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Case Report

Radiation proctitis as a differential of lower GIT bleeding in Nigeria: A case series.

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Abstract

Pelvic radiotherapy is an acceptable and promising treatment modality for various pelvic malignancies. However, it is associated with radiation-induced injury on surrounding structures with a preference for the rectum, which is characteristically fixed in the pelvic region. Acute radiation proctitis is usually self-limiting, but in its chronic form, it can be debilitating. Recent advances in radiation therapy have significantly reduced the prevalence of radiation proctitis (RP) in high-income countries, contrary to the findings in low and middle-income countries witnessing an increasing burden of radiation proctitis. This observation can be attributed to the increased availability of radiation therapies with limited use of novel technologies designed to reduce the detrimental effects of radiotherapy and improve the detection of RP owing to improvements in endoscopic services in developing countries. This is a highlight of the trends in the presentation of RP, management modalities in various tertiary centers in Nigeria, and the limitations in care occasioned by the non-availability of argon plasma coagulation (APC) as an effective treatment modality in most tertiary health facilities in Nigeria.

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Introduction

Radiation proctitis (RP) is characterized by damage to the rectal epithelium resulting from the use of ionizing radiation therapy. It is a common but potentially debilitating complication associated with pelvic radiotherapy for pelvic malignancies including those of the genitourinary, gastrointestinal, and gynecological systems.[1] The increased availability of radiation delivery services in Nigeria has substantially increased the rate of radiation proctitis. This is intensified by the ineffectiveness of protective strategies implemented by radiation oncologists from shielding the rectum, which has a fixed position in the pelvis.[2] RP can occur acutely in just a few days to six weeks of pelvic radiation or chronically months to 30 years of exposure to radiation therapy.[3] Radiation-associated vascular ectasia is an entity characterized by chronic (radiation-induced) proctitis and bleeding from vascular ectasia.[4] RP can present with varying clinical signs and symptoms ranging from asymptomatic presentation to severe diarrhea, rectal pain, rectal bleeding, incontinence, and fistulation.[5] The endoscopic features include pallor, friability, telangiectasias, and advanced stages and chronic stages of fistulizing disease, including rectovaginal, rectourethral, and recto vesicular fistulas.[6,7] External beam radiation therapy (EBRT) and brachytherapy are the major modalities of radiation therapy for pelvic malignancies. The risk of complication is reduced with brachytherapy as very high doses of radiation are delivered directly into the tumour.[8] Although EBRT involves the use of a linear accelerator to deliver radiation from outside the body to the tumor through two or three-dimensional beam arrays posing a higher risk of radiation proctitis, revolutionary changes have been made on EBRT with increased utilization of targeted intensity-modulated RT (IMRT) which enables the delivery of higher doses of radiation therapy to target tissues without damaging the adjacent tissues.[2,3] This has reduced the incidence of RP in these countries, however in Africa due to the increasing availability of radiation therapy and endoscopic facilities, there is an increase in the detection rate of RP. The diagnosis relies on a combination of clinical features, endoscopic findings, and histological evaluation. Management of RP depends on the severity of symptoms and may include conservative measures, medical therapy, and in extreme cases, surgical intervention.

In this case series, we present eight patients who developed radiation proctitis following pelvic radiotherapy for varying types of malignancies. We aim to illustrate the diverse clinical presentations, diagnostic approaches, and treatment modalities employed in managing these cases and to raise awareness among doctors of the increasing frequency of occurrence with more access to radiation therapy.

Case series

Case 1

A 64-year-old male presented with a one-year history of radiation to the pelvis for prostate cancer. He had worsening symptoms of loose stools, which were followed by bleeding from the rectum two weeks later. He was offered a colonoscopy, and the findings revealed multiple punctate erythema's in the rectum with hemorrhoids. He was treated with antibiotics, metronidazole, and Mesalamine. He had a significant improvement

Case 2

A 63-year-old male hypertensive, presented with abdominal pain and loose stools of three months duration. There was associated tenesmus, fecal urgency, fecal incontinence with easy fatiguability, loss of appetite, and unintentional weight loss. He had radiotherapy for prostate cancer a few days before the onset of symptoms combined with chemotherapy containing prednisolone, hydroxychloroquine, and Abiraterone. An assessment of radiation proctitis was entertained. He had an unremarkable CT scan, but a colonoscopy revealed diffuse edema and erythema of the rectum with prominent submucosal vessels and friable mucosa suggestive of proctitis and a rectal polyp. The patient commenced on Tabs

Sulfasalazine 500mg tds and Tab Rifaximin 400mg b.d for 2 weeks. Oral Rehydration Salts and Bismuth sucralfate were also administered. He was subsequently followed up in an outpatient clinic with remarkable improvement.

Case 3

A 60-year-old male was diagnosed with localized prostate cancer. He had 6 chemotherapy courses and 20 sessions of pelvic radiation. He developed hematochezia on the second cycle of radiotherapy. Prednisolone was prescribed at this time with Anusol suppository one tablet nocte for one week, with complete resolution of hematochezia 4-months post completion of radiotherapy. He developed copious mucoid stool and hematochezia. Colonoscopy reported findings showed inflamed distal rectal mucosa with neovascularization and an ulcer >3cm, which was consistent with acute proctitis on histology. Treatment included enema prednisolone 20mg (in 50ml of water) BD for 2 weeks, then nocte for 1 week with symptoms resolution after 1 week and subsequent follow-up.

Case 4

A 61-year-old male was diagnosed with localized prostate cancer. He had 6 courses of chemotherapy and 28 cycles of pelvic radiotherapy and was on oral Prednisolone 10mg daily during the period of chemotherapy. He later developed recurrent hematochezia 10 months after radiotherapy, about 20ml per episode. A colonoscopy revealed florid neovascularization at the distal rectum, with easily bruised distal sigmoid mucosa. He was started on Metronidazole 400mg tds PO and prednisolone 20mg. Antepsin (sucralfate) 2gram enema (in 100ml of water) BD was prescribed for 2 weeks but the patient did not get it due to the non-availability of the medication and the symptoms persisted.

Case 5

This was a 67-year-old man who presented with painless haematochezia of 3 weeks duration. It was bright red, recurrent, about 10-20mls per episode with occasional diarrhea episodes. He had five sessions of radiation therapy for prostatic cancer a year before the onset of symptoms. He is not well-known hypertensive or diabetic. He does not smoke cigarettes. At colonoscopy, multiple telangiectasia was noted in the rectum with contact bleeding. He was commenced on sucralfate enemas with some improvement in clinical symptoms.

Case 6

This was a 71-year-old gentleman who presented with recurrent rectal bleeding about 2-3 times each year. He has radiotherapy following chemotherapy for prostate cancer and a few days after starting radiotherapy, he developed rectal bleeding for which topical steroids were administered. Following the presentation, he had a colonoscopy which revealed multiple hyperemic spots with neovascularization that are easily friable. He also had a single polyp with a histological diagnosis of tubular adenoma with low-grade dysplasia.

Case 7

This case is that of a 74-year-old male known hypertensive who presented with recurrent rectal bleeding of six months duration with no abdominal pains or proctalgia. He had a history of prostate cancer 11 years ago with a previous prostatectomy. He was diagnosed with a recurrence of Ca Prostate about 2 years ago for which he had sessions of radiotherapy, with the last session being about 16 months ago. He was also on hormonal therapy for prostate cancer (Bicalutamide)

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He had a colonoscopy which showed features of radiation proctitis and was placed on Anusol suppository, Tranexamic acid, and mesalazine suppository at various times without significant improvement. He was also on iron supplements and PPIs. A repeat colonoscopy showed internal hemorrhoids in the anorectal region. The rectal mucosa had patchy areas of marked erythema with some friable areas and a tuft of capillaries(telangiectasias). The mucosa of the Sigmoid, Descending, Transverse, and Ascending colon as well as the Caecum were grossly normal. He was referred abroad for argon plasma coagulation (APC).

Case 8

A 56-year-old post-menopausal grand multiparous woman presented to the gynecology unit with complaints of vaginal discharge of 6 months duration and vaginal bleeding of 4 months duration. She was diagnosed with invasive non-keratinizing squamous cell carcinoma of the cervix stage 3B. She received neoadjuvant chemotherapy (Paclitaxel and Cisplatin while being worked up for External beam radiation therapy (EBRT). While on chemo-radiotherapy and brachytherapy, she developed radiation-induced dermatitis and complained of passing blood in stool associated with mucus and abdominal bloating. A colonoscopy was requested and revealed patchy erythematous areas in the rectum with prominent blood vessels. A diagnosis of radiation proctitis was made. She was placed on steroids and noticed a cessation of blood in the stool.

Case 9

A 59-year-old male with a history of colorectal cancer. He had left hemicolectomy and very low rectal anastomoses with staples and subsequently had chemotherapy for 6 months using oxaliplatin and capecitabine for five courses. Subsequently, he had two sessions of radiotherapy over four weeks this was followed by bleeding per rectum, which was treated with platelet transfusion and apheresis due to an extremely low platelet count. He later presented to the gastroenterologist with complaints of constipation and passage of pencil-like stools for more than 3 months with the associated occasional passage of blood per rectum. A colonoscopy revealed proctitis with stenosis of the anastomotic site with colon and ascending colon polyp. The patient was treated with Tabs prednisolone 10mg daily for one week. The bleeding stopped, however, constipation and passage of pencil-like stools probably from radiation-induced stenosis persisted.

Case 10

This was a 57-year-old female being managed for cervical cancer, who initially received Paclitaxel with radiotherapy in 2021, which was substituted with Docetaxel due to excessive diarrhea from Paclitaxel. She received another radiotherapy in 2023 and subsequently presented with rectal bleeding (frank red blood in stool). Colonoscopy findings include hyperemic mucosa with ulcerated and bleeding areas and external hemorrhoids. The patient received Tab Mesalazine 1g tds x for one month as the budesonide enema was difficult to procure. Symptoms resolved, although the patients died later.

Case series	Age yrs	Sex	Condition	Presentation	Colonoscopic findings	Treatment
Case 1	64	M	prostate cancer	Diarrhea, bleeding per rectum	Multiple punctate erythema	Oral Metronidazole and Mesalamine
Case 2	63	M	prostate cancer	Abdominal pain, Diarrhea, tenesmus, fecal incontinence, loss of appetite and weight loss	Diffuse edematous and erythematous rectum, prominent submucosal vessels and friable mucosa, rectal polyp.	Tabs Sulfasalazine 500mg tds X 2/52 Tab Rifaximin 400mg b.d X 2/52 ORT Bismuth sucralfate
Case 3	60	M	prostate cancer	Copious mucoid stool and hematochezia.	Inflamed distal rectal mucosa with neovascularization and an ulcer >3cm.	Enema Prednisolone 20mg (in 50ml of water) BD x 2/52, then Nocte x 1/52.
Case 4	61	M	prostate cancer	Recurrent hematochezia	Florid neovascularization at the distal rectum, with easily bruised distal sigmoid mucosa.	Metronidazole 400mg tds PO for 1 week Prednisolone 20mg 1 week and Sucralfate 2g enema (in 100ml of water) BD x 2/5.
Case 5	67	M	prostate cancer	Haematochezia with occasional diarrhea	Multiple telangiectasias were noted in the rectum	Sucralfate enemas
Case 6	71	M	prostate cancer	Bleeding per rectum	Multiple hyperemic spots with neovascularization. Rectal polyp	Topical Steroids
Case 7	74	M	prostate cancer	Bleeding per rectum	Patchy erythematous rectal mucosa with some friable areas and tuft of capillaries (telangiectasias)	Anusol suppository, Tranaemic acid, and Mesalazine suppository, but no significant improvement, referred for APC.
Case 8	56	F	Cervical cancer	Hematochezia associated with mucoid stools and abdominal bloating	Patchy erythematous areas in the rectum with prominent blood vessels	Steroids
Case 9	59	-	Colorectal CA (low rectal anastomosis)	Constipation, passage of pencil-like stools, and occasional passage of blood per rectum	Proctitis with stenosis of the anastomotic site. Ascending colon polyp	Tabs prednisolone 10mg daily x 1 week.

Case 10	57	F	Cervical cancer	Rectal bleeding	Hyperemic mucosa with ulcerated and bleeding areas. Also, External hemorrhoids.	Tab mesalazine 1g tds x 1/12.

Table 1: Clinical summary of all the cases presented

Discussion

Radiation proctitis is a significant complication that arises from radiation therapy used in the treatment of pelvic malignancies. It involves inflammation and damage to the rectal mucosa due to exposure to ionizing radiation leading to symptoms such as rectal bleeding, pain, diarrhea, and fecal urgency. [7] This condition can significantly affect a patient's quality of life. In this case series, we describe the varying presentation RP in a population of Nigerians who have had radiotherapy for prostate cancer, rectal cancer, and cervical cancer.

The incidence and prevalence of radiation proctitis are dependent on the malignancy being treated, the dose and duration of radiation therapy, the area of exposure, the method of delivery, the use of cytoprotective agents, and individual patient characteristics. [6,9] The incidence of radiation proctitis can range from 5% to 20% in patients undergoing pelvic radiation therapy for conditions such as prostate cancer, cervical cancer, or rectal cancer. [10] There is an increased detection rate of RP and other complications of radiotherapy in Nigeria owing to the increased availability of radiotherapy services for pelvic malignancies.

The risk of developing radiation proctitis may increase with higher radiation doses, larger treatment volumes, and certain patient factors such as age, comorbidities, and genetic predisposition. Smoking, hypertension, diabetes mellitus, and atherosclerosis presumably increase vascular injury and intestinal ischemia following radiation and impair tissue repair. [3] 70% of our patients in this series were elderly above the age of 60 years and had radiation proctitis from the treatment of prostate cancer. Interestingly the mean age of our patients is above the life expectancy of Nigerians, which is 54 years; perhaps as the population gets older the prevalence of these medical conditions is likely to increase with their antecedent complications including radiation proctitis.

The underlying pathophysiology of radiation proctitis involves the direct toxic effects of ionizing radiation on the rectal mucosa or the indirect generation of free radicals from the ionization of water molecules and consequent oxidative stress injuries. Radiation therapy disrupts normal cellular processes and leads to inflammation, endothelial damage, fibrosis, and impaired tissue healing. Chronic radiation exposure can further exacerbate these changes, resulting in progressive damage to the rectal tissue. Additionally, vascular injury and ischemia may contribute to the development of radiation proctitis by compromising blood flow to the affected area and stimulation of neo-angiogenesis via increased expression of vascular endothelial growth factor (VEGF) and CD31. [11]

The clinical presentation of radiation proctitis can vary widely among individuals and may range from mild to severe symptoms. Common manifestations include rectal bleeding, which may present as bright red blood in the stool or on toilet tissue. Patients may also experience symptoms such as rectal pain, tenesmus, diarrhea, urgency, and incontinence. The severity and persistence of symptoms can significantly impact a patient's quality of life and may require medical intervention to alleviate discomfort and manage complications.

In the investigation of radiation proctitis, various diagnostic modalities can be employed to assess the extent of rectal injury and guide treatment decisions. Endoscopic evaluation, such as sigmoidoscopy or colonoscopy, allows direct visualization of the rectal mucosa and identification of characteristic features of radiation-induced damage, including telangiectasia, ulceration, and strictures. [11] Biopsy specimens obtained during endoscopy can aid in confirming the diagnosis and ruling out other potential causes of rectal symptoms.

In addition to endoscopy, imaging studies such as magnetic resonance imaging (MRI) or computed tomography (CT) scans may be utilized to assess the severity of tissue damage, identify complications such as fistulas or abscesses, and guide surgical planning if necessary.[1] Functional studies, such as anorectal manometry or defecography, can provide valuable information about rectal motor function and pelvic floor dynamics, which may influence treatment decisions and predict outcomes.

Circulating micro vesicles (platelet, monocyte, and endothelial-derived micro vesicles) assessed via flow cytometry correlate with the degree of radiation injury and can be used as a novel biomarker for the detection of patients with high grades of toxicity and prognostication of radiation therapy-associated complications. [12]

Treatment options for radiation proctitis aim to alleviate symptoms, promote mucosal healing, and prevent disease progression. Conventional approaches include pharmacological agents, endoscopic interventions, and surgical procedures while emerging therapies and clinical trials explore novel modalities to address the underlying pathophysiology of the condition.

Pharmacological agents commonly used in the management of radiation proctitis include topical rectal therapies such as sucralfate, mesalamine, corticosteroids, and lidocaine, which can help reduce inflammation, promote tissue repair, and alleviate symptoms. Sucralfate enemas seem to be the best available 'medical' therapy and are safe and well tolerated. [10] Four percent (4%) formaldehyde is a chemical sclerosant that has been used to treat chronic radiation proctitis with varying efficacy. [10] Oral medications such as anti-diarrheas, anti-inflammatory drugs, and agents targeting vascular endothelial growth factor (VEGF) may also be prescribed to manage diarrhea, pain, and vascular dysfunction associated with radiation-induced injury. Oral Metronidazole potentiates the effect of sucralfate. [10]

Endoscopic interventions offer targeted treatment options for patients with refractory symptoms or complications such as bleeding or strictures. Techniques such as argon plasma coagulation (APC), laser therapy, cryotherapy, and endoscopic mucosal resection (EMR) can be utilized to control hemorrhage, ablate telangiectasia, or alleviate obstruction caused by fibrotic strictures.[13] Endoscopic stent placement or balloon dilation may be employed to relieve luminal narrowing and improve bowel transit in select cases.

Hyperbaric oxygen therapy has emerged as a modality for the treatment of RP. It is believed to promote wound healing by improving tissue oxygenation, and angiogenesis, and decreasing bacterial overgrowth. [14]

Surgical management of radiation proctitis is reserved for patients with severe or refractory symptoms who fail conservative measures or endoscopic interventions. Surgical options may include partial or total rectal resection, colostomy formation, or diversionary procedures aimed at bypassing or diverting fecal flow away from the affected segment of the rectum. While surgery can provide definitive treatment for radiation-induced complications, it carries inherent risks and should be carefully considered in consultation with a multidisciplinary team.

In the realm of clinical research, ongoing trials are exploring innovative approaches to the treatment of radiation proctitis, including the use of mesenchymal stem cell therapy, growth factors, cytokine inhibitors, and biologic agents targeting inflammatory pathways implicated in tissue injury and repair. [15] These investigational therapies hold promises for improving outcomes and reducing the long-term sequelae of radiation-induced rectal damage.

In addition to conventional treatment modalities, some patients may seek out alternative or complementary therapies to manage symptoms and improve their quality of life. These may include acupuncture, herbal supplements, dietary modifications, and mind-body techniques such as yoga or meditation. [16] While the evidence supporting the efficacy of these interventions in the treatment of radiation proctitis is limited, they may offer symptomatic relief and psychological support for some individuals as part of a comprehensive care plan.

Despite advances in radiation therapy techniques and supportive care measures, there are still several knowledge gaps in the understanding and management of radiation proctitis. One significant gap lies in the prediction and prevention of radiation-induced toxicity in individual patients. Currently, there are limited tools or biomarkers available to accurately assess a patient's risk of developing radiation proctitis or to tailor treatment strategies accordingly. Another area of uncertainty is the optimal management approach for radiation proctitis. While various interventions such as topical agents, hyperbaric oxygen therapy, endoscopic treatments, and surgical interventions may offer symptomatic relief, their efficacy and long-term outcomes are not well-defined. Furthermore, there is a lack of consensus regarding the timing, duration, and sequencing of these interventions, leading to variability in clinical practice. Therefore, there is a need for further research to elucidate the underlying mechanisms of radiation-induced rectal injury and to identify potential targets for preventive and therapeutic interventions. A better understanding of the molecular pathways involved in radiation proctitis could pave the way for the development of novel treatment modalities aimed at mitigating tissue damage and improving patient outcomes.

The prognosis of radiation proctitis depends on the type and severity of the radiation-induced injury. Acute RP is often self-limiting with minimal complications. In the United States, RP readmissions constitute a significant healthcare burden with all-cause inpatient mortality for 30-, 60-, and 90-day readmissions of 3.58%, 3.89%, and 3.46%, respectively. [2]

Conclusion

Radiation proctitis presents a multifaceted clinical challenge requiring a tailored approach to diagnosis and management. While conventional treatments such as pharmacotherapy, endoscopic interventions, and surgery remain cornerstone therapies, ongoing research efforts and exploration of unconventional modalities are promising for advancing the field and improving outcomes for patients affected by this debilitating condition.

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