

Incidence of Testicular Cancer in Transfeminine Patients following Vaginoplasty with Orchidectomy

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Background: Little is known about the prevalence of testicular cancer in the transfeminine population. Only six cases have been reported in the literature. This case series reports six additional cases of various testicular cancers found in transfeminine patients who underwent vaginoplasty with orchidectomy in our institution.

Methods: In our institution, all specimens are routinely sent to pathology following vaginoplasty with orchidectomy. This permitted the identification of all positive cases of testicular cancer. A chart review was conducted to retrieve patient demographics, duration of hormone therapy, type of neoplasm, the context of its discovery, and cancer follow-up.

Results: A total of 2555 patients underwent vaginoplasty with orchidectomy between January 2016 and January 2021. All specimens were sent to pathology for analysis. A total of six (0.23% of patients) specimens revealed malignant lesions.

Conclusions: Increased societal awareness toward the transgender population encourages recourse to gender-affirming procedures. Little is known about the incidence of testicular cancer in the transfeminine population. In total, 0.23% of patients in our cohort presented with positive pathology findings indicative of testicular cancer. All cancers were found to be only locally invasive, and all patients were successfully treated. We therefore encourage routine pathology examination for all specimens following vaginoplasty with orchidectomy. (*Plast Reconstr Surg Glob Open* 2022;10:e4051; doi: [10.1097/GOX.0000000000004051](https://doi.org/10.1097/GOX.0000000000004051); Published online 18 April 2022.)

INTRODUCTION

Testicular cancer is the most prevalent solid neoplasia among men aged 18–39 years. Its incidence has almost doubled between 1971 and 2015, accounting for 7.06 per 100,000 individuals in Canada.¹ Nevertheless, it remains rare, as it represents 1% of all malignancies affecting the male population. Often, patients present with nonspecific conditions, such as painless testicular mass or scrotal edema, but may describe signs of more advanced disease such as inguinal adenopathies or symptoms of metastatic pulmonary lesions. Treatment is often a combination of bilateral orchidectomy, chemotherapy, and radiotherapy. The current 5-year survival rate with treatment is 97%.^{2,3}

Exposure to exogenous hormones may increase one's lifetime risk of developing gonadal cancer.⁴ Excessive circulating estrogen may alter testicular parenchyma similarly

to testicular dysgenesis syndrome—a predisposing condition to testicular cancer.⁵ This potential adverse effect is of particular importance in the transfeminine population, as transitioning often implies a prolonged intake of estrogen, consequently resulting in more frequent use of hormonal therapy.⁶ Known risk factors for the development of testicular cancer include life habits, family history, and genetic factors; however, no study has proposed evidence that links testicular cancer to exogenous estrogen intake.⁷ Further research is necessary to determine if hormone therapy may be a driver of malignancy in the cases of testicular neoplasia.

We conducted a retrospective study to elucidate the percentage of incidental findings of testicular cancer in transfeminine patients who underwent gender-affirming surgery at our institution. A secondary goal was to contribute to the paucity of literature on this subject.

METHODS

A retrospective review of transgender patients undergoing vaginoplasty with orchidectomy at our institution was completed. All cases between 2016 and 2020 were examined to report the number of positive instances of testicular cancer. Patients under the age of 18 were excluded. For positive cases, a chart review was conducted to retrieve patient demographic information (including

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age, BMI, smoking status), duration of hormone therapy, type of neoplasm, the context of its discovery, and modalities of cancer evaluation. The study was conducted in compliance with the principles of the Declaration of Helsinki.

RESULTS

A total of 2555 patients underwent vaginoplasty with orchidectomy between January 2016 and January 2021. All specimens were sent to pathology for analysis. Of all the submitted specimens for routine examination, six (0.23% of patients) revealed malignant lesions. All of these patients were asymptomatic preoperatively. Of these six malignant lesions, three were seminomas and three were intratubular germ cell neoplasia. Malignant changes in all the collected specimens did not extend beyond the basement membrane. All patients were referred to urology for appropriate workup, which revealed only locally invasive lesions (T1N0M0) in all cases.

For patients with positive pathology, the average age at the time of the surgery was 27.7 years (range 16–48) and all patients were on hormone therapy (average 3.5 years, range 2–6). The average BMI was 24.4±5.6, and one patient had a positive personal history of tobacco use. No patients had a personal or familial history of testicular cancer (Table 1).

Takeaways

Question: What is the risk of developing testicular cancer for transfeminine patients on hormone therapy?

Findings: The risk of developing testicular cancer for transfeminine patients on hormone therapy is 0.23%.

Meaning: Transfeminine patients have a comparable risk of developing testicular cancer relative to cisgender men, and we will continue to send surgical specimens to pathology so patients with cancer can be appropriately directed to urology for investigation.

DISCUSSION

Our retrospective review revealed six incidental findings of testicular cancer in asymptomatic transfeminine patients undergoing vaginoplasty with orchidectomy. This represents 0.23% of our patient population.

Only six other cases of testicular cancer in transfeminine patients have been reported in the literature.^{4,8–12} In these studies, four of the six patients had clinical manifestations of the tumor, whereas the other two cases were incidental findings after a gender-affirming surgery involving orchidectomy. Five of these patients had locally invasive disease, whereas one had metastatic disease (Table 2).

Table 1. Patient Demographics and Pathology Results

Year	Patient Age	BMI	Tobacco Use	Years of HRT*	Symptoms	Pathology	Staging
2021	26	31.9	Yes	3	None	8-mm seminoma	Locally invasive pT1 N0 M0
2018	20	19.6	No	6	None	Intratubular germ cell neoplasia and microscopic intertubular seminoma cells	Locally invasive pT1a N0 M0
2019	22	16.5	No	4	None	Intratubular germ cell neoplasia	Locally invasive pT1 N0 M0
2019	31	27.2	No	2	None	5-mm seminoma	Locally invasive pT1 N0 M0
2018	19	26.6	No	3	None	Intratubular germ cell neoplasia	Locally invasive pT1 N0 M0
2016	48	25.8	No	3	None	1-cm seminoma	Locally invasive pT1 N0 M0

*HRT, hormonal replacement therapy.

Table 2. Reported Cases of Testicular Cancer

Authors	Year	Patient Age	Years of HRT*	Symptoms	Pathology	Staging
Jacoby et al ¹⁰	2021	29	Yes, but duration not reported	None	Mixed germ cell tumor with embryologic and yolk sac components	Locally invasive
Elshimy et al ¹¹	2020	31	>1	Persistence of masculine characteristics and failure to suppress testosterone despite hormone therapy	3.1×3.1×2.3 cm hCG-secreting seminoma	Locally invasive pT1b, Nx, M0
Kvach et al ⁹	2019	30	1.75	None	2.1-cm seminoma	Locally invasive 1A
Chandhoke et al ⁴	2018	38	1.25	Right-sided scrotal swelling, abdominal and back pain, fatigue, and weight loss of 7 kg	Germ cell tumor	Metastatic disease I1C
Wolf-Gould and Wolf-Gould ¹²	2016	28	2	Persistence of masculine characteristics and failure to suppress testosterone despite hormone therapy	Germ cell tumor with embryonal carcinoma (75%), immature teratoma, seminoma (9%), and yolk sac tumor (<1%)	Locally invasive Stage 1 T2N0M0
Kobori et al ⁸	2015	30	2	Testicular mass	Testicular teratoma	Locally invasive

*HRT, hormonal replacement therapy.

To this day, evidence describing the effect of estrogenic hormone therapy on the testicular matrix remains sparse and inconclusive. Some studies bring forth a theoretical risk of testicular cancer with exogenous hormone therapy.^{5,13} Excessive circulating estrogen leads to the remodeling of testicular parenchyma by acting on endocrinological pathways. These subsequent histological changes are similar to those found in patients with testicular dysgenesis syndrome—a known risk factor for testicular neoplasia.⁵ However, a recent retrospective study examined 135 specimens from transfeminine patients who had an orchidectomy, of which 75.6% (102/35) had been on hormone therapy. No specimens displayed premalignant or malignant histologic changes.¹⁴

The current Endocrine Society's guideline regarding the treatment of gender-dysphoric and gender incongruent individuals does not recommend routine screening tests for testicular cancer in the transfeminine population. These current recommendations are the same as those offered to the cisgender population.¹⁵ However, there are no recommendations regarding best practices for pathology post orchidectomy. More research is needed to determine if there exists a link between exogenous hormone therapy in transfeminine patients and the risk of developing testicular cancer. Limitations of this article include its retrospective and unicentric nature.

CONCLUSIONS

The growing societal acceptance of the transgender population has led to increased demand and access to gender-affirming procedures.⁶ Over the last 5 years, six transfeminine patients were found to have testicular cancer on routine pathology examination following vaginoplasty with orchidectomy in our institution. We therefore will continue the routine pathology examination for all specimens following vaginoplasty with orchidectomy.

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