Urethrocutaneous fistula after use of Tegress bulking agent: Case report and review of the literature

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Cite as: *Can Urol Assoc J* 2013;7(11-12):e833-6. http://dx.doi.org/10.5489/cuaj.481
Published online December 5, 2013.

Abstract

We report a case of a 68-year-old man who presented with a urethrocutaneous fistula after off-label use of Tegress (C. R. Bard, Inc., Murray Hill, NJ) Urethral Implant for post-prostatectomy incontinence. He was treated for prostate cancer with an open radical retropubic prostatectomy and adjuvant external beam radiation therapy. He was treated unsuccessfully for stress incontinence with a Tegress Urethral Implant and presented to our clinic initially with extrusion of the material urethrally. Four years later he re-presented with a large bullous skin lesion on his suprapubic area. Contrast-enhanced magnetic resonance imaging and retrograde urethral cystogram demonstrated a urethrocutaneous fistula. Subsequent cystoscopy revealed the calcified extruded material in the same location as the site of Tegress injection. The patient underwent simple cystectomy with ileal diversion. He recovered well postoperatively. This appears to be the first reported case of urethrocutaneous fistula after use of a Tegress Urethral Implant for post-prostatectomy stress urinary incontinence.

Case report

A 68-year-old man initially presented with a 4-year history of persistent stress urinary incontinence (SUI) requiring diapers, severe perineal pain, and recurrent occasional urinary retention requiring catheterization. He had a history of prostate cancer treated in 2003 with open radical retropubic prostatectomy (RRP) and adjuvant external beam radiation therapy. He had no open surgical procedures for incontinence, but had 2 Tegress (C. R. Bard, Inc., Murray Hill, NJ) Urethral Implant injections in 2006 to treat his incontinence, which had no effect. After the injections he developed painful urination, increased frequency and urgency, blood in his urine, perineal pain and penile discharge described as "a solid substance, gravel-like." He then presented at our institution in 2007 where, on physical examination, he had significant urinary leakage from the urethral meatus and tenderness to deep palpation of the perineal area. The scrotum, testes, and epididymis were normal. Urinalysis showed +2 leukocytes, positive nitrites, trace protein, and 50 heme. Urine cytology was negative for neoplasm. Cystoscopy was performed and showed material at both the 12 (anterior) and 6 o'clock (posterior) position, with only the 6 o'clock position showing material extrusion. The patient was then followed for several years by our clinic with 9 separate cystourethroscopies to debride the extruding Tegress material from the 6 o'clock position since the anterior position was epithelialized. These were performed utilizing a resectoscope with a cold loop. He was also found to have an acquired bladder neck contracture, which was dilated during these procedures. He was started on a trial of solifenacin 10 mg to manage his urinary incontinence. The severe, chronic perineal pain was managed initially with ibuprofen 800 mg twice a day and then duloxetine 60 mg once a day when he complained of being unable to "sit for more than an hour" without significant pain. His American Urological Association (AUA) symptom index score ranged from 31 to 33 out of 35 and he stated at multiple visits that his quality of life was "terrible" or "awful" due to his urinary symptoms. The ultimate treatment goal was to remove the entire extruded bulking agent to allow healing of the urethra to later allow placement of an artificial urinary sphincter. After discussing this plan with the patient and with the patient agreeing, we determined to go with this plan. We also discussed other reconstructive and urinary diversion options in depth, which the patient opted to postpone.

In 2012, he presented semi-urgently with an inflamed, swollen and erythematous 3-cm bullous area on his anterior abdominal wall in the location of his prostatectomy scar. A pelvic MRI with contrast revealed a urethrocutaneous fistula extending from the previously undisturbed area in the urethra with the bulking agent (anterior) to the skin of the lower anterior abdominal wall (Fig. 1).

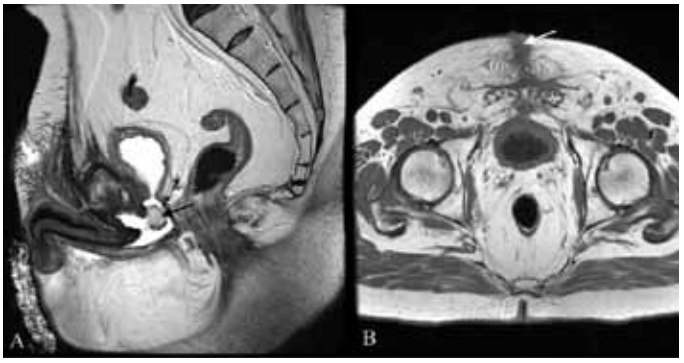

Fig. 1. T2 weighted magnetic resonance imaging (MRI) of urethrocutaneous fistula and urethral Tegress (C. R. Bard, Inc., Murray Hill, NJ) material. (A) MRI sagittal section. Material is entirely in the anterior position (black arrow) with the posteriorly placed material having been previously debrided. (B) MRI coronal section. Note the fistula tract (white arrow) extending from the Tegress material in the urethra to the abdominal wall.

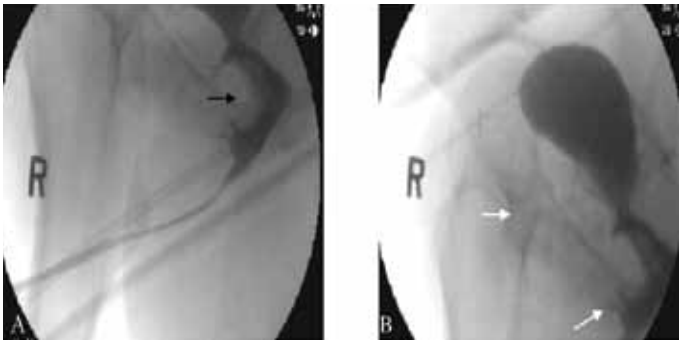

Fig. 2. Retrograde urethrogram of fistula and urethral Tegress (C. R. Bard, Inc., Murray Hill, NJ) material. (A) Filling defect demonstrating presence of the Tegress material in the anterior urethra (black arrow). (B) Communication of the urethra to the abdominal wall with contrast accumulating at abdominal wall (white arrows).

A retrograde urethrogram (RUG) and cystoscopy were performed with evidence of communication of the urethra to the abdominal wall (Fig. 2) and presence of the bulking agent only anteriorly (Fig. 3).

Treatment options

The available options discussed with the patient included: open abdomino-perineal debridement of the fistula and removal of all Tegress with excision of the diseased urethra and re-anastomosis to the bladder neck followed by a staged artificial sphincter several months later ***or*** a simple cystectomy with debridement of the fistula and Tegress and an ileal conduit. The patient opted for the latter given his desire to avoid a staged surgical procedure.

The surgical procedure was performed abdominally without complications and the remaining Tegress was removed with excision of the urethrocutaneous fistula tract. His pubic bone was uninvolved with the fistula. Postoperatively, he had a short, uneventful course in hospital, was discharged on postoperative day 6, and was off of all pain medications since his perineal pain was gone. Five months later, the patient continued to have no perineal pain and minimal drainage from his urethra, stable renal function and a normal renal ultrasound. He had resumed all normal physical activity and had no difficulty managing his ostomy appliance.

Discussion

The use of peri-urethral bulking agents to treat SUI has been well-described over the last 3 decades. Optimal bulking agents should be biocompatible, produce little or no immunogenic response in the host, and be stable and non-migratory on injection. Host-tissue response to the implanted agent should demonstrate minimal fibrosis, extracapsular inflammatory response, and resorption of injected material.

The ethylene vinyl alcohol co-polymer implant (Tegress) was approved by the FDA in December 2004 for use in adult women with intrinsic sphincter deficiency (ISD). It is a sterile, non-pyrogenic device composed of 8% ethylene vinyl alcohol copolymer (EVOH) and dimethyl sulfoxide (DMSO), which possesses unique phase-change properties on exposure to body temperature fluids causing it to expand. Exposure to blood or extracellular fluid at physiologic temperatures causes the DMSO to diffuse from the hydrophobic copolymer, leading to the precipitation of the EVOH into a cohesive spongiform mass. This phase change occurs quickly, with the mass developing within one minute after injection.[1] According to early studies, Tegress offered significant advantages over previous generations of bulking agents (Teflon, Dupont, Wilmington, DE; Contigen, Bard Urological, Covington, GA; Coaptite, Boston Scientific, Natick, MA). There were no required preoperative skin testing, excellent maintenance of volume and bulk without shrinkage or migration, ease of injection, and durability against degradation or reabsorption by the body.[2]

Despite the successful clinical trial[3], Tegress was reported in post-market studies to have a significant risk of urethral erosions or exposed material events. The first report reviewed the manufacturer and user facility device experience (MAUDE) database. Their search revealed 129 reports for 113 different adverse events (84 urethral erosions, two vaginal erosions, three bladder erosions, nine cases of urinary retention and 16 cases of bladder calculi) between January 2005 and July 2006.[4] Additionally, the manufacturer's own multicentre, randomized controlled trial comparing transurethral injections of Tegress with Contigen in women revealed the same problem: 16% of patients undergoing treatment with Tegress experienced erosions or exposed material in the urethra.[5]

Hurtado and colleagues retrospectively reviewed female patients who received Tegress between 2005 and 2006. After an average of 1.4 injections, 37% of patients experi-

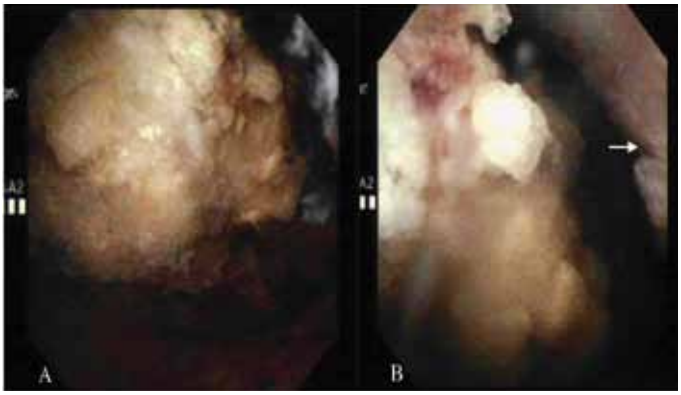

Fig. 3. Cystoscopic image of urethral Tegress (C. R. Bard, Inc., Murray Hill, NJ) material. Cystoscopy showing calcified extruded Tegress™ material in anterior urethra near bladder neck (white arrow).

enced urethral erosion. Only 10.5% reported at least a 50% subjective improvement in symptoms. They conclude that Tegress is less effective with more complications than initially reported in FDA trials, particularly in patients receiving prior injections.[6] One series demonstrated a 45% continence rate without any erosion in 38 women receiving cystoscopic injections of Tegress;[7] however, these results have not been duplicated. Hurtado and colleagues released another study on Tegress injections for use in male SUI.[8] While Tegress was approved only for use in women, it had also been used off-label for incontinence in men, particularly after RRP. A retrospective review of adult male patients undergoing treatment with Tegress from 2005 to 2006 was performed. Complete follow-up was available in 17 men, with most experiencing incontinence after RRP (89%). The patients had a mean subjective improvement of 31.8%. The most common procedural complication was erosion into the urethra (41.1%).

As a result of these studies and increasing clinician reports of complications with Tegress, the manufacturer, C.R. Bard, Co., voluntarily withdrew the bulking agent from the market in December 2007.

In developed countries, like the United States, urethral fistulas are usually related to previous urologic or gynecologic surgery, severe pelvic pathology, radiation therapy, or iatrogenic injury.[9] While pelvic diseases, such as epididymitis and balanitis, have been reported to cause urinary fistulas in men, the etiology of the patient's fistula reported herein is believed to be a combination of radiation to his pelvis, which has been associated with urinary fistulas,[10] and the known urethral erosion of his Tegress, which was injected 6 years prior.

Our patient is an example of a severe complication as a result of the off-label use of Tegress to treat male SUI. Like most male patients described in the study by Hurtado and colleagues, our patient experienced SUI after radical prostatectomy and received Tegress injections. He did not experience improvement and, actually, had worsening of the incontinence in the years after receiving treatment. He was eventually diagnosed at our institution with urethral erosion significant enough to form a patent sinus tract from his anterior urethra to the skin of his lower anterior abdomen. Other injectable urethral bulking agents, such as carbon beads (Durasphere, Coloplast, Minneapolis, MN) have been associated with migration,[11] while the use of dextranomer/hyaluronic acid (Zuidex, Q-Med AB, Uppsala, Sweden) is linked to formation of pseudoabscesses and sterile abscesses.[12, 13] As such, providers must use caution in selecting a bulking agent, especially given the increasingly common trend of using these agents off label.[14]

Reports of urethrocutaneous fistulas are rare in the literature: one associated with treatment for painful priapism[15] and another associated with a prostatic urethral calculus.[16]

Conclusion

Use of the urethral bulking agent Tegress is strongly associated with urethral erosions and urinary fistulas. Although complications are associated with many urethral bulking agents, their use should be guided by clinician experience and knowledge of the most recent clinical trials. This is the first report, to our knowledge, of the development of a urethrocutaneous fistula after the off-label use of Tegress for male SUI.

Competing interests: Mr. Mukkamala, Dr. Latini and Dr. Cameron all declare no competing financial or personal interests.

This paper has been peer-reviewed.

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