Rectal Ulcers and Rectoprostatic Fistulas after ^{125}I Low Dose Rate Prostate Brachytherapy

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Purpose: Radiation induced rectal ulcers and fistulas are rare but significant complications of low dose rate prostate brachytherapy for localized prostate cancer. We describe the incidence of ulcers and fistulas, and associated risk factors.

Materials and Methods: We reviewed the records of 4,690 patients with localized prostate cancer who were treated with low dose rate ^{125}I prostate brachytherapy to a dose of 144 Gy with or without 6 months of androgen deprivation therapy. Patient, disease, comorbidity, treatment, dosimetric and posttreatment intervention factors were analyzed for an association with ulcer or fistula formation.

Results: At a median followup of 53 months 21 cases were identified, including 15 rectal ulcer cases, of which 6 progressed to fistulas, and an additional 6 cases of fistulas with no prior documented ulcers. Overall 9 rectal ulcer cases (0.19%) and 12 fistula cases (0.26%) were identified. In 8 of 15 patients ulcers healed with conservative management. No fistulas healed without surgical management. Two patients with fistulas died. Eight patients diagnosed with rectal ulcers subsequently underwent rectal biopsies, after which fistulas developed in 3. One patient with a de novo fistula underwent a preceding biopsy. Urinary interventions such as transurethral resection of the prostate were performed after brachytherapy in 5 of 12 patients with fistulas compared to 0 of 9 with ulcers alone. Argon plasma coagulation of the rectum for hematochezia was performed after brachytherapy in 3 of 12 patients with fistulas.

Conclusions: Rates of post-brachytherapy rectal ulcers and fistulas are low as previously described. Post-brachytherapy interventions such as rectal biopsy, argon coagulation and urinary intervention may increase the risk of fistulas.

Key Words: prostatic neoplasms, brachytherapy, ulcer, fistula, iatrogenic disease

Abbreviations and Acronyms

ADT = androgen deprivation therapy

APC = argon plasma coagulation therapy

IBD = inflammatory bowel disease

LDR = low dose rate

NCCN® = National Comprehensive Cancer Network®

PB = prostate brachytherapy

UI = urinary intervention

V100 = relative prostate volume covered by 100% of prescribed dose

VR100 = volume of rectum receiving 100% of prescribed dose

Low dose rate PB (ultrasound guided transperineal implantation of radioactive seeds) is an established, effective treatment of localized prostate cancer.[1–3] According to the updated PCRSG (Prostate Cancer Results Study Group) the use or inclusion of LDR PB has achieved high biochemical control rates in all risk categories of localized prostate cancer.[4] Generally, LDR PB is well tolerated with low rates of severe late urinary and rectal

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toxicity.[5–8] However, radiation induced rectoprostatic fistulas are a rare but significant complication associated with LDR PB. In the literature incidence rates of rectoprostatic fistulas after LDR PB range from 0.2% to 1.0%.[9–12] Rectal ulcers have been described as preceding fistulas.[10–12] Previously described risk factors for significant rectal toxicity after LDR PB include rectal biopsy after LDR PB,[10] active inflammatory bowel disease,[13] increased rectal radiation dose[11,14] and external beam radiotherapy combined with LDR PB.[10]

In this study we reviewed all known cases of rectal ulcers and fistulas in a large, consecutive, prospectively followed cohort of patients who received ^{125}I monotherapy. We describe the incidence, presentation, treatment and outcomes in these patients and identify associated risk factors.

MATERIALS AND METHODS

Patient Selection

In this research ethics board approved study we reviewed our institutional prospective electronic LDR PB patient database and selected the charts of 4,690 patients with NCCN low or intermediate risk localized prostate cancer treated with LDR PB between July 1998 and May 2013. NCCN low risk cases were treated with prostate brachytherapy alone. Prior to February 2005 patients with NCCN intermediate risk disease received 3 months of neoadjuvant and 3 months of adjuvant ADT. ADT was also administered in patients who required prostate size reduction to allow implantation or who were started on ADT by a urologist before referral. After February 2005 ADT was no longer mandatory in patients at NCCN intermediate risk.

Brachytherapy Technique

The brachytherapy technique has been previously described.[2,3] The supplementary material (http://jurology.com/) shows the details of our treatment.

Case Identification and Followup

Patients were seen by a radiation oncologist 6 weeks after implantation, every 6 months for 2 to 3 years, annually until year 5 and biannually thereafter. At each visit patients were asked to complete urinary, gastrointestinal and sexual function surveys. They were also asked about new or ongoing toxicity or dysfunction. Supplementary medical records and reports were retrieved from other health care providers to corroborate identified toxicity when possible.

Prostate specific antigen was measured every 6 months after implantation. Minimum followup in this study was 6 months. Potential cases of rectal ulcers or fistulas were identified by querying the database for patients with recorded grade 3 or 4 urinary or gastrointestinal toxicity as defined by the RTOG® scoring system or any accompanying database notes suggesting symptoms of ulcers or fistulas. Prostate brachytherapists were contacted and asked about any patients with suspected or known occurrences of rectal ulcers or fistulas. We then manually reviewed the charts of patients with suspected ulcers or fistulas.

Data Analysis

The supplementary Appendix (http://jurology.com/) lists the patient, disease and treatment factors that were reviewed.[15,16]

Dosimetric details were taken from the database and reviewed using VariSeed™ brachytherapy planning software. Rectal doses in the database were calculated on rectal contours performed in a standard manner on postimplantation computerized tomography.[6] Urethral doses were determined by contouring the Foley catheter when present, or by estimating the dose when there was no catheter by generating a deviated urethra surrogate in VariSeed using the technique described by Bucci et al.[17]

Univariate analysis was done by comparing patients with rectal ulcers alone vs patients with fistulas. The Fisher exact test was used for nominal variables and ANOVA was used for continuous variables with SPSS®, version 21. Due to the small number of events multivariable analysis was not performed.

We additionally reviewed the charts of 238 patients in the database who were reported to have grade 2 or 3 RTOG rectal toxicity but no rectal ulcers or fistulas. We did this to determine the proportion of these patients who underwent rectal or urinary intervention after brachytherapy.

RESULTS

Rectal ulcers or fistulas developed in 21 of the 4,690 patients. The crude rates of ulcers and fistulas were 0.19% and 0.26%, respectively, of all implants.

Clinical Course

Rectal ulcers developed in 15 patients, including 1 with a history of inflammatory bowel disease (table 1). In the latter patient a rectocutaneous fistula developed, which was categorized as a rectal ulcer in this study. These conditions developed a median of 18 months (range 3 to 79) following LDR PB. In 8 patients (53%) the ulcers healed spontaneously with nonsurgical management between 13 and 40 months after ulcer diagnosis. The rectocutaneous fistula was treated surgically with loop colostomy and a stoma. Medical therapy included mesalamine, and rectal and oral corticosteroids. Six of the 15 ulcer cases progressed to fistulas between 1 and 17 months later, including 1 treated with surgical diversion for ulcers and 2 treated with hyperbaric oxygen.

Six patients presented with de novo fistulas without preceding ulcers a median of 33 months (range 8 to 53) after LDR PB. One patient with a fistula was treated with 2 transurethral resections of the prostate for locally recurrent prostate cancer and resection of colon cancer. Fistulas developed in 12 patients and none healed without surgical intervention. Surgical intervention consisted of