

# Pouchitis Associated With Pelvic Radiation for Prostate Cancer

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## ABSTRACT

Radiation therapy is a viable option in managing potentially life-threatening malignancies including prostate cancer. It is known that pelvic radiation can result in injury of the distal large bowel with the development of radiation proctitis. Despite reports from retrospective studies, there is a lack of direct endoscopic and histologic evidence of external pelvic radiation injury to the ileal pouch-anal anastomosis. We present a case of a 68-year-old male with pouchitis resulting from pelvic radiation for prostate cancer.

## INTRODUCTION

Restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) is the surgical treatment for ulcerative colitis patients with medically refractory disease or colitis-associated neoplasia. In IPAA surgery, the distal ileum is fashioned into a fecal reservoir. The alteration in the bowel anatomy as well as underlying inflammatory bowel disease can result in various complications in ileal pouch patients. Pouchitis is the most common complication, which can be triggered by dysbiosis, infection from pathogens, ischemia, autoimmune disorders, and the use of nonsteroidal anti-inflammatory drugs. Pelvic radiation has also been reported to be a risk factor.

In 2015, there were 220,800 newly reported cases of men with prostate cancer and a mortality of 12.4% in the United States.<sup>1</sup> More than 50% of those patients with prostate cancer were older than 65 years. Prostate cancer is the second leading cause of death, with a cancer mortality of 3%.<sup>1</sup> The management strategies for prostate cancer include active surveillance, radical prostatectomy, androgen deprivation therapy, chemotherapy, brachy radiotherapy, and external beam radiation therapy (EBRT). There is a concern in radiation therapy for the treatment of prostate cancer in male pouch patients and uterine or cervical cancer in female pouch patients.

## CASE REPORT

The patient was a 68-year-old male with diagnosis of ulcerative colitis in 1979 status post restorative proctocolectomy and 2-stage IPAA for colitis-associated dysplasia in 1991. For many years, he had been doing well with pouch, except that he developed perianal cryptogenic abscess in 2008. The abscess was successfully treated with incision and drainage along with antibiotics, and it did not recur. There was no further evidence of Crohn's disease (CD) during a long-term follow-up. The patient has been conscientious about the health status of the pouch and underwent pouchoscopy for disease monitoring every 1-3 years.

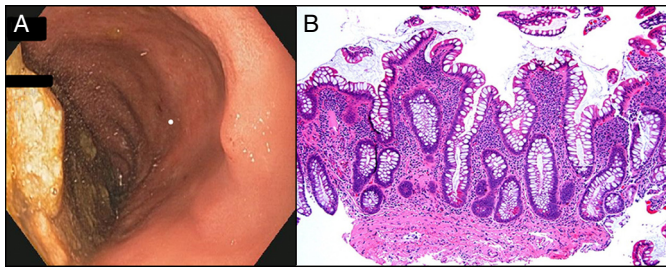
He started experiencing painful urination and saw a local urologist in December 2014. Prostate biopsy revealed low-grade prostate adenocarcinoma. The patient elected to have intensity-modulated radiation treatment with 44 fractions to a total dose of 7920 cGy to the prostate, using Calypso radiofrequency markers. The patient received EBRT from January to March 2015, 5 times per week. However, he experienced increased bowel incontinence during and after EBRT.

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**Figure 1.** (A) Endoscopy of pouch body before radiation therapy. (B) Histology of pouch body before radiation with mild villi blunting (40x).

During a routine clinic visit 7 months prior to his radiation therapy, the patient was free of major bowel symptoms. In May 2014, pouchoscopy showed normal pouch mucosa and only chronic minimally active inflammation in the pouch body and cuff on histology (Figure 1). Six months after radiation in September 2015, the patient presented to our Center for Ileal Pouch Disorders for increased bowel frequency, urgency, and incontinence. His postradiation pouchoscopy showed an inflammatory polyp in the afferent limb, typical arteriovenous malformation-like friable mucosa, and a bleeding ulcer in the distal pouch and cuff (Figure 2).

Suspected radiation injury was confirmed by classic histologic features of radiation enteritis. Biopsies from the terminal ileum, pouch body, and rectal cuff showed vascular abnormalities, such as telangiectatic vessels, focal perivascular hyalinization, and vessels with thickened walls, in addition to chronic active enteritis and erosions in the pouch body. Moreover, the rectal cuff biopsies showed focal lamina propria hyalinization and a focal fibrin thrombus. Those endoscopic and histologic features, along with clinical symptoms of increased bowel frequency and incontinence, were new since EBRT.

## DISCUSSION

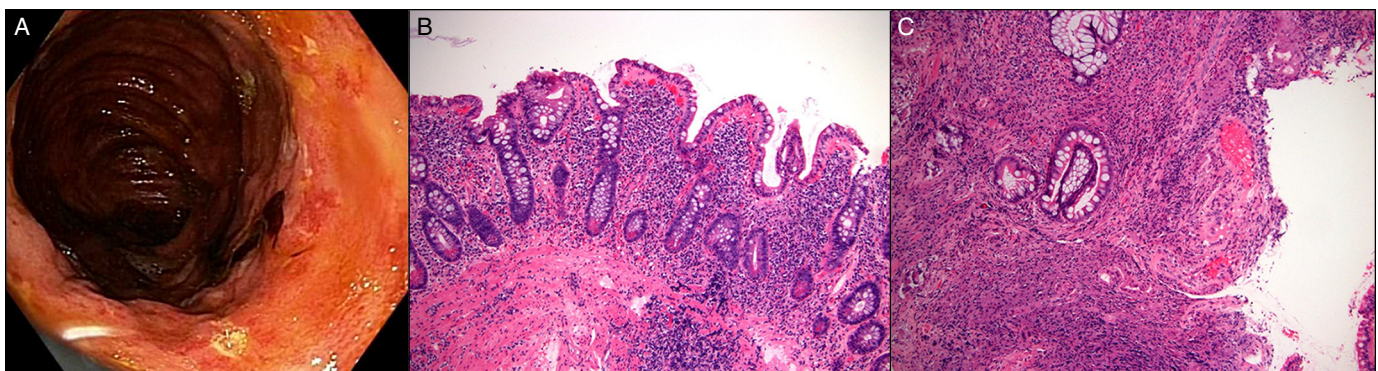
The risks and benefits of radiation therapy to any pelvic organ in pouch patients must be carefully balanced. The small bowel

mucosa, including pouch mucosa, is more vulnerable to radiation injury than solid organs, skin, muscles, and bones.<sup>2</sup> Radiation injury can affect the intestinal vasculature that may lead to ischemia-type injury, fibrosis, and stricture or fistula formation. Radiation injuries to the pouch can cause acute as well as chronic pouchitis in those patients.

It is estimated that 3%-13% of patients with a preoperative diagnosis of ulcerative colitis or indeterminate colitis develop CD or a CD-like condition of the pouch.<sup>3</sup> CD of the pouch can occur after diagnosis of CD before surgery, intraoperative diagnosis of CD upon examination of surgical colectomy specimens, or development of postoperative de novo CD. The latter condition is most common. The reported risk factors for CD of the pouch include smoking,<sup>4</sup> family history of CD,<sup>5,6</sup> and being Ashkenazi Jews.<sup>7</sup>

Diagnosis of CD of the pouch is mainly based on a combined assessment of clinical, endoscopic, radiographic, and histologic features. Classic features of CD of the pouch are segmental disease distribution in the pouch body and/or afferent limbs, multiple ulcerated strictures, particularly at the afferent limb, and the presence of late-onset perianal or vaginal fistula (>12 months after ileostomy closure). In some patients, histology may show noncaseating, nonmucinous granulomas. Our patient did not have those features. At one point after the surgery, he developed a self-limited simple perianal fistula, which is believed to be due to cryptoglandular abscess and not due to CD. The exclusion of CD or a CD-like condition in IPAA patients is critical, since radiation therapy can potentially aggravate CD of pouch.

Management of prostate cancer using medical versus surgical versus radiation therapy should be carefully considered. It is difficult to accurately predict the preoperative or postoperative effects of radiotherapy with or without chemotherapy on bowel's structure and function in patients with prostate cancer. Several factors need to be carefully analyzed in



**Figure 2.** (A) Endoscopy of pouch body after radiation revealed mucosal inflammation with ulcers and erythema, predominantly at the distal pouch and cuff. Histology of the (B) distal pouch body (40x) and (C) afferent limb (100x) showed chronic active enteritis with erosions, telangiectatic vessels, focal perivascular hyalinization, and vessels with thickened walls.

determining radiotherapy, including age of the patient, comorbidities, quality of life, and overall patients' and clinicians' expectations. For instance, the origin of malignancies (uterine, cervix, ovary, rectum, or prostate) and the presence of prior pelvic surgery in the area, such as total proctocolectomy and IPAA, will affect the decision on whether and what radiation therapy is performed. Our previous historic cohort study has shown that preoperative pelvic radiation in patients with a history of inflammatory bowel disease-related colorectal cancer and restorative proctocolectomy seemed to have poor pouch outcomes, with a higher risk for pelvic abscess and chronic pouchitis.<sup>8</sup> Importantly, most patients post IPAA seemed to become prone to develop pouch dysfunction and even pouch failure. Interestingly, a recent retrospective study showed that permanent prostate brachytherapy could be a better option in IPAA patients.<sup>9</sup> The permanent prostate brachytherapy would protect the pouch from excessive radiation by using the mesenteric pad as an "anatomical buffer zone" in between the anterior pouch wall and the prostate.<sup>9</sup>

## DISCLOSURES

Author contributions: G. Kulkarni reviewed the data and prepared the manuscript. X. Liu reviewed the histology and the manuscript. B. Shen reviewed the manuscript and is the article guarantor.

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Informed consent was obtained for this case report.

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