extremely rare condition with an estimated incidence of 1 in 100,000 live births (Blackless et al., 2000). The etiology and pathogenesis remain incompletely understood, but it is believed to be influenced by the expression of the Y chromosome and specific gene mutations. The most common karyotype in OT-DSD is 46, XX though 46, XY and 46, XX/46, XY chimerism are also observed (Nistal et al., 2015). Diagnosis requires the presence of both testicular and ovarian tissues in the same individual, either within the same gonad or in separate gonads. OT-DSD can be categorized into three types, including bilateral ovotestis (Type I), unilateral ovotestis (Type II), and unilateral ovary with contralateral testis (Type III) (Nistal et al., 2015). The external genitalia often exhibit varying degrees of ambiguity, depending on the amount of functional testicular tissue present. Internal genitalia are typically incompletely differentiated, influenced by the degree of gonadal differentiation (Sandberg and Gardner, 2022). This report describes a 24-year-old female with OT-DSD complicated by dysgerminoma, highlighting the importance of multidisciplinary analysis in diagnosis and treatment.

2. Case Presentation

A 24-year-old female presented to the Gynecology Department in April 2015 with a 20-year history of clitoral hypertrophy. Chromosomal analysis performed at an external hospital revealed a chimeric karyotype of 46, XX/46, XY (Fig. 1A). The patient reported a regular menstrual cycle of 28 days, lasting 5 days, with moderate flow and no dysmenorrhea, but had a small amount of vaginal discharge. Gynecological examination revealed female external genitalia with clitoral hypertrophy measuring 4 × 5 cm (Fig. 1B, C). Physical examination also noted the presence of a laryngeal prominence (Adam's apple). Hormonal assays indicated normal levels of estradiol, follicle-stimulating hormone, luteinizing hormone, and prolactin during the early follicular phase, but slightly elevated testosterone levels, likely due to the presence of testicular tissue in the ovotestis (Table 1). Routine blood tests, electrolyte levels, urinalysis, liver function tests, and coagulation profiles were within normal limits, and tests for hepatitis B virus and syphilis were negative. Gynecological ultrasound revealed a uterus measuring 4 × 3.8

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× 3 cm, endometrial thickness of 0.5 cm, left ovarian volume of 2.2 × 1.2 cm, and right ovarian volume of 1.7 × 1.4 cm. Chest X-ray, abdominal ultrasound, and cardiac ultrasound showed no significant abnormalities.

Given the increased risk of malignancy, a laparoscopic biopsy of both gonads was performed. Laparoscopic intraoperative findings revealed that the right ovary resembled an ovoid testicle, covered by the tunica albuginea. Frozen section pathology indicated that the left ovary contained ovarian tissue with a reduced number of follicles, while the right ovary exhibited dysgerminoma measuring 1.5 × 1.4 cm. In view of the intraoperative pathological diagnosis, the right ovary was resected after consultation with the patient's family (Fig. 1D). In addition, according to the patient's wishes, plastic surgery of the vulva was performed at the same time (Fig. 1E). Postoperative pathological examination of the right ovary confirmed dysgerminoma arising in an ovotestis, with positive expression of placental alkaline phosphatase (PLAP), octamer-binding transcription factor 3/4 (OCT3/4), and cytokeratin (CK). Ki-67 expression exceeded 30 %, while other markers, including CD117, CD30, alpha-fetoprotein (AFP), inhibin α, vimentin, and leukocyte common antigen (LCA), were negative. Based on these findings, the diagnosis of true hermaphroditism with ovarian dysgerminoma was confirmed. The patient was discharged without complications and reported satisfaction with the appearance and sensation of the clitoris at the 3-month follow-up (Fig. 1F). In August 2024, the patient returned for a follow-up visit, reporting good recovery. The patient did not have any children, but she had experienced two pregnancies during this period, both ended with voluntary abortion.

3. Discussion

Dysgerminoma, also referred to as seminoma in testicular tissue, is a low-grade malignant germ cell tumor. It is the most common malignant germ cell tumor of the ovary and requires prompt diagnosis and treatment (Euscher, 2019). Pathological and immunohistochemical analyses are critical for diagnosis. OCT3/4, a marker of pluripotency and self-renewal in embryonic stem and germ cells, is a well-established diagnostic marker for malignant germ cell tumors (Bica et al., 2024). High expression of PLAP and positivity for CD117 are also commonly used to confirm the diagnosis (Reiswich et al., 2021). Additionally, markers such as cytokeratin, Ki-67 and lactate dehydrogenase (LDH) provide insights into tumor proliferation and invasion, while AFP and beta human chorionic gonadotropin (β-hCG) levels may offer prognostic information.

Table1
Patient's sex hormone levels in early-follicular phase.

Tests	Results	Normal values
FSH	7.94	1.7–134.8 mIU/ml
LH	5.01	1.0–95.6 mIU/ml
E	32.12	5–498 pg/ml
T	0.85	0.06–0.82 ng/ml
PRL	9.42	4.79–23.30 ng/ml

FSH = follicle stimulating hormone, LH = luteinizing hormone, E = estradiol, T = testosterone, PRL = prolactin.

Dysgerminomas typically occur in the second and third decades of life and are often diagnosed at an early stage. Fertility preservation is a critical consideration, as these tumors frequently affect young women. For patients desiring fertility, conservative surgical management, including preservation of the uterus, fallopian tubes, and contralateral ovary, is recommended, even in metastatic cases, due to the tumor's chemosensitivity. For postmenopausal women or premenopausal patients with bilateral ovarian involvement, total abdominal hysterectomy and bilateral salpingo-oophorectomy (BSO), along with comprehensive surgical staging, are advised (Saani et al., 2023). Adjuvant chemotherapy or radiotherapy may be considered for patients beyond stage IA, depending on individual circumstances (Saani et al., 2023). However, in OT-DSD patients with 46, XY karyotype, the contralateral ovary's fate depends on its histology and functional potential. If the ovary is dysgenetic or contains Y chromosome material, BSO is recommended due to a high risk of malignant transformation. Conversely, if the ovary demonstrates normal histology and hormonal activity, preservation with rigorous surveillance (annual pelvic ultrasound, serum AFP/β-hCG) may be considered until puberty completion, provided the patient/family accepts residual risk (Kilberg et al., 2019). The long-term prognosis for ovarian dysgerminoma is excellent, with a 90 % disease-free survival rate for stage I patients. Even in advanced stages, the 5-year overall survival rate exceeds 90 %, and recurrence rates are low. In cases of recurrence, salvage therapy is often successful (Vicus et al., 2010). In this patient, surgical resection of the lesion was performed, and she was advised to return for follow-up one month postoperatively. Since the patient expressed strong female gender identity, vulvar plastic surgery was performed after consultation with the patient and her family. Fertility potential was assessed positively, and the patient was advised to pursue conception under the guidance of a specialist.

The karyotypes associated with OT-DSD include 46, XX, 46, XX/46, XY mosaicism, 46, XY/47, XXY, 45, X0/46, XY, 46, XX/45, X0, 46, XX/

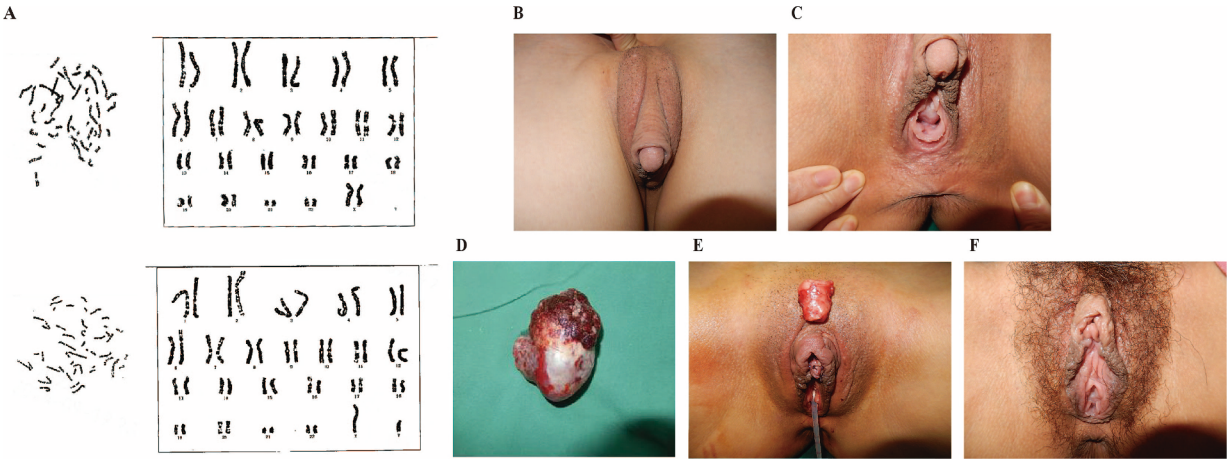

Fig. 1. The diagnosis of patient with true hermaphroditism. A: The chromosomal analysis showed the karyotype was a chimerism of 46XX,/46XY. B: Gynecological assessment revealed 4 × 5 cm clitoral hypertrophy. C: External genitalia was female, with visible vaginal opening. D: The surgically resected tumor specimen. Ovoid, the ovarian tissue forms a cap on the testicular parenchyma. E: Hypertrophic clitoris that was removed during surgery. F: The shape of vulva recovered after the plastic surgery of the vulva.

47, XXY, and 46, XY (Nistal et al., 2015). Among these, 46, XX is the most frequent, while 46, XY is rare. In patients with a chimeric karyotype of 46,XX/46,XY, the incidence of tumors is estimated at 10 %, with the most common types being gonadoblastoma, dysgerminoma, choriocarcinoma, and yolk sac tumor (Nistal et al., 2015). In this case, dysgerminoma was identified in the patient's right ovary.

While endocrine function in OT-DSD patients varies, most retain fertility potential. The article by Zeki Bayraktar et al. summarized four cases of pregnant 46, XX/46, XY chimera patients, three of whom had bilateral ovotestes and underwent unilateral removal surgery in their infantile period (Bayraktar, 2018). The remaining case involved a patient with a single ovoteste who did not undergo surgery. However, similar to the case at hand, this patient opted for an abortion. Future research should focus more on fertility preservation strategies (Kilberg et al., 2019).

Additionally, literature highlights the lack of psychological support and care for patients with disorders of sex development (DSD) and their families. Many patients and families face challenges in accessing reliable information and achieving social acceptance (Sandberg and Gardner, 2022). Increased awareness and societal support are needed for individuals with DSD.

4. Conclusion

This report presents a rare case of OT-DSD complicated by dysgerminoma. The pathogenesis, diagnosis, and treatment of OT-DSD are discussed, emphasizing the critical role of early diagnosis and surgical intervention based on cytogenetic and histomorphological findings. As well as the case highlights the importance of respecting the patient's psychological, cultural, and fertility concerns. Multidisciplinary care, including psychological support and fertility potential, is essential for optimizing outcomes in patients with OT-DSD. This report underscores the need for comprehensive medical and psychological support for patients and their families, ensuring informed decision-making and improved quality of life.

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CRediT authorship contribution statement

Yafei Xue: Writing – original draft, Conceptualization. **Shuqi Zuo:** Writing – review & editing, Supervision. **Min Cui:** Supervision, Resources. **Xingbo Zhao:** Supervision, Resources. **Xiaoyi Qi:** Writing – review & editing, Supervision, Funding acquisition.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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