

## Abstract

Pelvic Radiation Disease (PRD) is radiation-induced toxicity of tissues resulting in acute or chronic gastrointestinal and genitourinary complications. Some of these complications include rectal/urinary bleeding, ureteral strictures, fistulas, and osteonecrosis. Although a rare occurrence, the variability in presentation and the time between undergoing radiation therapy and the onset of symptoms can make diagnosis challenging. This case presents a 68-year-old patient with a history of cervical cancer who underwent a total abdominal hysterectomy followed by pelvic radiation therapy in 1992. She had no known complications until a traumatic fall in 2023 which led to the incidental finding of hydronephrosis. Through a series of hospital visits over the next six months, a sequela of other complications, including extensive gastrointestinal and genitourinary fistulas, ureteric stenosis, severe rectal and vaginal bleeding, and osteomyelitis of the pubic symphysis, arose. With growing rates of survivability from pelvic cancers, it is imperative that physicians are aware of the long-term, late complications of pelvic radiation therapy and effective management options. Early intervention using multidisciplinary teams can lead to more optimal patient outcomes.

## Background

- Pelvic Radiation Disease is radiation induced toxicity of nearby tissues resulting in acute or chronic complications
  - Chronic pelvic radiation disease can present as hematochezia, hematuria, ureter stricture, necrotic bladder masses, fistulas, chronic osteomyelitis, and sexual dysfunction
- Most common applications of radiotherapy in the pelvis include treatment of prostate, gynecological, and anorectal cancer. Radiotherapy damages the DNA of cancer cells through direct or indirect ionization.
- Even with the new advances in radiation therapy including intensity modulated radiotherapy (IMRT), toxicity to healthy tissue has been reduced but not eliminated
- Over 50% of patients who have undergone pelvic radiation state that their quality of life is affected by gastrointestinal symptoms

## Pathogenesis

- The earliest pathogenesis was explained as radiation induced necrosis of tissue that leads to fibroblast proliferation and fibrosis. As a result, neovascularization ensues which gives rise to abnormal blood vessels and friable tissue
- Other theories have proposed that radiation induces damage to the enteric nervous system or causes changes in the gut microbiota which all influence intestinal toxicity

## Case Presentation

**1992:** At 36 years old, patient underwent total abdominal hysterectomy with subsequent pelvic radiation due to cervical cancer

**7/23/2023:** At 67 years old, she was admitted to the hospital due to a traumatic fall causing subarachnoid hemorrhage. Upon abdominal imaging, incidental bilateral hydronephrosis was discovered.

- **8/10/2023:** Patient was discharged from the hospital to a rehab facility
- **10/4/2023:** Admitted to the hospital due to urosepsis. A new rectovesicular fistula, necrotic bladder mass, and persistent hydronephrosis was identified upon admission. At this time, degenerative changes of the sacroiliac and pubic symphysis joints were noted.
- **10/7/2023:** Underwent cystoscopy to biopsy bladder mass (benign) and place right ureteral stent
- **10/9/2023:** PEG tube placed due to failed response to oral stimulants. Patient was transitioned to total parenteral nutrition (TPN) due to persistent nausea, vomiting, and diarrhea with PEG tube feeds.
- **10/10/2023:** Percutaneous nephrostomy tube was placed to increased drainage of right kidney
- **10/23/2023:** Underwent transverse loop colostomy due to persistent stooling from vagina and rectum
- **10/30/2023:** Patient diagnosed with bilateral deep venous thrombosis (DVT) so she was put on Heparin
- **11/2/2023:** IVC filter placed due to development of heparin-induced thrombocytopenia (HIT)
- **11/16/2023:** Percutaneous cholecystostomy due to emphysematous cholecystitis
- **11/28/2023:** Tertiary facilities declined acceptance of patient, and therefore she was discharged to a long-term nursing facility
- 12/3/2023:** Returned to hospital due frank blood in her ostomy bag
- **12/4/2023:** CT abdomen/pelvis (CTAP) showed numerous fistulous tracts from the posterior bladder to the anterior rectum and to the vagina, sigmoid colon, as well as cecum. Further imaging noted more fistulas going from the dome of the bladder to the small bowel loops. The cecum and terminal ileum were noted to be adherent to the right ureter and iliac vessels. Imaging also suggested possible rupture/dehiscence of the bladder. CTAP additionally showed osteomyelitis of pubic symphysis that was likely chronic in nature.
  - Fistulas were large and difficult to measure on CT but estimated to be 14.1 cm on coronal imaging
- **1/5/2024:** Discharged back to long-term care facility
- 2/2/2024:** Returned to hospital due to continued bleeding through her colostomy and nephrostomy
- **2/9/2024:** GI performed colonoscopy which led to numerous fistulous tracts. Friable tissue with reduced vasculature noted but no polyps or lesions concerning for a cancerous process were visualized.
- **2/13/2024:** Urology removed the right ureteral stent at bedside to attempt bleeding control
- **2/16/2024:** Throughout this hospital admission, advanced GI, ACS, luminal GI, urology, OBGYN, and gynecology-oncology were all consulted and agreed that patient was a poor surgical candidate. Patient declined conversations regarding palliative care. She was discharged back to long-term nursing facility.

## Images



Figure 1. CTAP with contrast in a coronal view, showing 14.1 cm fistulous tract from the bladder wall to the cecum

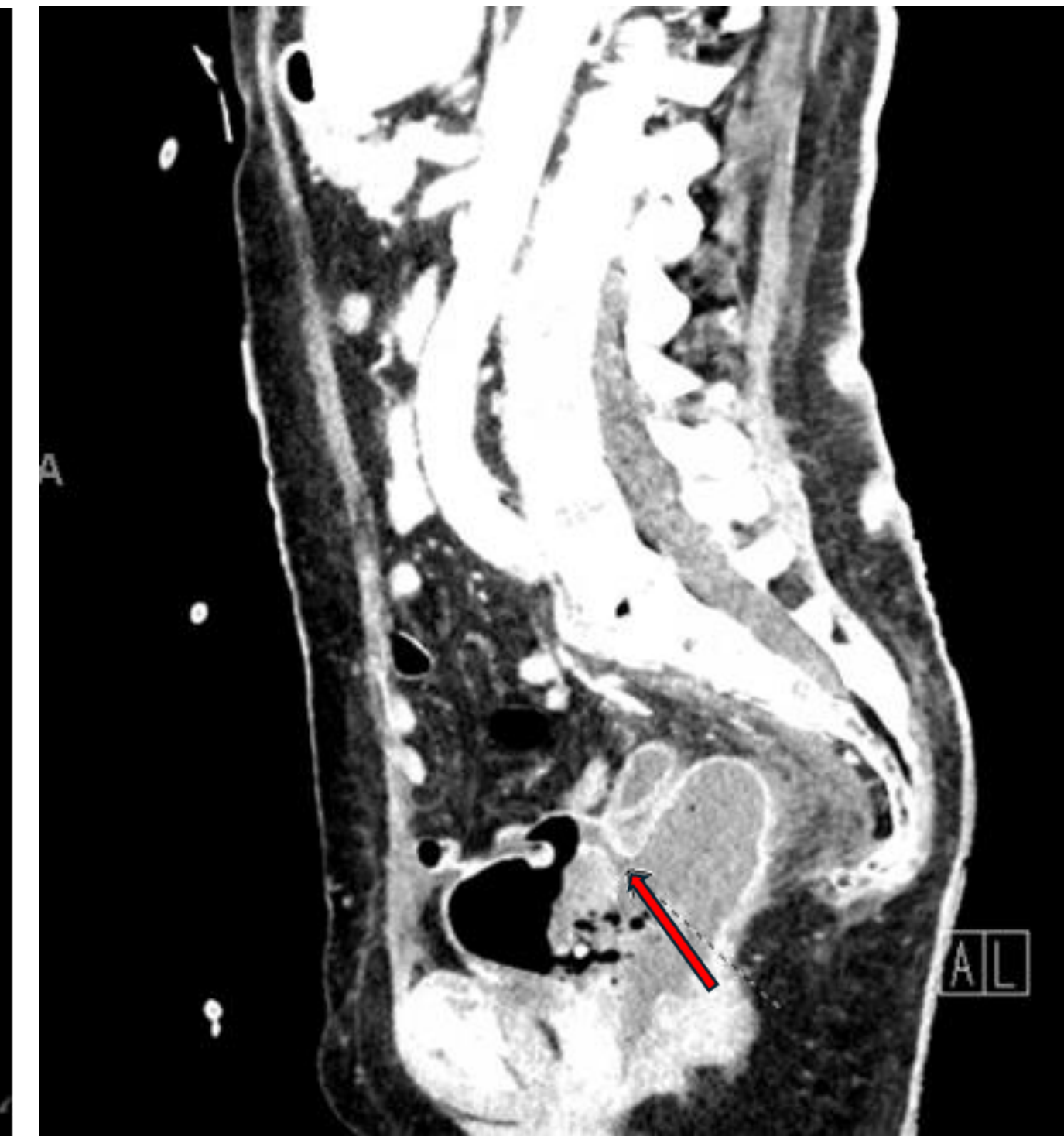


Figure 2. CTAP with contrast in a sagittal view. Red arrow demonstrates a fistulous tract between the anterior rectum and bladder wall.

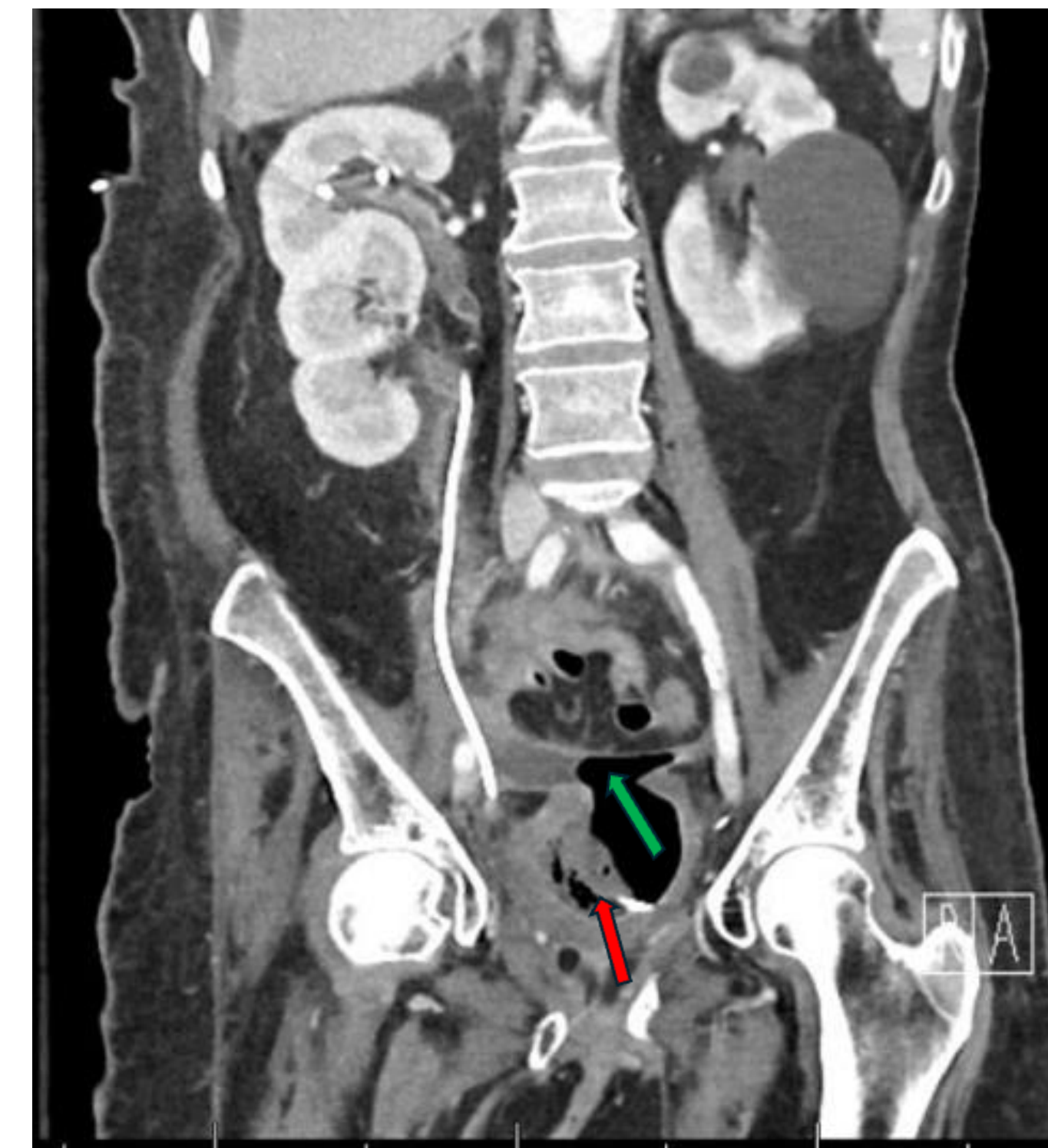


Figure 3. CTAP in a coronal view. Red arrow shows fecal material within the bladder. Green arrow shows fistulous tract between dome of the bladder and small bowel.

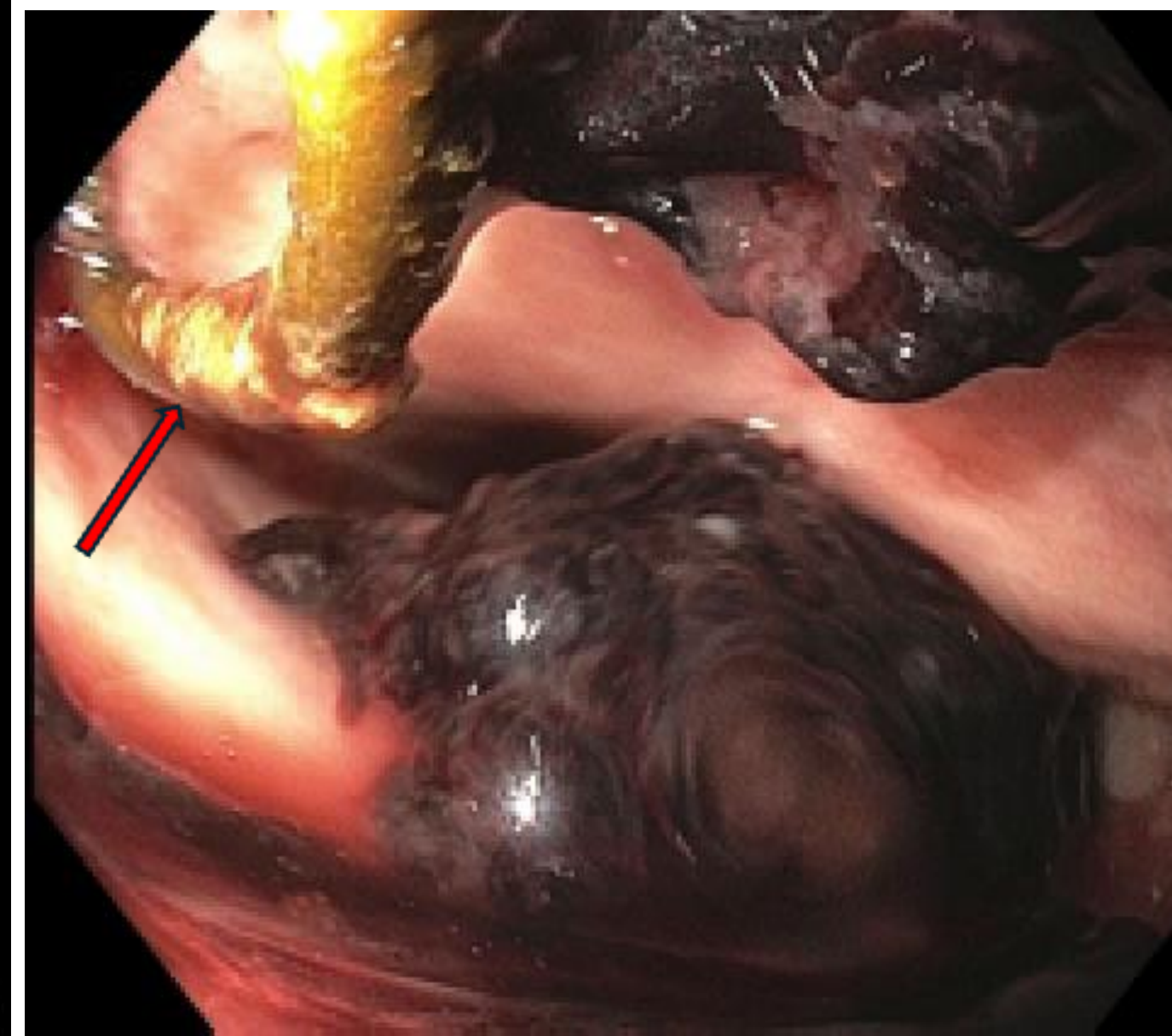


Figure 4. Gastroscope entered through the colostomy stoma, which led to an orifice. The orifice was hard to identify anatomically, but a plastic stent was seen traversing through the defect.

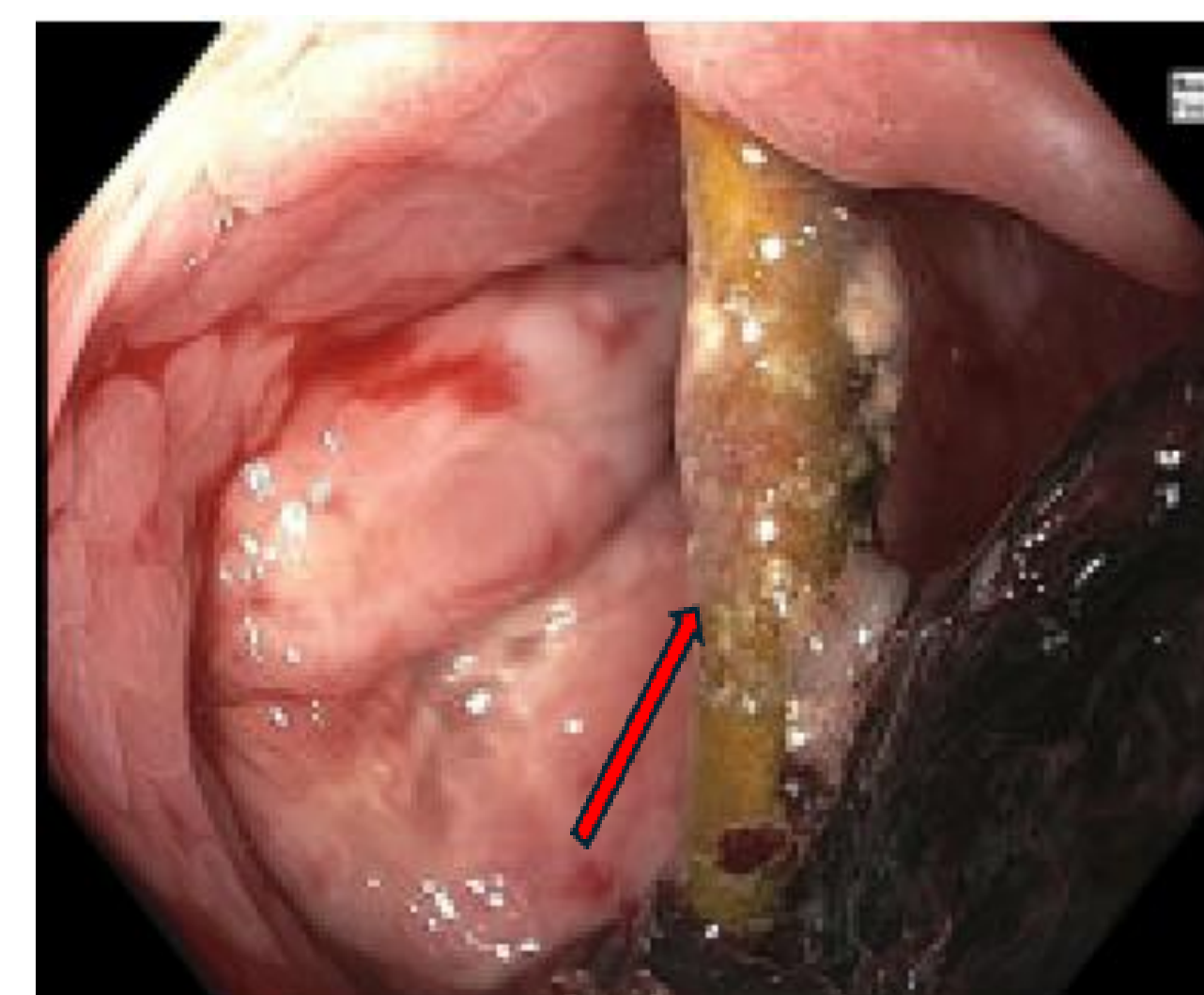


Figure 5. Gastroscope reinserted through the rectum. Clots noted as well as the plastic stent (red arrow) traversing an orifice through the rectal wall into the rectum. Friable tissue visualized.

## Management

### Ureteral stricture:

- Short term treatment includes ureteric stent placement
- Long term management includes surgical resection with re-implantation of the ureter using a bladder flap technique or ileal interposition
  - For more complicated cases, diversion and nephrectomy remains an option

### Hematochezia:

- Multiple treatments of argon plasma coagulation (APC) via colonoscopy or flexible sigmoidoscopy
  - If this fails, Formalin 4% topical instillation
- Sucralfate enemas and metronidazole
- For more severe cases, HBO therapy and surgical resection of the bowel segment

### Hematuria:

- Resuscitation, anticoagulation reversal, and catheterization with a three-way indwelling catheter. The catheter should be used to wash out the bladder, evacuate clots, and continuously irrigate
  - If bleeding and clotting is too extensive then manual clot evacuation using cystoscopy may be needed along with electro- or laser coagulation
  - Tranexamic acid can be used for severe persistent bleeding, but the data is limited
- Aluminum salt irrigation, formalin, or glycosaminoglycan replacement although the efficacy and long-term benefit is poorly understood
- Hyperbaric oxygen therapy (HBO) shows complete response rates of up to 65%
- Severe cases can be managed with surgical urinary diversion with an ileal conduit with or without cystectomy
  - Due to the poor wound healing and ureter fibrosis in the setting of PRD, this surgery has high morbidity and mortality

### Fistula:

- Initial workup to assess bladder and rectal anatomy as well as exclude alternate causes of fistula development such as malignancy are recommended. This includes MRI, cystoscopy, urethrogram, urodynamic studies, and flexible sigmoidoscopy. To assess for malignancy, biopsies should be taken and if any cancer is found, a surveillance or staging CT or PET should be performed prior to surgery.
- Small to medium sized fistulas:
  - Colostomy diversion for up to 6 months. During this time, optimizing nutrition, treating any underlying infection, and implementing HBO can support tissue healing
  - Once diversion is complete, a cystoscopy should be used to restage the fistula based on size which will guide further surgery
- Large defects (>3cm) or failed initial repair have options of permanent diversion or total pelvic exenteration
- In a study comparing results of restorative resection and pull-through coloanal anastomosis with a prophylactic colostomy versus simple colostomy without resection, the restorative resection showed better remission of tenesmus and perineal mucous discharge

### Osteonecrosis of pubic symphysis:

- Initial therapy is with pain management and physiotherapy
  - Treat any secondary complication (i.e. abscess, urinary tract infection (UTI), cutaneous or rectal fistula)
- For surgical candidates who seek long term treatment, a combination of cystectomy, loop urinary diversion, and complete pubic symphysis resection have improved pain and function

## Discussion

- Failure to recognize PRD can lead to a misdiagnosis of an inflammatory process and subsequent treatment with anti-inflammatory agents which are not helpful since radiation induced injury is due to tissue necrosis
- Often, PRD presents with multi-organ involvement therefore if a patient with a history of pelvic radiation presents with an isolated symptom or finding that fits the clinical picture of PRD, the physician should be queued to actively look for other areas of involvement
- Multidisciplinary teams including specialties such as urology, gastroenterology, hematology/oncology, obstetrics and gynecology, gynecology-oncology, plastic surgery, general surgery and more are needed to treat patients with PRD

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