Case Report

Ischemic proctitis after low-dose-rate brachytherapy using hydrogel spacer for prostate cancer

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Abbreviations & Acronyms
ADT = androgen deprivation therapy
IP = ischemic proctitis
LDR = low-dose-rate
PSA = prostate-specific antigen

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Introduction: Recently, an absorbable hydrogel spacer is becoming more widespread to reduce rectal radiation dose for radiation therapy for localized prostate cancer.

Case presentation: A 79-year-old male patient was referred to our hospital for radical treatment of organ-confined prostate cancer. Low-dose-rate brachytherapy was performed, and the hydrogel spacer injection was added. The spacer was properly injected between the prostate and the rectum, causing no acute complications during hospitalization. Two months after low-dose-rate brachytherapy, the patient visited our hospital with constipation and melena, without fever. He was diagnosed with ischemic proctitis based on clinical courses and examinations. He was hospitalized for 19 days and made a complete recovery with conservative treatment.

Conclusions: Herein, we report the first case of ischemic proctitis after low-dose-rate brachytherapy using hydrogel spacer for prostate cancer.

Key words: brachytherapy, hydrogels, ischemic colitis, proctitis, prostatic neoplasms.

Keynote message
Recently, the absorbable hydrogel spacer is becoming more widespread for radiation therapy for localized prostate cancer. We experienced a case of ischemic proctitis after low-dose-rate brachytherapy using hydrogel spacer. We should be aware of the possibility of ischemic proctitis as a hydrogel spacer complication.

Introduction
Low-dose-rate (LDR) brachytherapy for organ-confined prostate cancer is a well-established method worldwide.1–6 Recently, SpaceOAR system (Augmenix, Waltham, MA, USA), an absorbable hydrogel spacer, is becoming more widespread to reduce rectal radiation dose of radiation therapy for localized prostate cancer.7–9 However, rectal-related complications have been reported to occur in the wrong indication by SpaceOAR although in a small number.10 Defecation control is one of the most important issues in radiotherapy because elderly patients often have potential defecation disorders.11 Herein we report a case of early postoperative ischemic proctitis (IP) after LDR brachytherapy using SpaceOAR. To our knowledge, this is the first report that describes IP as a complication of hydrogel spacer for prostate cancer.

Case report
A 79-year-old male patient was referred to our hospital for radical treatment of organ-confined prostate cancer. The initial prostate-specific antigen (PSA) was 10.5 ng/mL, cT2aN0M0, Gleason score 3 + 4 = 7. He had a history of hemorrhoid surgery, but did not have an anal stenosis, defecation problems, and cardiovascular diseases. And he was not taking any medication. We planned LDR brachytherapy combined with 6 months of androgen deprivation therapy (ADT). After 3 months of neoadjuvant ADT, LDR brachytherapy was performed and 10 mL of hydrogel spacer was properly injected between the prostate and the rectum and outside the rectal serosa (Fig. 1), causing no acute complications during
hospitalization. The prescribed radiation dose was 145 Gy and $V_{100prostate}$ (the percentage of the prostate volume receiving 100% of the prescribed dose) was 99.24%; however, $V_{100rectum}$ (the rectal volume receiving 100% of the prescribed dose) was 0.00 mL due to the spacer separating the rectum and the prostate by 11 mm (Table 1).

Two months after the LDR brachytherapy, the patient visited our hospital with constipation and melena, without fever. Constipation lasted for 2 weeks before the visit but did not improve with laxatives. Contrast-enhanced computed tomography indicated suspicious proctitis, and colonoscopy was performed for a definitive diagnosis (Fig. 2). Colonoscopy revealed some localized longitudinal rectal ulcers, without the point of hemorrhage (Fig. 3).

The stool culture upon hospitalization showed positive for methicillin-resistant Staphylococcus aureus and Escherichia coli, and C-reactive protein was high at 10.57 mg/dL and the serum procalcitonin was low at 0.06 ng/mL, excluding infectious disease as a diagnosis. We finally diagnosed him as IP based on clinical courses and examinations.

He was hospitalized and treated conservatively with fasting, and cefmetazole was administered to prevent secondary infection. Endoscopy was performed again 2 weeks after hospitalization, which revealed ulcer improvement (Fig. 3). The histopathological findings of rectal biopsy indicated active ulcer with necrotic tissue and negative for malignancy. The length of fasting, antimicrobial agent administration, and hospitalization were 8 days, 10 days, and 19 days, respectively. The PSA level at the second hospitalization was below sensitivity, indicating a well-controlled prostate cancer.

### Discussion

We experienced a case of proctitis 2 months after LDR brachytherapy using hydrogel spacer, which was diagnosed as IP.
IP is a disease of ischemic colitis localized to the rectum. The most common site of ischemic colitis is the descending colon to the sigmoid colon, and the rectum is rarely reported. The patient with ischemic colitis presents abdominal pain (49.4%–73%) and diarrhea (14.2%–68%). The colonoscopy often reveals a longitudinal ulcerated or inflamed colon stripe. The present case is consistent with these clinical appearances.

One of the etiologies of ischemic colitis is reported to be transient mucosal ischemia of the colon. Teh et al. reported that one of the possible mechanisms of rectal injury with hydrogel spacer use is the ischemic injury based on the excessive tension from hydrogel spacer at the anterior rectal wall. Additionally, for patients with hemorrhoid, the most commonly demonstrated physiological abnormality is an increased resting anal pressure. In the present case, the spacer may have physically compressed the rectal mucosa, and further abdominal pressure due to constipation that lasted for 2 weeks may have triggered IP. Elderly people often have some kind of defecation disorder, and defecation should be properly controlled in patients undergoing radiotherapy.

IP diagnosis is difficult because it presents with nonspecific symptoms, and excluding differential diagnoses is...
necessary. First of all, we proposed some differential diagnoses – radiation, infectious, drug-induced, or ischemic proctitis; colonic diverticulitis; and inflammatory bowel diseases such as Crohn’s disease and ulcerative colitis. Drug-induced proctitis and inflammatory bowel disease were excluded as a diagnosis because of the clinical course. Infectious proctitis was also excluded since the serum procalcitonin level was low and the lesion was located at the rectum only. Therefore, it was considered different from typical bacterial enteritis. Additionally, the absence of anal intercourse history ruled out proctitis due to sexually transmitted disease. Furthermore, a colonoscopy revealed no sign of colonic diverticulitis.

The possibility of radiation proctitis is a little higher. Acute radiation proctitis occurs during or within the first 3 months of radiation therapy, and patients usually present symptoms such as diarrhea, an urgency to defecate, tenesmus, cramping pain, and mild rectal bleeding. However, with the help of radiation oncologists and gastroenterologists, we diagnosed him as IP based on the low rectal radiation dose and more specific longitudinal ulcer findings in IP.

Concerning prostate cancer treatments, hydrogel spacer is indicated not only in LDR brachytherapy but also in high-dose-rate brachytherapy or external beam radiotherapy. However, to our best of knowledge, no previous report has described IP after any method of radiotherapy with hydrogel spacer for prostate cancer. To prevent the adverse events after using hydrogel spacer, proper use of hydrogel spacer and defecation controls (e.g., perioperative use of laxatives) should be required.

Conclusion

This is the first case report of IP after LDR brachytherapy for prostate cancer using hydrogel spacer worldwide. Physicians should pay attention to the possibility of IP as a complication of hydrogel spacer.

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Author Contributions

Ren Toriumi: Data curation; investigation; project administration; resources; visualization; writing – original draft; writing – review and editing. Hiroshi Yaegashi: Conceptualization; project administration; resources; visualization; writing – review and editing. Takayuki Sakurai: Data curation; investigation; resources; visualization; writing – original draft; writing – review and editing. Shigeyuki Takamatsu: Supervision; writing – review and editing. Kazuyoshi Shigehara: Writing – original draft; writing – review and editing. Yosuke Shimizu: Writing – review and editing. Yoshifumi Kadono: Supervision; writing – review and editing. Atsushi Mizokami: 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

Not applicable.

Registry and the registration no. of the study/trial

Not applicable.

References

1 Stone NN, Stock RG, Cesaretti JA, Unger P. Local control following permanent prostate brachytherapy: effect of high biologically effective dose on biopsy results and oncologic outcomes. Int. J. Radiat. Oncol. Biol. Phys. 2010; 76: 355–60.
2 Taira AV, Merrick GS, Butler WM et al. Long-term outcome for clinically localized prostate cancer treated with permanent interstitial brachytherapy. Int. J. Radiat. Oncol. Biol. Phys. 2011; 79: 1336–42.
3 Zelenisky MJ, Chou JF, Pei X et al. Predicting biochemical tumor control after brachytherapy for clinically localized prostate cancer: the Memorial Sloan-Kettering Cancer Center experience. Brachytherapy. 2012; 11: 245–9.
4 Yorozu A, Kuroiwa N, Takahashi A et al. Permanent prostate brachytherapy with or without supplemental external beam radiotherapy as practiced in Japan: outcomes of 1300 patients. Brachytherapy. 2015; 14: 111–7.
5 Tanaka N, Asakawa I, Nakai Y et al. Comparison of PSA value at last follow-up of patients who underwent low-dose rate brachytherapy and intensity-modulated radiation therapy for prostate cancer. BMC Cancer. 2017; 17: 573.
6 Ito K, Saito S, Yorozu A et al. Nationwide Japanese prostate cancer outcome study of permanent iodine-125 seed implantation (J-POPS): first analysis on survival. Int. J. Clin. Oncol. 2018; 23: 1148–59.
7 Morita M, Fukagai T, Hiyama K et al. Placement of SpaceOAR hydrogel spacer for prostate cancer patients treated with iodine-125 low-dose-rate brachytherapy. Int. J. Urol. 2020; 27: 60–6.
8 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.
9 Neilsen AD, Sindhu KK, Moshier E et al. The impact of a rectal hydrogel spacer on dosimetric and toxicity outcomes among patients undergoing combination therapy with external beam radiotherapy and low-dose-rate brachytherapy. Brachytherapy. 2021; 20: 296–301.
10 Vaggers S, Rai BP, Chegdy ECP et al. Polyethylene glycol-based hydrogel rectal spacers for prostate brachytherapy: a systematic review with a focus on technique. World J. Urol. 2021; 39: 1769–80.
11 DeB B, Prichard DO, Bharucha AE. Constipation and fecal incontinence in the elderly. Curr. Gastroenterol. Rep. 2020; 22: 54.
12 Matsumoto S, Tsuji K, Shirahama S. Clinical investigation of 41 patients with ischemic colitis accompanied by ulcer. World J. Gastroenterol. 2007; 13: 1236–9.
13 Nikolic AL, Keck J. Ischaemic colitis: uncertainty in diagnosis, pathophysiology and management. ANZ J. Surg. 2018; 88: 278–83.
14 Theodoropoulou A, Koutroubakis IE. Ischemic colitis: clinical practice in diagnosis and treatment. World J. Gastroenterol. 2008; 14: 7302–8.
15 Teh AYM, Ko H, Barr G, et al. Rectal ulcer associated with SpaceOAR hydrogel insertion during prostate brachytherapy. BMJ Case Rep. 2014; bcr2014206931.
16 Sandler RS, Peery AF. Rethinking what we know about hemorrhoids. Clin. Gastroenterol. Hepatol. 2019; 17: 8–15.
17 Tabaja I, Sidani SM. Management of radiation proctitis. Dig. Dis. Sci. 2018; 63: 2180–8.
18 Armstrong N, Bahl A, Pinkawa M et al. SpaceOAR hydrogel spacer for reducing radiation toxicity during radiotherapy for prostate cancer. A systematic review. Urology. 2021; 156: e74–85.