Radiation proctitis: Clinical manifestations, diagnosis, and management

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INTRODUCTION

Radiation injury to the lower intestine may result following treatment of cancers of the rectum, anus, cervix, uterus, prostate, urinary bladder, and testes. The rectum and sigmoid colon are most often affected.

Radiation proctitis is inflammation of the rectum that occurs as a result of acute damage to the rectum sustained from pelvic radiation. In patients with chronic radiation injury, the term chronic radiation proctitis is generally used but is somewhat misleading, since it inaccurately implies a chronic inflammatory condition of the rectum [1,2]. The term "radiation-associated vascular ectasias" ("RAVE") has been proposed for cases in which bleeding from vascular ectasias, rather than fibrosis and ischemia, is the predominant feature in patients with chronic radiation injury [3]. Chronic radiation injury may also manifest as radiation proctopathy, defined as epithelial damage to the rectum due to radiation that is associated with minimal or no inflammation. This topic will review the clinical features, diagnosis, and treatment of acute radiation proctitis and chronic radiation injury (RAVE and chronic radiation proctopathy). The adverse effects of radiation therapy on the esophagus, stomach, small and large intestine, anus, and liver are discussed separately. (See "Overview of gastrointestinal toxicity of radiation therapy" and "Diagnosis and management of chronic radiation enteritis".)

EPIDEMIOLOGY AND PATHOGENESIS

Incidence — Acute radiation proctitis occurs during or within six weeks of radiation therapy. Reliable estimates of the incidence of radiation proctitis are not available due to variability in the definition and reporting of radiation proctitis. However, the incidence of radiation proctitis in patients treated with brachytherapy alone is estimated to range from 8 to 13 percent and up to 21 percent when used in combination with other modalities [4].

Chronic radiation injury may occur as a continuation of acute radiation proctitis or have a delayed onset (9 to 14 months following radiation exposure to 30 years after exposure) [5-7]. The reported incidence of chronic radiation injury ranges from 2 to 20 percent [8].

Risk factors — Risk factors for radiation proctitis include the dose of radiation, area of exposure, and method of delivery. Doses of radiation <45 Gy are associated with few long-term radiation side effects. In contrast, doses between 45 and 70 Gy cause more complications, and doses above 70 Gy cause significant and longstanding injury to the surrounding area [9,10].

The method of radiation delivery is an important predictor of the risk of radiation proctitis. External beam radiation, typically administered by a linear accelerator, results in significantly greater exposure to surrounding organs as compared with brachytherapy, where radiation is administered via radioactive implants. Newer modalities of external beam radiation delivery, including three-dimensional conformal radiation therapy, intensity-modulated radiation therapy (eg, image-guided radiation therapy, volumetric-modulated arc therapy), and the use of heavy particles including protons and neutrons, minimize the dose of radiation to the rectum while maximizing the dose to the tumor. (See "Radiation therapy techniques in cancer treatment", section on 'External beam radiation therapy' and "Radiation therapy techniques in cancer treatment", section on 'Brachytherapy'.)

Other potential risk factors include inflammatory bowel disease and HIV/AIDS, which may increase the susceptibility of the underlying mucosa to the adverse effects of radiation [11-13]. There are data to suggest that genetic predisposition may play a role [14].

Use of adjunctive medical therapy (eg, amifostine) to decrease the risk of radiation proctitis has had only a minimal effect, and such agents are not widely used. Sucralfate has also been evaluated for prophylaxis against acute radiation injury. However, placebo-controlled phase III trials have detected no benefit from either topical or oral sucralfate [15,16]. In one randomized trial, the use of aloe vera topical ointment during radiotherapy resulted in reduction in the incidence of symptoms of radiation proctitis as compared with placebo, but further studies are

needed to validate these results [17]. (See "External beam radiation therapy for localized prostate cancer", section on 'External beam radiation therapy techniques'.)

Mechanism of injury — Acute radiation proctitis is caused by direct mucosal damage from radiation exposure. Chronic radiation proctitis results from progressive epithelial atrophy and fibrosis associated with obliterative endarteritis and chronic mucosal ischemia. The pathogenesis of radiation-induced injury to the intestine is discussed in detail separately. (See "Overview of gastrointestinal toxicity of radiation therapy", section on 'Pathogenesis'.)

CLINICAL MANIFESTATIONS

- **Acute radiation proctitis** — Symptoms of acute radiation proctitis include abdominal or pelvic pain, diarrhea, mucus discharge, urgency, and tenesmus. Rectal bleeding is rare.

- **Chronic radiation injury** — Patients with chronic radiation injury can present with symptoms of acute radiation proctitis that persist or with new onset of symptoms months to years following radiation therapy. The most common manifestation is rectal bleeding and iron deficiency anemia due to bleeding secondary to radiation-associated vascular ectasia (RAVE). Patients may also present with chronic radiation proctopathy with symptoms of urgency, change in stool caliber and consistency, constipation resulting from underlying fibrosis, and, rarely, fecal incontinence due to overflow diarrhea and increased mucus.

  Concomitant injury to the genitourinary tract or small bowel may lead to fistulas, small bowel obstruction, and small intestinal bacterial overgrowth. Patients with rectovaginal fistulas may present with uncontrollable passage of gas or feces from the vagina, a malodorous vaginal discharge, and fecal soiling of the undergarments. These symptoms may be more pronounced when patient bowel movements are loose. Occasionally, a small fistula may be asymptomatic. Patients with a colovesicular fistula generally present with lower urinary tract symptoms, of which pneumaturia, fecaluria, and suprapubic pain are the most frequent. (See "Rectovaginal and anovaginal fistulas", section on 'Clinical manifestations' and "Colovesical fistulas", section on 'Clinical manifestations' and "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Clinical features'.)

DIAGNOSTIC APPROACH

Evaluation of a patient with suspected radiation proctitis serves to exclude other causes of proctitis and a malignancy, establish the diagnosis of radiation proctitis, and determine the extent and severity of the disease.

Clinical suspicion — The diagnosis of acute radiation proctitis should be suspected in patients with diarrhea, mucus discharge, urgency, tenesmus, or bleeding during or within six weeks of radiation therapy. Chronic radiation proctitis should be suspected in patients with a history of pelvic radiation exposure who present with symptoms of constipation, rectal pain, rectal bleeding, or urgency.

Evaluation — The goal of the evaluation is to exclude other etiologies and confirm the diagnosis of radiation proctitis.

History — A history of risk factors for other causes of colitis should be sought. This includes a history of recent travel to areas endemic for parasitic infections including amebiasis, recent antibiotic use that might predispose to an infection with *Clostridioides difficile*, and a history of or risk factors for sexually transmitted diseases (eg, *Neisseria gonorrhoeae* and herpes simplex virus [HSV]) that are associated with proctitis. Atherosclerotic disease or prior ischemic episodes are suggestive of chronic colonic ischemia. A history of nonsteroidal antiinflammatory drug (NSAID) exposure should be sought, as these drugs (and others) may also be associated with colitis. In an immunocompromised patient, cytomegalovirus (CMV) can cause colitis. (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults", section on 'Differential diagnosis' and "NSAIDs: Adverse effects on the distal small bowel and colon" and "Colonic ischemia".)

Laboratory studies

- Laboratory evaluation should include a complete blood count, electrolytes, albumin, and markers of inflammation (eg, erythrocyte sedimentation rate/C-reactive protein [CRP]).
- In patients with diarrhea, stool studies should include stool *C. difficile* toxin, routine stool cultures (*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*), and specific testing for *Escherichia coli* O157:H7. Microscopy for ova and parasites (three samples) and a Giardia stool antigen test should also be performed, particularly if the patient has risk factors such as recent travel to endemic areas.
- In patients with rectal symptoms including urgency and tenesmus, testing for sexually transmitted infections, including *C. trachomatis, N. gonorrhoeae,* HSV, and *Treponema pallidum,* may be warranted, particularly in men who have sex with men. (See "Clinical manifestations and diagnosis of *Neisseria gonorrhoeae* infection in adults and adolescents"

and "Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus in patients with HIV" and "Syphilis: Screening and diagnostic testing".)

Endoscopy — Endoscopic findings in patients with radiation proctitis are nonspecific. Endoscopic features of acute radiation proctitis include edematous, erythematous mucosa that may have ulceration or sloughing. Rectal biopsies should be performed carefully when the diagnosis of acute radiation proctitis is in doubt and should take into account the timing, dose, and fractionation of previous pelvic radiation therapy. If required, they should be directed at the posterior and lateral walls to avoid the irradiated areas. Although studies have reported fistula formation following rectal biopsies over the prostate, it is likely that patients in whom this occurred had severe necrosis, and hence, the contribution of the biopsy to the fistula formation is unclear [18].

Endoscopy remains the mainstay of diagnosis for chronic radiation changes in the rectum, and the hallmark feature includes the presence of vascular ectasias. Other endoscopic findings include mucosal edema and pallor. Rare cases of strictures and fistulas can be diagnosed with endoscopy or imaging.

Mucosal features consistent with chronic radiation injury include pallor with friability and telangiectasias, which can be multiple, large, and serpiginous. These changes tend to be continuous, without skip lesions, but can be varying in intensity [19]. In patients with chronic radiation proctopathy, the rectum appears pale, edematous, and noncompliant, and may have strictures, fistulas, and areas of mucosal hemorrhage.

Biopsies in patients with vascular ectasias show dilated and tortuous mucosal capillaries lined by endothelial cells with prominent nuclei and surrounded by a cuff of hyalinized lamina propria, dilated blood vessels, and microthrombi that closely resemble the histologic appearance of gastric antral vascular ectasias.

In patients with chronic radiation proctopathy, findings include fibrosis of the lamina propria and a variable degree of epithelial injury, crypt distortion, and Paneth cell metaplasia. Important distinguishing characteristics include a lack of inflammatory cell infiltrates and ulcerations. Although mucosal biopsies are not specific, they can help to exclude other causes of proctitis such as infection or inflammatory bowel disease [20]. A histologic classification system has been proposed, but its role has not been defined [21]. (See "Endoscopic diagnosis of inflammatory bowel disease in adults".)

Imaging in selected patients — Abdominal imaging should be performed in selected patients with a suspected colovesical fistula and in patients with obstructive symptoms. The evaluation of patients with a colovesical and rectovaginal fistula is discussed in detail separately.

(See "Colovesical fistulas", section on 'Evaluation and diagnosis' and "Rectovaginal and anovaginal fistulas", section on 'Evaluation and diagnosis'.)

Establishing the diagnosis — The diagnosis of radiation proctitis is based on endoscopy and histology in the setting of supportive history after the exclusion of alternative diagnoses.

Differential diagnosis — The differential diagnosis of radiation proctitis includes other causes of proctitis, including infectious colitis, inflammatory bowel disease, diversion colitis, ischemic colitis, chronic graft-versus-host disease, diverticular colitis, and medication-associated colitis. These conditions can be distinguished from radiation proctitis by history, laboratory studies, and, if permissible, biopsies of the colon and are discussed in detail separately. (See 'Diagnostic approach' above and "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults", section on 'Differential diagnosis'.)

MANAGEMENT

There have been no large controlled trials evaluating the treatment of radiation proctitis [22]. Thus, experience is derived mostly from case reports and small clinical trials [23-31]. Clinical practice guidelines have been published by the American Society of Colon and Rectal Surgeons [32].

Acute radiation proctitis — While acute proctitis is self-limiting, up to 20 percent of patients undergoing external beam radiation will require short interruptions in their treatment to improve symptoms. We treat patients with acute radiation proctitis with supportive treatment consisting of hydration and antidiarrheals as needed. In addition, we use sodium butyrate enemas for three weeks to induce remission of symptoms [33,34]. The efficacy of sodium butyrate, a short-chain fatty acid, was demonstrated in a small randomized cross-over trial in which 20 patients with acute radiation proctitis were assigned to topical sodium butyrate or saline enemas for three weeks [33]. Topical butyrate led to remission of symptoms, with a reduction in clinical symptom severity score at the end of treatment. In one retrospective study that included 31 patients with acute radiation proctitis, 74 percent experienced an improvement in symptom severity within eight days of treatment [34]. However, in this study, the use of sodium butyrate enemas for acute radiation proctitis did not impact the incidence and severity of late proctitis [34]. Prophylactic use of butyrate enemas does not appear to decrease the incidence, severity, or duration of radiation proctitis [35].

Chronic radiation injury

Mild symptoms — Specific therapy may not be necessary in those who have only mild and infrequent symptoms, such as occasional hematochezia or mild tenesmus. In patients with bothersome symptoms, the choice of treatment is based on the pattern of symptoms [36].

- Sucralfate **enemas** – We treat patients with bothersome or persistent rectal pain or tenesmus or bleeding with sucralfate enemas (20 mL of a 10 percent sucralfate suspension in water twice daily). Several studies have suggested that topical sucralfate may improve symptoms of radiation proctitis or proctosigmoiditis [23,37-42]. The rationale for its use is based upon its favorable effects on epithelial microvascular injury [43,44]. In a randomized trial, 37 patients with radiation-induced proctosigmoiditis were assigned to a four-week course of oral sulfasalazine plus prednisolone enemas or sucralfate enemas [23]. Clinical improvement was noted in both groups at the end of the study. Although the endoscopic response was not different between groups, the clinical response for sucralfate enemas was better as compared with oral sulfasalazine and prednisolone enemas. Sucralfate enemas were also better tolerated.

  Remission of bleeding may be sustained following discontinuation of sucralfate. A prospective study included 26 patients with moderate to severe radiation proctosigmoiditis who were treated with sucralfate enemas (20 mL of a 10 percent suspension twice daily) until bleeding stopped or failure of therapy was acknowledged [37]. Reduction in the severity of bleeding was observed in 77 percent of patients by four weeks and 92 percent by 16 weeks. At a median follow-up of 46 months (range 5 to 73 months) after cessation of bleeding, 17 (71 percent) patients had no further bleeding, while 7 (22 percent) had recurrence of bleeding. Further studies are needed to confirm these results.

- **Stool softeners** – We use stool softeners for patients with mild obstructive symptoms, such as constipation related to strictures. However, endoscopic therapy may be needed in patients with persistent symptoms. (See "Management of chronic constipation in adults", section on 'Surfactants'.)

Endoscopic therapy for severe or persistent symptoms

Patients with bleeding — We treat patients with persistent bleeding despite a four-week trial of sucralfate enemas or with severe bleeding with endoscopic therapy. Argon plasma coagulation (APC) is effective in reducing the short-term symptoms (<6 weeks) of chronic radiation injury [30]. A variety of other endoscopic methods have also been used to treat radiation colitis. Other reasonable alternatives to APC include bipolar electrocoagulation, heater probe, radiofrequency ablation, and cryoablation [45]. However, there is significant

heterogeneity in the studies evaluating the efficacy of these endoscopic therapies, and few studies have directly compared them [46]. Due to the potential risk of rectourethral fistulas in the first six months to two years after radiation therapy, the decision to pursue endoscopic management should be made with a urologic radiation oncologist [18]. Avoidance or minimal therapy of the distal 2 cm of the rectum may reduce postprocedure tenesmus and fecal incontinence.

- **Argon plasma coagulation** – APC uses high-frequency energy transmitted to tissue by ionized gas.

  The efficacy of APC has been suggested in several case series [47-52]. An illustrative report included 28 patients with persistent bleeding despite medical therapy [47]. The majority of patients had improvement in bleeding and anemia after a median of 2.9 sessions (range one to eight). All visible lesions were targeted at each session, and follow-up procedures were scheduled in four-week intervals to allow the tissue to heal (picture 1). The mean hemoglobin rose by 1.2 g/dL and by 1.9 g/dL among individuals presenting with anemia. Some patients experienced postprocedure rectal pain and cramps, but no major complications occurred. In a study of 35 patients with chronic radiation proctitis following external beam radiation therapy for prostate cancer, bleeding was controlled in 30 (85.7 percent) after a median of two sessions (range 1 to 13) of APC [53]. Other reports have demonstrated that APC may control bleeding even after unsuccessful treatment using other methods [48,49]. Special care is required to avoid spraying too close to the dentate line.

  Mesalamine suppositories and/or glucocorticoid enemas are often used to help treat rectal ulceration associated with APC [54]. In order to minimize the risk of bowel explosion with perforation due to the accumulation of combustible colonic gas, a complete bowel lavage should be performed prior to the use of APC [55]. The use of APC to treat other bleeding lesions in the gastrointestinal tract is discussed in detail separately. (See "Argon plasma coagulation in the management of gastrointestinal hemorrhage".)

- **Bipolar electrocoagulation (BiCap) and heater probe** – BiCap and heater probe have several advantages as compared with laser therapy. They cause less tissue injury and permit tangential application of cautery, and the equipment needed is widely available and relatively inexpensive. However, it is unclear if they are more effective in treating chronic radiation proctitis as compared with other modalities. BiCap and heater probe were evaluated in a study involving 21 patients with chronic recurrent hematochezia and anemia due to radiation-induced injury who were followed for 12 months [25]. Patients were treated with either BiCap or heater probe therapy as needed. Severe bleeding

diminished significantly after these treatments as compared with the previous 12 months of medical therapy (75 versus 33 percent and 67 versus 11 percent, respectively). There were no major complications.

- **Radiofrequency ablation** – Radiofrequency ablation (RFA) has been used in case reports to treat radiation proctitis refractory to APC [56,57]. RFA has the advantage over other methods in that it covers a broader surface area and has a uniformly shallow depth of injury (<1 mm), making it ideal for radiation proctitis. However, additional studies are needed to assess the long-term effects of RFA and its role in the treatment of radiation proctitis [57].

- **Other endoscopic therapies with unclear role**

  - **Band ligation** – A case report and a case series have described band ligation to control bleeding from chronic radiation proctitis [58,59].

  - **Lasers** – Argon, Nd:YAG, and diode lasers have been used to coagulate bleeding ectatic vessels throughout the gastrointestinal tract [60-65]. A systematic review of four studies that included 65 patients treated with Nd:YAG laser found an improvement in symptoms in 78 percent of patients (range 58 to 87 percent) [61]. However, the Nd:YAG laser is expensive and not widely available.

  - **Cryoablation** – Controlled trials are needed to establish the safety and efficacy of cryoablation for radiation proctitis [66]. In a pilot study, 7 out of 10 patients with radiation proctitis responded to cryoablation with a decrease in rectal telangiectasia density and improvement in radiation proctitis symptom severity. One complication of cecal perforation due to gas overdistention was observed.

  - **Formalin** – Formalin induces coagulative tissue necrosis on contact, providing the rationale for its use in patients with radiation proctitis who have significant bleeding [67-76]. Although the procedure has generally been well tolerated, and several studies have reported an improvement in symptoms, APC may be more effective in treating radiation proctitis as compared with formalin therapy; however, in one study, the endoscopic therapeutic success rate of endoscopic installation of formalin was over 92 percent and equivalent to that for APC [77]. Overall, there is insufficient evidence to support the use of formalin [30]. In addition, serious complications, including the development of fistulas requiring colostomy and bowel necrosis requiring resection, have also been described [70].

Patients with obstructive symptoms — Stricture dilation (balloon or Savary-Gilliard) can be effective in patients with obstructive symptoms from strictures that do not respond to stool softeners, provided that the strictured segment is short [78]. The risk of perforation is increased in patients with a long or angulated stricture. Surgery may be preferable in such cases. (See 'Surgery for intractable symptoms and complications' below and "Endoscopic interventions for nonmalignant esophageal strictures in adults", section on 'Types of dilators'.)

Surgery for intractable symptoms and complications — Surgery is reserved for patients who have intractable or progressive symptoms despite pharmacotherapy and/or endoscopic therapy (eg, pain, bleeding) or those that are not amenable to endoscopic therapy (eg, long/angulated stricture, perforation, fistula). Anastomotic breakdown of irradiated tissue is a potential complication of surgery [79]. Surgery may also be technically demanding due to adhesions and has been associated with a high risk of complications (15 to 80 percent) and mortality (3 to 9 percent) [7,80-82]. In one study of 48 patients with severe refractory radiotherapy complications that had failed initial treatment, surgery was generally required for patients with a fistula, and permanent diversion was more likely in patients with severe radiation enteritis and a distal colonic stricture [83]. In patients with severe and intractable bleeding, a diverting loop colostomy only rarely controls bleeding and leaves the patient at risk of further complications, including perforation and abscess formation [84]. In such cases, proctectomy may be the only option. In this setting, construction of an ileocecal reservoir has been associated with a good functional outcome [85]. The management of rectovaginal fistulas is discussed in detail separately. (See "Rectovaginal and anovaginal fistulas".)

Other therapies with an unclear role — Several other therapies have been evaluated in patients with radiation proctitis. However, there is limited evidence to support their use [22,30].

- **Hyperbaric oxygen** – Hyperbaric oxygen (HBO) therapy is expensive, not widely available, and therefore an impractical means of treating chronic radiation proctitis outside of centers specializing in this approach. HBO therapy has been associated with improved outcomes in patients with radiation proctitis in observational studies and in a randomized controlled trial [86-92]. However, these studies have methodologic limitations. As an example, a randomized trial included 120 patients with refractory radiation proctitis who were assigned to HBO or to a sham procedure [87]. The clinical response rate was significantly higher in the intervention group as compared with the sham control group (89 versus 63 percent). In addition, symptom improvement was accompanied by a decreased requirement for other treatments. However, the study was potentially limited by a large number of dropouts after allocation. The mechanism of action of HBO,

technique, and complications associated with HBO therapy are discussed in detail separately. (See "Hyperbaric oxygen therapy".)

- **Hormonal therapy** – There are limited data to support the use of hormonal therapy with estrogen (with or without progesterone) in patients with chronic radiation proctitis [93]. However, side effects of hormonal therapy observed during treatment of patients with angiodysplasias are common, and reports of the efficacy of therapy have been conflicting. (See "Angiodysplasia of the gastrointestinal tract", section on 'Hormonal therapy'.)

- **Antioxidants** – The possible role of oxidative injury in chronic radiation proctitis provided the rationale for a study of antioxidants, but controlled trials are needed before antioxidant therapy can be recommended [94,95]. A small uncontrolled study involving 10 patients suggested that treatment with vitamin E (400 international units three times daily) and vitamin C (500 mg three times daily) was associated with improvement in diarrhea and urgency [94]. Important limitations of the study include a high dropout rate, relatively subjective endpoints used, and absence of a control group.

  A potential role for vitamin A was suggested in a pilot randomized trial in which 18 patients with radiation proctitis were assigned to oral retinol palmitate or placebo for 90 days [96]. Patients randomized to retinol palmitate were significantly more likely to respond as compared with placebo (70 versus 22 percent). In addition, five nonresponders who initially received placebo subsequently responded when treated with retinol palmitate. Larger studies are needed to validate these results.

- **Topical** metronidazole **and glucocorticoids** – The efficacy of glucocorticoid enemas alone has been poorly studied, and clinical experience with topical steroids has been disappointing. However, studies suggest that metronidazole may have synergistic effects with glucocorticoids in treating the symptoms of chronic proctitis. The efficacy of metronidazole was evaluated in a study that included 60 patients with rectal bleeding and diarrhea who were randomly assigned to treatment with mesalamine plus betamethasone enemas with or without metronidazole (400 mg orally three times daily) [28]. The frequency of rectal bleeding and mucosal ulcers was lower in the metronidazole group at four weeks, three months, and 12 months. Diarrhea and edema were also reduced in the metronidazole group.

- Mesalamine **(5-aminosalicylic acid [5-ASA])** – There is no role for mesalamine enemas in patients with chronic radiation proctitis. Although some reports and anecdotal experience have suggested that mesalamine and sulfasalazine may be successful in treating chronic radiation proctitis, the results in other series have been conflicting [97,98]. The

combination of rectal prednisolone enemas and oral sulfasalazine improved symptoms in a controlled trial in which combined therapy was compared with sucralfate enemas [23]. However, the clinical response for sucralfate enemas was better as compared with oral sulfasalazine and prednisolone enemas. Sucralfate enemas were also better tolerated. (See 'Mild symptoms' above.)

- **Fecal transplantation** – A single case report has described improvement in hematochezia and diarrhea after four courses of fecal microbial transplantation [99].

- **Mesenchymal stem cell injection** – Mesenchymal stem cell injections have been reported to reduce fibrosis and increase mucosal proliferation in a rat model of radiation proctitis [100]. Human trials are awaited.

PROGNOSIS

- **Disease course** – Up to 20 percent of patients with acute radiation proctitis will have symptoms that are severe enough to necessitate an interruption in radiation treatment. Acute radiation injury usually resolves after radiation is discontinued, although some patients report persistent symptoms for at least one year [5,101,102]. Among patients with symptoms severe enough to require hospitalization, the inpatient mortality rate is 1.7 percent; the highest rates are in older persons and those with protein-calorie malnutrition [103]. Acute radiation proctitis may increase the risk of chronic radiation proctitis [15,29]. In addition, raised levels of fecal calprotectin and fecal lactoferrin four weeks after completion of radiation in patients with acute radiation proctitis may be predictive of progression to chronic proctitis [104,105].

  In patients with chronic radiation injury, prognosis depends upon the disease severity. In one series, for example, bleeding subsided spontaneously within six months in 35 percent of patients who initially had only mild rectal bleeding [6]. In contrast, patients whose symptoms are more severe may not have such a favorable prognosis, and symptoms are associated with a significant decrease in health-related quality of life in up to 30 percent of patients [106-109].

- **Cancer risk** – Patients with radiation proctitis, by virtue of having received abdominal radiation, are at increased risk of secondary malignancies, the majority of which are colorectal cancers [110-113]. The magnitude of risk is similar to that observed in patients with a family history of colonic adenomas; however, increased surveillance is not recommended in this group. The impact of pelvic radiation on cancer risk and guidelines

for colorectal cancer screening in patients who have received abdominal radiation are discussed in detail separately. (See "Radiation therapy techniques in cancer treatment", section on 'Radiation side effects' and "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Other risk factors'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Radiation-induced gastrointestinal toxicity".)

SUMMARY AND RECOMMENDATIONS

- Radiation proctitis (or proctopathy) is defined as epithelial damage to the rectum due to radiation that is associated with minimal or no inflammation. Acute radiation proctitis occurs during and within six weeks of radiation therapy. Chronic radiation injury may occur as a continuation of acute radiation proctitis or have a delayed onset (9 to 14 months following radiation exposure to 30 years after exposure). (See 'Epidemiology and pathogenesis' above.)

- Acute radiation proctitis is caused by direct mucosal damage from radiation exposure. Chronic radiation proctitis is due to progressive epithelial atrophy and fibrosis associated with obliterative endarteritis and chronic mucosal ischemia. Risk factors for radiation proctitis include the dose of radiation, area of exposure, and method of delivery. (See 'Risk factors' above and 'Mechanism of injury' above.)

- Symptoms of acute radiation proctitis include diarrhea, mucus discharge, urgency, tenesmus, and, uncommonly, bleeding. The most common manifestation of chronic radiation injury to the rectum is rectal bleeding and iron deficiency anemia due to bleeding secondary to radiation-associated vascular ectasias (RAVE). Patients may also present with chronic radiation proctopathy with symptoms of urgency, change in stool caliber and consistency, constipation resulting from underlying fibrosis, and, rarely, fecal incontinence due to overflow diarrhea and increased mucus. (See 'Clinical manifestations' above.)

- As the clinical features of radiation proctitis are nonspecific, establishing the diagnosis requires the exclusion of other causes of colitis by history, laboratory studies, endoscopic evaluation of the colon, and, if permissible, biopsies of the rectum. Rectal biopsies should

be performed carefully depending upon the dose and fractionation of previous pelvic radiation therapy and in consultation with a radiation oncologist. If performed, biopsies should be directed at the posterior and lateral walls to avoid the irradiated areas. (See 'Diagnostic approach' above.)

- In patients with acute radiation proctitis, treatment is supportive (eg, hydration and antidiarrheals as needed). Butyrate enemas may improve symptoms and accelerate healing in acute radiation proctitis. (See 'Management' above.)

- The choice of treatment of chronic radiation proctitis is based on the pattern and severity of symptoms and available endoscopic and surgical expertise. Specific therapy may not be necessary in those who have only mild symptoms, such as occasional hematochezia or mild tenesmus.

- In patients with tenesmus, rectal pain, or bleeding due to radiation-associated vascular ectasias, we suggest an initial trial of sucralfate enemas (**Grade 2C**). In patients with bleeding due to radiation-associated vascular ectasias who fail to respond to sucralfate therapy for four weeks and in patients with severe symptoms, we suggest a trial of endoscopic therapy with argon plasma coagulation (**Grade 2C**). Endoscopic therapy in the setting of prostate necrosis is associated with an increased risk of fistula formation. Therefore, the decision to perform endoscopic therapy and the timing of such therapy should be made with a urologic radiation oncologist. (See 'Patients with bleeding' above.)

- In patients with mild obstructive symptoms related to strictures, we use stool softeners for management of constipation. In patients with a narrow stricture and continued symptoms despite stool softeners, we suggest endoscopic dilation provided that the strictured segment is short (**Grade 2C**). The risk of perforation is increased in patients with long or angulated strictures; such patients may require surgery. (See 'Mild symptoms' above and 'Endoscopic therapy for severe or persistent symptoms' above and 'Surgery for intractable symptoms and complications' above.)

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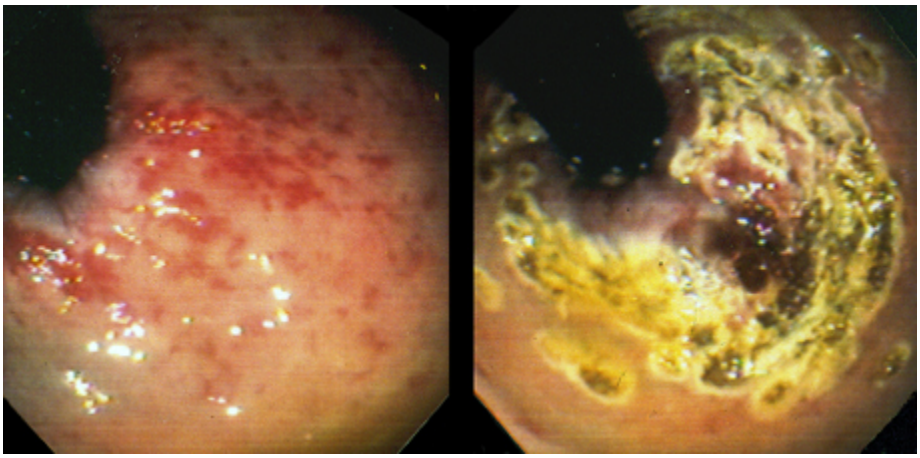
GRAPHICS

Radiation telangiectasias



Left panel: Endoscopy shows hemorrhagic areas in the rectum in a patient with radiation telangiectasias and chronic hematochezia. Right panel: The hemorrhagic areas have been treated with argon plasma coagulation.

Courtesy of Jonathan Cohen, MD.

Graphic 64264 Version 2.0

Contributor Disclosures

Lawrence S Friedman, MD Other Financial Interest: Elsevier [Gastroenterology]; McGraw-Hill [Gastroenterology]; Wiley [Gastroenterology]. All of the relevant financial relationships listed have been mitigated. **Theodore S Hong, MD** Equity Ownership/Stock Options: PanTher Therapeutics [Pancreatic cancer]. Consultant/Advisory Boards: Synthetic Biologics [IAP/microbiome]. All of the relevant financial relationships listed have been mitigated. **Christopher G Willett, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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