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Incidental testicular germ cell tumor in a transgender woman: A case report

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ABSTRACT

Testicular cancer found incidentally during gender-affirming orchiectomy is infrequently reported in the literature. This report details a 27-year-old transgender woman whose testicular cancer was discovered incidentally upon routine histopathologic examination of the orchiectomy specimen. The patient did not present with any clinical signs of malignancy. There was no evidence of metastases after further workup and the patient was able to resume hormone therapy after surgery. Transgender individuals must be screened according to their natal anatomy and even in absence of clinical signs excised tissue should be examined for possible malignancy.

1. Introduction

With an estimated 1.3 million American adults identifying as transgender, the number of patients seeking gender-affirming surgery nearly tripled from 2016 to 2019; this rate of increase is projected to continue over the next decade.[1,2] To relieve the incongruence between their anatomy and gender identity, patients assigned male at birth (AMAB) who identify as women often pursue orchiectomy in isolation or as part of a gender-affirming vaginoplasty.[2] Of significance, the peak age group for patients undergoing gender-affirming orchiectomy coincides with the peak incidence of testicular malignancies.[3] Because routine cancer screening for testicular cancer is less likely to occur in transgender patients, surgeons performing gender-affirming orchiectomy should both appropriately evaluate patients pre-operatively and must routinely submit orchiectomy specimens for pathological examination.[4–6] To emphasize this point, we present a case of testicular germ cell tumor discovered incidentally in an orchiectomy specimen from a transgender woman following gender-affirming vaginoplasty.

2. Case presentation

A 27-year-old AMAB patient identifying as female was referred to us for a gender affirming vaginoplasty. The patient fulfilled all WPATH SOC8 Standards of Care criteria for gender-affirming surgery, including having marked and sustained gender incongruence, demonstrating capacity to consent, understanding the impact of surgery on fertility and reproductive options, excluding other causes of gender incongruence, assessment of physical and mental health conditions that could impact her surgical outcome, discussing surgery's risks and benefits, and stability on gender-affirming hormone treatment for >6 months.[7] She had been on cross-sex hormone therapy for 3 years, with a current regimen of 20mg estrogen injections every 5 days, and 50mg of spironolactone daily. Past medical history was notable only for obesity, asthma, and longstanding gender dysphoria. The patient had no history of testicular mass or other abnormality, and physical examination confirmed normal testes bilaterally, without mass, hydrocele, or varicocele. Pre-operative preparation included cessation of hormone therapy 3 weeks prior to surgery. The patient underwent an uncomplicated penile inversion vaginoplasty including a bilateral orchiectomy with submission of the testes for pathologic examination. Surgical pathology evaluation of the right testicle demonstrated malignant stage 0 germ cell tumor of the testis (pTis) with focal intratubular classic seminoma and extensive germ cell neoplasia in situ (GCNIS); immunohistochemistry for OCT4 was supportive of these findings (Figure 1). The rete testis was not involved by the tumor and there was no lymphovascular invasion. Her left testicle had no evidence of tumor or germ cell neoplasia, and only showed benign testicular tissue with atrophic changes (consistent with patient's history of hormonal therapy). Due to identification of germ cell tumor within the orchiectomy specimen, the entire testicular parenchyma from both slides was submitted for histologic evaluation.

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Urologic Oncology was consulted to guide further workup. On CT there was no evidence of retroperitoneal adenopathy or visceral metastatic disease. L dehydrogenase, alpha fetoprotein, and β-hCG were all within normal limits. Because the tumor had no extra-testicular spread and imaging and tumor markers were within normal limits, the orchiectomy constituted definitive treatment. The risk of recurrence or metastasis was determined to be negligible and surveillance and further screening were deemed unnecessary. For this patient's clinical circumstance, exogenous estrogen therapy did not pose a risk of promoting testis malignancy, so hormone therapy was resumed post-operatively.

3. Discussion

Although the true incidence is unknown, testicular malignancy in transgender women appears to be very uncommon. A thorough literature search turned up only thirteen reported cases of testicular cancer and an additional three cases of intratubular germ cell neoplasia; these cases are summarized in Table 1. Despite this apparent low incidence, this case of incidentally discovered testicular malignancy in a transgender woman illustrates a number of important considerations.

The first is to emphasize surveillance in transgender women prior to orchiectomy. As noted in Table 1, testicular malignancy, including metastatic malignancy, has been observed in transwomen with retained testes, despite ongoing estrogen therapy. In many of these cases a scrotal mass, orchalgia, or failed suppression of testosterone with spironolactone prompted further investigation to confirm the diagnosis. Specific to transgender women, any failure of testosterone-suppression medication to have the expected clinical effects should prompt further investigation. However, four studies describe cases diagnosed by orchiectomy specimen pathology alone. Therefore, for transgender women, whether on cross-sex hormone therapy or not, routine health maintenance should include screening for testicular malignancy that does not vary from that in cisgender men. Furthermore, because patients may not disclose their transgender identity to other healthcare providers, surgeons performing gender-affirming procedures have a unique responsibility to ensure adequate health-maintenance screening for their patients.[4]

The second consideration is the need to evaluate for the possibility of occult testicular malignancy at the time of orchiectomy. While there are cases of testicular cancer in transgender women discussed in the literature, half of the studies discuss patients who were not asymptomatic; these are summarized in the second half of Table 1.[12–16] A literature review found only four studies that collectively report a total of 9 patients who were diagnosed with testicular cancer due only to specimen pathology after gender-affirming orchiectomy.[8–11] Of note, six of the nine cases came from single institution where all specimens are routinely sent for pathology.[11] At present, there are no published guidelines or standards dictating pathologic examination of all orchiectomy specimens in transgender patients as well as a paucity of publications discussing the spectrum of histologic changes occurring in patients on feminizing hormone therapy.[17] A recent study interrogating orchiectomy specimens performed for gender affirmation surgery has proposed submitting 3 tissue sections per orchiectomy for histologic evaluation (one representing spermatic cord margin and two representing testicular parenchyma including rete testis and epididymis); however, if a mass is seen or features of malignancy like tumor regression, GCNIS, or invasive germ cell tumor, additional sampling is critical for evaluating and staging germ cell tumor.[18] Because insurance coverage for gender-affirming vaginoplasty varies widely, at least some proportion of patients self-pay for the surgery and may object to the additional cost of the pathologic examination. Based on the literature and our experience with this case, we consider sending all orchiectomy specimens for pathologic evaluation mandatory. It is incumbent on the surgical team to educate the patient regarding this necessity. Additionally, surgical pathology evaluation of such specimens by pathologists who frequently encounter testicular resections, or by subspecialty trained genitourinary pathologists, is recommended to faithfully diagnose germ cell tumors in such clinical scenarios.

For patients where a testicular mass is noted, American Urologic Association (AUA) guidelines should be followed; these include

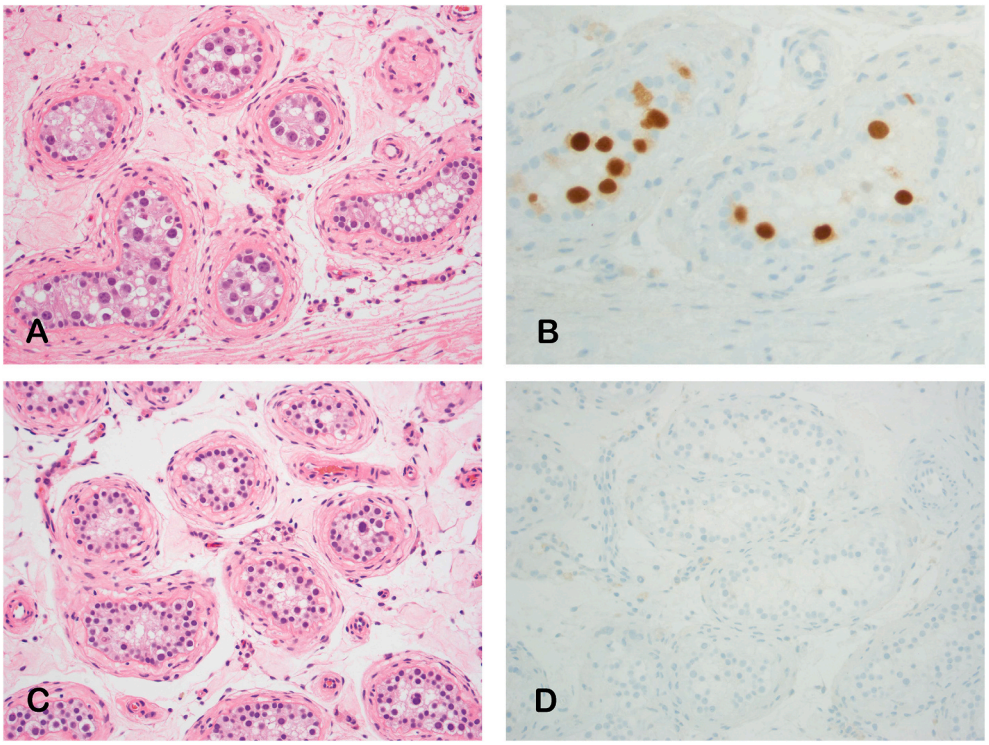

Fig. 1. Germ cell neoplasia in situ. A. H&E image, and B. Immunohistochemistry in A with OCT4 highlighting GCNIS. Benign testicular parenchyma with atrophic changes. C. H&E image, and D. Immunohistochemistry in C with negative OCT4 expression.

Table 1
Reported Cases of Testicular Cancer in Transgender Women.

Authors	Total # of cases	Year	Symptoms	Pathology	Hormone Therapy Status
Asymptomatic Presentation, diagnosed after orchiectomy:					
Kvach et al.[8]	1	2019	None	Seminoma	On HRT for 1.75 years
Jacoby et al.[9]	1	2020	None	Mixed germ cell tumor	On HRT for undisclosed duration
de Nie et al.[10]	3	2021	Painless scrotal mass (2 cases) None (1 case)	Nonseminoma (1 case) Seminoma (2 cases)	On HRT for 1–3 years
Bonapace-Potvin et al.[11]	6	2022	None	Seminoma (3 cases) Intratubular germ cell neoplasia (3 cases)	On HRT for average of 3.5 years
Symptomatic Presentation, diagnosed prior to orchiectomy:					
Kobori et al.[12]	1	2015	Rapidly growing painless mass in the right scrotum	Testicular teratoma	On HRT for 2 years
Wolf-Gould & Wolf-Gould[13]	1	2016	Aberrant high testosterone and estradiol levels in the context of hormonal suppression	Nonseminomatous germ cell tumor	On HRT for 2 years
Chandhoke et al.[14]	1	2018	Right-sided scrotal swelling, abdominal and back pain, fatigue, and weight loss of 7 kg	Germ cell tumor, likely seminoma	On HRT for 1.25 years
Elshimy et al.[15]	1	2020	Aberrant high testosterone in the context of hormonal suppression	bHCG-secreting seminoma	On HRT for >1 year
Fine et al.[16]	1	2022	Left scrotal discomfort	Mixed germ cell tumor	On HRT for 1 year

performing a thorough history and physical exam; drawing tumor markers, alpha-fetoprotein, human chorionic gonadotropin, and lactate dehydrogenase; and obtaining staging scans of the chest, abdomen, and pelvis to rule out local or metastatic spread.[19] These same AUA guidelines should be followed if, as in our patient, a mass was not noted prior to orchiectomy but is discovered on pathologic examination of the orchiectomy specimen. In all cases, consultation with a Urologic Oncology specialist should be considered.

The final consideration is the advisability and timing of resuming estrogen therapy. These decisions will be critically dependent on individual clinical scenarios and must be made on a patient-by-patient basis. Our patient received the standard of care for post-orchiectomy testicular cancer, allowing detailed discussion of prognosis and need for further follow-up. She was able to ask questions about her risk of recurrence and need for ongoing treatment as well as be reassured that the orchiectomy itself was curative. When the patient raised concerns about how her hormone therapy may have contributed to her development of cancer, we were able to assure her that estrogen has no known role in promoting testis malignancy, so there is no contraindication to resumption of hormone use.

4. Conclusion

Considering the growing number of gender-affirming surgeries being performed, it is our recommendation that population-specific guidelines be established based on studies focused on care of transgender people. Because at present there are still very few cases in the literature of testicular cancer in transgender women, it is our conviction that sending orchiectomy specimens to pathology for each patient is mandatory. This will contribute to a greater understanding of the incidence of testicular malignancy in this population and have the additional benefit of contributing to an as yet paucity of data published regarding the spectrum of histologic changes occurring in patients on feminizing hormone therapy. Once a diagnosis is made, AUA guidelines can then guide the development of an individual plan of care for each patient. Because transgender individuals already face potential discrimination and delays even within healthcare, gender affirming surgeons have a responsibility to provide holistic care, including pre-operative and ongoing health maintenance screening after surgery.

CRediT authorship contribution statement

R. Evey Aslanian: Writing – review & editing, Writing – original draft, Visualization, Project administration, Investigation, Data curation. **Cole Roblee:** Writing – review & editing, Methodology, Conceptualization. **David C. Smith:** Writing – review & editing, Validation, Conceptualization. **William M. Kuzon:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

None of the authors has any financial conflicts of interest to disclose.

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References

1. Herman J, Flores A, O'Neill K. *How Many Adults and Youth Identify as Transgender in the United States?* Williams Institute; June 2022.
2. Wright JD, Chen L, Suzuki Y, Matsuo K, Hershman DL. National estimates of gender-affirming surgery in the US. *JAMA Netw Open.* 2023;6(8), e2330348.
3. Fung C, Dinh PC, Fossa SD, Travis LB. Testicular cancer survivorship. *J Natl Compr Cancer Netw.* 2019;17(12):1557–1568.
4. Panichella JC, Araya S, Nannapaneni S, et al. Cancer screening and management in the transgender population: review of literature and special considerations for gender affirmation surgery. *World J Clin Oncol.* 2023;14(7):265–284.
5. Seelman KL, Colón-Diaz MJP, LeCroix RH, Xavier-Brier M, Kattari L. Transgender noninclusive healthcare and delaying care because of fear: connections to general health and mental health among transgender adults. *Transgend Health.* 2017;2:17–28.
6. Bradford J, Reisner SL, Honnold JA, Xavier J. Experiences of transgender-related discrimination and implications for health: results from the Virginia Transgender Health Initiative Study. *Am J Publ Health.* 2013;103(10):1820–1829.
7. Coleman E, Radix AE, Bouman WP, et al. Standards of care for the health of transgender and gender diverse people, version 8. *Int J Transgend Health.* 2022;23 (Suppl 1):S1–S259. https://doi.org/10.1080/26895269.2022.2100644. Published 2022 Sep. 6.
8. Kvach EJ, Hyer JS, Carey JC, et al. Testicular seminoma in a transgender woman: a case report. *LGBT Health.* Jan 2019;6:40–42.
9. Jacoby A, Rifkin W, Zhao L, et al. Incidence of cancer and premalignant lesions in surgical specimens of transgender patients. *Plast Reconstr Surg.* 2021;147:194–198.
10. de Nie I, Wiepjes CM, de Blok CJM, et al. Incidence of testicular cancer in trans women using gender-affirming hormonal treatment: a nationwide cohort study. *BJU Int.* 2022;129:491–497.
11. Bonapace-Potvin M, Bijou-Coulon S, Medor MC, et al. Incidence of testicular cancer in transfeminine patients following vaginoplasty with orchidectomy. *Plast Reconstr Surg Glob Open.* 2022;10, e4051.
12. Kobori Y, Suzuki K, Iwahata T, et al. Mature testicular teratoma with positive estrogen receptor beta expression in a transgendered individual on cross-sex hormonal therapy: a case report. *LGBT Health.* 2015 Mar;2:81–83.
13. Wolf-Gould CS, Wolf-Gould CH. A transgender woman with testicular cancer: a new twist on an old problem. *LGBT Health.* 2016 Feb;3:90–95.
14. Chandhoke G, Shayegan B, Hotte SJ. Exogenous estrogen therapy, testicular cancer, and the male to female transgender population: a case report. *J Med Case Rep.* 2018;12:373.
15. Elshimy G, Tran K, Harman SM, et al. Unmasked testicular seminoma during use of hormonal transgender woman therapy: a hidden hCG-secreting tumor. *Journal of the Endocrine Society.* July 2020;4, bvaa074.

16. Fine N, Abbott T, Wintner A. Testicular mixed germ cell tumor in a transgender woman. *Urol Case Rep*. 2021;40, 101861.
17. Andrews AR, Kakadekar A, Schmidt RL, et al. Histologic findings in surgical pathology specimens from individuals taking feminizing hormone therapy for the purpose of gender transition. *Arch Pathol Lab Med*. 2022;146:252–261.
18. Cornejo KM, Oliva E, Crotty R, et al. Clinicopathologic features and proposed grossing protocol of orchiectomy specimens performed for gender affirmation surgery. *Hum Pathol*. 2022;127:21–27. https://doi.org/10.1016/j.humpath.2022.05.017.
19. Stephenson A, Eggener SE, Bass EB, et al. Diagnosis and treatment of early stage testicular cancer: AUA guideline. *J Urol*. 2019 Aug;202(2):272–281.