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CASE REPORT

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Massive prolapse of the urethral mucosa following periurethral injection of calcium hydroxylapatite for stress urinary incontinence

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Abstract The injection of bulking agents into the urethral submucosa is designed to create artificial urethral cushions that can improve urethral coaptation and hence restore continence. Ideally, a urethral bulking agent should be non-immunogenic and biocompatible, leading to minimal inflammatory and fibrotic response. The authors present a case report of a granulomatous reaction leading to urethral prolapse, 3 months after the transurethral injection of calcium hydroxylapatite. To our knowledge, this is the first granulomatous reaction described after calcium hydroxylapatite injection.

Keywords Bulking agents · Urinary incontinence · Granuloma · Calcium hydroxylapatite

Introduction

The use of calcium hydroxylapatite (CaHA) as a bulking agent for the treatment of sphincteric insufficiency has been proposed with several advantages: it is readily available, biocompatible and involves a minimally invasive procedure [1]. The mechanism of achieving continence is based on increasing urethral coaptation, which increases leak point pressure [2].

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We presented a patient who developed an inflammatory reaction leading to a massive prolapse of the urethral mucosa after periurethral injection of CaHA. To our best knowledge, such a complication of calcium hydroxylapatite injection has not been reported previously.

Case report

A 55-year-old woman underwent surgical treatment for a complex pelvic bone fracture. Stress urinary incontinence developed in the early postoperative period. Physical examination did not show any urethral abnormalities. Urodynamic evaluation was performed 6 months later and demonstrated Valsalva leak point pressure (VLPP) of less than 50 cm H_2O.

The patient underwent one session of periurethral CaHA injection. The procedure was performed in lithotomy position, under spinal anesthesia, on an outpatient basis. Using a 21 Fr cystoscope and 30-degree optic, transurethral injections were performed at urethral submucosa from the bladder neck to the midurethra using a 21 Ga endoscopic needle. After the insertion of at least 5 mm of the needle into the urethral submucosa, CaHA was gently injected under simultaneous endoscopic control of urethral coaptation. Three punctures were needed at 3, 6 and 9 o'clock positions, and 2.5 ml of CaHA was injected. At the end of the procedure, an excellent urethral coaptation was achieved. No urethral catheter was left in place postoperatively.

Although continence improved in the early postoperative period, the patient reported on the 3-month follow-up a 3-cm nodule that prolapsed through the urethral meatus during voiding (Fig. 1) and urinary incontinence.

The prolapsed tissue was removed by an incision around its base, and the urethral mucosa was sutured with interrupted 4.0 chromic catgut stitches. Histopathological analysis showed a lymphomonocytic inflammatory response and a chronic granulomatous inflammatory response with giant cells and macrophages surrounding hydroxylapatite particles (Fig. 2). Moreover, mild to moderate fibroblast reaction inside the graft was observed. The

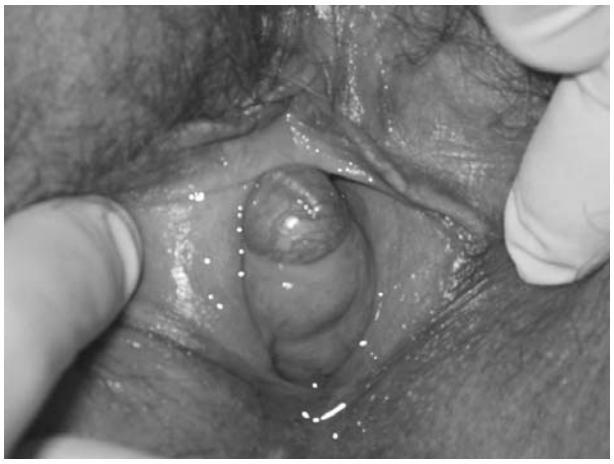

Fig. 1 Prolapsed nodule through the urethral meatus during voiding

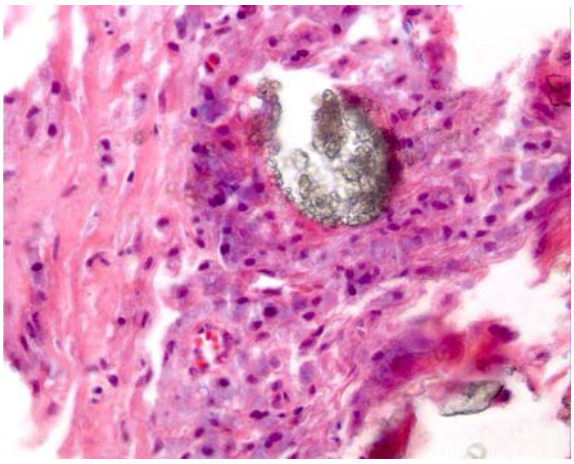

Fig. 2 Foreign body granulomatous reaction and particles of calcium hydroxylapatite ceramic (hematoxylin and eosin × 330)

patient was submitted to an aponeurotic sling 3 months later and became continent.

Discussion

A urethral bulking agent should ideally be non-immunogenic and biocompatible, leading to minimal inflammatory and fibrotic response. The particles that make up the agent should be of sufficient size to prevent them migrating away from the site of injection (diameter >80 μm), and it should also be of sufficient durability to maintain their effect over time [2].

The bulking agent used for periurethral injection in this patient is a non-pyrogenic injectable mixture of spherical particles (75 to 125 μm) of CaHA in an aqueous-based gel carrier of water, glycerin and sodium carboxymethylcellulose. The gel is dissipated in vivo, while the particles remain to provide permanent bulking.

The prolapse of urethral mucosa after periurethral lipoinjection was described in the past. When injected in the urethral submucosa, autologous fat also induced foreign body-type reaction, due to liberation of intracellular components from the adipocytes [3].

Calcium hydroxylapatite is a synthetic material identical to the primary constituent of teeth and bones. It is highly biocompatible, forming a well-defined injection site. The CaHA particles allow the cells from the injection site to grow directly on its surface, without reaction or encapsulation process [1]. Based on this concept, it can be supposed that the carrier gel could elicit the granulomatous reaction.

It has been proposed that the transurethral approach permits maximal coaptation with minimal amount of the material, probably because the proper submucosal injection is achieved.

To our knowledge, this is the first granulomatous reaction described after calcium hydroxylapatite injection. We believe that proper depth injections, from the bladder neck to the midurethra, could avoid this complication.

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