

Case reports: periurethral bulking agents and presumed urethral diverticula

Disha Kumar · Melissa R. Kaufman ·
Roger R. Dmochowski

Received: 28 October 2010 / Accepted: 30 January 2011 / Published online: 22 February 2011
© The International Urogynecological Association 2011

Abstract Urethral bulking agents are a commonly employed modality utilized for treatment of female stress urinary incontinence. These primarily collagen-based agents are placed in the proximal urethra to facilitate mucosal coaptation during increases of intra-abdominal stress. Several known complications of these agents exist, including urethral prolapse, retention, and urinary infection. Herein, we report two cases diagnosed as urethral diverticuli which were ultimately determined anatomic aberration secondary to prior bulking agent therapy. Recognition of this potential sequela of bulking agent placement is important for the female pelvic surgeon to recognize to avoid the morbidity of potential invasive interventions.

Keywords Diverticula · Urethral bulking agents · Female stress urinary incontinence · Collagen

Introduction

Periurethral bulking agents have become increasingly utilized over the past several decades for treatment of female stress urinary incontinence (SUI) [1]. Injectable agents, primarily collagen-based, are an attractive treatment

options as they are minimally invasive and may often be placed without the need for a general anesthetic. Current compounds enjoy both efficacy and an acceptable safety profile. Despite improved outcomes with definitive surgical interventions, patient satisfaction, and improvement in quality of life following injection therapy compares favorably to traditional surgical treatment in randomized trials [2]. Overall, complications were significantly less frequent and less severe in the injection group. Several studies employing collagen reported cure and improved rates ranging on average from 40–60% with up to 1 year of follow-up [1]. However, there is sparse literature regarding potential long-term sequela of periurethral bulking agents. Reports of durability vary by type of injectable, and comparisons are difficult due to vastly differing study methodologies. In one randomized trial comparing the efficacy and durability of Contigen to Durasphere, treatment was initially effective in 63% of both groups, but decreased by 36 months 21% in the Durasphere group, and 9% in the Contigen group [3]. In addition to issues with overall durability, multiple injections may be required to achieve and maintain effect. As such, a certain proportion of patients will ultimately decide to undergo surgery after initial injection therapy in an effort to obtain a more sustained outcome.

Potential long-term issues involving collagen injections include migration of the particles and loss of efficacy. Preliminary studies have determined placement of bulking agents is not deleterious with regard to future sling placement [4]. However, more obscure complications and presentations are sparsely reported in the current literature. Herein, we present two cases of misdiagnosis of urethral diverticulum in patients who had undergone prior periurethral bulking agent implant.

D. Kumar · M. R. Kaufman (✉) · R. R. Dmochowski
Department of Urologic Surgery,
Vanderbilt University Medical Center,
A-1302 Medical Center North,
Nashville, TN 37232, USA
e-mail: melissa.kaufman@vanderbilt.edu

R. R. Dmochowski
e-mail: roger.dmochowski@vanderbilt.edu

Case #1

Mrs. BC, a 69-year-old female, was referred from an outside urologist for evaluation and management of a urethral diverticulum. She presented with primary symptoms of a vaginal bulge and associated vaginal pressure. She additionally reported occasional dribbling incontinence, but otherwise did not have lower urinary tract symptoms and did not regularly utilize incontinence pads.

Her past medical history was significant for cervical cancer and stress urinary incontinence. She had previously undergone hysterectomy with brachytherapy implants and several anti-incontinence procedures including two bladder suspensions or unknown type as well as periurethral collagen injections.

On physical exam in the clinic, she demonstrated a large cystic suburethral mass which was ballotable and extended from the mid-urethra to the bladder neck. She, otherwise, demonstrated no pelvic organ prolapse or other abnormalities.

Outside hospital imaging included a pelvic magnetic resonance imaging (MRI) exam revealing a 4-cm cystic mass which appeared to wrap around the urethra, bulging into the floor of the urinary bladder, and causing some compression of the bladder (Fig. 1a). She additionally underwent a voiding cystourethrogram that demonstrated a smooth filling defect on the floor of the urethra due to an extrinsic mass effect (Fig. 1b).

She underwent operative cystoscopy with bilateral retrograde pyelograms. No ostia were identified within the urethra, but cystoscopic exam did demonstrate an extrinsic compressing defect at the level of the left bladder neck. She subsequently underwent operative exploration with resection of the complex urethral mass and placement of an autologous fascia pubovaginal sling. Following dissection of the vaginal mucosa and periurethral fascia, a large periurethral lesion was encountered (Fig. 2a). Upon sharp opening of the mass, large amounts of a white foreign body substance exuded (Fig. 2b). The cyst was completely dissected without evidence of communication with the urethral lumen (Fig. 2c). The periurethral cyst wall was sent to pathology and identified as a benign fibrous cyst.

Postoperatively, the patient convalesced without incident. At last follow-up, approximately 24 months following her operative intervention, she was without SUI and reported normal voiding with the exception of rare episodes of urge incontinence for which she declined any further treatment.

Case #2

A 74-year-old female was referred for evaluation of recurrent urinary tract infections and possible urethral diverticulum identified on CT imaging (Fig. 3a). The patient had undergone operative cystoscopy and bilateral retrograde

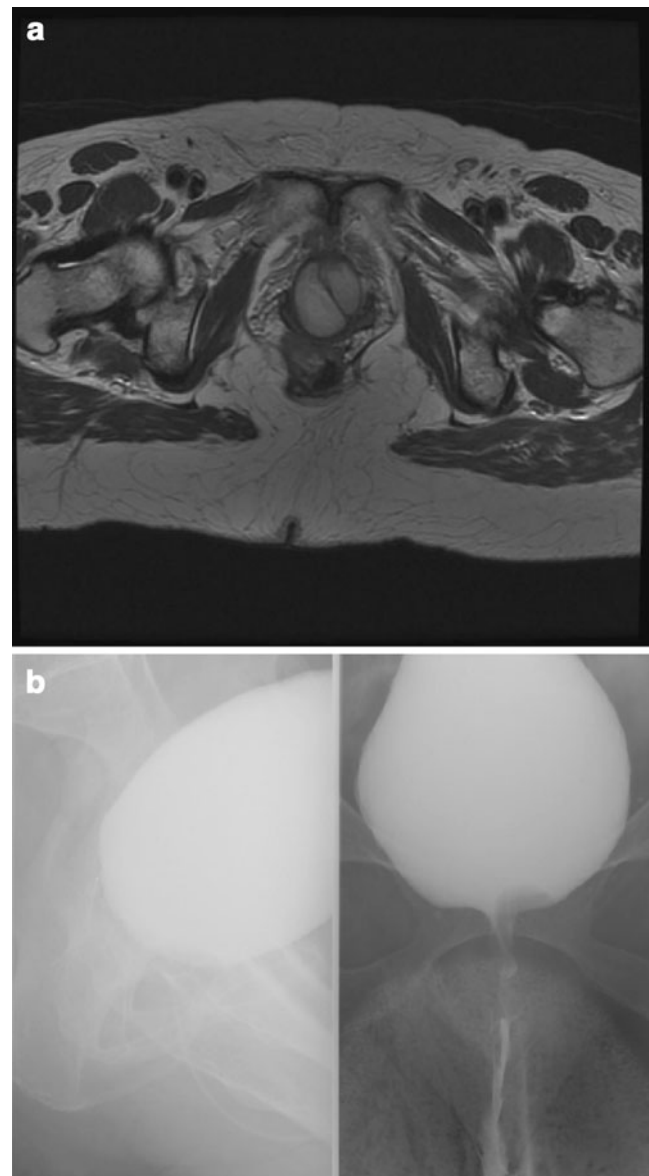


Fig. 1 **a** A pelvic MRI revealing a 4-cm cystic mass which appeared to wrap around the urethra and bulge into the floor of the urinary bladder. **b** Voiding cystourethrogram demonstrated a smooth filling defect on the floor of the urethra due to an extrinsic mass effect

pyelograms at an outside hospital prior to presentation which failed to reveal any urethral abnormalities or a diverticular ostium. The patient described a 20-year history of chronic UTI with voiding symptoms that included dysuria, urgency, frequency, urge urinary incontinence, and systemic chills. She reports these symptoms would transiently resolve with antibiotic therapy.

Her past medical history was significant only for a history of stress urinary incontinence for which she had undergone placement of a mid-urethral sling approximately 5 years prior to presentation. The patient indicated that

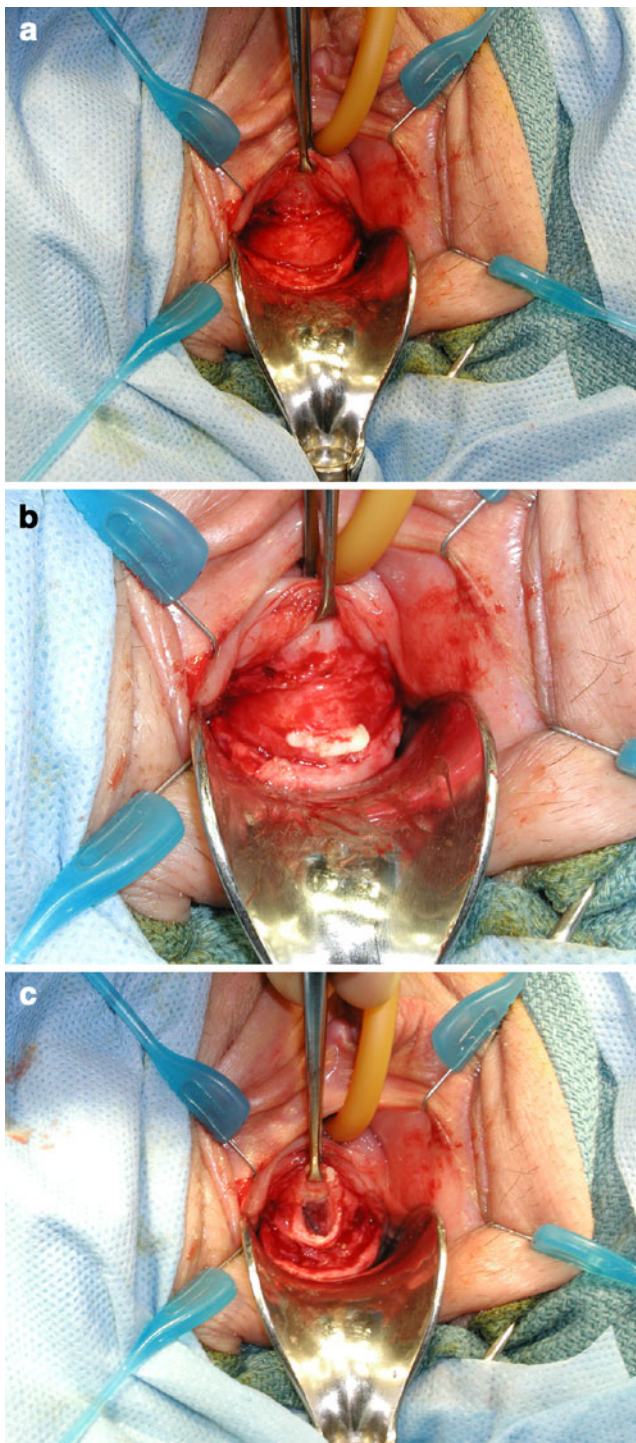


Fig. 2 **a** Dissection of the vaginal mucosa and periurethral fascia reveals a large periurethral lesion. **b** Upon sharp opening of the mass, large amounts of a white foreign body substance exuded. **c** The cyst was completely dissected without evidence of communication with the urethral lumen

preceding her sling surgery she underwent several periurethral collagen injections. She noted the interventions for her SUI did not change the recurrence of her symptoms of urinary infection.

Physical exam did not reveal evidence for a periurethral mass, urethral discharge, or anatomic abnormality. She additionally did not demonstrate pelvic organ prolapse.

At presentation she underwent pelvic MRI which additionally elucidated periurethral calcifications but failed to definitively reveal presence of a urethral diverticulum (Fig. 3b). She was treated with transvaginal estrogen cream and anticholinergic medication with resolution of her symptoms.

Discussion

Urethral diverticula are presumed to arise from periurethral glands, most likely due to recurrent infection and obstruction with suburethral abscess formation and rupture of the glands into the urethral lumen [5]. There is often a discrete connection between the diverticulum and the urethral lumen, but anatomical variations do exist. These include

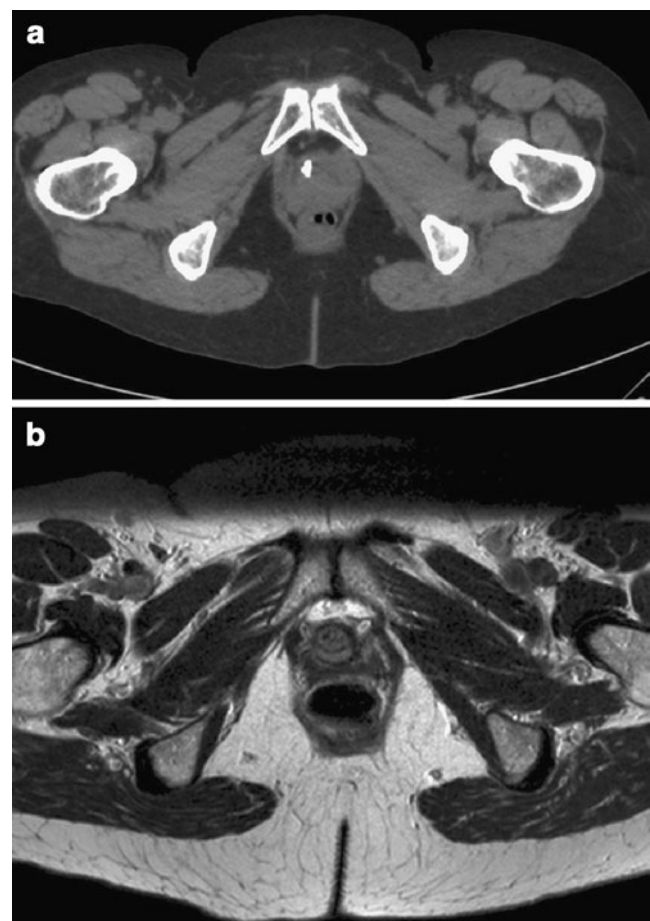


Fig. 3 **a** CT imaging of a possible urethral diverticulum in a 74-year-old female referred for evaluation of recurrent urinary tract infections. **b** At presentation pelvic MRI additionally elucidated periurethral calcifications but failed to definitively reveal presence of a urethral diverticulum

partial extension around the urethra, dorsal to the urethra, or circumferentially around the urethra [6]. Size can also vary depending on the level of inflammation, intermittent obstruction of the ostium, and drainage into the urethral lumen. The classic presentation of urethral diverticula includes dyspareunia, dysuria, and post-void dribbling. Fifty percent of women with a urethral diverticulum demonstrate stress urinary incontinence as well. As demonstrated in these cases, long-term sequela of periurethral bulking agents may present similarly to classic diverticuli.

The FDA approved the use of collagen injections for treatment of stress urinary incontinence in 1993 as an effective and low-risk alternative to surgery. Recent meta-analysis determined urethral injection therapy, a viable modality of treatment for most patients with uncomplicated stress urinary incontinence, and may be offered as a first-line option for patients who have failed pelvic floor exercises or pharmacological therapy [7]. With greater use of urethral bulking agents for treatment of stress urinary incontinence, local complications were inevitable although poorly described in the literature. Early studies on collagen injections did not adequately report outcomes and complications over 24 months following therapy. Overall, collagen injection therapy has proven to be relatively safe in the short run for patients, with few local or systemic complications documented. However, many patients need reinjections to maintain the desired outcome.

Prior literature reports one other documented case of urethral diverticulum following transurethral collagen injection therapy [8]. In this case, the patient had normal physical exam findings 4 months after the last injection for stress urinary incontinence, but developed urinary retention postoperatively from a dental procedure. Similar to the presentation in case #1, this patient also had symptoms related to the mass effect from the urethral diverticulum. Upon surgical exploration, a non-communicating urethral diverticulum was found. It was hypothesized that the previous collagen injections caused obstruction of periurethral glands due to accumulation of glandular secretions, especially since there was no history of urinary tract infections and no connection between the urethra and diverticulum where the collagen was injected.

Other documented complications after collagen injection therapy include urinary tract infections, transient periods of complete urinary retention, and de novo frequency and urgency [9–15]. Rare occurrences of suburethral swellings have been reported with use of collagen, polytetrafluoroethylene, carbon-coated zirconium beads, and non-animal stabilized hyaluronic acid/dextranomer gel. It has been proposed that the suburethral swellings are related to a tissue reaction to the injectable agent, and resolve with needle drainage [7, 16–23]. Hypersensitivity reactions have also been reported in 3% of patients with use of collagen

and previous collagen exposure [23]. Recent studies have revealed periurethral use of substances other than collagen, such as dextranomer hyaluronic acid, for stress urinary incontinence has not been shown to be safe or efficacious [24]. In this report, dextranomer hyaluronic acid was associated with increased incidence of pseudoabscesses, de novo urge incontinence, and poor efficacy.

Sterile and non-sterile abscess formation [25, 26] and periurethral pseudocyst formation after transurethral collagen injections [27] are documented complications. Patients often present with irritative voiding symptoms and suburethral swelling and tenderness and require open for treatment. Sterile abscess formation has been reported to occur from use of a periurethral injection of Zuidex (dextranomer/hyaluronic copolymer) [26]. Reports of abscess formation from collagen injections are limited [16]. Pseudocyst formation has been previously documented to occur through distal migration of the collagen along the urethra to create a non-tender collagen-filled periurethral mass at the meatus. Distal particle migration has also been described in non-biodegradable agents such as silicone and carbon-coated zirconium beads [7]. Accumulation of these substances could be harmful, especially with risks of granuloma formation and carcinogenesis.

Another documented complication of periurethral collagen injections was urethral prolapse causing recurrent episodes of cystitis [28]. This possibly manifested due to collagen intervening between mucosa and the underlying muscle wall. However, distal migration of the collagen along the urethra could not be ruled out in this circumstance.

Conclusion

Based on these patient's presentation, imaging, and pathology, it was reasonable to conclude that their lower urinary tract symptoms were most likely iatrogenic from the use of collagen urethral bulking agents. With the increasing use of such bulking agents, awareness of these potential complications is paramount to allow appropriate counseling and avoid the morbidity of possible unnecessary operative interventions.

Conflicts of interest None.

References

1. Kotb AF, Campeau L, Corcos J (2009) Urethral bulking agents: techniques and outcomes. *Curr Urol Rep* 10(5):396–400
2. Handel LN, Leach GE (2008) Current evaluation and management of female urethral diverticula. *Curr Urol Rep* 9(5):383–388, Review
3. Chrouser KL, Fick F, Goel A, Itano NB, Sweat SD, Lightner DJ (2004) Carbon coated zirconium beads in β -glucan gel and bovine glutaraldehyde cross-linked collagen injections for intrinsic

- sphincter deficiency: continence and satisfaction after extended follow-up. *J Urol* 171(3):1152–1155
4. Koski ME, Enemchukwu E, Padmanabhan P, Kaufman MR, Scarpero HM, Dmochowski RR (2011) Safety and efficacy of sling after bulking injection for persistent stress urinary incontinence. *Urology* 2011 Jan 7. [Epub ahead of print]
 5. Rovner ES (2007) Urethral diverticula: a review and an update. *Neurourol Urodyn* 26(7):972–977
 6. Rovner ES, Wein AJ (2003) Diagnosis and reconstruction of the dorsal or circumferential urethral diverticulum. *J Urol* 170:82–86
 7. Chapple CR, Wein AJ, Brubaker L, Dmochowski R, Pons ME, Haab F, Hill S (2005) Stress incontinence injection therapy: what is best for our patients? *Eur Urol* 48(4):552–565
 8. Clemens JQ, Bushman W (2001) Urethral diverticulum following transurethral collagen injection. *J Urol* 166(2):626
 9. Corcos J, Fournier C (1999) Periurethral collagen injection for the treatment of female stress urinary incontinence: 4-year follow-up results. *Urology* 54(5):815–818
 10. Shortliffe LMD, Freiha FS, Kessler R et al (1989) Treatment of urinary incontinence by the periurethral implantation of glutaraldehyde cross-linked collagen. *J Urol* 141:538–541
 11. Herschorn S, Radomski SB, Steele DJ (1992) Early experience with intraurethral collagen injections for urinary incontinence. *J Urol* 148:1797–1800
 12. O'Connell HE, McGuire EJ, Aboseif S et al (1995) Transurethral collagen therapy in women. *J Urol* 154:1463–1465
 13. Moore KN, Chetner MP, Metcalfe JB et al (1995) Periurethral implantation of glutaraldehyde cross-linked collagen (Contingen) in women with type I or III stress incontinence: quantitative outcome measures. *Br J Urol* 75:359–363
 14. Winters JC, Appell RA (1995) Periurethral injection of collagen in the treatment of intrinsic sphincter deficiency in the female patient. *Urol Clin North Am* 22:673–678
 15. Stothers L, Goldenberg SL, Leone EF (1998) Complications of periurethral collagen injection for stress urinary incontinence. *J Urol* 159(3):806–807
 16. Sweat SD, Lightner DJ (1999) Complications of sterile abscess formation and pulmonary embolism following periurethral bulking agents. *J Urol* 161:93–96
 17. Kershen RT, Dmochowski RR, Appell RA (2002) Beyond collagen: injectable therapies for the treatment of female stress urinary incontinence in the new millennium. *Urol Clin North Am* 29:559–574
 18. McKinney CD, Gaffey MJ, Gillenwater JY (1995) Bladder outlet obstruction after multiple periurethral polytetrafluoroethylene injections. *J Urol* 153:149–151
 19. Lightner DJ, Itano NB, Sweat SD, Chrouser KL, Fick F (2002) Injectable agents: present and future. *Curr Urol Rep* 3:408–413
 20. Hartanto VH, Lightner DJ, Nitti VW (2003) Endoscopic evacuation of Durasphere. *Urology* 62:135–137
 21. Chapple C, Sultan AH, Cervigni M (2004) Efficacy and safety of the Zuidex system for the treatment of stress urinary incontinence: 6-month results of an open, multicentre study. Joint Meeting of the International Continence Society and Urogynecological Association, Paris, France, 23–27 August 2004. Abstract 314
 22. van Kerrebroeck P, ter Meulen F, Larsson G, Farrelly E, Edwall L, Fianu-Jonasson A (2004) Efficacy and safety of a novel system (NASHA/Dx copolymer using the Implacer device) for treatment of stress urinary incontinence. *Urology* 64:276–281
 23. Stothers L, Goldenberg SL (1998) Delayed hypersensitivity and systemic arthralgia following transurethral collagen injection for stress urinary incontinence. *J Urol* 159:1507–1509
 24. Lightner DJ, Fox J, Klingele C (2010) Cystoscopic injections of dextranomer hyaluronic acid into proximal urethra for urethral incompetence: efficacy and adverse outcomes. *Urology* 75(6):1310–1314
 25. McLennan MT, Bent AE (1998) Suburethral abscess: a complication of periurethral collagen injection therapy. *Obstet Gynecol* 92:650
 26. Coull N, Dover K, Walker RMH (2008) Sterile abscess formation following periurethral injections for stress urinary incontinence—an underestimated complication. *Br J Med Surg* 1:142–144
 27. Wainstein MA, Klutke CG (1998) Periurethral pseudocyst following cystoscopic collagen injection. *Urology* 51:835
 28. Harris RL, Cundiff GW, Coates KW, Addison WA, Bump RC (1998) Urethral prolapse after collagen injection. *Am J Obstet Gynecol* 178(3):614–615