Urology Case Reports 10 (2017) 60–62

Contents lists available at ScienceDirect

Urology Case Reports

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

Trauma and Reconstruction

# Development of Squamous Cell Carcinoma of Buccal Mucosa Graft Used for Urethroplasty: A Case Report

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ARTICLE INFO

*Article history:*
Received 27 September 2016
Accepted 1 November 2016

*Keywords:*
Urethral stricture
Urethroplasty
Buccal mucosa graft
Squamous cell carcinoma

ABSTRACT

Urethroplasty may involve the use of tissue substitution including buccal mucosa graft (BMG), penile fasciocutaneous flaps, or skin grafts. Stricture recurrence and fistula formation are some uncommon complications that can result from surgery. The development of squamous cell carcinoma (SCC) after BMG substitution urethroplasty is a new complication that we encountered that has not been described in the literature. We present the first reported case of a patient who developed SCC of the buccal mucosa graft used to reconstruct the urethra.


## Introduction

Current AUA guidelines for management of male urethral strictures include urethral dilation, direct visual internal urethrotomy, and urethroplasty. Stricture recurrence and fistula formation are some uncommon complications that may result from surgery. We present a previously unreported complication of the development of SCC of the BMG used for urethroplasty.

## Case presentation

Our patient is a 43 year old white male with a history of urolithiasis who was referred to our Urology clinic for urethral stricture management. He had a 20 pack year history of cigarette smoking and quit six years prior to presentation. He had no history of oral tobacco use. At age 39, he developed lower urinary tract symptoms (LUTS) including frequency, urgency, decreased force of stream and recurrent UTIs. Cystoscopy and retrograde urethrography revealed a 2 cm bulbar urethral stricture and subsequently underwent urethral dilation with temporary (one month) improvement in his urinary symptoms.

He was then referred to our clinic due to a recurrence of severe LUTS and was found to have an AUA symptom score of 24, a Uroflowmetry Qmax of 12.3 mL/s, and a post void residual of 297 mL. Cystoscopy showed urethral stricture recurrence with an 8F opening at the distal bulbar urethra and blanched mucosa. Retrograde urethrography demonstrated a 2.5 cm distal bulbar urethral stricture. The patient underwent one-stage, augmented anastomotic dorsal onlay BMG urethroplasty in standard fashion. The pathology report of the excised stricture tissue showed fragments of urethra and surrounding erectile tissue with focal chronic inflammation and stromal fibrosis, but no overt malignancy identified. At 16 months post-urethroplasty, the patient was voiding well, but he had persistent microscopic hematuria. He underwent cystourethroscopy, which revealed a papillary lesion at the distal end of the BMG anastomosis (Fig. 1). This lesion was biopsied, which demonstrated moderately differentiated carcinoma with squamous differentiation. He then underwent a more comprehensive cystoscopic evaluation with urethral biopsies revealing invasive SCC (Fig. 1). Staging PET/CT and chest X-ray were negative for metastatic disease. Subsequently, he underwent partial urethrectomy of the involved segment and one-stage urethral reconstruction utilizing a dorsally placed split thickness skin graft from the thigh and a ventral penile fasciocutaneous flap (Fig. 2). Frozen sections from the distal and proximal urethral margins as well as the underlying corpora were all negative for carcinoma. The patient recovered from the procedure without complication. Final pathology was consistent with pT1Nx, SCC of the urethra with verrucous features and focal subepithelial invasion with extensive SCC *in-situ*.

## Discussion

Primary urethral cancer (PUC) is very rare, accounting for about 1% of all urological malignancies[1,2] with an annual age-adjusted

Funding: None.
Informed consent: Obtained from patient.
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http://dx.doi.org/10.1016/j.eucr.2016.11.002

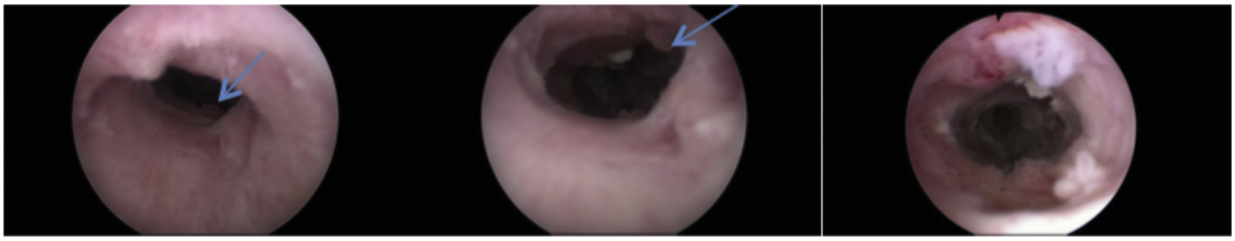

**Figure 1.** Urethroscopy 16 mo post-urethroplasty showing papillary lesions (left and middle images). Urethroscopy for further biopsies of papillary lesions (right image). Arrows showing the papillary lesions in buccal mucosa graft.

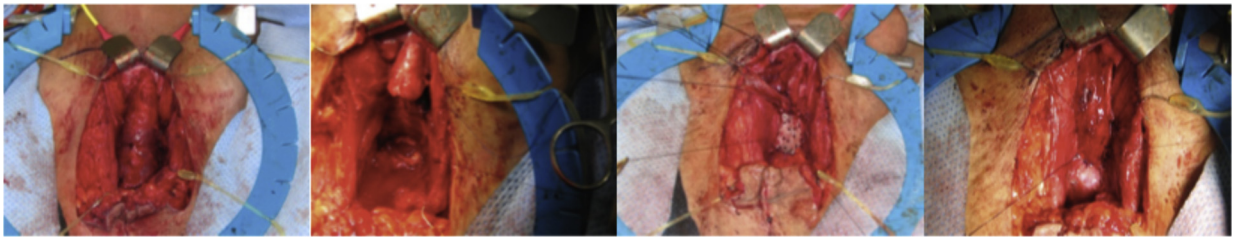

**Figure 2.** Partial urethrectomy with one-stage urethral reconstruction utilizing dorsal split thickness skin graft from a thigh with ventral penile fasciocutaneous flap.

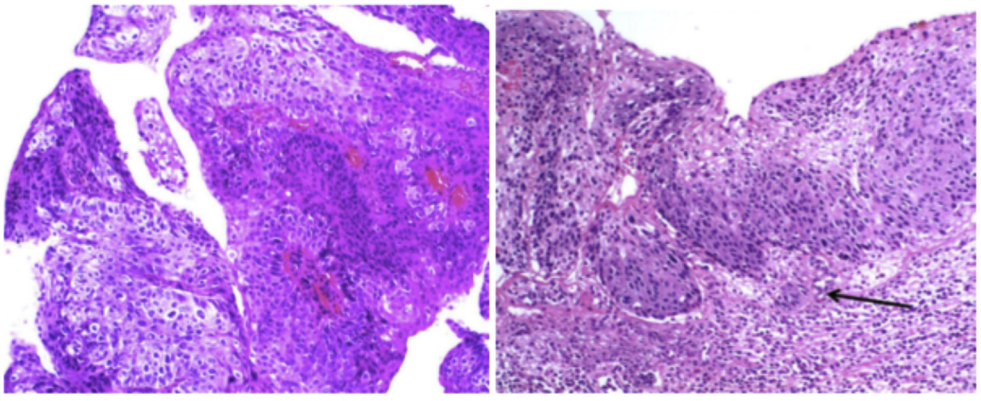

**Figure 3.** Left picture: Urethral biopsy shows invasive SCC, focally keratinizing; P16INK immunostain was negative, not shown (H&E 10×). Right picture: Partial urethrectomy shows superficially invasive SCC (H&E 10×). Arrow showing superficially invasive squamous cell carcinoma.

incidence rate of 4.3 and 1.5 per million in males and females respectively[3] and with the vast majority histologic type of SCC in both males and females encompassing close to 70%–80% of cases.[2] In males, the highest risk factor is urethral stricture disease, followed by human papilloma virus and other sexually transmitted diseases, and traumatic injuries.[2] As with our patient, the most common symptoms at presentation include obstructive and irritative urinary symptoms as well as hematuria, and at the time of diagnosis the disease is likely to have spread to local-regional lymph nodes.[2] Management of PUC is not standardized and it revolves mainly around local-regional disease control and it may require a multimodal approach with chemoradiation and surgical excision.[2] However, one should first evaluate the origin of the disease to later provide the best overall management.

In determining the etiology of this malignancy, we focused our evaluation on defining if this was a cancer originally developing in the oral cavity or if the buccal mucosa underwent malignant transformation once transposed to the urethra. Furthermore, we considered viral versus chronic inflammatory processes as the cause of malignancy. We referred our patient to an otolaryngologist for a thorough head and neck examination. Fiber optic nasal-laryngoscopy was performed, which did not reveal any suspicious oral, nasal, or laryngeal lesions. This made the hypothesis that the BMG tissue most likely had undergone malignant transformation once transposed to the urethra more plausible.

To evaluate for possible human papilloma virus induced malignancy originating from either the oral mucosa or the urethra, p16 immunohistochemistry analysis was performed on the biopsies. These studies were negative, largely excluding associated human papilloma virus related SCC as an etiology (Fig. 3). Chronic inflammation was the main histologic pattern in the first biopsy of this patient's urethral stricture tissue, strongly suggesting that inflammation was the most likely cause of malignant transformation.

This unique case illustrates the importance of a thorough evaluation in the presence of microhematuria, even in someone with a history of urethral reconstruction, to rule out recurrence of urethral stricture or development of malignancy among other causes of hematuria. In our patient, we were able to perform a resection of the involved segment of urethra and prior BMG. A

ventral fasciocutaneous penile skin flap and dorsal split thickness skin graft were chosen for one-stage reconstruction of the urethra, as opposed to a repeat BMG, because of the suspicion that the malignancy likely originated from the BMG. At 3 months of follow-up, the patient was free from recurrence of urethral stricture and malignancy as demonstrated by cystoscopy, retrograde urethrography and urine cytology. He will undergo periodic cystoscopic surveillance of the reconstructed urethra to monitor for tumor recurrence.

## Conclusion

The development of SCC in a BMG used for urethoplasty is a rare complication of this surgery that has not been reported previously in the literature. Management revolves around local-regional disease control. In patients who present with persistent LUTS and/or microhematuria after urethroplasty, evaluation by cystourethroscopy is warranted to rule out stricture recurrence, or rarely, the development of malignancy in the urethra.

## Conflict of interest

None.

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