Case Report

Bladder stone formation around polyethylene glycol after use of SpaceOAR Hydrogel

Gen Tanaka, Ichiro Tsuboi, Kazutaka Mitani, Saori Yoshioka, Shuhei Yokoyama, Yusuke Kobayashi, Hirochika Nakajima, Taichi Nagami, Kohei Ogawa and Koichiro Wada

[1]Department of Urology, Shimane University Faculty of Medicine, Izumo, Shimane, Japan

Abbreviations & Acronyms
BPH = benign prostatic hyperplasia
CT = computed tomography
HU = Hounsfield unit
IMRT = intensity-modulated radiation therapy
MRI = magnetic resonance imaging
PEG = polyethylene glycol
PSA = prostate-specific antigen

Correspondence: Ichiro Tsuboi M.D., Department of Urology, Shimane University Faculty of Medicine, 89-1, Enya-cho, Izumo, Shimane 693-8501, Japan. Email: ichiro.tsuboi0810@gmail.com

How to cite this article: Tanaka G, Tsuboi I, Mitani K *et al*. Bladder stone formation around polyethylene glycol after use of SpaceOAR Hydrogel. *IJU Case Rep*. 2023; 6: 353–356.

Received 25 May 2023; accepted 3 August 2023. Online publication 18 August 2023

Introduction: Radiation therapy is used as primary, adjuvant, and salvage therapy for prostate cancer. When using radiation therapy, the SpaceOAR® system is considered easy to use and useful for reducing the irradiated dose and toxicity to the rectum. Although SpaceOAR® system have been reported some adverse event including death.
Case presentation: A 74-year-old male was diagnosed with prostate cancer of clinical stage cT2aN0M0 and intermediate risk by the National Comprehensive Cancer Network guidelines. We inserted the SpaceOAR® Hydrogel before performing intensity-modulated radiation therapy, as the patient had ulcerative colitis. We did not recognize any complications during or after the procedure, although magnetic resonance imaging revealed hydrogel in the bladder retrospectively. Fourteen months after the procedure, the patient was presented with macrohematuria and we found a bladder stone including hydrogel.
Conclusion: We report the first case of a bladder stone after use of SpaceOAR® Hydrogel. We must be careful of taking place it.

Key words: bladder stone, polyethylene glycol, SpaceOAR®.

Keynote message

An adverse effect of radiation therapy for localized prostate cancer can reduce using the SpaceOAR® system. The SpaceOAR® system is relatively easy to insert. However, we should understand the unexpected adverse effect of inappropriate insertion.

Introduction

Radiation therapy has been widely used as a treatment for prostate carcinoma. Although the devices and technology used for radiation therapy have improved, such as IMRT, the rectal dose and toxicity have remained major sources of adverse events, including proctitis, bloody diarrhea, fistula, bowel obstruction, and secondary cancer.

Therefore, the SpaceOAR® System (Boston Scientific, Marlborough, MA, USA) is used to make space between the prostate and the rectum with hydrogel, and its main ingredient is PEG. PEG remains in place for 3–6 months before it hydrolyses and liquefies and is absorbed. It has been established that its insertion significantly reduces the rectal dose and toxicity.[1]

However, some reports of complications associated with the use of the SpaceOAR® Hydrogel have arisen.[2–4] Aminsharifi *et al*. reported many severe complications, such as acute pulmonary embolism, severe anaphylaxis, prostatic abscess, and rectal fistula, among others. They also indicated that the number of cases with complications increased with each passing year.[4]

Herein, we present a case of bladder stone formation around the PEG of the SpaceOAR® Hydrogel. To the best of our knowledge, this is the first report of a bladder stone as a complication of using the SpaceOAR® System.

Case presentation

A 74-year-old male was referred to our institution due to a PSA elevation. His PSA level was 4.3 ng/mL. MRI indicated prostate cancer in the right transitional zone and could not indicate

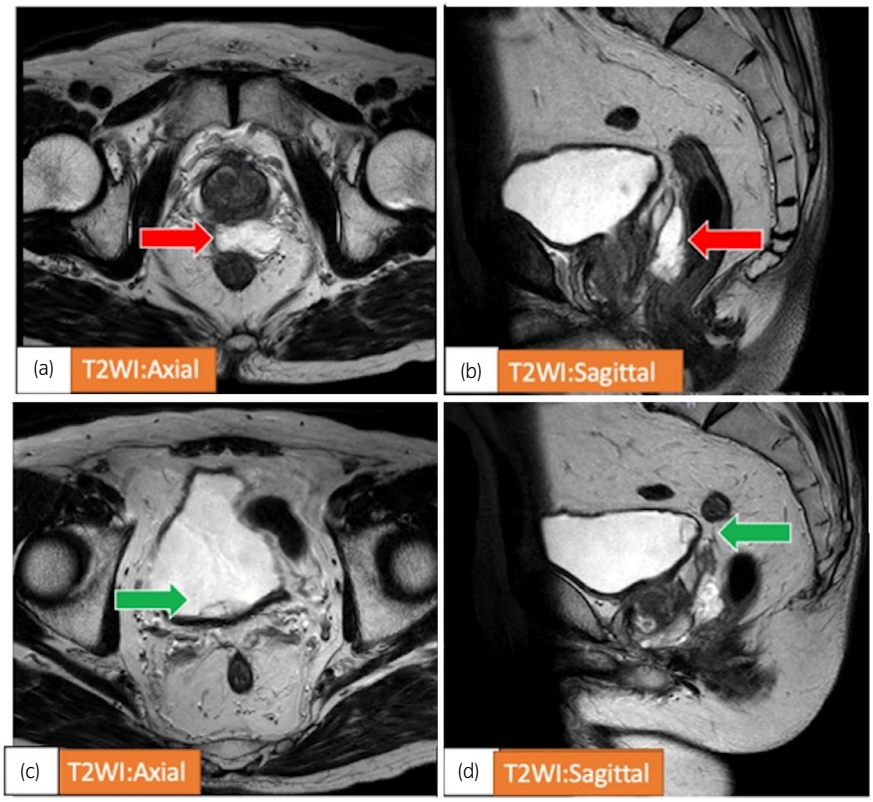

Fig. 1 MRI was performed 2 weeks after insertion of the SpaceOAR® Hydrogel. (a, b) Red arrow shows the hydrogel in the correct space between the prostate and the rectum. (c, d) Green arrow shows the hydrogel in the bladder.

the bladder stone at that time. Ultrasound-guided transrectal prostate biopsy and histopathological findings revealed Grade Group 2 adenocarcinoma in one of nine specimens. He was diagnosed with intermediate-risk prostate cancer by the National Comprehensive Cancer Network guidelines, stage cT2aN0M0. CT for the clinical staging could not reveal the stone or foreign matter in his bladder. His past medical history included ulcerative colitis and BPH. He did not have urinary tract stone in his history. His medication history was methotrexate, mesalazine, prednisolone, and silodosin. We recommended radical prostatectomy or IMRT as a definitive treatment, and he chose IMRT. Before we performed IMRT (78 Gy in 39 fractions), we inserted the SpaceOAR® Hydrogel to make a space between the prostate and the rectum. There were no intraoperative or postoperative complications. MRI was performed to confirm that the SpaceOAR® Hydrogel was inserted in the correct position 2 weeks after the placement of it (Fig. 1a,b).

Retrospectively, there was already what appeared to be PEG in the bladder (Fig. 1c,d). Two weeks after we inserted the SpaceOAR® Hydrogel, a treatment planning CT scan was also performed, and although it showed that a calcification had formed around the low-density material (Fig. 2), nobody noticed it then. As the patient complained of macrohematuria 14 months later, we performed cystoscopy and CT (Fig. 3a,b). As it showed a bladder stone, transurethral lithotripsy by holmium laser was performed. Although the surrounding area was of usual hardness, similar to a calcium stone, we continued the procedure and at last recognized that the interior material was gel-like material inside the stone (Fig. 3c). Stone analysis identified the calcium stone (Calcium oxalate: 53%, Calcium phosphate: 47%). We asked Boston Scientific

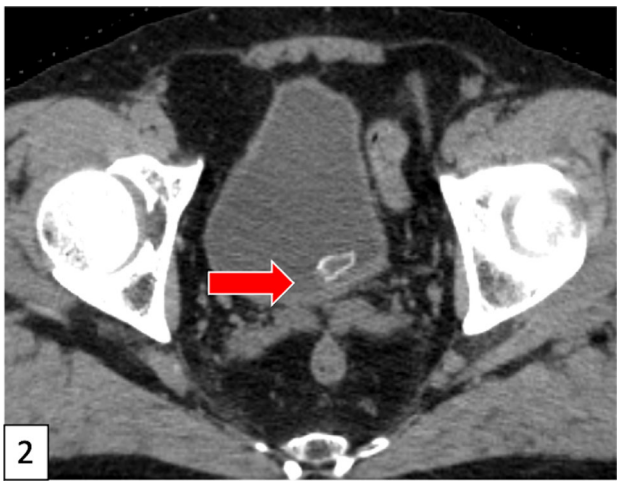

Fig. 2 Two weeks after inserting the hydrogel, a treatment planning CT revealed that a calcification had formed around it.

to analyze the gel-like material found within the calcium stone whether the gel was PEG or not. According to the analysis, the provided sample had contained PEG, but testing was inconclusive. (Fig. 3d).

Discussion

The SpaceOAR® Hydrogel, which consists of absorbable PEG, has been used for reducing irradiation toxicity to the anterior rectal wall. It contributes to a decrease in both acute and chronic symptoms, such as rectal pain, bowel movement frequency, bleeding, fecal incontinence, ulceration, and fistula

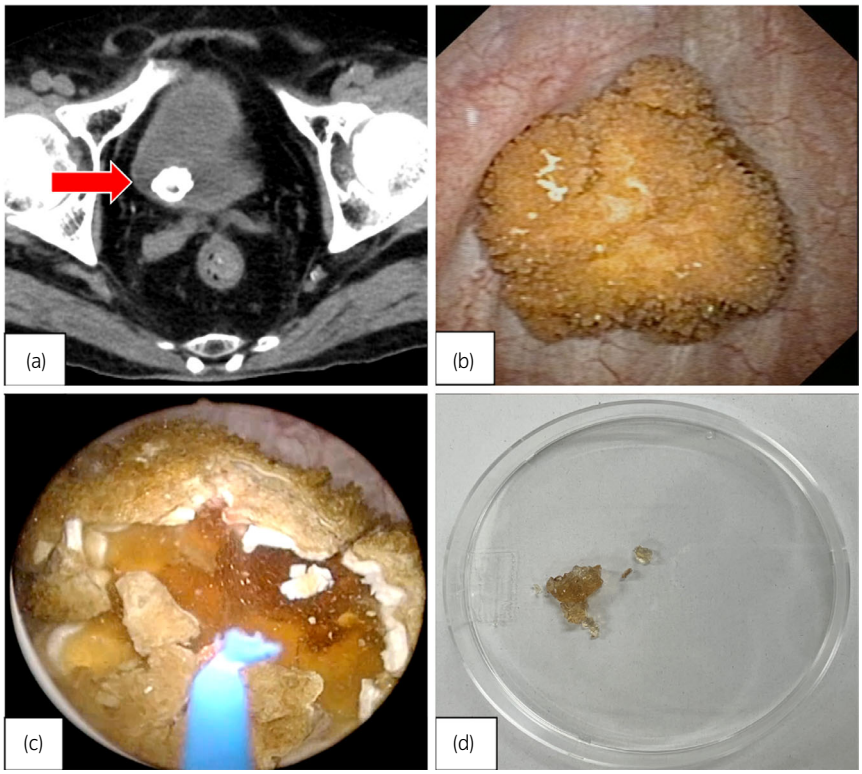

Fig. 3 (a, b) A CT scan performed 6 months after inserting the hydrogel and a cystoscopy scan show a bladder stone of 1.5 × 1.5 × 1.1 cm. The average CT HU was 308 HU. (c, d) Transurethral lithotripsy by holmium laser revealed the hydrogel inside the stone.

formation. A randomized study demonstrated that it not only reduced the rectal radiation dose by 25% and reduced the incidence of grade I–III rectal adverse events (National Cancer Institute Common Terminology Criteria), but also improved bowel-related quality of life at both 15 months and 3 years.[1] In our case, as the patient had ulcerative colitis, we considered this a good use of SpaceOAR® Hydrogel.

Some reports have described adverse events associated with the use of SpaceOAR® Hydrogel. Most have been written about the rectum and the prostate, such as proctitis, rectourethral fistula, prostatic abscess, etc.[2–4] As far as we investigated, there has been no report about the bladder stone.

In our case, MRI, which was performed after inserting the SpaceOAR® Hydrogel to confirm its location, revealed retrospectively that hydrogel was in the bladder. At that point, we had two questions: (i) how the hydrogel was inserted into the bladder and (ii) why was the PEG not absorbed so that a stone formed around it. We have two hypotheses regarding these two questions. First, we think that the hydrogel, which was inserted via the seminal vesicle or ampulla of the vas deferens, reached the bladder because the patient was prone to retrograde ejaculation due to silodosin. Another possibility is that the needle punctured the bladder or urethra directly. Secondly, as the patient took prednisolone for over 30 years due to ulcerative colitis, urinary calcium creatinine ratio was high (0.52; reference value: <0.3), which could have caused a stone to form around the PEG.

This report suggested we consider performing bladder irrigation to remove the PEG when we recognized it in the bladder. If we could recognize it and perform bladder irrigation, stone formation could be prevented in this case.

Conclusion

We have reported a rare case of a bladder stone that formed around the PEG of SpaceOAR® Hydrogel. This report suggested the one of complications after using SpaceOAR® Hydrogel. We clinicians need to know the possibility of this complication after insertion of the hydrogel.

Author contributions

Gen Tanaka: Writing – original draft. Ichiro Tsuboi: Supervision; writing – original draft; writing – review and editing. Kazutaka Mitani: Writing – review and editing. Saori Yoshioka: Writing – review and editing. Shuhei Yokoyama: Writing – review and editing. Yusuke Kobayashi: Writing – review and editing. Hirochika Nakajima: Writing – review and editing. Taichi Nagami: Writing – review and editing. Kohei Ogawa: Writing – review and editing. Koichiro Wada: Supervision; writing – review and editing.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

References

1 Hamstra DA, Mariados N, Sylvester J *et al*. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. *Int. J. Radiat. Oncol. Biol. Phys.* 2017; **97**: 976–85.
2 Kashihara T, Inaba K, Komiyama M *et al*. The use of hyperbaric oxygen to treat actinic rectal fistula after SpaceOAR use and radiotherapy for prostate cancer: a case report. *BMC Urol.* 2020; **20**: 196.
3 Teh AY, Ko HT, Barr G, Woo HH. Rectal ulcer associated with SpaceOAR hydrogel insertion during prostate brachytherapy. *BMJ Case Rep.* 2014; **2014**: bcr2014206931.
4 Aminsharifi A, Kotamarti S, Silver D, Schulman A. Major complications and adverse events related to the injection of the SpaceOAR hydrogel system before radiotherapy for prostate cancer: review of the manufacturer and user facility device experience database. *J. Endourol.* 2019; **33**: 868–71.

Editorial Comment

Editorial Comment to Bladder stone formation around polyethylene glycol after use of SpaceOAR hydrogel

SpaceOAR is currently the only hydrogel spacer available in Japan and has been actively used in conjunction with radiation therapy for prostate cancer since its introduction in 2018.

A multicenter randomized controlled trial involving its use with IMRT showed a significant reduction in the frequency of Grade 2 or higher late rectal toxicities.[1] The reports also included descriptions of the ease of the procedure, despite their initial experience, with 98.7% of operators rating it as "very easy" or "easy." However, while the procedure is perceived as easy, the number of reported procedure-related adverse events are increasing each year. In some cases, the radiation therapy itself could not be performed due to high-grade procedure-related adverse events. High-grade adverse events are frequently attributed to the gel misplacement within the rectal wall caused by intraoperative manipulation, leading to rectal ulcers or fistulas. The problem with such ectopic gel placement is that, although it is probably caused by some operation during the procedure, most cases end the procedure without noticing any problems.

In this study, the authors report a rare case of gel misplacement into the bladder and the subsequent formation of a bladder stone within a short period.[2] Unfortunately, the details of the procedure are unknown, and the specific cause of the ectopic placement into the bladder remains unclear. However, if the cause is the indwelled gels in the seminal vesicles, as the authors speculated, it is highly possible that puncture of the seminal vesicles occurred during the puncture process, and it should be noted that such calculus formation may occur afterward. Therefore, it is important to carefully perform each procedure process, and it may also be important to objectively confirm the indwelling state by MRI early after the procedure. Early detection of ectopic placement may allow action to be taken to avoid high-grade adverse events.

Author contributions

Masashi Morita: Writing – original draft; writing – review and editing.

Masashi Morita MD, PhD
Department of Urology, Showa University Koto Toyosu Hospital, Tokyo, Japan
morita34@med.showa-u.ac.jp

DOI: 10.1002/iju5.12634

Conflict of interest

The author declares no conflict of interest.

References

1 Mariados N, Sylvester J, Shah D *et al*. Hydrogel spacer prospective multicenter randomized controlled pivotal trial: dosimetric and clinical effects of perirectal spacer application in men undergoing prostate image guided intensity modulated radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2015; **92**: 971–7.
2 Tanaka G, Tsuboi I, Mitani K *et al*. Bladder stone formation around polyethylene glycol after use of SpaceOAR hydrogel. *IJU Case Rep.* 2023; **6**: 353–6.