

## Rectal ulcer and pseudomalignant epithelial changes after prostate seed brachytherapy: A rare complication with a diagnostic pitfall



Hwajeong Lee<sup>a</sup>, Natallia Sheuka<sup>a</sup>, Osama El-kadi<sup>a</sup>, Brian P. Murray<sup>b</sup>, Hugh A. Fisher<sup>c</sup>, Bhaskar V.S. Kallakury<sup>a,d</sup>, Edward C. Lee<sup>e</sup>, Ann Boguniewicz<sup>a</sup>, Timothy A. Jennings<sup>a,\*</sup>

<sup>a</sup> Anatomic Pathology, Albany Medical College, Albany, NY, USA

<sup>b</sup> Urology, St Peter's Health Partner Medical Associates, Albany, NY, USA

<sup>c</sup> Urology, Albany Medical College, Albany, NY, USA

<sup>d</sup> Pathology, Georgetown University, Washington, DC, USA

<sup>e</sup> General Surgery, Albany Medical College, NY, USA

### ARTICLE INFO

#### Keywords:

Brachytherapy  
Radiation atypia  
Rectal ulcer  
Pseudomalignant gland  
Pitfall

### ABSTRACT

**Background:** Implant brachytherapy (IBT) is a well-recognized treatment modality for early stage prostate cancer. Rectal ulcer and rectourethral fistula complicating IBT may cause an alteration of the normal anatomic landmarks. In this context, pseudomalignant radiation-induced changes within prostatic epithelium may be misinterpreted as a primary rectal malignancy. Such challenging and misleading findings have not been described, and may not be recognized as such.

**Materials and methods:** We present the clinical and pathologic aspects of two patients who underwent IBT for low stage prostate cancer that was complicated by deep rectal ulcer. Both patients underwent extensive palliative surgical resection for disease control.

**Results:** The histologic changes in both cases were noteworthy for extensive necrosis and inflammation of the prostate, associated with loss of recto-prostatic anatomical landmarks. Prostatic glands showed striking radiation-induced atypia and pseudomalignant epithelial changes extending to the rectal ulcer bed, with no residual viable tumor. The first patient had undergone a biopsy of the rectal ulcer bed that was misinterpreted as a rectal adenocarcinoma prior to surgery. The similarity between atypical glands of the biopsy and the benign prostatic tissue with radiation-induced atypia in resection specimen confirmed their benign nature.

**Conclusions:** Deep rectal ulcer complicating IBT may lead to distortion of the normal recto-prostatic anatomical landmarks, resulting in detection of pseudo-malignant prostatic glands at the ulcer base. Such findings may be mistaken for a primary rectal malignancy in limited biopsy material if not familiar to the pathologist.

### 1. Introduction

For localized low stage prostate cancer, implant brachytherapy (IBT) has emerged as a treatment of choice with overall good health related quality of life compared to radical prostatectomy and/or external beam radiation therapy (EBRT) [1]. IBT has the advantages of shorter treatment time, lower cost, significantly lower incidence of acute and late complications and comparable cure rates compared to EBRT or prostatectomy [2,3].

The optimal choice of IBT seed type, whether loose or stranded, has been a subject of controversy [4–6], which may be attributed to the heterogeneity of study design and varying follow-up intervals [6,7]. Generally, however, the use of loose seeds seems to result in a higher

rate of seed migration and pulmonary embolism, with no definite impact on radiation dose [7,8]. In contrast, stranded seeds might be associated with decline in the median curative dose administered to the surrounding prostatic tissue following tissue retraction, due to their non-adjustable nature [4,9].

Despite the relative safety of this procedure, complications may still occur, to include bowel and erectile dysfunction, and urinary symptoms [3,10]. Rare but serious colorectal complications of IBT that are associated with high rate of surgical intervention are rectal ulceration, rectourethral fistula and intractable bleeding [2,3,11,12]. Secondary malignancies associated with IBT are extremely rare, but have been reported [13,14].

Altered histology of prostatic tissue following radiation therapy is

\* Corresponding author at: 47 New Scotland Ave. MC81, Albany, NY 12208, USA.

E-mail addresses: [leeh5@amc.edu](mailto:leeh5@amc.edu) (H. Lee), [sheukan@amc.edu](mailto:sheukan@amc.edu) (N. Sheuka), [fisherH@amc.edu](mailto:fisherH@amc.edu) (H.A. Fisher), [kallakub@gunet.georgetown.edu](mailto:kallakub@gunet.georgetown.edu) (B.V.S. Kallakury), [leeE@amc.edu](mailto:leeE@amc.edu) (E.C. Lee), [Bogunia@amc.edu](mailto:Bogunia@amc.edu) (A. Boguniewicz), [JenninT@amc.edu](mailto:JenninT@amc.edu) (T.A. Jennings).

<https://doi.org/10.1016/j.anndiagpath.2018.03.011>

relatively well documented in the literature [15–18]. However, deep rectal ulcer as a complication of IBT associated with pseudomalignant epithelial changes due to altered recto-prostatic anatomic landmarks mimicking a primary rectal malignancy has not been reported. We present two such patients who developed deep rectal ulcer following IBT that were surgically treated at our institution. In one of the patients, a pre-operative rectal ulcer bed biopsy containing atypical prostate glands was initially misdiagnosed as a rectal adenocarcinoma.

## 2. Materials and methods

The study was approved by the institutional review board (IRB). Radiation protection protocol was followed. The tissue was fixed in 10% buffered formalin, routinely processed and paraffin-embedded. In both cases, the ulcer bed and the adjacent more preserved rectal mucosa were extensively sampled. The prostate glands were entirely embedded as whole mounts in patient A, including the contiguous rectal ulcer base. In patient B, routine representative sections (not whole mounts) were taken to include recto-urethral fistula. Four-micrometer thick tissue sections were stained with Hematoxylin & Eosin. Patients' history was obtained from the medical records.

## 3. Results

### 3.1. History

Patient A was 50 years old, presented with elevated PSA of 9.5 ng/ml. Prostate biopsy showed adenocarcinoma, Gleason score 3 + 3 = 6/10, localized to the right apex, involving 10% of the submitted tissue. The rest of the biopsies were negative for malignancy. The patient was treated with loose seeds IBT with I-125 of 144 Gy that was complicated by rectal ulcer 18 months later. A biopsy of this rectal ulcer revealed highly atypical glands that initially were misinterpreted as a rectal adenocarcinoma at an outside institution. Subsequently he underwent abdomino-perineal resection with prostatectomy at our institution. Outside biopsy material was re-reviewed at our institution following the surgery.

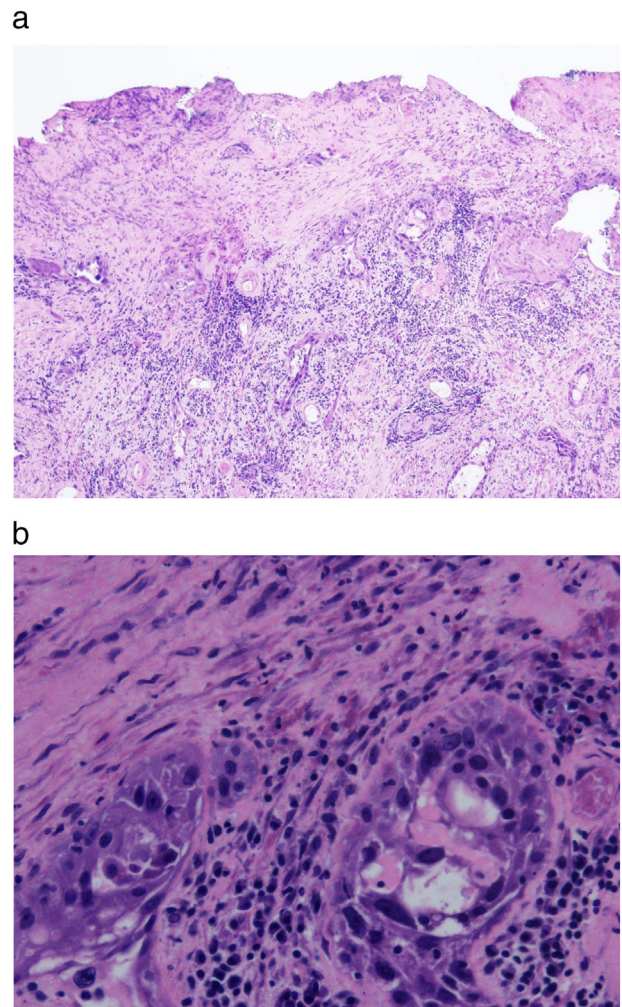
Patient B was 70 years old, presented with elevated PSA of 12 ng/ml. Prostate biopsy showed adenocarcinoma, Gleason score 3 + 3 = 6/10. Initially he received EBRT of 7020 cGy with subsequent local failure (three consecutive rises in serum PSA after post-radiation nadir, and biopsy proven residual tumor) in 26 month. He was then treated with loose seeds IBT with I-125 at 100 Gy. Forty two months later, this was complicated by bloody diarrhea and rectal pain, and rectourethral fistula was diagnosed. The patient underwent diverting colostomy, followed by total pelvic exenteration.

### 3.2. Gross examination

Both specimens showed dense adhesions between the rectal wall and the posterior aspect of the prostate. The anterior rectal wall, in both specimens, also displayed a deep ulcer, flanked by friable and hemorrhagic rectal mucosa without obvious tumor. Serial transverse cross-sections of the prostate revealed a largely blurred recto-prostatic junction with indurated and hemorrhagic cut surfaces, and loss of the normal anatomic landmarks.

### 3.3. Microscopic examination

The histologic changes in both cases were similar, and were noteworthy for extensive necrosis of the prostate tissue, associated with an inflammatory reaction and hyalinizing fibrosis. No residual viable carcinoma was seen in either case. Examination of the areas with residual benign prostatic glands showed marked radiation atypia. The radiation atypia encompassed nuclear enlargement, pleomorphism, and hyperchromatic or vesicular nuclei, with prominent nucleoli. Some of



**Fig. 1.** [Patient A] Low magnification view of the rectal ulcer bed of the resection specimen shows markedly atypical glands, in a background of granulation tissue and necrosis (1a). The glands show nuclear enlargement, pleomorphism and hyperchromasia with prominent nucleoli (1b).

the atypical glands were present in the rectal ulcer bed, surrounded by granulation tissue and necrosis [Figs. 1 and 2]. While the cytologic atypia was striking, the architecture of the atypical prostatic glands was considered to be benign with lobular configuration and atrophic features. The rectal mucosa adjacent to the ulcer bed showed radiation induced changes with atrophy and mucin loss.

For patient A, given the potential discrepancy between the findings in the pre-operative rectal biopsy and resection specimen, the outside rectal biopsy was re-reviewed at our institution. The biopsy contained highly atypical glands with marked nuclear enlargement and pleomorphism, associated with acute and chronic inflammation, necrosis, stromal fibrosis and granulation tissue element. From a purely histopathologic standpoint, the overall features were indeed highly suspicious for carcinoma [Fig. 3]. However, comparing the atypical glands in the rectal biopsy specimen to those in the prostate resection specimen revealed a striking similarity, which confirmed that the atypical glands in the rectal biopsy were prostatic in origin, and that the process was benign in nature. Therefore, a final diagnosis of “benign prostate glands with marked radiation induced atypia” was rendered.

### 3.4. Follow-up

Patient A and B have been followed for 16 and 11 years, respectively, at which time both were alive, free of disease, with radiation

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