

Oncology

Papillary urothelial carcinoma of the vagina: A case presentation and review of the literature

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A B S T R A C T

A 92-year-old woman with history of right nephroureterectomy for low grade Ta urothelial carcinoma (UC) of the renal pelvis and proximal ureter and high grade Ta and carcinoma-in-situ of the bladder presented for surveillance cystoscopy in 2019. She was found to have no evidence of disease within bladder or upper tract, however demonstrated a large papillary lesion within the vagina. This lesion stained for p40+, p16 patchy+, and GATA3+, all markers of UC, and the same molecular makeup of her prior bladder tumor.

Introduction

Urothelial carcinoma (UC) is a molecularly diverse cancer. It is known to affect the gamut of the urinary tract beginning at the apex of the collecting system down to the proximal portion of the urethra. One classic feature of urothelial carcinoma is its ability to manifest as multifocal disease. There are two popular theories as to the pathogenesis of multifocal urothelial carcinoma: the field hypothesis and monoclonal hypothesis. There is ongoing debate over which theory correctly explains the spread of urothelial cancer, and neither has been accepted fully as dogma.

In the following case report, we present a patient with history of upper tract UC and prior bladder cancer who now experiences recurrent papillary UC of the vagina without synchronous bladder or upper tract tumors. To our knowledge, this is the only case described in the literature of recurrent vaginal disease without concurrent bladder or upper tract disease.

Case presentation

Our patient is a 92 year-old female with history of prior supracervical hysterectomy, status post right nephroureterectomy in October 2012 for low grade Ta urothelial carcinoma of the renal pelvis and proximal ureter, and an 18-year history of urothelial carcinoma of the bladder previously treated with intravesical mitomycin C and induction BCG for high grade T1 and carcinoma in situ (CIS). After a series of negative cystoscopies, she presented one year ago for evaluation of recurrent gross hematuria. Cystoscopy in 2018 revealed a new papillary lesion on the left lateral bladder wall with pathology confirmed high grade Ta as

well as a vaginal lesion that initially was read as “small focus of severely atypical epithelium, worrisome for carcinoma, different in appearance from the bladder tumor.” Further special staining confirmed the vaginal lesion to be of urothelial origin, with the vaginal lesion staining positive for p40+, p16 patchy+, and GATA3+.

Our patient returned in early 2019 for surveillance cystoscopy. There were no lesions within the bladder that required biopsy or resection. After removing the scope from the patient’s urethra, a vaginal exam was performed which revealed two large papillary-appearing lesions towards the proximal vagina. The left lesion was fulgurated with Bovie coagulation and a biopsy was taken of the right lesion. (Fig. 1). Repeat cystoscopy/vaginotomy a few months later again revealed a papillary lesion within the vagina with a negative cystoscopy. (Fig. 2).

Pathology specimens from both resections showed recurrent high grade Ta. Specimens stained positive for p40, p16, as well as GATA3 with prominent nests of urothelial cells seen interspersed with vaginal epithelial cells. (Fig. 3). Imaging of the upper tract with computed tomography (CT) scan did not reveal any suspicious lesions within the contralateral kidney or ureter, further confirming the presence of metachronous urothelial carcinoma of the vagina.

Discussion

In a case report by Warzecha et al., the genetic makeup of non-invasive urothelial carcinoma of the vagina was discussed.¹ They performed numerous immunostains of a papillary vaginal lesion discovered during colposcopy in a 75 year old female patient with no significant past urologic history. The tumor was negative for p16 but stained positive for GATA3, CK20, CK7, all of which were negative in the

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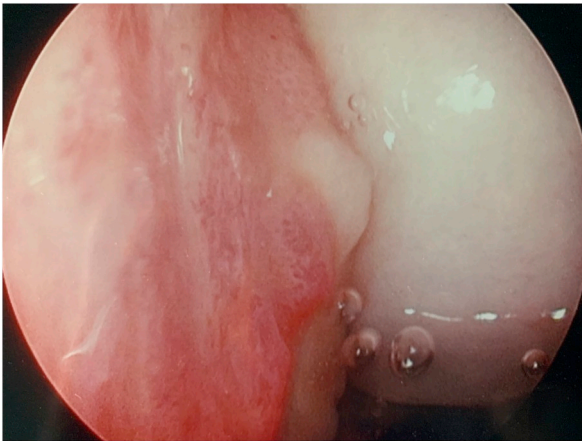


Fig. 1. Gross appearance of vaginal lesion from initial 2019 resection.



Fig. 2. Gross appearance of vaginal lesion from repeat 2019 resection.

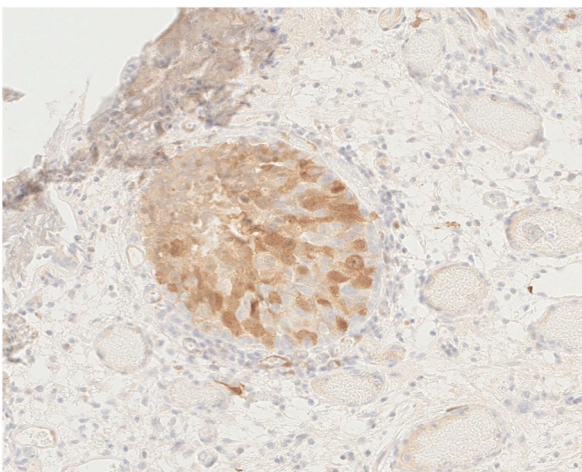


Fig. 3. Immunohistochemical staining of vaginal lesions showing nests of urothelial cells within background of vaginal epithelial cells.

surrounding tissue. Their patient then underwent abdominal imaging and was found to have synchronous tumors within the bladder and renal pelvis. Further resection of those sites revealed the bladder lesions having similar molecular profile to the vaginal lesion, with the renal pelvic lesion having a wild type genetic makeup.

There have been a handful of case reports describing vaginal UC, with the majority of patients having synchronous lesions of the urinary tract.²⁻⁴ What is of particular interest in our current case report is the absence of concurrent bladder or upper tract lesions. Our patient truly had a primary vaginal UC, manifesting similarly to how primary UC of the bladder or upper tract presents—with frequent local recurrences. Her two presentations in 2019 showed a similar grade of vaginal involvement and had an identical molecular makeup to the lesion excised in 2018, supporting the theory of drop metastasis rather than the theory of field cancerization.

Warzecha et al. commented on the preponderance of primary vaginal UC in older women, suggesting a component of dysfunctional voiding as a mechanism by which tumor cells from the urinary tract can seed the gynecologic system.¹ Additionally, older women with a history of bladder cancer, simply by virtue of age, are instrumented more. Our patient had an 18-year history of bladder UC, implying nearly two decades of cystoscopy. What is more, she had moderate urinary incontinence after her hysterectomy, with chronic pooling of urine in her vagina. The effects of this pooling can be seen by the location of her vaginal lesions—just adjacent to the cervix where urine can collect in the vaginal fornices.

Embryology can help explain the ability of vaginal tissue to express urothelial carcinoma—the proximal vagina is derived from endoderm, as is the entire genitourinary tract. The renal pelvicalyceal system and ureter are derived from the Wolffian ducts, and distally form the bladder trigone. The remainder of the bladder, urethra, and distal vagina are derived from the urogenital sinus, with the proximal vagina forming from the paramesonephric duct via extension of the uterine canal. While all endoderm in origin, the vagina is embryologically more similar to the bladder and urethra than the renal pelvis and ureter.

Conclusions

With this case report, we contribute further evidence to the body of literature on the pathogenesis of urothelial carcinoma, with our evidence supporting spread by drop metastasis. There are three further conclusions we hope to put across. First, vaginal involvement of UC is exclusively a presentation of the old, with various risk factors including degree of prior instrumentation, prior gynecologic surgery, and dysfunctional voiding and incontinence being predisposing factors. Second, vaginal UC frequently is of the same clone as concomitant or metachronous bladder UC but unlikely to derive from a clone of upper tract disease. Finally, the fact that vaginal epithelium can even manifest urothelial carcinoma can be explained by a common embryologic progenitor organ—the urogenital sinus.

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Declaration of competing interest

Authors have no conflicts of interest to report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2019.101091>.

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