



# Prophylactic Radical Cystectomy for the Management of Keratinizing Squamous Metaplasia of the Bladder in a Man With Tetraplegia

Camilo M. Castillo, MD<sup>1</sup>; Chang Y. Ha, MD<sup>2</sup>; David R. Gater, MD, PhD<sup>1,2</sup>; Baruch M. Grob, MD<sup>2</sup>; Adam P. Klausner, MD<sup>2</sup>

<sup>1</sup>Hunter Holmes McGuire VA Medical Center, Richmond, Virginia; <sup>2</sup>Virginia Commonwealth University Health Systems, Richmond, Virginia

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## Abstract

**Background/Objective:** To report a case of keratinizing squamous metaplasia of the bladder treated with radical cystectomy.

**Design:** Case report and discussion of management options.

**Methods:** Keratinizing squamous metaplasia of the bladder is a rare entity that can result from chronic irritative stimuli involving the bladder. It is considered a premalignant condition associated with invasive squamous cell carcinoma. A case report is presented describing the diagnosis and management of keratinizing squamous metaplasia of the bladder in a tetraplegic man with a chronic indwelling urinary catheter.

**Results:** Radical cystectomy with an Indiana continent reservoir was performed after cystoscopy with biopsy confirmed keratinizing squamous metaplasia. Final pathology revealed focal erosion and diffuse keratinizing squamous metaplasia of the bladder with prostatic adenocarcinoma as an incidental finding.

**Conclusions:** Patients with spinal cord injury who use indwelling catheters for bladder management are at higher risk of developing keratinizing squamous metaplasia. Surveillance for early detection of this entity is recommended. Prophylactic cystectomy is sometimes warranted; however, observation and frequent cystoscopic surveillance to identify potential malignant transformation can be an alternative strategy. An interdisciplinary approach is recommended before consideration of bladder resection.

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**Key Words:** Spinal cord injuries; Cystectomy; Neurogenic bladder; Tetraplegia; Metaplasia; Squamous; Epithelial growth factor receptor; Prostate

## INTRODUCTION

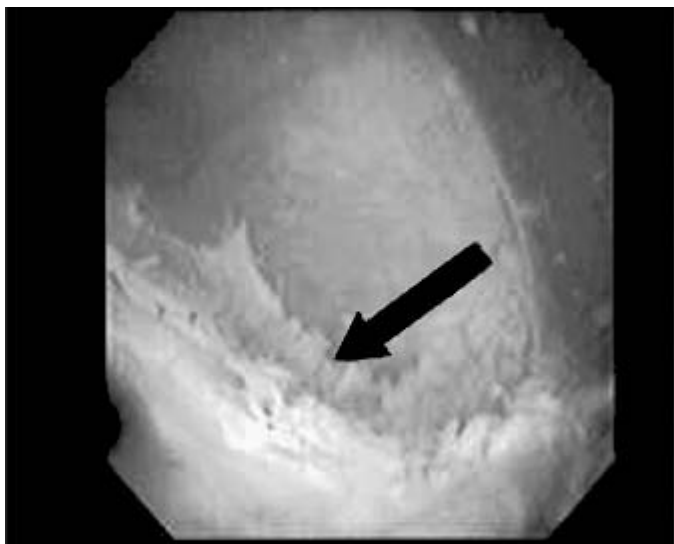
After exposure to chronic irritative stimuli, the transitional epithelium of the bladder can occasionally undergo a histologic transformation to keratinizing squamous metaplasia. Although several theories have been proposed, chronic inflammation and infection are considered the most likely etiologic factors. Because of the frequent use of chronic indwelling catheters for bladder management, patients with spinal cord injury (SCI) are at increased risk of developing this condition. The diagnosis is made histologically after cystoscopy and biopsy are

performed. However, once the diagnosis is made, it is controversial whether to perform surveillance by cystoscopy to look for potential malignant transformation or to perform a prophylactic radical cystectomy. We describe a case of keratinizing squamous metaplasia identified in the bladder of a man with SCI who used a chronic indwelling urinary catheter.

## CASE REPORT

A 54-year-old man with tetraplegia who used a chronic indwelling catheter for bladder management was evaluated by the urology service for detrusor sphincter dyssynergia. As part of the work-up, a routine cystoscopy was performed. The bladder mucosa appeared abnormal, and the patient was taken to the operating room for repeat cystoscopy and biopsy, during which moderate to

Please address correspondence to Camilo M. Castillo, MD, McGuire VA Medical Center, 1201 Broad Rock Road, Richmond, VA 23249; phone: 804.675.6741; fax: 804.675.6742 (e-mail: camilo.castillo@va.gov).



**Figure 1.** Bladder wall showing flaky, white, plaque-like lesions during cystoscopy (arrow).

severe trabeculation was noted with multiple diverticula in the bladder wall. In addition, the mucosa was covered by flaky, white, plaque-like lesions (Figure 1). Multiple cold-cup biopsies were performed, and the pathologic diagnosis revealed squamous metaplasia with keratinization. The patient was subsequently taken back to the operating room for a cystoscopy and attempt at complete transurethral resection of this lesion; however, because of diffuse involvement of the bladder mucosa and growth within diverticula, complete resection was not possible. Pathologic diagnosis again revealed squamous metaplasia with keratin but no evidence of malignancy.

An interdisciplinary team was formed in which medical providers, a social worker, nursing staff, and family members took an active role so that the patient was able to make an informed decision. He was offered continued observation vs prophylactic radical cystoprostatectomy. Because of the premalignant nature of this unresectable lesion, the patient elected to undergo radical cystectoprostatectomy with an Indiana pouch continent reservoir. The procedure was performed, and the patient experienced no complications in the perioperative period. Final pathologic diagnosis revealed diffuse keratinizing squamous metaplasia with no evidence of urothelial malignancy. However, incidentally, a small focus (<5%) of Gleason 3+4 adenocarcinoma of the prostate was identified with negative surgical margins. The patient has not needed additional treatment for prostate cancer, and his prostate-specific antigen remains undetectable. The patient was discharged home with instructions to perform clean intermittent catheterization of his continent reservoir every 4 hours. On 18-month follow-up, he had no evidence of malignancy and was able to manage his continent reservoir adequately.

## DISCUSSION

Keratinizing squamous metaplasia is considered a premalignant condition with a reported incidence of 23% in patients with SCI who use indwelling catheters for bladder management (1,2). In patients diagnosed with keratinizing squamous metaplasia, the subsequent risk of developing bladder cancer has been estimated to be 21% to 32% (1,2). Khan et al (1) reviewed 34 patients with histologically proven keratinizing squamous metaplasia and postulated that some cases with synchronous or metachronous bladder cancer progress to carcinoma in situ and ultimately invasive tumor. Likewise, Guo et al (4) recently described findings of 5 patients diagnosed with keratinizing squamous metaplasia. Two of 5 (40%) were found to have invasive squamous cell carcinoma identified on cystectomy performed within 1 year of the initial diagnosis, and an additional 1 of 5 (20%) had persistent keratinizing squamous metaplasia on repeat bladder biopsy.

Although the exact pathophysiology underlying the transformation from keratinizing squamous metaplasia to squamous cell carcinoma is unknown, several etiologic factors have been linked its development (1,15). Chronic inflammation caused by indwelling catheters and stones, as well as infection secondary to parasites, are considered to be the most likely etiologic agents (1,3,4,8,12,13). Histopathologically, Guo et al (4) recently reported enhanced activity of epithelial growth factor receptor (EGFR) in keratinizing squamous metaplasia after cystectomy in patients with hematuria, as well as patients with urinary retention. EGFR is a tyrosine kinase that transduces signals controlling cell proliferation. Stonehill et al (2) reviewed 208 charts of patients with SCI with neurogenic bladder and chronic indwelling catheters and concluded that nearly all patients had inflammatory changes or squamous metaplasia of the bladder, whereas 1 patient had keratinizing squamous metaplasia.

Because of this increased risk, many centers recommend frequent surveillance to diagnosis lesions at a curable phase (2). For patients with SCI who have been managed with indwelling urinary catheters for less than 5 years and found to have limited keratinizing lesions, several investigators recommend annual cystoscopy and urinary cytology (1,2,6). For patients with SCI managed with indwelling urinary catheters for greater than 10 years with more extensive keratinizing lesions, attempts at reductive therapy with cauterization or silver nitrate fulguration are recommended (1,6). However, because of limited data on these types of protocols, no approach can be considered superior (1,2,10), and some have been proven ineffective (1,6,7). Most recently, some authors have suggested that EGFR could potentially be used as logic therapeutic target for keratinizing squamous metaplasia, among other bladder lesions, that are difficult to manage clinically (4,15). However, some investigators advocate for a more aggressive management with radical

bladder resection to avoid development of malignant transformation (1,3,5–7).

Patients with SCI may experience significant difficulty adjusting to life-altering events including radical surgery (16–20). The psychologic and quality-of-life impact of prophylactic radical cystectomy in patients with keratinizing squamous metaplasia is unknown; however, performance of a radical cystectomy may affect many quality-of-life issues including stoma care, catheter use, and presence of incontinence, body image, and sexual dysfunction (21–25). Because of these significant concerns, we recommend that a team be formed including SCI specialists, urologists, nurses, social workers, psychologists, and family members to construct an individualized treatment for each affected patient.

## CONCLUSION

Keratinizing squamous metaplasia of the bladder is a rare premalignant lesion, associated with chronic inflammation and infection. Management of this histologic entity remains controversial. Risk of development of keratinizing squamous metaplasia in patients with SCI is elevated, and radical bladder resection should be considered in certain cases. However, because of significant quality-of-life impact associated with prophylactic surgery, a team approach is advised to individualize treatment plans and to allow affected patients to make more informed decisions. Additionally, clinicians are encouraged to consider EGFR as a potential therapeutic target for interventions, although further research in this area is warranted.

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