Gynecologic Oncology Reports 57 (2025) 101686

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case report

# Neovaginal squamous cell carcinoma in a transgender woman: Case report, treatment insights, and literature review

Manengue Arsene [a], Nantier Émilie Marie-Christine [b], Pelland Marie-Ève [b,c], Beauchemin Marie-Claude [b], Bourque Jean-Marc [b,c,*]

[a] Faculty of Medicine, Université de Montréal, Roger-Gaudry Pavilion, 2900 Édouard-Montpetit boulevard, Montréal, Quebec H3T 1J4, Canada
[b] Radiation Oncology Department, Centre Hospitalier de l'Université de Montréal, 1055, rue Sanguinet, Pavilion C, SS3, Montreal, Quebec H2X 3E4, Canada
[c] CHUM Research Center, Pavilions R and S,900, Saint-Denis Street, Montreal, QC H2X 0A9, Canada

ARTICLE INFO

*Keywords:*
Neovaginal squamous cell carcinoma
Transgender health
Gender-affirming surgery
Cancer disparities
Radiation therapy
Case report
Equity in cancer care

## 1. Introduction

Approximately 1 % of the population identifies as transgender, with 2 % to 3 % of those under 25 identifying as transgender or gender diverse (Jackson and Hammer, 2023). Transgender is an umbrella term for persons whose gender identity, gender expression or behavior does not conform to that typically associated with the sex to which they were assigned at birth (American Psychological Association, 2024). With the growing accessibility of gender affirming care and surgeries, it's important to raise awareness among healthcare workers about these procedures (Fierz et al., 2019) and how they may guide cancer care. For male-to-female reassignment surgery, the technique of inverting the penile and scrotal skin, with the glans forming the neovaginal apex, is a commonly used and established method. In this report, we present a case of neovaginal cancer, which is uncommon (Fernandes et al., 2014). In this case study, we describe the eighth reported case of neovaginal squamous cell carcinoma in a transgender woman and the associated cancer treatments, 23 years after gender confirmation surgery.

## 2. Case presentation

A 49-year-old transgender female presented with foul-smelling vaginal discharge, spotting, and a feeling of a mass in her neovagina for the past 6 months. She had no urinary symptoms, and otherwise, the review of symptoms was negative. She underwent male to female reassignment surgery 23 years ago, which included a vaginoplasty and penile and testicular resection. The neovagina was formed using the Stuteville technique, in which the inverted penile skin forms the vaginal lining and the scrotal tissue is used to construct the labia majora (Pandya and Stuteville, 1973). Past medical history included a breast implant surgery, acid reflux and a possibility of deep vein thrombosis, for which she had no treatment. She was on hormone replacement therapy for 5 years and ceased approximately 20 years ago. The patient had no history of HPV vaccination nor cytologic smear test. She denied having STIs, although she had previously been followed for condyloma. Family history included a sister with breast cancer, and a grandfather with colon cancer. The patient had a 15 pack-year tobacco smoking history ceased a year ago but continues to vape and smokes cannabis occasionally. Gynecological exam revealed a necrotic lesion located at the vaginal apex focused on the left fornix that extended to the lower third on the anterior, posterior, and left vaginal walls.

Histopathology revealed a moderately differentiated vaginal squamous cell carcinoma. HPV status was unknown and the pathology report did not include p16 stains. A pelvic MRI showed a 4.6 × 3.6 × 3.1 cm vaginal mass with an invasion of bilateral seminal vesicles and extensive inguinal and pelvic adenopathy. PET-CT scan showed hypermetabolism

* Corresponding author at: Radiation Oncologist, 1055, rue Sanguinet, Radio-oncologie, Pavillon C, porte C.S3.5258, Montreal, Quebec H2X 3E4, Canada.
*E-mail address:* %20jean-marc.bourque.med@ssss.gouv.qc.ca (B. Jean-Marc).

https://doi.org/10.1016/j.gore.2025.101686
Received 16 December 2024; Received in revised form 24 January 2025; Accepted 26 January 2025
Available online 27 January 2025

of the primary lesion and multiple metastatic pelvic lymphadenopathies, including one mesorectal, but no visceral or bone metastasis. The case was evaluated by a multidisciplinary team composed of gynecologic oncologists, radiation oncologists, pathologists, and radiologists. Consensus was reached to procced with treatment according to cervical cancer guidelines as is commonly practiced with metastatic squamous cell carcinomas of suspected gynecologic origin, knowing the patient has never had a uterine cervix.

As per the INTERLACE protocol (recently implemented by our institution for locally advanced cervical cancer), the patient was first treated with 6 cycles of weekly carboplatin-docetaxel followed by radiation therapy with concurrent cisplatin. Neo-adjuvant chemotherapy was well tolerated without any grade 2 or greater side-effects. After the 6 cycles, we observed a partial response on physical examination and pelvic MRI.

For radiation planning, GTV (Gross Tumor Volume) corresponding to the macroscopic vaginal tumor was contoured using fused MRI images. Clinical Target Volume (CTV) corresponding to the microscopic disease included the whole vagina as well as all pelvic lymph nodes (bilateral common, internal and external iliac and pre-sacral). As suggested by Smart et al. (2023), bilateral inguinal lymph nodes were also included in the field. As the usual lymphatic drainage can be altered depending on the technique of the re-assignment surgery, all relevant operating reports of the region are vital to volume contouring. For our patient, the perineum skin was used to create the neovagina for which the drainage is mainly inguinal. Due to the presence of a mesorectal adenopathy, we included the whole mesorectum in the CTV as well.

We treated the PTV to a cumulative dose of 4500 cGy in 25 fractions with a simultaneous integrated boost to the macroscopic lymph nodes to 5750 cGy. The shrinkage of the vaginal mass, especially in thickness, allowed a dose complement on the residual vaginal disease using endocavitary brachytherapy. The superior half of the vagina including the vaginal residual tumor was treated to a dose of 2000 cGy in 4 fractions twice weekly prescribed to the surface of the applicator (total dose to the primary tumor EqD2 = 7000 cGy).

Radiotherapy was completed and the patient was seen by a gynecologic oncologist, who performed a thorough examination and found no evidence of disease. Follow-up pelvic MRI and PET scans are pending. A high-risk HPV test was conducted and was negative. Additionally, the Gardasil vaccine was prescribed as part of her ongoing care.

## 3. Review of literature

This report identifies the eighth case of neovaginal squamous cell carcinoma (SCC) in a transgender woman after male-to-female reassignment surgery. The ages of patients at the time of surgery ranged from 21 to the 50 s, with a median of 36–40 years. Seven patients had undergone the Stuteville technique, while the eighth patient underwent vaginoplasty with an unknown technique. Our patient also had a penectomy and bilateral orchiectomy, retaining an intact prostate and seminal vesicles. Ages at diagnoses among the reviewed cases varied from ages 42 to 78, with a median age of 60. The latency period from surgery to diagnosis spanned 10 to 47 years, averaging 28.5 years. Most patients (n = 5) initially presented with foul-smelling discharge; others reported urinary issues, with a painful lesion or vulvovaginal discomfort fistulas, or vaginal bleeding. Gynecological exams revealed either an ulcerative or necrotic mass located in the anterior or posterior vagina [Table 1]. Lymph node enlargement occurred in four cases, including ours, with one patient having lung metastasis.

No standardized first-line treatment exists for SCC of the vagina in transgender women having undergone gender confirming surgery. Treatments among the reviewed cases included surgery and combined chemoradiotherapy. Four patients received a chemotherapy-radiotherapy combination, with brachytherapy added in two cases, while three underwent surgical approaches, with varying subsequent treatments. One patient had a total neovaginal resection followed by chemoradiotherapy. Another underwent tumor exenteration followed by chemoradiotherapy, and one patient had tumor exenteration with urethroplasty without additional treatment. One case was palliative intent as per terminal stage of disease at presentation. Histopathological confirmation of SCC was obtained in seven cases. No transvaginal biopsy was possible for the metastatic patient due to heavy bleeding, but the pathology of the lung metastasis was suggestive of SCC. One patient was diagnosed with verrucous carcinoma, two with HPV-related squamous cell carcinoma, and one with high-grade SCC. One case presented a well-differentiated squamous cell carcinoma, another was moderately differentiated SCC, and the last was poorly differentiated SCC. Our patient was diagnosed with moderately differentiated SCC. Three patients were disease-free at their 6-month, 2-year, and 2.5-year follow-ups. One patient with HPV-related SCC showed a regression on PET/CT three months after treatment. The transgender woman with high-grade SCC died two years after diagnosis, and the transgender woman diagnosed with well-differentiated SCC died due to sepsis and multi-organ failure after two months. The patient with the lung lesion died four months after diagnosis due to terminal stage disease (Fierz et al., 2019; Fernandes et al., 2014; Arruza-Frau et al., 2023; Wang, 2020; Bollo et al., 2018; Lang et al., 2024; Braun et al., 2017) [Table 2].

**Table 1**
Summary of reported cases of neovaginal squamous cell carcinoma in transgender women, including surgical history, latency period, clinical presentation, and physical examination findings.

| Reference | Age of reconstruction | Procedure | Age at diagnosis | Years/ between | Presentation symptoms | Physical examination |
|---|---|---|---|---|---|---|
| *HM. Fernandes et al.* | 30, 31 | Skin graft | 53 | 21 | Bloody, foul-smelling discharge | 4 cm necrotic mass, apex of neovagina |
| *R. Fierz et al.* | 21 | Presumably penile and scrotal skin inversion | 43 | 22 | Vaginal bleeding, foul-smelling discharge | 4.6 cm ulcerative tumour, anterior vagina |
| *C. Arruza-Frau et al.* | 27 | Unknown technique | 74 | 47 | Urinary difficulty and a painful lesion | 4 cm white plaque with visible ulceration, anterior vagina |
| *G. Wang et al.* | 25 | Penile and scrotal skin inversion | 69 | 44 | Lung metastasis | No information |
| *J. Bollo et al.* | 33 | Penile and scrotal skin inversion | 78 | 45 | Genital discomfort, vaginal discharge | Bulky mass, posterior vagina |
| *SM. Lang et al.* | 50′s | Penile and scrotal skin inversion, penectomy and bilateral orchiectomy | 60′s | 10 | Urinary incontinence and vulvovaginal discomfort | No information |
| *H. Braun et al.* | 24 | Penile and scrotal skin inversion | 42 | 18 | Increasing vaginal discharge, fistula | Mass, posterior vagina |
| Present case | 26 | Penile and scrotal skin inversion | 49 | 23 | Foul-smelling discharges, spotting, and with feeling of a mass | Necrotic lesion at the vaginal dome, anterior, posterior, and left vagina wall |

**Table 2**
Summary of primary treatment approaches, pathological findings, lymph node involvement, therapeutic outcomes, and additional clinical details for reported cases of neovaginal squamous cell carcinoma in transgender women.

| Reference | Primary Treatment | Pathology | Lymph nodes | Result/therapy | Additional clinical data |
|---|---|---|---|---|---|
| *HM. Fernandes et al.* | Combined chemoradiotherapy | Moderately differentiated SCC | No information | Disease-free follow-up for at least 2 years | No history of STIs including warts, negative p16 immunohistochemistry |
| *R. Fierz et al.* | Combined chemoradiotherapy | High grade squamous carcinoma | Positive | Death 2 years after diagnosis | High-risk HPV (type 51) infection, HIV infection, multiple osseous metastases at time of diagnosis |
| *C. Arruza-Frau et al.* | Tumour exenteration with urethroplasty; Additional proximal excision | Verrucous carcinoma | Negative | Disease free at 6-month follow up | Negative p16 immunohistochemistry, positive margins |
| *G. Wang et al.* | Palliative radiotherapy | Lung lesion: poorly differentiated squamous cell carcinoma<br>No transvaginal biopsy due to heavy bleeding | Lung metastasis. Positive | Death 4 months after the diagnosis | Previous history of left kidney renal cell carcinoma of clear cell, grade 4 with osseous metastasis.<br>Positive p16 immunohistochemistry<br>Death due to terminal stage |
| *J. Bollo et al.* | Tumour exenteration and chemoradiotherapy | Well-differentiated SCC | Negative | Death after 2 months | High-risk HPV (type 16)<br>Infection, death due to sepsis and multi-organ failure |
| *SM. Lang et al.* | Chemoradiotherapy followed brachytherapy | HPV-related invasive SCC | Positive | Decrease in size on PET/CT 3 months after treatments | No further information |
| *H. Braun et al.* | Total resection of neovagina and chemoradiotherapy | HPV-induced SCC of the penis | Negative | Disease-free follow-up for 2.5 years | Previous history of chronic venereal warts (low-risk HPV infection) |
| Present case | Chemotherapy followed by chemoradiotherapy | Moderately differentiated SCC | Positive | Ongoing… | |

## 4. Discussion

We discuss a case of primary vaginal cancer in a transgender woman who underwent gender-affirming surgery with a creation of a neovagina using the perineal skin 23 years prior.

Vaginoplasty using penile and scrotal skin inversion provides anatomical benefits, such as preserving sweat glands and the absence of hair follicles, recreating physiological characteristics of the vagina, including its pH balance and microbiological environment. However, it may lead to chronic irritation, increasing cancer risk due to inflammation or infection. A recent study by Grosse et al. (2017) analyzed the cytology of 20 neovaginal tissue samples from both transgender (n = 12) and cisgender (n = 8) women with congenital or chromosomic abnormalities and found inflammation in 40 % of the cases. The risk of long-term malignant degeneration is increased by factors such as chronic inflammation, lacerations, and the presence of heterotopic glans and prepuce, particularly in individuals with a history of HPV infection (Fierz et al., 2019; Bollo et al., 2018).

Malignancies in neovaginal tissue often reflect their tissue origin with squamous cell carcinomas arising from skin grafts while adenocarcinomas are associated with bowel grafts. Studies suggest that the type of graft used in vaginoplasty influences the likelihood of malignant transformation. In their case report, Steiner et al. (2002) analyzed 16 cases of neovaginal carcinoma, focusing on cisgender women born with congenital vaginal malformations. Histopathological analysis revealed 11 cases of squamous cell carcinoma and five cases of adenocarcinoma. All five adenocarcinomas were linked to intestinal transplants, with one case occurring in a woman with a neovagina constructed solely from a skin graft. Among the 11 cases of squamous cell carcinoma, ten originated from skin, peritoneal, and dura grafts, as well as from neovaginal tissue formed through vaginal traction without grafts. These findings suggest that the choice of tissue for vaginoplasty plays a crucial role in shaping the pathogenesis and influencing the development of malignant conditions (Fierz et al., 2019).

It has been documented that transgender women exhibit a high prevalence of sexually transmitted infections, particularly HIV and HPV (Baral et al., 2013; van der Sluis et al., 2016). The latter is also a significant factor in male genital carcinogenesis. It is estimated that high-risk HPV infections are responsible for malignant transformation in approximately 40–50 % of penile carcinoma cases. Transgender women face a high risk of HPV infection due to the generally high prevalence of HPV in the male genital region, which can reach up to 76 %. Additionally, many transgender women identify as heterosexual or bisexual and are likely to have male sexual partners. Since the risk of pregnancy is not a concern, condom use may be reduced and thus HPV and STI transmission risk may increase (Fierz et al., 2019; Arruza-Frau et al., 2023; Wang, 2020). This highlights the importance of widespread HPV vaccination programs for all transgender women.

Early self-detection of neovaginal masses is challenging due to their typical location in the posterior cavity. Moreover, only 4 % of transgender women seek gynecological exams after initial follow-up (Fierz et al., 2019; Wang, 2020). Post-genital reconstruction surgery cancer risks may emerge years later, emphasizing the importance of ongoing gynecological check-ups for early detection. Recommended exams, such as speculum and digital neovaginal assessments, are crucial for transgender women even beyond the initial postoperative follow-up. Additionally, transgender women should have cytologic smear tests every three years, starting at age 21 and continuing up to age 70, especially if they have a history of genital warts, in line with recommendations for cisgender women (Fierz et al., 2019; Fernandes et al., 2014; Wang, 2020).

Discrimination, stigma, and other societal factors amplify healthcare vulnerabilities for transgender individuals, contributing to higher cancer risks, delayed diagnoses, and poorer oncological outcomes. A study conducted in the US found that 63 % of transgender participants reported significant acts of discrimination related to their gender identity, which has severe consequences for emotional and physical well-being. Higher levels of emotional distress may lead to harmful coping mechanisms, including higher rates of alcohol and tobacco use and lower levels of physical activity—each of which is a significant risk factor for cancer. Disparities in access to preventive services, such as smoking cessation programs and cancer screenings, exacerbate these issues, resulting in worse outcomes for cancers prevalent among this population. As such, transgender individuals are more likely to be diagnosed with cancer at later stages, less likely to receive timely treatment, and face a higher risk of mortality from cancers such as prostate cancer, non-Hodgkin lymphoma, and bladder cancer (Jackson and Hammer, 2023).

## 5. Conclusion

Transgender individuals experience heightened cancer risks due to discrimination and healthcare barriers, necessitating inclusive and equitable care (Jackson and Hammer, 2023). This report presents a rare case of squamous cell carcinoma of the neovagina in a transgender woman and offers insights into treatment, particularly concerning radiation therapy. Further research is essential to establish definitive guidelines for managing and preventing SCC in neovaginas. Understanding the long-term outcomes of different therapeutic approaches, along with enhanced screening protocols, could significantly improve patient care. To address these disparities, the development of specialized clinics with culturally trained staff is crucial, ensuring a supportive and informed environment for this vulnerable population. Additionally, fostering patient-centered care models tailored to the unique needs of transgender individuals will help mitigate healthcare barriers and promote better outcomes.

* Written informed consent was obtained from the patient for publication of this case report and accompanying images.

## 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.

## References

American Psychological Association, 2024. Answers to your questions about transgender people, gender identity, and gender expression.

Arruza-Frau, C., López-García, A., Morales-López, R., 2023. Squamous cell carcinoma of the neovagina 47 years after gender-affirming surgery. Urol. Case Rep. 50, 102488. https://doi.org/10.1016/j.eucr.2023.102488.

Baral, S.D., Poteat, T., Strömdahl, S., Wirtz, A.L., Guadamuz, T.E., Beyrer, C., 2013. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. Lancet Infect. Dis. 13 (3), 214–222. https://doi.org/10.1016/S1473-3099(12)70315-8. Epub 2012 Dec 21 PMID: 23260128.

Bollo, J., Balla, A., Rodriguez Luppi, C., Martinez, C., Quaresima, S., Targarona, E.M., 2018. HPV-related squamous cell carcinoma in a neovagina after male-to-female gender confirmation surgery. Int J STD AIDS 29 (3), 306–308. https://doi.org/10.1177/0956462417728856.

Braun, H., Nash, R., Tangpricha, V., Brockman, J., Ward, K., Goodman, M., 2017. Cancer in transgender people: evidence and methodological considerations. Epidemiol. Rev. 39 (1), 93–107. https://doi.org/10.1093/epirev/mxw003.

Fernandes, H.M., Manolitsas, T.P., Jobling, T.W., 2014. Carcinoma of the neovagina after male-to-female reassignment. J. Low. Genit. Tract Dis. 18 (2), E43–E45. https://doi.org/10.1097/LGT.0b013e3182976219.

Fierz, R., Ghisu, G.-P., Fink, D., 2019. Squamous carcinoma of the neovagina after male-to-female reconstruction surgery: a case report and review of the literature. Case Rep. Obstet. Gynecol. 2019, 1–7. https://doi.org/10.1155/2019/4820396.

Grosse, A., Grosse, C., Lenggenhager, D., Bode, B., Camenisch, U., Bode, P., 2017. Cytology of the neovagina in transgender women and individuals with congenital or acquired absence of a natural vagina. Cytopathology 28 (3), 184–191. https://doi.org/10.1111/cyt.12417. https://www.apa.org/topics/lgbtq/transgender-people-gender-identity-gender-expression.

Jackson, S.S., Hammer, A., 2023. Cancer risk among transgender adults: a growing population with unmet needs. Acta Obstet. Gynecol. Scand. 102 (11), 1428–1430. https://doi.org/10.1111/aogs.14686.

Lang, S.M., Reddy, R.A., Renz, M., 2024. Neovaginal human papilloma virus–related squamous cell carcinoma in a transgender woman. JAMA Netw. Open 7 (3), e242537. https://doi.org/10.1001/jamanetworkopen.2024.2537.

Pandya, N.J., Stuteville, O.H., 1973. A one-stage technique for constructing female external genitalia in male transsexuals. Br. J. Plast. Surg. 26 (3), 277–282. https://doi.org/10.1016/0007-1226(73)90015-5. PMID: 4737729.

Smart, A.C., et al., 2023. Gender-affirming surgery and cancer: considerations for radiation oncologists for pelvic radiation in transfeminine patients. Int. J. Rad. Oncol. Biol. Phys. 117 (2), 301–311. https://doi.org/10.1016/j.ijrobp.2023.05.028.

Steiner, E., Woernle, F., Kuhn, W., Beckmann, K., Schmidt, M., Pilch, H., Knapstein, P.G., 2002. Carcinoma of the neovagina: case report and review of the literature. Gynecol. Oncol. 84 (1), 171–175. https://doi.org/10.1006/gyno.2001.6417. PMID: 11748997.

van der Sluis, W.B., Buncamper, M.E., Bouman, M.B., Elfering, L., Özer, M., Bogaarts, M., Steenbergen, R.D., Heideman, D.A., Mullender, M.G., 2016. Prevalence of neovaginal high-risk human papillomavirus among transgender women in The Netherlands. Sex. Transm. Dis. 43 (8), 503–505. https://doi.org/10.1097/OLQ.0000000000000476. PMID: 27414682.

Wang, G., et al., 2020. HPV-related neovaginal squamous cell carcinoma presenting as lung metastasis after male-to-female gender confirmation surgery. Case Rep Oncol 13 (1), 17–22. https://doi.org/10.1159/000504936.