Urology Case Reports 50 (2023) 102488

Contents lists available at ScienceDirect

Urology Case Reports

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

Trauma and reconstruction

Squamous cell carcinoma of the neovagina 47 years after gender-affirming surgery

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ARTICLE INFO

Keywords:
Squamous cell carcinoma
Verrucous carcinoma
Neovagina
Transgender female

ABSTRACT

A 74-year-old transgender female presented with urinary difficulty and a painful lesion at her neo-vagina, 47 years after undergoing gender-affirming vaginoplasty. Initial biopsy reported Low-Grade Squamous Intraepithelial Lesion (LGSIL), while MRI revealed no inguinal or pelvic lymphadenopathy. Patient underwent partial neo-vaginectomy with wide local excision and formal urethroplasty. Pathology revealed verrucous carcinoma of the neovagina, a rare neoplasm in transgender female patients. This case highlights the importance of considering squamous cell carcinoma in the differential diagnosis of patients presenting lesions at neo-vagina and the need of screening methods for early detection of such neoplasms.

1. Introduction

Vaginosplasty has been performed for over 200 years on cisgender female patients with Mayer-Rokitansky-Kuster-Hauser Syndrome or those with significant vaginal canal shortening after cancer treatment.[1] The technique has improved with advances in endocrinology and plastic surgery. In 1952, Danish plastic surgeon Paul Fogh-Andersen initiated the modern era for gender-affirming surgery by using penile skin as a full-thickness graft to line the neovagina.[2] The technique has evolved to increase length, diameter, and functionality of the neovagina. Today, penile inversion, peritoneal flap, or intestinal vaginoplasty are the most common techniques. Postoperative complications from this procedure include chronic lacerations, abscesses, neovaginal or urethral stenosis, and recto-neovaginal fistulas.[1] However, a less reported sequelae is the development of neoplasms in the neovaginal canal, raising questions about long-term management and the possible need for screening protocols for these patients. Reported cases regarding squamous cell carcinoma (SCC) of the neovagina in transgender female patients are scarce. Our case is the fifth reported discussing a transgender female patient with SCC of the neovagina, but the first reported as verrucous carcinoma.

2. Case presentation

A 74-year-old transgender female presented with urinary difficulty and a painful lesion at her neovagina for the past two years. Physical exam revealed pinpoint meatus, neovaginal atrophy, and an approximately 4 cm white plaque with visible ulceration at the anterior wall of neovagina. The patient underwent male-to-female gender-affirming surgery 47 years ago, by an unknown technique. Past medical history includes hypothyroidism, cardiac arrhythmia and deep vein thrombosis, for which she was on Apixaban. The patient reported a 50-year-long marriage, with vaginal penetration and last sexual intercourse over 15 years ago. She was not on hormone replacement.

Gynecology performed a biopsy of the lesion, revealing low-grade squamous intraepithelial lesion (LGSIL). A pelvic MRI (Fig. 1) was suggestive of penile skin inversion vaginoplasty without inguinal or pelvic lymphadenopathy.

The patient was taken to the operating room for wide local excision of her verrucous lesion (Fig. 2), as well as urethroplasty to alleviate her symptoms of bladder outlet obstruction. The procedure was carried out by dissecting the urethra away from the anterior vaginal canal (Fig. 2). After adequate urethral dissection, a circumscribing incision was made at introitus to allow release of neovaginal skin away from lateral walls bilaterally and anterior rectus fascia posteriorly. Cystoscopy revealed non-prostatic obstruction. Urethroplasty with mucosal advancement was effective for urinary symptoms (Fig. 3).

Pathology revealed Squamous Cell Carcinoma consistent for verrucous carcinoma, negative for p16 human papillomavirus (HPV), and with positive margins. The pathologic stage pT1B was assigned. Given

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https://doi.org/10.1016/j.eucr.2023.102488
Received 22 June 2023; Accepted 25 June 2023
Available online 26 June 2023

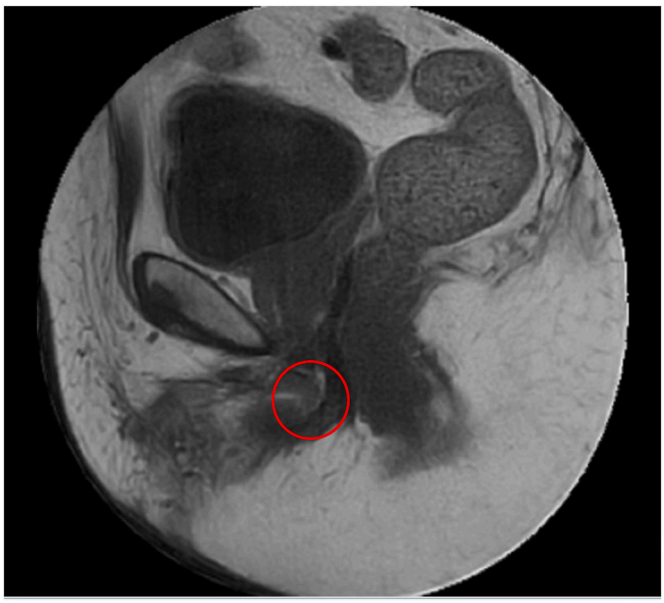

Fig. 1. Preoperative sagittal MRI of pelvis showing the bladder, the prostate and the rectum, with hyperintense lesion (circled) on anterior wall of neovagina. Imaging suggests penile skin inversion vaginoplasty.

the margin status, the patient was taken back to the operating room for a more proximal excision until achieving negative margins. Hematology oncology recommended no further medical treatment. Patient with no recurrence at 6-month follow-up.

3. Discussion

To our knowledge, only four cases of neoplasm in the vagina after genital reconstruction in transgender female patients have been reported. The mean age at presentation was 54 years old, and the diagnosis ranged between 18 and 45 years after genital reconstruction, as seen in the literature review conducted by Fierz et al.[1] In three cases, penile and scrotal skin grafts were used for vaginal canal construction, as suspected in our case. The presenting symptoms included vaginal bleeding or secretions, discomfort, and a visible mass. In our case, the patient had neovaginal atrophy, which led to meatal stenosis. Two cases were treated with chemotherapy and radiation, while the others were treated with local excision and adjuvant chemotherapy. Unfortunately, all patients succumbed to their malignancies or sepsis related to immunosuppression within 3 years from diagnosis.[1]

Our case was negative for HPV, which is rare in cases of SCC of the genitalia, including those of transgender patients. Among the four cases documented, only Fernandes' et al. reported a negative p16 immunohistochemistry, as seen in our case.[1] Glans and prepuce infections are common in cisgender men. These parts are used to recreate the clitoris and labia minora during vaginoplasty, potentially increasing the risk of genital cancer. While HPV-related lesions like condyloma acuminatum and SCC have been documented in transgender female patients, HPV

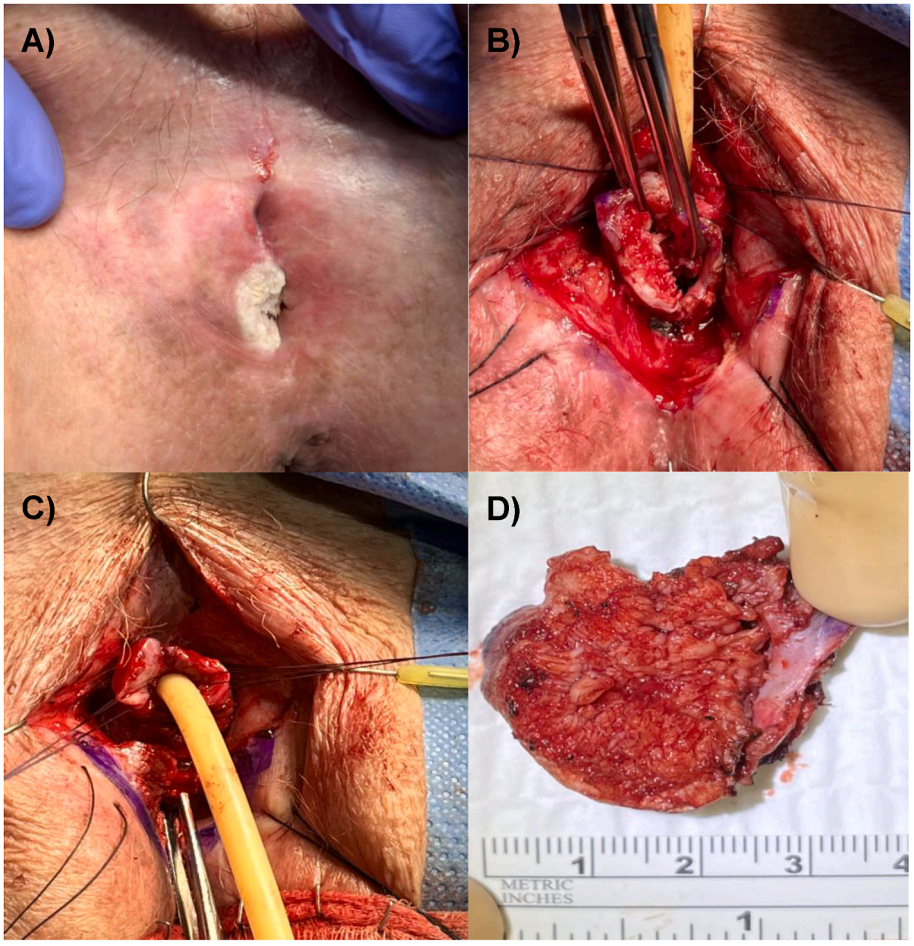

Fig. 2. A) Preoperative photo of lesion seen at the anterior and right wall of neovagina introitus. B) Intraoperative photo showing dissection of the lesion at the anterior vaginal canal. C) Intraoperative photo showing intact dissection of the urethra away from the lesion. D) Gross specimen of neovaginal lesion.

Fig. 3. Postoperative photo of the urethra with indwelling catheter and neovagina canal opening.

likely has clinical implications in neovaginal malignancies, warranting tailored screening and care. Since incidence of primary vaginal malignancy in cisgender females is extremely rare, no screening protocols for early detection have been developed. These reported cases raise concern for the need of HPV cytology screening on transgender female patients with neovagina, and emphasize the importance of HPV vaccination protocols for the trans population.

Verrucous carcinoma is defined as a rare, low-grade, well-differentiated squamous cell carcinoma that rarely metastasizes.[3] However, it is known for its locally aggressive, expanding warty growth that can affect function and aesthetic in the local area. The literature has characterized verrucous carcinoma as predominantly negative for HPV, negative or patchy p16 staining, and associated with chronic inflammation such as lichen sclerosus and lichen simplex chronicus.[3] Penile and vulvar verrucous carcinoma, a rare type of SCC, has poorly understood etiology, diagnosis and treatment.[4,5] Surgery is considered the most appropriate treatment. However, it is important to note that this type of SCC has a high chance of local recurrence, requiring close follow-up and potential re-excision.[5] Currently, there is no literature reviewing this specific type of SCC in the anogenital area of the transgender community.

Even though 25 million people in the world identify as transgender, the incidence of reproductive tract cancers in this population is limited. Establishing recommendations for screening and preventive care in this population has been challenging, which makes cases like ours particularly important to report and study.

4. Conclusion

With an increased number of gender-affirming surgeries in the United States, it is imperative for urologists to understand and recognize pathologies specific to the transgender patient population, especially those related to cancer. Although carcinoma of the neovagina has seldom been reported, it should be considered part of the differential diagnosis in transgender females. Surgical treatment, as shown here, is an option to prevent long-term complications or metastasis.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Abbreviations:

LGSIL: Low-Grade Squamous Intraepithelial Lesion
SCC: Squamous cell carcinoma
HPV: Human papillomavirus