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Case Report

Treatment With a Nonaromatizable Androgen for Transgender Man With a Hormone-sensitive Ovarian Cancer

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Abstract

Gender-affirming hormone therapy (GAHT) is increasingly prescribed to transgender men and gender diverse individuals to better align their affirmed gender identity and somatic phenotype, aiming to improve psychosocial well-being. However, the long-term outcomes of GAHT, especially risk of hormone-related malignancy, remains unclear. We report a case of transgender man on long-term GAHT with testosterone who developed recurrent hormone-sensitive endometrioid ovarian cancer. Treatment with medroxyprogesterone acetate effectively suppressed serum estradiol (measured by liquid chromatography–mass spectrometry) but resulted in intolerable physical and mental health symptoms from hypogonadism. The nonaromatizable androgen 19-nortestosterone (nandrolone) was initiated as an alternative and successfully improved quality of life while maintaining bone and muscle health. This case underscores the importance of coordinated care within a multidisciplinary team.

Key Words: transgender, ovarian cancer, nandrolone, nonaromatizable androgen

Introduction

Hormone-related cancer remains a serious but uncommon issue in transgender and gender diverse individuals. Its rarity is partly attributable to the relatively younger age of this population, lack of consistent screening strategy and uptake as well as limited therapeutic alternatives to conventional gender-affirming hormone therapy (GAHT), which may be contraindicated in certain cases. The decision to maintain or discontinue GAHT, particularly testosterone in transgender men following a diagnosis of hormone-sensitive cancer, is complex and requires careful consideration of alternative options by both the patient and multidisciplinary team. Here, we report a case of a transgender man who developed recurrent hormone-sensitive, low-grade endometroid ovarian cancer and outline the challenges encountered in management.

Case Presentation

A 51-year-old transgender man had first presented in 2015 at the age of 43 years seeking GAHT for marked and persistent life-long gender incongruence. He was otherwise in good physical and mental health, apart from mild asthma and morbid obesity (body mass index, 42 kg/m^2). He used no regularly prescribed or over-the-counter medications. He was a life-long nonsmoker or drinker. He could not recall onset of menarche but reported regular menstrual cycle without dysmenorrhea or menorrhagia. He was not sexually active and had never been pregnant. There was absence of any benign or malignant gynecological condition in the family.

Short-acting intramuscular testosterone enanthate (Primoteston 250 mg) at 2 to 3 weekly intervals was commenced in November 2015 and switched to longer acting intramuscular testosterone undecanoate (Reandron 1000 mg, 12 weekly) a few months later. Cessation of menses occurred 4 months into testosterone and other desired physical changes including deepening of his voice, self-reported body fat redistribution, and mild acne were observed. Because of the shape and size of the nipples and breasts on a background of obesity, he was recommended to first undergo nipple reduction and chest liposuction in October 2016, followed by bilateral mastectomies in May 2017. He was pleased with the surgical outcome and continued intramuscular testosterone undecanoate with clinical reviewed every 6 months.

In November 2017, he reported recurrence of almost daily menstrual spotting for about 6 weeks, which eventually

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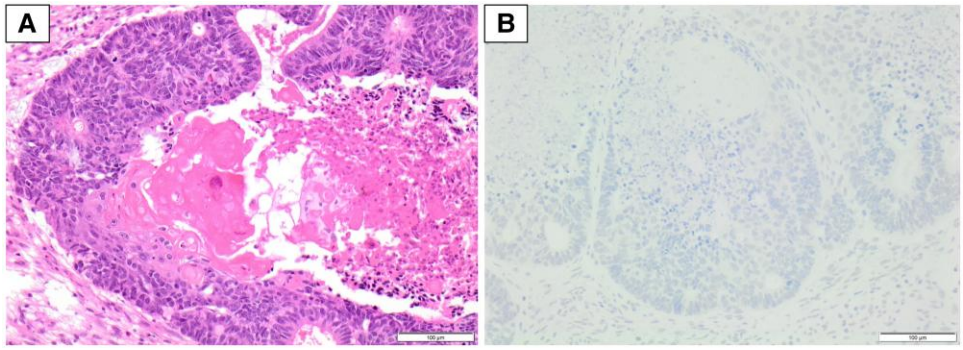

Figure 1. (A) Metastatic adenocarcinoma from pelvic nodule recurrence (hematoxylin and eosin stain). (B) Pelvic nodule recurrence demonstrated negative staining with androgen receptor immunohistochemistry.

ceased spontaneously. A suggested gynecological referral was not taken up. In January 2019, the spotting recurred lasting for 1 day. A diagnosis of diverticular disease was also made at the time based on clinical symptoms and radiographic evidence of diverticular disease. A gynecology referral was again sought with a view to hysterectomy.

Diagnostic Assessment

The patient underwent hysteroscopy with uterine dilation and curette in November 2019, which revealed a benign endometrial polyp on histology. Imaging identified a left ovarian mass, and he underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Histopathological examination of the left ovary confirmed The International Federation of Gynaecology and Obstetrics (FIGO) grade 1 endometrioid carcinoma, with carcinoma extending to the ovarian serosal surface. No malignancy was identified elsewhere. Immunohistochemistry revealed strong nuclear staining for estrogen and progesterone receptors in approximately 5% to 10% of tumor cells. He recovered well from surgery. He was considered surgically cured and did not require adjuvant therapy. He continued on intramuscular testosterone undecanoate 1000 mg every 14 weeks.

In February 2021, at routine review, he reported abdominal pain. Colonoscopy and abdominal computed tomography scan confirmed diverticular disease but also 3 soft tissue nodules in the pelvis. A positron emission tomography scan detected intensely avid uptake in the nodules with maximum standardized uptake value 15.2 without significant activity elsewhere. The case was reviewed at gynecological cancer multidisciplinary meeting and thought to represent recurrent disease.

Treatment

The patient underwent laparotomic excision of pelvic masses and omentectomy in March 2021. The histopathology showed metastatic well-differentiated adenocarcinoma in the resected pelvic nodules (Fig. 1A), with no evidence of malignancy in the omentum. Immunohistochemistry of the pelvic nodules was negative for estrogen, progesterone, androgen receptors, and caudal type homeobox transcription factor 2. The adenocarcinoma was only patchy positive for special AT-rich sequence binding protein immunostaining (Figure 1B). A differential diagnosis between recurrent ovarian endometrioid adenocarcinoma and primary colorectal adenocarcinoma was raised. Consensus agreement at a multidisciplinary tumor board meeting favored a final diagnosis of recurrent ovarian endometrioid adenocarcinoma based on clinical history and normal colonoscopy.

Unfortunately, an abdominal computed tomography scan 2 months postoperatively detected a residual nodule measuring 30×29 mm in the left pelvic wall, consistent with recurrence. Tumor markers were negative. The recommended treatment modality was endocrine therapy with local pelvic radiotherapy.

Because aromatization of injectable testosterone would produce estradiol with potential to stimulate the hormone-sensitive cancer, testosterone therapy was discontinued in May 2021. Endocrine therapy with oral medroxyprogesterone 200 mg daily was commenced. Pretreatment serum estradiol measured by liquid chromatography–mass spectrometry at 29.7 pg/mL (109 pmol/L) (normal reference range: 9.8-42 pg/mL; 36-155 pmol/L).

Throughout the follow-up review, he had no disease recurrence but struggled with progressive weight gain, lethargy, and deterioration in bone mineral density, effects considered likely due to untreated hypogonadism with lack of testosterone. A decision was made to commence injectable 19-nortestosterone (nandrolone decanoate) starting at 50 mg every 2 weeks in February 2023.

Outcome and Follow-up

The patient continued to do well at last review in May 2024, without evidence of disease recurrence clinically, biochemically, and radiologically. The dose of nandrolone was uptitrated to 150 mg every 2 weeks based on clinical symptoms; the patient did not report any undesirable adverse effects. Table 1 summarized serial laboratory results throughout his treatment.

Discussion

Epithelial ovarian cancer is a rare malignancy, with an estimated lifetime risk of 1.2% for Australian women to be diagnosed before the age of 85 years [1]. Among the subtypes, endometrioid ovarian cancer represents a distinct form, accounting for approximately 10% to 13% of all epithelial ovarian cancers [2]. This subtype can be associated with endometriosis and tends to present at an earlier stage, compared to other epithelial ovarian cancers, which may contribute to its generally more favorable prognosis. However, outcomes can vary depending on factors such as tumor grade and extent of disease at diagnosis.

Table 1. Serial laboratory profile and timeline over the course of our patient's treatment

		Pretransition	During testosterone treatment (Primoteston)	During testosterone treatment (Reandron)	During testosterone treatment (Reandron)	After TAH-BSO	Prepelvic surgery	Post pelvic Surgery Testosterone cessation	During testosterone cessation	During Nandrolone	Follow up
	Date	**Oct 2015**	**Mar 2016**	**May 2017**	**Jan 2019**	**Feb 2020**	**Feb 2021**	**May 2021**	**Feb 2023**	**May 2023**	**Feb 2024**
Laboratory parameter	**Reference ranges**										
Blood Hemoglobin	13-17 g/dL (130-170 g/L)	13.2 g/dL (132 g/L)	15.3 g/dL (153 g/L)	14.0 g/dL (140 g/L)	16.9 g/dL (169 g/L)	16.3 g/dL (163 g/L)	17.1 g/dL (171 g/L)	13.6 g/dL (136 g/L)	12.7 g/dL (127 g/L)	15.0 g/dL (150 g/L)	16.8 g/dL (168 g/L)
Blood hematocrit	40-50% (0.40-0.50 L/L)	40% (0.4 L/L)	46% (0.46 L/L)	42% (0.42 L/L)	51% (0.51 L/L)	51% (0.51 L/L)	53% (0.53 L/L)	40% (0.40 L/L)	38% (0.38 L/L)	46% (0.46 L/L)	53% (0.53 L/L)
Serum LH	2.0-12.0 IU/L (2.0-12.0 mIU/mL)	9.0 IU/L (9.0 mIU/mL)	2.8 IU/L (2.8 mIU/mL)	2.6 IU/L (2.6 mIU/mL)	2.8 IU/L (2.8 mIU/mL)	3.8 IU/L (3.8 mIU/mL)	2.1 IU/L (2.1 mIU/mL)	5.8 IU/L (5.8 mIU/mL)	31.9 IU/L (31.9 mIU/mL)	< 0.1 IU/L (<0.1 mIU/mL)	<0.3 IU/L (<0.3 mIU/mL)
Serum FSH	1.0-10 IU/L (1.0-10 mIU/mL)	3.0 IU/L (3.0 mIU/mL)	3.3 IU/L (3.3 mIU/mL)	4.7 IU/L (4.7 mIU/mL)	3.2 IU/L (3.2 mIU/mL)	5.0 IU/L (5.0 mIU/mL)	3.0 IU/L (3.0 mIU/mL)	7.6 IU/L (7.6 mIU/mL)	54.6 IU/L (54.6 mIU/mL)	3.4 IU/L (3.4 mIU/mL)	2.3 IU/L (2.3 mIU/mL)
Serum Testosterone (trough)	288-865 ng/dL (10-30 nmol/L) (male range)	51.9 ng/dL (1.8 nmol/L)	775.8 ng/dL (26.9 nmol/L)	504 ng/dL (17.5 nmol/L)	562 ng/dL (19.5 nmol/L)	369.2 ng/dL (12.8 nmol/L)	467 ng/dL (16.2 nmol/L)	438.4 ng/dL (15.2 nmol/L)	25.9 ng/dL (0.9 nmol/L)	118 ng/dL (4.1 nmol/L)	383.6 ng/dL (13.3 nmol/L)
Serum SHBG	1.42-7.6 µg/mL (15-80 nmol/L)	4.08 µg/mL (43 nmol/L)	2.28 µg/mL (24 nmol/L)	2.98 µg/mL (31.4 nmol/L)	2.94 µg/mL (31 nmol/L)	2.38 µg/mL (25 nmol/L)	3.13 µg/mL (33 nmol/L)	2.69 µg/mL (28.4 nmol/L)	2.05 µg/mL (21.6 nmol/L)	1.26 µg/mL (13.3 nmol/L)	1.41 µg/mL (14.8 nmol/L)
Serum estradiol	9.8-42 pg/mL (36-155 pmol/L)	129 pg/mL (476 pmol/L)	47.4 pg/mL (174 pmol/L)					29.7 pg/mL (109 pmol/L)[a]	5.9 pg/mL (22 pmol/L)[a]	8.17 pg/mL (30 pmol/L)[a]	9.5 pg/mL (35 pmol/L)
Serum creatinine	0.68-1.24 mg/dL (60-110 µmol/L)	0.79 mg/dL (70 µmol/L)	1.1 mg/dL (97 µmol/L)		1.05 mg/dL (93 µmol/L)			1.02 mg/dL (90 µmol/L)		1.1 mg/dL (98 µmol/L)	
Serum ALP	30-110 U/L (0.5-1.8 µkat/L)	82 U/L (1.4 µkat/L)	92 U/L (1.5 µkat/L)		90 U/L (1.5 µkat/L)		92 U/L (1.5 µkat/L)	101 U/L (1.7 µkat/L)			
Serum ALT	10-50 U/L (0.1-0.8 µkat/L)	14 U/L (0.2 µkat/L)	15 U/L (0.25 µkat/L)		20 U/L (0.3 µkat/L)		24 U/L (0.4 µkat/L)	18 U/L (0.3 µkat/L)			
Serum AST	10-35 U/L (0.17-0.58 µkat/L)	13 U/L (0.2 µkat/L)	16 U/L (0.27 µkat/L)		17 U/L (0.28 µkat/L)		19 U/L (0.3 µkat/L)	17 U/L (0.28 µkat/L)			
Blood glucose (fasting)	61.2-97.3 mg/dL (3.4-5.4 mmol/L)	91.8 mg/dL (5.1 mmol/L)			100 mg/dL (5.6 mmol/L)		90 mg/dL (5.0 mmol/L)				
HbA1c	4.0-6.0% (20-42 mmol/mol)	5.5% (37 mmol/mol)			5.9% (41 mmol/mol)		5.8% (40 mmol/mol)				
Total cholesterol (fasting)	151-201 mg/dL (3.9-5.2 mmol/L)	139 mg/dL (3.6 mmol/L)			153 mg/dL (3.96 mmol/L)		131.4 mg/dL (3.4 mmol/L)				
HDL (fasting)	38.6-115 mg/dL (1.0-3.0 mmol/L)				40.1 mg/dL (1.06 mmol/L)		42.5 mg/dL (1.1 mmol/L)				
LDL (fasting)	19.3-135.3 mg/dL (1.0-3.0 mmol/L)				92.8 mg/dL (2.4)		73.4 mg/dL (1.9)				

(*continued*)

Table 1. Continued

	Pretransition	During testosterone treatment (Primoteston)	During testosterone treatment (Reandron)	During testosterone treatment (Reandron)	After TAH-BSO	Prepelvic surgery	Post pelvic Surgery Testosterone cessation	During testosterone cessation	During Nandrolone	Follow up
Date	Oct 2015	Mar 2016	May 2017	Jan 2019	Feb 2020	Feb 2021	May 2021	Feb 2023	May 2023	Feb 2024
Triglycerides (fasting)	44.2-150.4 mg/dL (0.5-1.7 mmol/L)	70.8 mg/dL (0.8 mmol/L)		96.4 mg/dL (1.09 mmol/L)		86.7 mg/dL (0.98 mmol/L)				
Serum CA 125	0-35 kU/L (0-35 U/mL)							12 kU/L (12 U/mL)	15 kU/L (15 U/mL)	
Serum LDH	120-250 U/L (2.0-4.2 µkat/L)							230 U/L (3.8 µkat/L)	239 U/L (3.9 µkat/L)	

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA 125, cancer antigen 125; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDH, lactate dehydrogenase; LDL, low-density lipoprotein;TAH-BSO, total abdominal hysterectomy, bilateral salpingo-oophorectomy.
[a]Serum estradiol measured by liquid chromatography-mass spectrometry.

The symptoms of ovarian cancer are often nonspecific and can be mistaken for other conditions, specifically gastrointestinal problems, not dissimilar to our patient. A retrospective population-based study examined the factors impacting the time to diagnosis based on prespecified classic symptoms (abdominal/pelvic pain, bloating, urinary symptoms, and difficulty eating) [3]. A total of 18 693 women were identified as having stage II to IV primary epithelial ovarian cancer. Of these, 74.2% (13 872 women) had codes for at least 1 prespecified symptom. The time to diagnosis differed significantly by first symptom, number of symptoms, and first physician specialty seen. This highlights the importance of being vigilant to screen for ovarian cancer in the presence of nonspecific symptoms and appropriate referral to gynecologist.

The treatment of ovarian carcinomas is highly dependent on the subtypes, with emerging evidence for targeted molecular therapies [4]. In endometrioid ovarian carcinoma, surgery remains the cornerstone of treatment, with primary objectives to achieve complete cytoreduction and accurate staging [5]. The role of adjuvant therapy in low-grade endometrioid ovarian cancer is nuanced. In early-stage disease, observation of regular follow up is generally recommended. In advanced-stage disease, the decision to administer chemotherapy or endocrine therapy is individualized, taking into account factors such as residual disease postsurgery and patient comorbidities. For recurrent disease, endocrine therapy offers a treatment option, especially in patients with hormone receptor-positive disease, by exerting an antiestrogenic effect, inducing cellular differentiation, apoptosis, and anti-inflammation.

The prevalence of ovarian cancer in transgender men remains very low and reported in either case reports or case series only. In a systematic review published in 2018 on breast and reproductive cancers in transgender population, only 5 cases of ovarian cancers were reported [6]. We have further identified an additional 6 cases since then and summarized all reported cases to date in Table 2 [7-16]. The sole unifying observation is the much younger age of ovarian cancer in transgender population compared with cisgender women but the paucity of reported malignant cases highlighted the limited screening and management strategies available for such patients.

There is no convincing direct association between testosterone and development of ovarian cancer in transgender population. However, there is potential implication of androgen receptor signalling in ovarian tumorigenesis and malignant transformation [9, 17]. Our patient is unique in that although androgen receptor status was negative, he had estrogen and progesterone receptor positivity in the original tumor, making the ongoing use of aromatizable testosterone as gender-affirming care risky for cancer recurrence. Yet the discontinuation of testosterone led to worsening underlying gender dysphoria and hypogonadal symptoms. Hence, after careful consideration, testosterone treatment was discontinued and eventually switched to intramuscular injectable 19-nortestosterone (nandrolone decanoate) following treatment for the ovarian disease.

Nandrolone is one of the most commonly used androgens, as a derivatives of testosterone lacking the C19 methyl group (=19-nor) with the injectable pro-drug product in the form of an ester of decanoic acid in an oil vehicle [18]. Nandrolone is metabolized by the 5α-reductase enzyme into 5α-dihydro 19-nortestosterone, a weakened androgen unlike the 5α reduction of testosterone to the more potent, pure, (nonaromatizable)

Table 2. Ovarian tumor (malignant and nonmalignant) in transgender men—published case reports (terminology used directly adopted from respective case reports)

Author/year published/ country	Patient demographic (at time of publication)	Symptoms	On testosterone	Medical history	Investigations	Treatment	Histology	Immunohistochemistry/ receptor status	Subsequent management after histology
Hage et al/2000/ The Netherlands [7]	46-year-old female to male transexual	Chronic abdominal pain and change in defecation pattern (1998) Right lower abdominal quadrant tumor palpated	Yes (since 1980)	Bilateral mastectomy (1980) Abdominal hysterectomy (1981) Multistaged phalloplasty (between 1990 and 1994)	CT scan: right adnexa multicystic tumor with mesenteric and omental infiltration CA125 4253 kU/L (4253 U/mL) CA 15.3 171 kU/L (171 U/mL)	Resection of multicystic tumor invading right ovary, 40-cm colon descendens, supracolic omentectomy and left oophorectomy	FIGO stage IIIc papillary serous cystadenocarcinoma of the right ovary	VEGF positive, EGF-R positive	Chemotherapy (Taxol, epirubicin, cis-platinum)
Dizon et al/ 2006/USA [8]	46-year-old female to male transgender	Abdominal distension and early satiety	Yes (since 2001)	Ulcerative colitis, hypertension, asthma Previous bilateral mastectomy	CT pelvis: predominantly cystic mass within the pelvis 14.7 × 27 × 26-cm CA 125; 94 kU/L (94 U/mL)	TAH, BSA, omentectomy, pelvic and para-aortic node dissection, peritoneal staging biopsies	Stage 2A Well differentiated cystic endometriod adenocarcinoma of the left ovary and fallopian tube	AR positive	Six cycles of chemotherapy (carboplatin and paclitaxel) Testosterone discontinued
Aubrey et al/ 2021/Canada [9]	36-year-old transmasculine	Acute pelvic pain, nausea, bloating, incomplete voiding	Yes	None reported	Pelvic US: right adnexal mass 10.7 × 7.3 × 9.8-cm	Initial lap. Right salpingo-oophorectomy Completion staging—TAH, left salpingo-oophorectomy, pelvic and paraaortic lymphadedectomy and omentectomy	FIGO Grade 2 ovarian endometroid carcinoma of right ovary, metastatic in the left ovary	Diffuse ER, PR expression Normal CKDN2A AR positive in 70% of tumor cell	Six cycles chemotherapy (carboplatin and paclitaxel) Testosterone discontinued
Bilash et al/ 2022/USA [10]	? 50s (self-narrative story)	Not reported	Not at presentation	PCOS	Not reported	TAH and BSO at age 30	Stage III3 serous tumor	Not reported	Testosterone commencement
Smrz et al/2023/ USA [11]	19-year-old transgender male	Abdominal pain, bloating, anorexia, and worsening indigestion	Yes (1 year before presentation)	Gastroesophageal reflux disease, anxiety, depression Oocyte preservation pretestosterone	CT scan: Bulky partially cystic and calcified mass within the pelvis CA 125; 720 kU/L (720 U/mL)	Diagnostic and therapeutic paracentesis En bloc resection of uterus, cervix, bilateral fallopian tubes, ovaries, appendix and total colon, splenectomy, ileocecal resection with an end ileostomy and resection of umbilical cord nodule	Low-grade serous ovarian carcinoma	Positive WT1, CK7, PAX8, ER and p16, wild-type expression of p53 AR positive	Systemic chemotherapy followed by maintenance endocrine therapy (Letrozole) Referral to radiation oncology for stereotactic body radiation
Tumas et al/ 2024/USA [12]	33-year-old female to male transgender	Initial presentation aged 26 years (2017) with pleuritic chest pain, pulmonary embolism	Yes (4 years after initial surgery in 2021)	Obesity, anxiety, depression, venous thromboembolism and stroke Gender-affirming mastectomy (2021)	CT scan: 14-cm complex adnexal mass and ascites CA 125; 532 kU/L (532 U/mL) CT scan Aug 2022? vaginal cuff recurrence	Exploratory laparotomy, TAH, BSO, omentectomy, pericolic and diaphragmatic biopsies June 2023—exploratory laparotomy and mass resection	FIGO stage 1C, adult type granulosa cell tumor Recurrent granulosa cell tumor with ovary primary	PR positive, AR positive	Adjuvant chemotherapy (cisplatin, etoposide, bleomycin) 3 cycles—complete response Advised to stop testosterone and Letrozole commenced Bicalutamide added

(*continued*)

Table 2. Continued

Author/year published/ country	Patient demographic (at time of publication)	Symptoms	On testosterone	Medical history	Investigations	Treatment	Histology	Immunohistochemistry/ receptor status	Subsequent management after histology
Hage et al/2000/ The Netherlands [7]	39-year-old female to male transexual	Asymptomatic	Yes (since 1997)	Subcutaneous mastectomy (1998)	Preoperative ultrasound: 8 × 7 × 7 cm mass to the left of the uterus	Hysterectomy and BSO, para-aortic lymphadenectomy, resection of tumor plaque on colon descendens	Multicystous serous papillary borderline tumor of the left ovary FIGO stage IIc	ER positive PR positive VEGF positive EGF-R positive	Close follow up, no adjuvant radiotherapy or chemotherapy needed
Kwiatkowska et al/2020/ Poland [13]	17-year-old female	Irregular menses aged 15	Not documented	Hypothyroidism, insulin resistance, psoriasis, hirsutism	Serum testosterone 14.96 nmol/L CA 125 27.96 kU/L (27.96 U/mL)	Laparoscopic enucleation of left ovarian tumor Ultrasound surveillance at 9 months post: 7-cm tumor in the left ovary Patient demanded TAH and BSO given gender dysphoria history, but parent declined given age of minor Agreed to unilateral removal of appendages and staging	FIGO stage 1A Folliculoma Unilateral FIGO 1A relapse of juvenile granulosa cell tumor	Not documented	Declined adjuvant chemotherapy
Ferreira et al/ 2021/ Portugal [14]	23-year-old female to male transgender	asymptomatic	Yes (since 2016)	Asthma	Routine ultrasound: complex cyst lesion left ovary 3.0 cm Pelvic MRI: complex cystic lesion from left ovary 4.0 × 4.3-cm, another mixed mass involving both ovaries CA 125 ; 133 kU/L (133 U/mL)	Total abdominal hysterectomy, BSO, and multiple biopsies of the peritoneum	Bilateral borderline ovarian serous tumor with noninvasive desmoplastic implants	Positivity for WT1, RE, RP, p53 wild-type labelling, p16, Ki 67 and AR	Refer to oncology department for further evaluation. Testosterone temporarily suspended
Millington et al/ 2021/USA [15]	17-year-old transgender male	Acute right lower quadrant pain and nausea	Yes (12 weeks before presentation)	Obesity, anxiety	Ultrasound: large right sided mass with solid and cystic component	Elected salpingo-oophorectomy (right)	FIGO stage 1A serous papillary borderline tumor	AR positive	Testosterone restarted 2 months after surgery Five years periodic surveillance ultrasound
Ing et al/2023/ USA [16]	34-year-old transgender male	Left lower quadrant pain Early satiety and bloating	Yes (since 2016)	Ollier's disease (enchondroma, low-grade chondrosarcoma) Anxiety, depression, obesity	CT chest/abdomen/ pelvis: 15-cm cystic and solid right ovarian mass, 4.9-cm uterine fundal fibroid, endometrial thickness 1.4 cm Pap smear atypical endometrial cells, and HPV 16 positive	Exploratory laparotomy, TAH, BSO, omentectomy, radical optimal tumor reductive surgery	Stage 1 A juvenile granulosa cell tumor confined to right ovary Atypical endometrial hyperplasia	Positive for ER, PR, AR	Ongoing surveillance Still desire top surgery and to be restarted on testosterone therapy

Reference ranges: CA125—cancer antigen 125 (0-35 kU/L; 0-35 U/mL); CA 15.3—cancer antigen 15.3 (reference range <30 kU/L; <30 U/mL).

Abbreviations: AR, androgen receptor; BSO, bilateral salpingo-oophorectomy; EGF-R, epidermal growth factor receptor; ER, estrogen receptor; FIGO, The International Federation of Gynaecology and Obstetrics; HPV, human papillomavirus; MRI, magnetic resonance imaging; PR, progesterone receptor; RP, regulatory peptides; TAH, total abdominal hysterectomy; US, ultrasound; VEGF, vascular endothelial growth factor; WT1, Wilms' Tumor Gene 1.

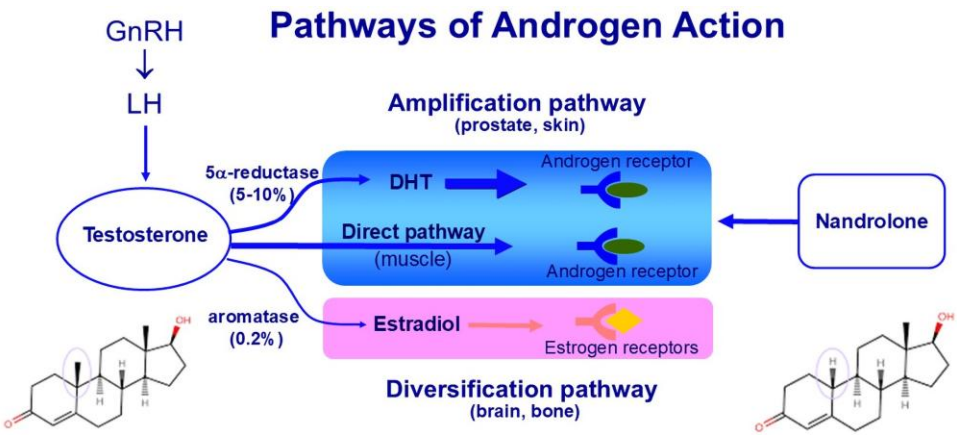

Figure 2. Pathways of action between testosterone and nandrolone.

androgen dihydrotestosterone (Fig. 2). Nandrolone is also metabolized to 19-norandrosterone and 19-noretiocholanolone, which are inactive androgen metabolites.

Nandrolone has been used in various clinical conditions with catabolic state such as burns, anemia, chronic kidney disease, osteoporosis, sarcopenia, and HIV associated wasting syndrome [18], but its virilizing properties largely preclude its use in women and children. It is also among the most frequent androgens abused in sports doping and body building [19]. The therapeutic dose for humans can be 0.4 mg/kg/day [18] but is usually administered as 50 mg every 1 to 3 times weekly. Although 19-nortestosterone is an intermediate in the aromatization reaction converting testosterone to estradiol in the aromatase enzyme complex, paradoxically, exogenous nandrolone is not converted to estradiol in men [20]. It is this nonaromatizable characteristic that prompted the use of nandrolone as an alternative gender-affirming masculinizing therapy in our patient to maintain the androgen effects but without generating estradiol by aromatization that may promote cancer recurrence while also improving androgen deficiency symptoms and maintaining bone density and muscle mass.

In summary, this case highlights the challenges in balancing provision of gender-affirming care for better psychosocial well-being when a hormone-sensitive cancer occurs, which precludes using aromatizable testosterone for risk of promoting tumor recurrence. It provides an opportunity for use of nandrolone as an alternative masculinizing hormone as GAHT and relief for androgen deficiency symptoms while maintaining androgen effects on muscle, bone, and brain without risking recurrence of a hormone-sensitive cancer. It also emphasizes a coordinated multidisciplinary team is essential for optimal patient outcome.

Learning Points

- Ovarian cancer can occur in transgender men, but diagnosis and management present unique challenges. As in cisgender women, there are no established screening guidelines for ovarian cancer. However, in transgender men, health care avoidance may further complicate early detection. Maintaining clinical awareness and a high index of suspicion is crucial for timely diagnosis.
- The impact of discontinuing gender-affirming testosterone therapy requires careful discussion. Risks and benefits must be evaluated in a multidisciplinary team setting, taking into account the patient's quality of life, mental health, and the risk of hormone-sensitive cancer recurrence.
- Nandrolone is a plausible alternative gender-affirming masculinizing therapy. It may help avoid androgen deficiency symptoms while maintaining bone and muscle health and reduce the risk of hormone-sensitive cancer recurrence compared to testosterone therapy.

Contributors

All authors made individual contributions to authorship. S.L., L.C., and Y.C.L. were involved in diagnosis and management of the patient. D.J.H. suggested the use of nandrolone as alternative treatment. S.L., R.P., and D.J.H. were involved in manuscript drafting. K.T. was involved in histopathology reporting and preparation of the histology images. All authors approved the final manuscript.

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Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent directly obtained from patient.

Data Availability Statement

Original data generated and analyzed during this study are included in this published article.

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