Unexpected outcome (positive or negative) including adverse drug reactions

Conservative treatment of a recto-urethral fistula due to savage HIFU for local recurrence of prostate cancer, 5 years after radical prostatectomy and external beam radiotherapy

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Summary

Recto-urethral fistula is one of the most serious complications caused by high-intensity-focused ultrasound used as salvage treatment for recurrence of prostate cancer after brachytherapy or external beam radiotherapy (EBRT). We report the case of a recto-urethral fistula in a 68-year-old patient, who previously had undergone radical prostatectomy and EBRT for prostate cancer (pT3 N0 Mx). The fistula was treated conservatively by an indwelling Foley catheter, without the creation of an intestinal diversion. The fistula was assessed initially by a retrograde and a CT scan of the pelvis with contrast medium and reassessed periodically by means of retrograde urethrograms. To date, 24 months after this episode, no evidence of recurrence of the fistula has been found.

BACKGROUND

This is a rare case of conservative treatment of a recto-urethral fistula (RUF). To our knowledge, this is the first described case of conservative treatment after high-intensity-focused ultrasound (HIFU).

CASE PRESENTATION

A 68-year-old patient, in good physical and mental conditions, came to our observation 5 years after radical retro-pubic prostatectomy and subsequent external beam radiotherapy (EBRT) for prostate cancer (pathological stage, pT3b N0 Mx, Gleason 8), both performed in other centres. Since a rise of the serum PSA levels (2.8 ng/ml) was noticed, the patient underwent a whole-body 18F-choline positron emission tomography (PET)/CT.

The PET/CT showed a positive nodule, located by the vesico-urethral anastomosis, on the postero-right lateral face of the urethra. No further suspect findings were observed.

Because of the good life expectancy of the patient and due to the absence of obvious distant recurrence of PCa, it was deemed possible to try a local treatment with savage HIFU in order to postpone the use of hormonal therapy. Even though this is not a standard indication, we decided to carry out this treatment on the basis of a promising experience, already published by our group¹ on HIFU used as salvage therapy for local recurrence of PCa after radical prostatectomy. Therefore, the patient underwent a salvage HIFU treatment using the Ablatherm system (EDAP-TMS, Vaulx-en-Velin, France) in a single 1 h session. The patient was catheterised before surgery using a 16 Ch Foley catheter. Surgery was carried out under spinal anesthesia, with the patient lying on his right side. The postoperative hospital stay was 2 days. The catheter was maintained in place for 7 days after surgery.

Seven days after the catheter removal, the patient returned to our observation complaining urgency episodes,

associated with no micturition and subsequent defecation of liquid stools.

INVESTIGATIONS

We performed a retrograde cystography to confirm the suspect of a RUF (figure 1). The exam showed the leakage of the contrast medium at the level of the bladder neck. We performed a CT scan of the pelvis, soon after the cystography, to exclude the involvement of the bladder. The CT scan (figure 2) did not show any involvement of the bladder. The fistula was located just under the vesico-urethral anastomosis.

TREATMENT

We decided to try a conservative treatment, positioning a 16 Ch Foley catheter. Our decision was led by the fact that the patient did not report passage of faeces from the urethra, nor leakage of urine from the anus before the urgency episodes. Furthermore, the patient had performed a urodynamic examination showing detrusor overactivity (DO). Thus, we speculated that the passage of urine into the rectum could have been due to the rise of bladder and urethral pressure, caused by an involuntary contraction of detrusor muscle, with a closed urethral sphincter. Therefore, the opening of the fistulous tract, that was closed during bladder filling, would be avoided by the use of an indwelling catheter. Furthermore, the fistulous tract presented a small diameter.

The patient was treated with antibiotics (metronidazole 500 mg and ceftriaxone 1 g/10 days) and afterward with ciprofloxacin 500 mg twice a day for 1 month. We scheduled a close follow-up constituted by monthly outpatient retrograde urethrograms.

OUTCOME AND FOLLOW-UP

At the first outpatient assessment, 30 days later, the patient neither complain symptoms of urinary tract

Figure 1 (A) Retrograde cystography performed 7 days after the catheter removal. Oblique radiograms of the bladder after full repletion with contrast media. The expansion of contrast media could be better observed in the oblique projections. (B) Retrograde cystography performed 7 days after the catheter removal. In delayed oblique projection, the fistulous tract is more visible, as well as a certain amount of contrast in the rectum. However, it is not possible to exclude with absolute certainty a partial involvement of the bladder.

infection (UTI) nor pain, nor presence of liquid stool, but the urethrogram showed persistence of the fistula. A second urethrogram, performed 60 days after the catheter positioning (figure 3), showed the complete resolution of the RUE. The catheter was thus removed and a further urethrogram, performed 15 days after catheter withdrawal, confirmed the absence of the fistula.

We decided to treat the patient with an antimuscarinic drug (solifenacin 5 mg) to manage the overactive bladder syndrome reported by the patient.

Figure 2 Pelvic CT scan with VR reconstruction. Pelvic CT scan was acquired before emptying the bladder of the contrast media, in order to confirm that the bladder was not involved in the problem and that only the urethra was affected by the fistula. VR reconstruction allows to see the fistulous tract that connect the bladder to the rectum better than cystourethrography.

Moreover, since the patient was at high risk (Gleason score=8) and because of his young age, we decided to use an adjuvant hormonal treatment with triptorelin 1125 mg for 1 year. To date, 24 months after the treatment and 12 months after discontinuation of triptorelin, the patient is still in good clinical condition, he does not complain of the recurrence of the fistula and his PSA level is still low (last check 0.1 ng/ml) without evidence of recurrences of PCa.

Figure 3 Retrograde cysto-urethrography after conservative treatment. Oblique radiograms of bladder after full repletion with contrast media, acquired 60 days after the catheter positioning, depict the closure of the fistulous tract.

Discussion HIFU is a minimally invasive therapy used in the treatment of prostate cancer. This technique consists of focused ultrasound waves emitted from a transducer, causing tissue damage by mechanical and thermal effects as well as by cavitation.²

The guidelines of the European Association of Urology (EAU) and of the American Association of Urology do not recommend HIFU as a standard treatment of a primary organ confined prostate cancer (PCa) and consider it still experimental or investigational. In the EAU guidelines, HIFU is considered a possible salvage treatment after EBRT: according to Murat³ local cancer control can be achieved in 73% of patients. In a recent experience, HIFU has been proposed for the salvage treatment of palpable local recurrent PCa after radical prostatectomy.¹

In our case, HIFU was proposed to the patient, after an extensive explanation of its potentialities, limits and complications, for several reasons. In a 68-year-old patient, with evidence of local recurrence of PCa after RP and subsequent EBRT, HIFU could represent a treatment with possible curative intent. In any case, such an approach could reduce tumor burden in the possible context of cytoreductive therapy, as proposed for other solid tumors.⁴⁻⁶ Therefore, even though this surgical approach might not be associated with a durable response over time, tumor load might be decreased and further cancer progression might be delayed. In addition, it might be speculated that this option might also aim at postponing the delivery of long term hormonal therapy, therefore reducing the exposure to such therapy.⁷

Reported HIFU complications are transient urinary retention, urinary incontinence and impotence. RUF is a well-known complication of HIFU treatment. Its presentation rate varies from 1% described by Lukka *et al*⁸ (when HIFU is carried out as primary treatment) to 6% described by Gelet *et al*⁹ (in cases of HIFU used as salvage therapy).

Ahmed *et al* affirmed that RUF is a consequence of the previous radiotherapy and it is not directly linked to the HIFU procedure. In a study on 172 patients treated with HIFU as primary treatment, there was no evidence of any RUF, whilst RUF rate was of 6.5% in those patients receiving salvage HIFU after failed EBRT. This could be a result of poor tissue viability and periprostatic blood supply after radiation. Moreover it seems possible that RUF can be linked to repeated HIFU and rectal abnormalities or intestinal pathologies.¹⁰ This complication can lead to the passage of faeces in the urinary system and therefore to UTIs and urosepsis: in these situations, it is mandatory to perform an urgent surgical treatment. The treatment is usually complex and requires the creation of two different diversions (urinary and faecal) and a surgical treatment to repair the fistulous tract. Surgical repair of RUF can be challenging; several surgical techniques have been described and can be classified in single and staged repairs.

Conservative management of RUF is rarely reported in literature and shows poor success rate at a 5-year follow-up.¹¹ In our case we managed to treat conservatively the RUF using an indwelling catheter (maintained in place for 2 months) and avoiding the creation of a colostomy. This result was possible due to the small size of the fistula and to the fact that the opening of the

fistulous tract was observed only when the patient had urgency. He presented DO, previously diagnosed on urodynamic evaluation, and this condition was probably responsible of the urine leakage through the fistula, when the urethral sphincter was still closed because the patient was trying to hold urine. Moreover there was no evidence of faecaluria: therefore we chose not to create a faecal diversion.

It has been postulated that, if a RUF persists after 2 weeks of non-operative management, a surgical treatment should be performed¹²: our case report seems not to confirm this statement, because the RUF was persisting 37 days after the HIFU procedure, but it was cured only about 30 days later. To our knowledge, our report is one of the very few reports of a successful conservative treatment for a RUF and the only one regarding a RUF after HIFU.

Being this the only case of RUF after HIFU in our experience, it has not changed our behaviour regarding catheter use. We usually place a suprapubic catheter after HIFU used as first line therapy for prostate cancer; the patient is allowed to pass urine spontaneously the second day after the procedure. On the contrary, we maintain a transurethral catheter for 7 days after HIFU as salvage treatment after EBRT and/or radical prostatectomy. We believe that urine should not pass through the urethra for some days after the procedure, to avoid that a partial urethral damage could lead to fistula formation. It could be hypothesised that a longer permanence of the transurethral catheter or of an open suprapubic tube could reduce the risk of fistula: unfortunately, no conclusive data are available.

We do not support the routine use of non-operative management for RUFs, but we consider it possible in selected cases. The criteria to assess the possibility of a conservative management of RUFs may include the anatomy of the fistula and its dimensions, the patient's operative risk, and the ability to maintain close follow-up. Once these are assessed, the chances of successful non-operative management can be estimated. Close follow-up is essential for early detection of failure of non-operative management and prompt subsequent intervention.

Learning points

- ▶ The possible role of high-intensity-focused ultrasound (HIFU) in PCa recurrences after surgery and external beam radiotherapy (EBRT) needs to be investigated.
- ▶ RUF is a well known complication of HIFU, especially when used as salvage treatment after EBRT, and can be a result of poor tissue viability and periprostatic blood supply after radiation.
- ▶ Recto-urethral fistula can be treated in a conservative way depending on the dimensions of the fistula, on its anatomy and on the ability to maintain a close follow-up.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Asimakopoulos AD**, Miano R, Virgili G, *et al*. HIFU as salvage first-line treatment for palpable, TRUS-evidenced, biopsy proven locally recurrent prostate cancer after radical prostatectomy. A pilot study. *Urol Oncol* 2011.
2. **Madersbacher S**, Marberger M. High-energy shockwaves and extracorporeal high-intensity focused ultrasound. *J Endourol* 2003;**17**:667–72.
3. **Murat FJ**, Poissonnier L, Rabilloud M, *et al*. Mid-term results demonstrate salvage high-intensity focused ultrasound (HIFU) as an effective and acceptably morbid salvage treatment option for locally radio recurrent prostate cancer. *Eur Urol* 2009;**55**:640–7.
4. **Park SY**, Choi GS, Jun SH, *et al*. Laparoscopic salvage surgery for recurrent and metachronous colorectal cancer: 15 years' experience in a single center. *Surg Endosc* 2011;**25**:3551–8.
5. **Eeson G**, Foo M, Harrow S, *et al*. Outcomes of salvage surgery for epidermoid carcinoma of the anus following failed combined modality treatment. *Am J Surg* 2011;**201**:628–33.
6. **Yim JH**, Kim WB, Kim EY, *et al*. The outcomes of first reoperation for locoregionally recurrent/persistent papillary thyroid carcinoma in patients who initially underwent total thyroidectomy and remnant ablation. *J Clin Endocrinol Metab* 2011;**96**:2049–56.
7. **Keating NL**, O'Malley AJ, Freedland SJ, *et al*. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. *J Natl Cancer Inst* 2010;**102**:39–46.
8. **Lukka H**, Waldron T, Chin J, *et al*. Genitourinary cancer disease site group of cancer care ontario's program in evidence-based care. High-intensity focused ultrasound for prostate cancer: a systematic review. *Clin Oncol (R Coll Radiol)* 2011;**23**:117–27.
9. **Gelet A**, Chapelon JY, Poissonnier L, *et al*. Local recurrence of prostate cancer after external beam radiotherapy: early experience of salvage therapy using high-intensity focused ultrasonography. *Urology* 2004;**63**:625–9.
10. **Ahmed HU**, Ishaq A, Zacharakis E, *et al*. Rectal fistulae after salvage high intensity focused ultrasound for recurrent prostate cancer after combined brachytherapy and external beam radiotherapy. *BJU Int* 2009;**103**:321–3.
11. **Thompson IM**, Marx AC. Conservative therapy of rectourethral fistula: five-year follow-up. *Urology* 1990;**35**:533–6.
12. **Zilbert NR**, Sand M, Draper L, *et al*. Successful non-operative management of an iatrogenic recto-urethral fistula in a 13-year-old boy. *J Pediatr Urol* 2009;**5**:142–4.

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