Radiation Proctitis

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Abstract

Radiation proctitis is a troublesome complication of radiation therapy for as many as 75% patients after pelvic irradiation. Indications of pelvic irradiation are mainly cancers of prostate, ovary, cervix, and uterus. In this review we summarise the available options for the management of radiation proctitis with special emphasis on use of formalin, which is a cheap and easily available method in India.

Key words: Radiation proctitis, 4% formalin.

Introduction

Radiation proctitis is a common complication of radiation to lower abdomen and pelvis. Different modalities of treatment are available including aminosalicylic acid derivatives, corticosteroids, sucralfate, argon laser, bipolar electrocoagulation, and short chain fatty acids. Out of these, 4% formalin has been recently used and has shown remarkable success. Formalin is a simple, inexpensive, and effective treatment for haemorrhagic radiation proctitis, both as initial therapy, and for refractory cases.

History

In 1895, Wilhelm Roentgen discovered X-rays. In 1897, Walsh reported a case of abdominal pain and diarrhoea in a person working with the newly discovered radiation energy i.e., X-rays. He also found and reported that his symptoms stopped when he was shielded by lead1. In 1917, the first clinical report of a patient who developed severe intestinal injury following use of radiation therapy for treatment of malignant disease was published2. In 1930, factitial proctitis was described in a group of patients who had undergone pelvic radiation3.

Radiation proctitis is a troublesome complication as many as 75% of patients who undergo pelvic irradiation for any cause4. The incidence of late complications is about 2.5-30%5-8.

Any part of the gastrointestinal (GI) tract can be affected by the radiation, i.e., oesophagus, stomach, small intestine, colon, and rectum. The patient may present with different clinical symptoms according to the part affected.

In the early years, the radiation therapy by external beam ortho voltage equipment was limited by the tolerance of the overlying skin. The advent of newer supervoltage technique made it possible to give higher energy X-rays without skin injury.

More recent evaluation suggests that incidence of significant late GI complications may be less, especially when modern computerised techniques for delivery of therapeutic radiation are utilised6. It was said that it is the price paid for extension of life by the radiation therapy. The symptoms of radiation proctitis start appearing after 5,000 rads of radiation exposure10-12.

Predisposing conditions

Abdomino-pelvic surgery, pelvic inflammatory conditions, adhesions in the abdomen leading to immobility of loops of small intestine in the radiation field, hypertension, diabetes mellitus, body habitus (thin), collagen vascular disease, and concomitant or previous chemotherapy lead to increased chances of radiation proctitis.

Pathology

The gross pathologic changes can be acute, subacute, or chronic13-16.

Acute changes occur during and immediately after irradiation in the form of hyperaemia, oedema, and extensive inflammatory cell infiltration of mucosa17. Crypt abscesses consisting of acute inflammatory cells, eosinophils, and sloughed epithelial cells may be present; mucosa may ulcerate18, 19.
Subacute and chronic changes begin after 2-12 months of regeneration to a variable extent. The submucosa becomes thickened, fibrotic, and often contains large, bizarre-appearing fibroblasts\textsuperscript{13, 14}. In the vessels there may be endothelial swelling in arterioles leading to fibrosis of connective tissues and endarteritis of the arterioles. These pathological changes result in rectal tissue ischaemia leading to mucosal friability, bleeding, ulcers, strictures, and fistulae\textsuperscript{15, 20}.

**Clinical features**

Early symptoms can develop during the first or second week of radiation therapy. Nausea, and vomiting are seen with upper abdominal radiation therapy as opposed with pelvic radiation and may be related to acute gastroparesis\textsuperscript{21}. Involvement of small intestine leads to abdominal cramps, nausea, and watery diarrhoea. Large intestinal irradiation leads to diarrhoea, tenesmus, mucoid rectal discharge, and rectal bleeding if ulceration is present\textsuperscript{22}. However, many patients remain symptom free even with mucosal ulceration\textsuperscript{19}.

The late symptoms appear at an interval range of 3 months to 30 years. The most common symptom with small intestinal radiation damage is colicky abdominal pain, nausea, vomiting, and small intestinal obstruction can also occur. In small intestine, if the ileum is extensively involved, malabsorption may be prominent\textsuperscript{23, 24}. Patients with chronic radiation injury of rectum will have symptoms of proctitis, including tenesmus, mucoid rectal discharge, bleeding per rectum; occasionally, constipation could occur, and less commonly low-grade obstruction or fistulous tract into adjacent organs\textsuperscript{25}. Bleeding may be minimal to chronic and severe, requiring blood transfusion\textsuperscript{26}.

**Diagnosis**

There will be history of pelvic irradiation for malignancy. There may be history of tenesmus, diarrhoea, bleeding per rectum or fistulous communication.

During the early stage of radiation enteritis, there could be evidence of ileus on plain radiograph. Barium studies often demonstrate mucosal oedema and dilated loops of hypotonic small intestine\textsuperscript{27, 28}. Rectum during acute phase shows severe spasm; rarely, ulcer on anterior wall is seen on barium study.

In late radiation enterocolitis, recurrence of cancer should be excluded because the clinical manifestations of chronic radiation enteritis are non-specific. In late or chronic radiation enterocolitis, barium studies of small intestine may show mucosal oedema, separation of small intestine loops, and excessive secretion in the intestinal lumen\textsuperscript{29}. Enteroclysis (small bowel enema produced through the introduction of nasoduodenal tube) is superior to conventional small bowel follow-through because it provides better intestinal distension, thereby allowing a greater visualisation of any intestinal abnormality. In a review of 1,465 patients, the sensitivity and specificity of the small bowel enema was over 90\textsuperscript{\%}\textsuperscript{20}. Progressive fibrosis can produce narrowed, fixed, tubular, or poorly distensible intestinal segment, an increase in the pre-sacral space, stricture, or fistulae\textsuperscript{20}.

Colonoscopy or sigmoidoscopy may be required for investigation of rectal bleeding to locate the lesion, and may complement the barium enema for detection of tumour recurrence. During acute phase, a dusky oedematous and inflamed mucosa is seen with poorly visible vascular pattern; friability is not marked, and ulceration is infrequent. In late cases, the mucosa appears granular, friable; multiple telangiectasia, and ulceration of anterior rectal wall occur in 10\textsuperscript{\%} of cases\textsuperscript{31}.

In addition to these, USG, CT scan, or MRI of abdomen can be informative. Biopsy from the lesion is diagnostic, but there are chances of bleeding and perforation of the necrotic wall. Therefore it is not practicable.

**Treatment**

Treatment can be medical or surgical. Some patients may remain symptomatic or initially respond to medical therapy and then again become symptomatic requiring surgery. The interval from radiation to surgery may range from 3 months to 31 years\textsuperscript{22, 31}.

**Medical**

1. Aminosalicylic acid derivatives\textsuperscript{32-34}.
2. Corticosteroids\textsuperscript{32-34}.
3. Sucralfate

Sucralfate enema has been tried with good initial results, but the follow-up period has been less than 2 months. Melko GP (1999) opined that sucralfate suspension enema provides a viable treatment option in patients who are intolerant to, or refractory to, therapy for radiation-induced proctitis. Kochhar et al. treated 26 patients of proctosigmoiditis with 20 ml of 10% rectal sucralfate enema thrice daily until bleeding subsided. Sasai et al. treated three patients with oral sucralfate and found good results.

4. Argon laser

Some patients (6-8% according to Buch) developed prolonged and significant rectal bleeding resistant to above treatment. Argon laser may be successful in this difficult situation.

5. Bipolar coagulation

Another method used for treating haemorrhagic proctitis is bipolar electrocoagulation.

6. Short chain fatty acids

Anablea Pinto used short chain fatty acid enema in 19 patients of radiation proctitis for five weeks, and followed the patient for 6 months, and found that short chain fatty acid enema can accelerate the process of healing in chronic radiation proctitis; but the treatment has to be continuous.

7. Hyperbaric oxygen (HBO2)

14 patients with chronic radiation-induced proctitis were treated with HBO2. Eight patients experienced complete resolution of symptoms, and one patient had substantial improvement for a total response rate of 64%. Follow-up ranged from 5 to 35 months (mean: 17 months). Five patients (36%) were classified as non-responders. Three experienced significant improvement during treatment, but relapsed soon after therapy was discontinued, whereas two had no symptomatic improvement.

8. Formalin

Various investigators have used formalin in patients with radiation proctitis, and this method of treatment is cost-effective with respect to the Indian subcontinent where patients cannot afford other costly methods of treatment and present with frequent relapses.

Seow-Choeu F (1993) treated 8 patients of haemorrhagic radiation proctitis with formalin. Application time for formalin therapy was 20 minutes. 1 patient needed repeat formalin application after two weeks; bleeding ceased immediately in 7 patients. No further bleeding was noted nor was any blood transfusion needed.

Coyoli-Garcia et al. (1999) treated 7 patients of radiation proctitis post-radiotherapy for carcinoma cervix. The investigator applied a gauze soaked in 4% formalin through a rigid sigmoidoscope, and then kept gauze in contact for 4 minutes and repeated the procedure until bleeding ceased (median exposure time was 26 minutes). Bleeding ceased immediately in 6 patients; 1 patient continued with minor bleeding, and 2 patients had fever within 24 hrs. 3 patients required repeat formalin application. After that, 6 out of 7 patients had no further bleed or requirement of blood transfusions. He used peridural anaesthesia for application.

Counter et al. (1999) treated 11 patients of rectal bleeding after pelvic irradiation, 4% formalin was instilled into the rectum in four separate 20 cc aliquots with total mucosal contact of 15 minutes. The patient were followed-up after...
7-10 days and one month. Only 1 patient required repeat formalin application. In follow-up after 3-64 months, 100% success was reported.

Roche et al (1996) treated 6 patients of radiation proctitis. In 4 patients, bleeding ceased after a single application, but in 2 patients repeat application of 4% formaldehyde after 3 weeks led to controlled rectal bleed.

Saclarides et al (1996) treated 16 patients of refractory radiation-induced proctitis, initially treated with cautery, steroid, laser, but failed, and found that in 12 patients bleeding stopped after a single formalin 4% instillation. In 3 patients bleeding considerably reduced, 1 patient required three applications. He used local anaesthesia in 9, sedation in 4, and general anesthesia in 2 patients.

Biswal et al (1995) treated 16 documented cases of haemorrhagic radiation proctitis who did not respond to conventional steroid retention enemas, with 4% formalin application. It was observed that the rectal bleeding was controlled completely in 81% cases in median follow-up of 11 months (range: 6-17 months) and diversion colostomy could be avoided in all the cases.

Ismail et al (2002) analysed 20 patients presenting with haemorrhagic radiation proctitis, and treated with a formalin dab. 12 patients ceased to bleed following one session of formalin dab. 6 patients needed more than one session to effect haemostasis. 2 of 3 patients with torrential bleeding failed to respond to formalin dab and required surgical excision of the rectum.

We have experience of treating 10 patients at Indira Gandhi Medical College, Shimla. 7 patients improved after a single application of 4% formalin, 2 patients responded after second application, and one patient was lost to follow-up because she died of advanced malignancy, but her symptoms of proctitis had improved.

Surgical

Uncommonly, patients with radiation proctitis require surgery for persistent symptoms or local complications including pelvic fistulas (e.g., vaginal or bladder), and uncontrolled bleeding. Limited resection of the diseased intestine is the goal, but if the lesion is too diffuse a bypass procedure may also be attempted. Review of surgical literature revealed that surgical procedures should be simple and conservative and should be done as a last resort only as they can lead to post-operative complications such as local wound infections, sepsis, obstruction, and fistulae.

Prevention

Because of complexity of treatment options, it is desirable that preventive measures should be always tried to reduce the incidence of radiation proctitis. The preventive measures include surgical placement of a polyglycolic biodegradable mesh that supports the intestines out of pelvis. The patient should be instructed to maintain a full bladder, which displaces the intestines out of pelvis. Using modern radiation treatment techniques can also avoid the unnecessary exposure of intestines. Appropriate packing to push the rectum and bladder away from the radioactive source also helps in reducing the incidence of radiation proctitis. Pharmacotherapy in the form of amifostine has shown promising results in prevention of radiation proctitis. Most surgeons favour a diversion colostomy for a medically intractable proctitis. Others favour a more aggressive approach with resection of the inflamed rectal segment and the colo-anal pull-through anastomosis.

References


