

# Treatment and outcomes of patients with chronic radiation proctitis.

## A single-center experience and review of the literature



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Maurizio Gentile, Giovanni Cestaro\*\*, Cesare Formisano\*, Luigi Sivero\*\*\*

\*Department of General and Specialistic Surgery "Federico II" University of Naples, Naples, Italy

\*\*UOC General Surgery – P.O. "S. Maria degli Angeli" ULSS Polesana, Adria (Rovigo), Italy

\*\*\*Department of Biomedical Advanced Sciences "Federico II" University of Naples, Naples, Italy

### Treatment and outcomes of patients with chronic radiation proctitis. A single-center experience and review of the literature

*Chronic radiation proctitis is a frequent complication after radiotherapy for pelvic malignancies. It is reported that 1 to 5% of patients develop chronic radiation proctitis even with recent advances in external radiotherapy. Hematochezia, mucus discharge, urgency and tenesmus are common symptoms and they can vary in severity but bleeding is often the most debilitating to the patient. Different options are reported for treatment of this condition that always should keep in differential diagnosis in patients with history of pelvic radiotherapy. Treatments range from easy, with topic administration of formalina, to expensive and requiring specialized equipment such as hyperbaric oxygen therapy. Surgery is reserved to patients with failure of conservative treatments due to the high risk of leakage and high morbidity up to 60%.*

KEY WORDS: Argon beam, Bleeding, Formalin, Radiation, Proctitis, Sucralfate enema

### Introduction

Radiation therapy is commonly used for treatment of pelvic neoplasms such as prostate cancer, anal, cervical and rectal malignancies. It is used in about 50% of cancer patients and in 25% of these plays a crucial role. Despite it is effective on tumor control a lot of side effects are reported in GI tract <sup>1</sup>.

We can record early effects within 3 months of radiotherapy with patients often forced to interrupt the treatment with compromise of tumor control, and a late toxicity that is a progressive condition with a significant mobility and mortality. Chronic radiation proctitis can last from 8 to 12 months after the end of the treatment and patients compliant initially for diarrhea, mucus discharge, urgency and tenesmus. due to loss of microvilli ,

mucosal ulceration and edema of the wall <sup>1</sup>. The incidence of this condition was reported as high as 30% even if the advances in radiation therapy minimized collateral effects and is currently estimated that 1 to 5% of patients (2) develop a chronic radiation proctitis <sup>1,2</sup>. Colorectal surgeons are often called for management of the symptoms and many options are available for this aim.

The results of the treatment are strongly related to patient conditions such as diabetes, IBD, collagen vascular diseases and high BMI as protective factor; radiation related factors are the extent and proctitis area <sup>3</sup>. However the incidence of chronic radiation proctitis is mainly related to dose, while other factors include the field of irradiation and a concomitant chemotherapy <sup>4</sup>. Two cases of patients treated with radiotherapy for prostate cancer are presented followed by discussion about the most updated options for treatment of radiation proctitis

Final recommendations approved by the ASCRS Clinical Guidelines Committee and ASCRS Executive Committee were used in the present review. These recommendations are usually updated every three-five year <sup>2</sup>.

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Correspondence to: Maurizio Gentile, MD, Department of General and Specialistic Surgery Federico II University of Naples, Via S. Pansini 5, 80131 Naples, Italy (e-mail: magentil@unina.it)

## Cases Report

### CASE N. 1

A 65-year-old man operated for prostate cancer in 2017 and subsequently treated with external irradiation, was observed in our Department for diarrhea with mucus discharge and rectal blood loss 5 months after the end of radiotherapy. A colonoscopy showed the distal sigmoid and rectal wall involved in active inflammation with edema of the wall, teleangectasias and blood loss. He was prescribed oral sulfasalazine and 20 ml of 10% sucralfate enemas twice a day; after one month of treatment a good improvement was observed with healing of sigmoid and proximal rectal mucosa, but a persistent bleeding from the distal 5 cm of the rectum. With the use of digital proctoscopy topical 10% formaline solution was topically applied which resulted in a significant reduction of bleeding; a definite healing was obtained after further two weeks of sucralfate enemas with cessation of bleeding. The patient was followed up to 5 months when a complete healing of the mucosa was observed (Fig 1).

### CASE N. 2

A 76-year-old man treated with radiotherapy alone for prostatic cancer was observed in the office for diarrhea, pelvic pain, anal burning sensation and bleeding per rectum 8 months after treatment. He was strongly debilitated for blood loss and required hospitalization with fluid replacement and blood transfusion. Colonoscopy showed a severe rectal proctitis with confluent teleangectasias involving the entire rectal wall.

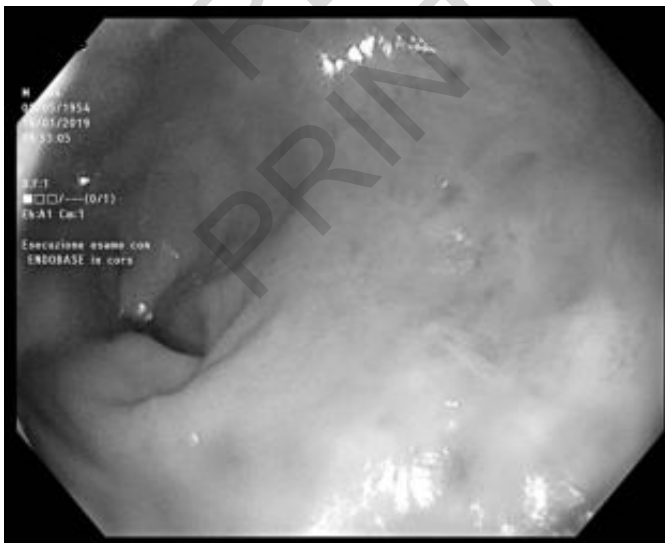


Fig. 1

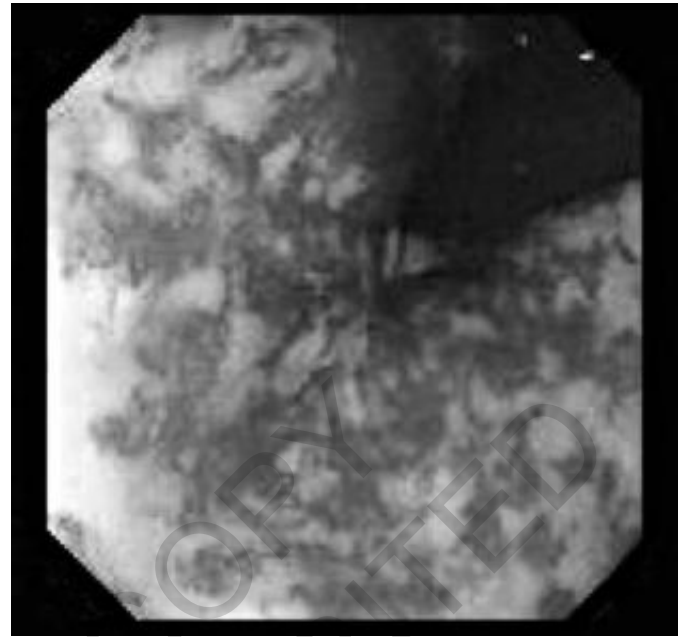


Fig. 2

The patient was treated at first with steroids enemas with poor results. After a week of treatment a 10% formalin solution was applied in the office with a mild improvement in symptoms but bleeding was persistent; finally, an Argon Plasma Coagulation was administered with cessation of bleeding after two treatments. The follow up showed a complete healing 4 months after treatment (Fig 2).

## Discussion

Radiation therapy is an essential treatment modality for pelvic cancers and is mainly used in treatment of prostate cancer. Radiation proctitis (RP) is a frequent complication with up to 40% of patients developing rectal hemorrhage. The radiation injury is due to a direct mucosal damage from radiation with inflammation or cell death. The process of chronic injury is different from the acute damage and ischemic and fibrotic changes are observed and predispose the involved rectum to bleeding or to develop strictures and fistulas<sup>4</sup>.

There is a general agreement that symptoms and frequency of rectal proctitis are closely related to type and radiation dose, the way of dissipating radiation energy and the route of delivery. Some modalities of radiation therapy such as 3-dimensional conformal radiation therapy, intensity modulated radiotherapy and brachithery allowed to deliver higher doses of radiation decreasing the incidence of radiation damage. Despite these innovations in the treatment some patient-related comorbidities such as diabetes, hypertension, IBD, HIV, can increase the risk of chronic proctitis (4). A study sug-

gested a decreased proctitis severity in patients treated with glutamine, but a randomized controlled trial suggested that there is no benefit from administration of oral glutamine. Some profilactic intraoperative measures as an omental pedicle flap and tissue expander were adopted in order to decrease the incidence of radiation proctitis but they are not routinely recommended and poorly evaluated<sup>6,7</sup>.

The patient with radiation proctitis present usually with hematochezia, tenesmus, urgency and loss of mucus. Since a radiation proctitis develop after a treatment for cancer it is important to assess the patient with clinical examination or imaging for recurrence of his primary cancer. A colonoscopy is always indicated or, at least, a proctoscopy to rule out malignancies and check the quality of the tissue<sup>4</sup>.

Many treatments are available for the cure of radiation proctitis with a different grade of recommendation from the ASCRS and we can consider medical treatments and interventional treatments<sup>2</sup>.

The use of topical formaldehyde (formalin) is considered the most effective treatment for radiation proctitis and its administration can vary from 4 to 10% and the application can be made topically with a sponge or by irrigation with a short contact time<sup>8</sup>.

In a Cleveland Clinic Florida experience 21 patients were treated with 4% formalin and in 80% of them a complete remission of symptoms was observed at first application. Some adverse effects were reported: 4 rectal pain, 2 fecal incontinence, and 1 colitis<sup>9</sup>. Lee et al. reported their experience with 4% formalin: the majority of patients had improvement of symptoms and cessation of bleeding after one treatment. The mean duration of symptoms was 15.6 months<sup>10</sup>. In another experience from Dziki et al., patients need more than one application, with an average of two (range 1-5 and about 50% stopped bleeding after one application)<sup>11</sup>.

Haas et al. reported a 93% of cessation bleeding with 10% topical application of formaline after 3.5 application at 2-to-4 week intervals<sup>12</sup>. It is strongly recommended by ASCRS based on moderate-quality evidence (1B)<sup>2</sup>. A sucralfate suspension in water or saline is an effective treatment of bleeding with a strong recommendation based on low quality evidence (1C)<sup>2</sup>.

In a retrospective study of 26 patients with chronic radiation proctitis treated with 20 ml of 10 % sucralfate enemas a significant decrease in bleeding was reported in 76% after 4 weeks and 88% had a complete healing after 16 weeks of treatment. In a study of 23 patients the administration of 2gr in 4,5 ml of water twice daily resulted only in a partial improvement (41%) of symptoms and a resolution in 32%. 13 Another two studies with application of 20g in 20-50 ml of water or saline reported healing of rectal ulcers and cessation of bleeding in 80-100% of patients<sup>14,15</sup>.

A lot of other enemas were topically used but steroids, mesalamine metronidazole<sup>16,17</sup> and ozone therapy are

not widely evaluated so are not recommended in treatment of radiation proctitis. Short-chain fatty acid, i.e butyrate, have some interest in treatment but studies are limited and reported that patients need to be treated for 5 weeks at least to achieve some results with a recurrence after the end of treatment<sup>18</sup>.

Endoscopic argon beam plasma coagulation (APC) is strongly recommended as safe and effective in treatment of radiation proctitis (moderate quality evidence-(1B)<sup>2</sup> with positive results ranging from 79% to 100% for cessation of bleeding<sup>19-22</sup>. Common flow reported is 1-2 lt per minute and the power 40 to 60 watts It needs a mean of 2 sessions (range 1-5) to achieve these results<sup>23</sup>. A controlled randomized trial versus formaline application APC reported positive results in 94% with no significant difference from topical formaline application (100%)<sup>22</sup>. The use of APC can be followed by mucus discharge, and rectal pain, while severe complication such as recto-vaginal fistula and rectal stricture are reported in about 3% of cases<sup>22-24</sup>. It is less effective in control of frequency and urgency and one prospective study reported no benefit for this aim<sup>22</sup>. Some adverse effects are reported such as perforation of the rectum and explosion after retrograde enema preparation<sup>20</sup>.

Hyperbaric Oxygen Therapy is widely used for non-healing wounds either traumatic, diabetic, septic or radiation induced, based on antibacterial and angiogenic power<sup>25</sup>. In Woo et al. experience in 18 patients with radiation proctitis only 4 of 13 had resolution of bleeding and 3 just improved<sup>26</sup>. Virginia Mason Medical Center reported the results of a series of 27 patients treated by hyperbaric oxygen with a follow-up of 5 years: a complete resolution was achieved in 48%, and a decrease of bleeding in 28%<sup>27</sup>.

It is not widely available even effective because it is expensive and requires a specialized equipment with treatment lasting several weeks. Its recommendation is based on moderate quality evidence<sup>2</sup>.

Other methods such as bipolar electrocoagulation, Nd-YAG laser, cryotherapy, have a limited evidence in support of the use with poor data about effectiveness and safety<sup>28</sup>.

Finally a surgical option is reserved for patients with failure of previous medical treatment, with the belief that radiotherapy increases the risk of leakage after resection<sup>1,29</sup>. A diversion is preferred and is useful for symptoms and bleeding control but in decision making other factors must be considered such as oncological history, patient status and prognosis. Both procedures are related to a high morbidity ranging from 30 to 65%<sup>29</sup>.

## Conclusions

Radiotherapy plays a primary role in multimodal treatment of pelvic cancers. Prostate cancer are often managed with high dose administration up to 7000-8000

cGy so increasing the risk of rectal radiation proctitis. About 10% of patients develop a bleeding requiring topical treatment so colorectal surgeons developed some effective and cost-effective methods of local treatment. Rectal instillation of formaline 4% was reported as successful treatment for radiation proctitis in 21 patients such as the direct application of 10% resulted in 93% of cessation of bleeding in 100 patients with a low incidence of complications (1.1%) The sucralfate enema administration demonstrated effective in a randomized double-blind controlled trial with 94% of patients compared to prednisolone enemas (53%) and 88% in a series of 26 patients.

Other medical options are not widely evaluated so cannot be indicated for routine treatment.

Interventional treatments are more complex and requires specialized equipments so are reserved to refractory cases. The Argon plasma coagulation is reported to be effective in 80 to 90% of case while Hyperbaric oxygen in 88% of patients but it is very expensive and lasts several weeks.

### Riassunto

La proctite cronica da radiazioni è una complicanza frequente dopo la radioterapia per le neoplasie pelviche. È stato riferito che l'1-5% dei pazienti sviluppa proctite cronica da radiazioni anche con i recenti progressi nella radioterapia esterna. Ematochezia, secrezione di muco, urgenza e tenesmo sono sintomi comuni e possono variare in gravità, ma il sanguinamento è spesso il più debilitante per il paziente. Diverse opzioni sono riportate per il trattamento di questa condizione che dovrebbe mantenere sempre una diagnosi differenziale nei pazienti con storia di radioterapia pelvica. I trattamenti vanno da soluzioni facili ed economiche come la somministrazione topica di formalina, a costose che richiedono attrezzature speciali come l'ossigenoterapia iperbarica.

La chirurgia è riservata ai pazienti con fallimento dei trattamenti conservativi a causa dell'elevato rischio di perdite e dell'elevata morbilità fino al 60%. In questo studio sono riportati due casi di pazienti trattati con radioterapia e con sintomatologia da probabile colite attinica. Entrambi i pazienti sono stati sottoposti a colonoscopia ed a trattamento topico e valutazione a distanza. In uno dei casi, visto il perdurare del sanguinamento, è stato necessario eseguire un trattamento con Argon Plasma Coagulator, per ottenere un risultato definitivo.

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