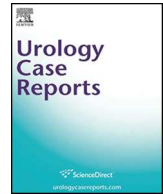




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## Oncology

## Primary adenocarcinoma of bulbomembranous urethra: An exceedingly rare carcinoma in a male patient

Igor Stukalin<sup>a</sup>, Yuan Gao<sup>b</sup>, Shelley Spaner<sup>c</sup>, Kiril Trpkov<sup>b</sup>, Geoffrey Gotto<sup>d,\*</sup><sup>a</sup> Faculty of Medicine, University of Calgary, Calgary, AB, Canada<sup>b</sup> Department of Pathology, University of Calgary, Calgary, AB, Canada<sup>c</sup> Department of Radiology, University of Calgary, Calgary, AB, Canada<sup>d</sup> Department of Surgery, University of Calgary, Calgary, AB, Canada

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## ABSTRACT

Primary urethral carcinomas are rare tumors and their incidence increases with age. Urothelial carcinoma is the most common histologic type of primary urethral carcinoma, followed by squamous cell carcinoma and adenocarcinoma. Adenocarcinoma arising in the male urethra is an exceedingly rare carcinoma that is much less frequent than urethral adenocarcinomas arising in females. The management protocol depends on the tumor location and the stage. We report on a 68-year-old male patient with high-grade bulbomembranous urethral adenocarcinoma (not otherwise specified), who was treated with en bloc radical cystoprostatectomy, urethrectomy and pelvic lymph node dissection.

## Introduction

The annual age-adjusted incidence of primary urethral carcinoma (PUC) in the United States is between 1.5 and 4.2 per million.<sup>1,2</sup> The incidence peaks in the 75-84-year age group, and men are almost three times more likely to develop PUC than women.<sup>1</sup> Patients of African ethnicity are twice as likely to develop PUC than Caucasians.<sup>2</sup>

Urothelial carcinoma is the most common primary type of urethral carcinoma, followed by squamous cell carcinoma and adenocarcinoma. The urethra is an unusual location for a primary adenocarcinoma particularly in males, and adenocarcinomas of the male urethra are much less common than those arising in females. Primary adenocarcinomas of the urinary tract typically arise in the bladder, and several histologic types have been described, including most commonly enteric (colonic) type adenocarcinoma, and adenocarcinoma, not otherwise specified (NOS). Other rarer histologic subtypes include signet ring cell, mucinous (colloid), clear cell, hepatoid, and mixed forms.

We report on patient with a primary high-grade urethral adenocarcinoma (NOS) arising in the bulbomembranous urethra, treated with en bloc radical cystoprostatectomy, urethrectomy and pelvic lymph node dissection.

## Case presentation

A 68-year-old male presented with urethral bleeding after a cardiac

coronary artery bypass grafting procedure. He had no other voiding or systemic symptoms. General and local examination were unremarkable and digital rectal examination was normal. Three years previously he was evaluated for a dense bulbar urethral stricture that was subsequently dilated; however, no tissue biopsy was performed at that time. Blood chemistry revealed anemia, hyperkalemia, high creatinine, a low glomerular filtration rate and hypertriglyceridemia. The patient was a former smoker with extensive coronary artery disease, dyslipidemia and mild chronic kidney disease.

Magnetic resonance imaging (MRI) of the pelvis showed a predominantly solid and partially necrotic mass measuring 5.1 × 2.2 × 2.6 cm, located at the base of the penis, centered on the bulbomembranous urethra (Fig. 1). The mass involved almost the entire bulbous urethra, expanding into the posterior aspect of corpus spongiosum. There was no definitive extension into the corpora cavernosa and adjacent soft tissues around the penile base. Multiple enlarged left external iliac lymph nodes were also found.

Cystoscopy revealed an expansile mass in the bulbar urethra, which on biopsy consisted of three small fragments demonstrating papillary, micropapillary and cribriform growth, suggestive of adenocarcinoma. The biopsy showed absence of normal urethral tissue and there was no evidence of either intestinal differentiation or mucin content. Immunohistochemistry work-up showed reactivity for CDX2, β-catenin (membranous only) and focally for AMACR, while GATA3, NKX3.1, PAX-8, PSA, PSAP, p63 and cytokeratin 5/6 were all negative (Fig. 2).

\* Corresponding author. Southern Alberta Institute of Urology, 7007 14 St SW, Calgary, AB, T2V 1P9, Canada.

E-mail address: [drgotto@gmail.com](mailto:drgotto@gmail.com) (G. Gotto).

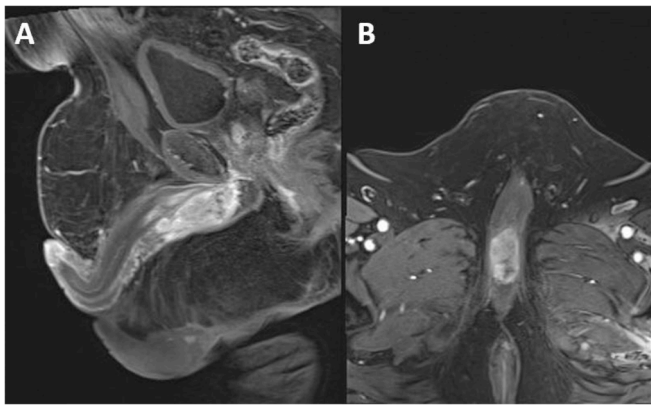
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**Fig. 1.** Magnetic resonance imaging findings A-B. Axial and Sagittal T1FS gadolinium enhanced images demonstrate a 5.1 × 2.2 × 2.6 cm heterogeneously enhancing mass centered in the base of the penis, infiltrating most of the bulbous urethral segment and expanding the posterior aspect of the corpus spongiosum. Proximally the tumor extends to the level of the urogenital diaphragm/external urethral sphincter.

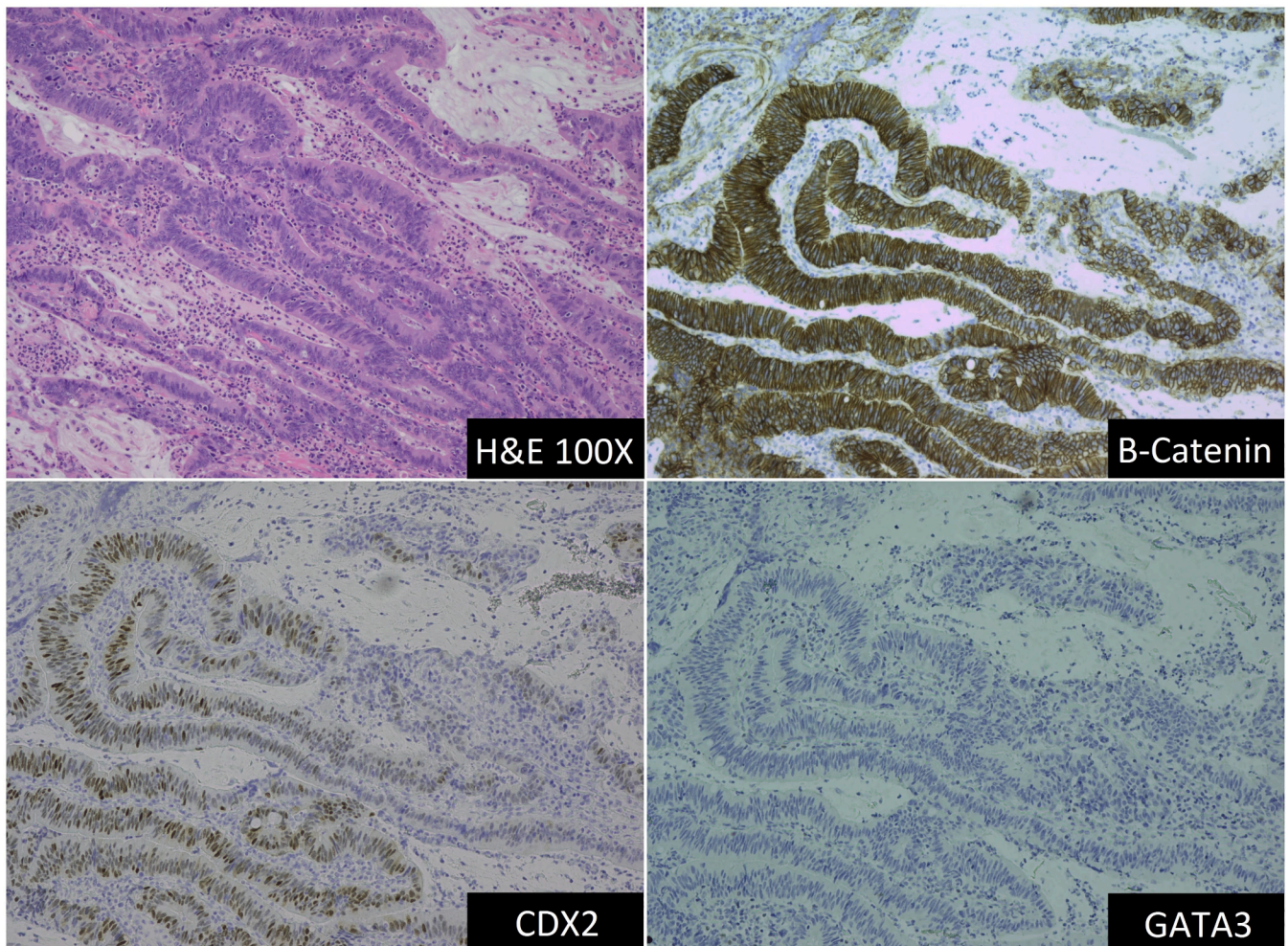
Based on the morphology and the immunoprofile, a diagnosis of high-grade adenocarcinoma (NOS) was established, which was presumed to be urethral primary.

En bloc radical cystoprostatectomy and a urethrectomy were performed (Fig. 3A/3B), including pelvic lymph node dissection, with

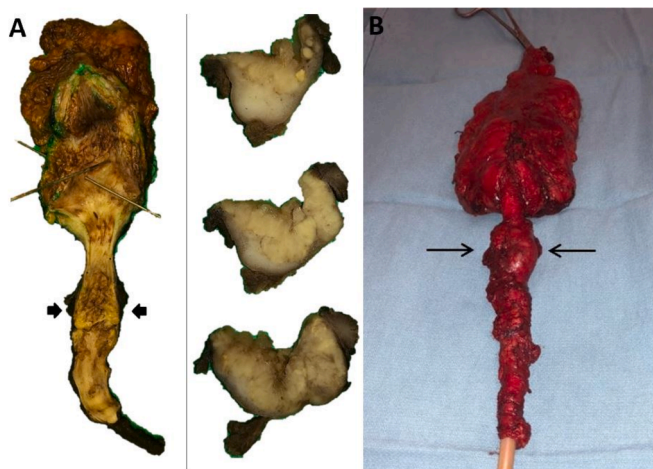
creation of an ileal conduit urinary diversion with bowel resection. The final pathology evaluation confirmed that this was indeed a high-grade invasive adenocarcinoma of the bulbomembranous urethra (NOS), which in addition to the glandular component, also exhibited a more solid component, with only focal mucinous differentiation. Importantly, the presence of dysplastic glandular epithelium in the adjacent membranous urethra was supportive of a primary urethral malignancy, and no primary urothelial carcinoma was identified. The absence of urothelial carcinoma in situ and the negative staining for GATA3, particularly in the more solid carcinoma component, ruled out the possibility of urothelial carcinoma with glandular differentiation. There was an extensive invasion into the subepithelial urethral tissue and into the corpus spongiosum (pT2). The neoplasm also focally involved the periurethral soft tissue resection margin. The resected pelvic lymph nodes showed no evidence of metastatic disease.

**Discussion**

Primary urethral adenocarcinoma is an exceedingly rare carcinoma in males, which typically demonstrates either mucinous or enteric (intestinal) differentiation. Adenocarcinomas without these features, as seen in the current patient, are considered adenocarcinoma, NOS. Urethral carcinomas are generally characterized according to the location and the histologic features. The bulbomembranous urethra (60%), penile urethra (30%) and prostatic urethra (10%) are the most common locations. The three most common histopathological subtypes



**Fig. 2.** Biopsy findings of the adenocarcinoma of the bulbomembranous urethra. A-D. Carcinoma demonstrated glandular differentiation with papillary, micro-papillary and cribriform growth. Immunohistochemistry showed immunoreactivity for CDX2, B-Catenin (membranous), while GATA3 was negative.



**Fig. 3.** En bloc excised specimen of radical cystoprostatectomy and urethrectomy (3A) and gross pathology specimen (3B). A. The dominant tumor encased the entire bulbomembranous urethral segment. The mass is marked by the black arrows. B. Open urethra (left) and urethral cross sections (right), show the location of the neoplasm in the bulbomembranous urethra. Carcinoma invaded extensively into the corpus spongiosum and extended to the resection margin.

of urethral carcinoma are urothelial carcinoma (54–65%), squamous cell carcinoma (16–22%) and adenocarcinoma (5%–10%).<sup>1,2</sup>

To our knowledge, only a handful of primary bulbourethral adenocarcinomas have been previously reported in males.<sup>3–5</sup> All patients presented with symptoms of urinary obstruction and were treated by surgery and other modalities.<sup>3–5</sup> The differential diagnosis of primary urethral adenocarcinoma includes ductal prostatic adenocarcinoma, urothelial carcinoma with glandular differentiation, direct invasion or extension from an adjacent organ (for example, rectum or bladder), metastatic carcinoma, as well as the exceedingly rare carcinoma of the Cowper's glands that typically demonstrates adenoid cystic appearance. On the basis of the clinical and other findings in the current patient, the topography of the neoplasm, its morphology and the immunoprofile, all listed possibilities were ruled out.

PUC is an uncommon and highly heterogeneous disease, and

currently no definitive treatment protocols exist for its management. Age > 65 years, African ethnicity, nodal involvement, presence of metastasis, larger tumor size, proximal tumor location and presence of concomitant bladder cancer are negative predictors of survival in PUC.<sup>2</sup> Early stage urethral cancers can be treated surgically, whereas more advanced tumors may require a multimodal approach, including chemotherapy and radiation. Superficial and early stage tumors have a favorable prognosis, particularly small, anterior urethral tumors that may be effectively resected with urethrectomy. Other surgical approaches include urethrectomy and cystoprostatectomy for locally invasive tumors and pelvic/iliac lymph node. Advanced tumors may require partial/total penectomy, en bloc radical cystoprostatectomy, and even inferior pubectomy.

### Conclusion

We document a rare case of primary urethral adenocarcinoma of the bulbomembranous urethra treated with en bloc radical cystoprostatectomy, urethrectomy and pelvic lymph node dissection. Although a rare malignancy, primary urethral adenocarcinoma should be considered in the differential diagnosis for any de novo urethral mass in male patients. The reported treatments have been variable, and multimodal interventions are recommended for more advanced disease.

### Conflicts of interest

All others have nothing to disclose.

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