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# Radiation Enteritis

## – a case report and literature review

### Enterite Rádica – apresentação dum caso clínico e revisão da literatura

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#### ABSTRACT

Chronic radiation enteritis is an uncommon clinical entity whose incidence has been gradually increasing even with the constant development of techniques that minimize radiotherapy damaging effects. There are different medical approaches concerning its control, however one third of patients need surgical treatment during the course of the disease. The criteria for the suitable timing and the adequate procedure for the surgical approach are not clearly defined. The authors present the case report of a 65-year-old woman with history of pelvic radiotherapy for cervical cancer who displayed symptoms of chronic radiation enteritis two decades after radiotherapy treatment. The patient was submitted to surgical treatment. After 12 months of follow-up, she was asymptomatic and presented a good physical condition. A brief review of the therapeutic options is made regarding this case.

**Key words:** *enteritis complications; radiation injuries/complications; chronic disease; treatment outcome.*

#### RESUMO

A enterite rádica crónica é uma entidade clínica pouco frequente que tem vindo a aumentar de incidência mesmo com a evolução de técnicas que minimizam os efeitos deletérios da radioterapia. São várias as abordagens médicas sugeridas para o seu controlo, no entanto 1/3 dos doentes necessitam de tratamento cirúrgico ao longo do curso da doença. Os critérios para o *timing* e do procedimento adequado para a abordagem cirúrgica não se encontram definidos. Os autores apresentam o caso clínico de uma mulher de 65 anos, com antecedentes de radioterapia pélvica por neoplasia do colo do útero, com manifestações de enterite rádica crónica cerca de duas décadas após a radioterapia. A doente foi submetida a tratamento cirúrgico. Aos doze meses de seguimento encontrava-se assintomática e com bom estado geral. A propósito deste caso é realizada uma breve revisão das opções terapêuticas.

**Palavras chave:** *complicações da enterite; lesões/complicações rádicas; doença crónica; resultado do tratamento.*

#### INTRODUCTION

Radiation enteritis (RE) results from the gut lesions which occur in response to radiotherapy (RT) used for

abdominal and pelvic malignancies<sup>1</sup>. According to the timing of occurrence of symptoms, radiation enteritis can be subdivided into “acute” and “chronic”. Acute RE occurs soon after exposure and symptoms resolve



spontaneously or with symptomatic treatment within 2 to 12 weeks. Chronic RE develops months to years after radiation exposure and is usually progressive or persists indefinitely<sup>1</sup>.

Improvements in the long-term survival of oncological patients and the increasing usage of radiotherapy as a modality of treatment for pelvic tumors have contributed to increase the incidence of chronic radiation enteritis (CRE)<sup>2,3</sup>. The real incidence of CRE is uncertain, but has been reported to range from 5% to 55% depending on the symptoms and definition of CRE<sup>2</sup>, and it is associated with significant morbimortality<sup>1</sup>. Among women treated for cervical cancer the incidence of severe cases lies between 10 to 15% 20 years after exposure<sup>4</sup>.

## CLINICAL CASE

### History of current disease

We present the case of a 65-year-old woman with history of extracorporeal pelvic radiotherapy for cervical cancer in 1992. Considering that she has been treated in another hospital institution the total radiation doses is unknown. Since then, she is in complete remission from the disease.

In 2009 the patient was referred to Internal Medicine due to weight loss, anemia and malnutrition. In addition, the patient also mentioned sporadic episodes of abdominal pain, diarrhea and vomits for about 4 years long. She was submitted to upper endoscopy and colonoscopy which did not reveal any lesions. In the course of clinical research, the patient underwent a plain abdominal radiography and computerized tomography that showed small bowel obstruction, with no identification of the obstruction site (figure 1).

The patient's assessment was then carried out in the General Surgery service. Based on the clinical history and the previous radiotherapy exposure, CRE was an important diagnosis to consider. Retrograde enteroscopy revealed a friable ulcerative stricture in the medium/distal ileum hindering endoscopic passage and a pale mucosa in the adjacent area, with tiny normal vascular pattern and some ulcerative zones – endoscopic signs consistent with radiation enteritis. Oral enteroscopy proceeded until the medium/distal ileum, which was distended and showed signs compatible with CRE.

Surgical treatment was proposed but the patient refused.

Thereafter the patient was admitted to the General Surgery service several times for medical treatment due to bowel occlusion episodes.

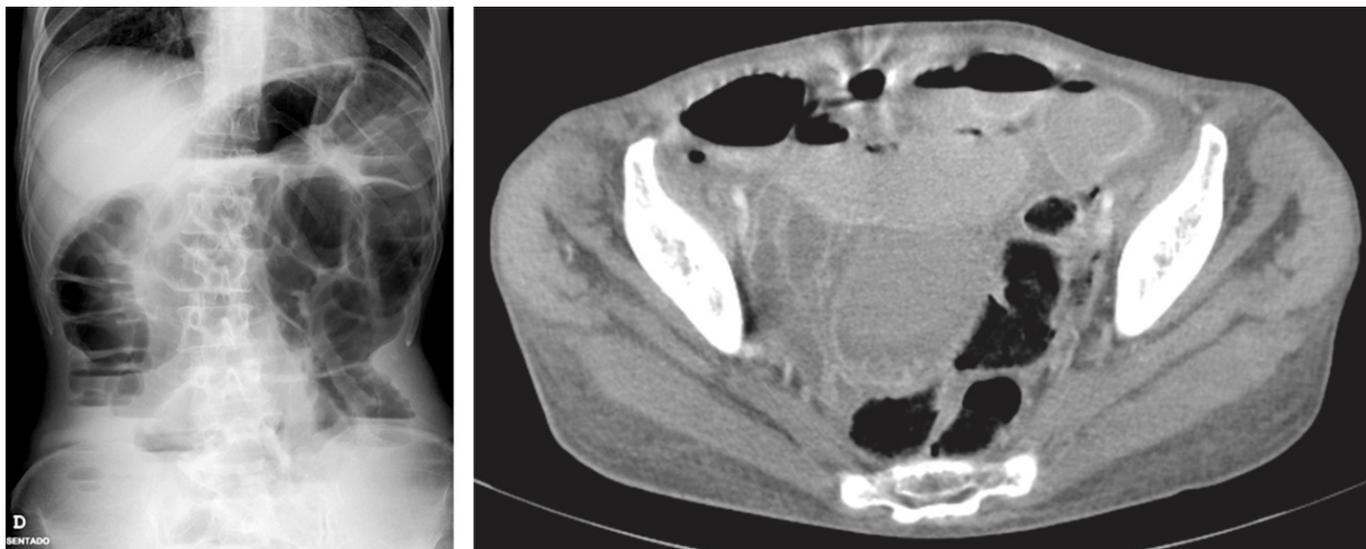


FIGURE 1 – Plain abdominal radiography and computerized tomography show markedly distended loops of small bowel with air-fluid levels.



In August 2013 she was admitted to our surgical unit with a new bowel occlusion episode, this time presenting impairment of her health status. The patient weighed 32,5 pounds, having lost 18 pounds since 2009, and only tolerating liquid diet. On the 4<sup>th</sup> day of hospitalization, with no response to medical treatment, she agreed to be submitted to exploratory laparotomy.

### Surgical Procedure

During surgery there was no evidence of inter-visceral adhesions and only one stenosis with about 3cm length was identified in the medium/distal part of the ileum. The exploration of the abdominal cavity did not reveal other changes. A segmentar enterectomy of 20cm of small intestine with primary anastomosis was performed, at about 50cm from the ileocecal valve. The length of the remaining bowel was of about 4,5m. The procedure was carried out without complications.

### Histology

Stricture compatible with chronic radiation enteritis injuries, without neoplasm structures (Figure 2).

### Postoperative

The postoperative period was complicated by infection and dehiscence of the operative wound, nosocomial pneumonia and sub-occlusive thrombosis of the superior vena cava as a consequence of central venous catheterization for parenteral nutrition (grade II, Clavien-Dindo classification).

The patient was discharged on the 40<sup>th</sup> day after surgery and continued her follow-up in the General Surgery, Vascular Surgery, Medicine and Nutrition services.

### Follow-up

At 12 months the patient presented with substantial clinical improvement. She had no signs of anemia, tolerated all food and had a weight gain of 17 pounds.

### DISCUSSION

The small intestine is the most common site for CRE. Intestinal mucosa is more susceptible to radiation



FIGURE 2 – Intraoperative findings and surgical specimen reveal single stricture with dilation of the small bowel upstream.



damage because of its high cell turnover<sup>1</sup>. The intestinal dysfunction induced by radiation may be a result of mucosal dysfunction (by atrophy, reduction of enzymatic activity of brush border membrane enzymes, decrease of blood and lymphatic supply), intestinal dysmotility with bacterial overgrowth and digestive dysfunction (by stricture formation and neuromuscular dysfunction)<sup>4</sup>. The functional absorption area is reduced which results in malabsorption and poor metabolism. Furthermore, the injuries progression can result in stricture, bleeding, perforation and fistula or local abscesses<sup>1</sup>. There are many symptoms of CRE and the most frequent include abdominal pain and diarrhea. Radiation enteritis is the main cause of functional malabsorption syndrome<sup>1</sup>.

The development and severity of radiation enteropathy are associated to individual factors (previous abdominal or pelvic surgery, comorbidities, inadequate nutrition, etc.) and radiotherapy factors (dose, concomitant chemotherapy, etc.). In order to prevent complications associated to RT, radioprotective agents or mechanical attempts are being developed to exclude gut from the radiation field<sup>5</sup>.

The diagnosis of CRE is established by the combination of appropriate clinical features, a history of radiation exposure and features established by endoscopic studies (friable, edematous, bloody, firm or fibrous mucosa), radiologic or intraoperative features (strictures, fistulae, extensive adhesions in formerly radiated areas) and/or pathologic alterations (fibrotic villi, ulceration, atrophic or absent lymphatic tissue, sub-mucosa severe diseases, hyalinization of arterioles and small arteries, distorted muscular layer or focally replaced by fibrosis) in the absence of other gastrointestinal pathologies, including the neoplastic<sup>1,4</sup>.

Medical management should be individualized and directed to the specific underlying abnormalities (correction of hydro-electrolytic imbalances and nutritional deficits, bile acids absorption increase, regulation of intestinal dysmotility and bacterial overgrowth). Nutritional support is essential for these patients, nevertheless long-term parenteral nutrition is accepted for CRE patients who cannot manage with oral supplementation alone<sup>1</sup>. Hyperbaric oxygen therapy

has shown promise in arresting weight loss but is not widely available and controlled trials are still required to support the expense of its use<sup>1</sup>.

About one third of CRE patients will need to be submitted to surgical treatment during follow-up. Surgery must be limited to those cases in which conservative treatment failed or to those in which symptomatic strictures, perforation, fistulae, severe bleeding or malnutrition occurred<sup>1,3,4,5</sup>. Symptomatic stricture is referred to be the main indication for surgery<sup>2,5</sup>. As for the medical management of patients with delayed radiation enteropathy, the surgical management should be highly individualized<sup>4</sup>.

Surgical management is associated with both an elevated morbidity (reported to be of 30-50%) and significant mortality (10-15%)<sup>1</sup>. Perioperative nutrition therapy is important for the success of surgery and it can decrease the morbidity and mortality of surgical procedures<sup>1</sup>. Operative mortality was significantly higher when the procedure was performed as an emergency rather than as elective surgery<sup>5</sup>. Even after apparently successful operations, symptoms may persist in a significant proportion of patients. Up to 60% of CRE patients undergoing surgery needed reoperation due to CRE recurrence. Risk factors for reoperation are associated to emergency surgery, "conservative" surgical procedures (bypass, adhesiolysis, and diverting enterostomy) and male sex<sup>2,5</sup>.

Intestinal resection of the injured segment is referred to be the preferred procedure by several authors and it should preserve the most gut as possible<sup>2,3,4,5</sup>. However, if in the resection of the distal part of the small bowel the remaining length of the ileum is less than 20 cm, it is suggested that the ileocecal junction be resected, even if the small bowel appears not to be affected by CRE, because this reduces the risk of anastomotic leaks and repeated surgery for CRE recurrence<sup>2</sup>. In addition, it is difficult to distinguish between the normal and the irradiated tissue area of the gut by gross evaluation during operation. Therefore, the accuracy in locating injured intestine may be improved by intraoperative endoscopic evaluation, which can detect radiation induced mucosal injury<sup>3</sup>.



Bypass procedures should be performed when resection is not possible, for instance in case of dense adhesions, or as temporary management in unstable patients<sup>3,4,5</sup>. However, this procedure is associated with blind loop syndrome and does not eliminate either the pathologic tissues or the risks of complications such as bleeding, perforation, occlusion, abscess and fistulae<sup>3,5</sup>. Another drawback of bypass procedures is the relative risk of radiation-induced cancer in irradiated bowel left in place, a single-digit risk rate<sup>5</sup>.

Simple diverting procedures are generally an unsatisfactory alternative. They should be reserved for highly unstable patients and must be seen as a transitory procedure<sup>4</sup>.

With regard to adhesiolysis and intestinal bypass there is little place for these procedures<sup>2</sup>.

Although uncommon, small bowel transplantation is an established surgical approach which may be considered in the pediatric population<sup>1,3</sup>.

In a retrospective study by Lefevre et al. the median hospital stay in patients submitted to surgical treatment was 21 (5-90) days<sup>2</sup>.

Wound complications, intestinal obstruction and anastomotic dehiscence are referred as the main

postoperative morbidities<sup>5</sup>. The risk of dehiscence is high, not only because of poor healing when anastomosis is performed using irradiated tissue but also because of the poor nutritional status of the patient<sup>3,4</sup>. Permanent dependency on home parenteral nutrition is not to be ruled out in CRE patients<sup>2</sup>.

## CONCLUSIONS

CRE must be suspected whenever patients present with symptoms suggestive of that diagnosis and have a history of previous radiation exposure. The symptoms and impact of CRE vary, so the approach must be individualized and multidisciplinary. The decision to perform surgical treatment should be based on the presence of symptomatic anatomical changes and symptoms refractory to medical treatment. Urgent surgery has a higher mortality rate than elective surgery. Surgery should be performed after evaluation of the lesion extension and optimization of the patient's functional and nutritional status in order to reduce surgical morbidity and mortality.

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