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**Retention enema and oral administration of modified Gegen Qinlian decoction for hemorrhagic chronic radiation proctitis: A case report**

Modified Gegen Qinlian decoction for hemorrhagic chronic radiation proctitis

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## **Abstract**

### **BACKGROUND**

Hemorrhagic chronic radiation proctitis (CRP) is a common late complication of irradiation of the pelvis and seriously impairs life quality. There is no standard treatment for hemorrhagic CRP. Medical treatment, interventional treatment, and surgery are available, but they are limited in their applications due to nondefinite efficacy or side effects. Chinese herbal medicine (CHM), as a complementary or alternative therapy, may provide another option for hemorrhagic CRP treatment.

### **CASE SUMMARY**

A 51-year-old woman with cervical cancer received intensity-modulated radiation therapy and brachytherapy with a total dose of 93 Gy fifteen days after hysterectomy and bilateral adnexectomy. She received six additional cycles of chemotherapy with carboplatin and paclitaxel. Nine months after radiotherapy treatment, she mainly complained of 5–6 times diarrhea daily and bloody purulent stools for over 10 days. After colonoscopy examinations, she was diagnosed with hemorrhagic CRP with a giant ulcer. After assessment, she received CHM treatment. The specific regimen was 150 mL of modified Gegen Qinlian decoction (GQD) used as a retention enema for 1 mo, followed by replacement with oral administration of 150 mL of modified GQD three times per day for 5 mo. After the whole treatment, her diarrhea reduced to 1–2 times a day. Her rectal tenesmus and mild pain in lower abdomen disappeared. Both colonoscopy and MRI confirmed its significant improvement. During treatment, there were no side effects, such as liver and renal function damage.

### **CONCLUSION**

Modified GQD may be another effective and safe option for hemorrhagic CRP patients with giant ulcers.

**Key Words:** Hemorrhagic chronic radiation proctitis; Chinese herbal medicine; Gegen Qinlian decoction; Retention enema; Case report

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**Core Tip:** We report a case of hemorrhagic chronic radiation proctitis (CRP) in a patient with a giant rectal ulcer who achieved significant remission *via* retention enema and oral administration of modified Gegen Qinlian decoction. As an alternative and complementary medicine, modified Gegen Qinlian decoction may be another effective and safe option for hemorrhagic CRP patients with giant ulcers in the absence of standard treatments.

## INTRODUCTION

In the case of pelvic cancer, radiation therapy is often used[1]. As a complication of radiation therapy, radiation proctitis frequently occurs. Acute radiation proctitis often occurs in the first 6 wk of radiation treatment; however, it usually subsides on its own. For chronic radiation proctitis (CRP), 5%–20% of patients with pelvic malignancies experience CRP after radiotherapy[2,3]. It can continue from the acute phase or occur after an asymptomatic period of 3 to 6 mo or even years after pelvic radiotherapy[4]. The most common symptoms of CRP are rectal bleeding, also called hemorrhagic CRP, due to neoangiogenesis and vascular ectasias[3,5,6]. Rectal ulcer is another symptom of CRP, which may lead to severe complications, such as perforation, fistulas, strictures, or even death, seriously affecting a patient's quality of life[7,8].

Although the Clinical Practice Guidelines Committee of The American Society of Colon and Rectal Surgeons issued Clinical Practice Guidelines for the Treatment of Chronic Radiation Proctitis in 2018, there are currently no standard treatment for

hemorrhagic CRP<sup>[9,10]</sup>. Current treatments for hemorrhagic CRP mainly include conventional medical therapies (e.g., anti-inflammatory medications, antioxidants, and formalin), endoscopic therapy, and surgery[3]. Due to their side effects and costs, as well as associated high recurrence rates, the above mentioned therapies are selected with caution<sup>[11]</sup>. In addition, accompanying symptoms such as intractable perianal pain, mucus discharge, diarrhea, urinary incontinence and urgency, tenesmus, and iron deficiency anemia in hemorrhagic CRP are usually difficult to manage[3]. As a complementary or alternative medicine, Chinese herbal medicine (CHM) may provide another option for patients with hemorrhagic CRP.

CHMs have been widely applied to treat ulcerative colitis[11,12]. Increasing evidence has demonstrated that CHMs have potentially positive effects on the relief of intestinal inflammation. Some clinical trials explored the efficacy of CHMs for acute radiation proctitis following oral administration or enema[13,14], but no reports were found on CRP or hemorrhagic CRP in the clinical setting. Here, we report a hemorrhagic CRP patient with a giant ulcer treated using CHM by means of retention enema and oral administration.

## **CASE PRESENTATION**

### ***Chief complaints***

A 51-year-old female patient first visited the Traditional Chinese Medicine Cancer Treatment Center in our hospital on September 13, 2021. She mainly complained of frequent diarrhea (5–6 times per day) and bloody purulent stools for over 10 days.

### ***History of present illness***

The patient presented mainly with frequent diarrhea (5–6 times a day), loose stool with blood and mucus accompanied by tenesmus and pain, and mild pain in the lower abdomen. We observed that her tongue was thin and red, with a thin, yellowish, and greasy coating. Her pulse was rapid and thready.

### *History of past illness*

In her past medical history, she was diagnosed with cervical cancer and received intensity-modulated radiation therapy and brachytherapy with a total dose of 93 Gy 15 days after hysterectomy and bilateral adnexectomy from October 30, 2020, to November 23, 2020. <sup>1</sup> Due to the presence of residual disease, she received six additional cycles of chemotherapy with carboplatin and paclitaxel on November 14, 21, and 28 and December 5, 12, and 19, 2020. Two-dimensional conventional radiotherapy was performed 5 times from December 4 to 30, 2020.

### <sup>2</sup> *Personal and family history*

The patient had no significant personal or family history.

### <sup>3</sup> *Physical examination*

On admission, the patient's temperature was 36.2 °C, heart rate was 86 bpm, respiratory rate was 18 breaths per minute, blood pressure was 108/65 mm Hg and body mass index was 20.5 kg/m<sup>2</sup>. The patient presented with a soft abdomen, and no mass was palpated. There was no tenderness in the abdomen and no rebound pain. Bowel sounds occurred 4 times/minute. <sup>3</sup>

### *Laboratory examinations*

A routine fecal occult blood test yielded positive results. No abnormalities were found in tests for cytomegalovirus antibody, *Clostridium difficile* antigen, or coagulation function or in the T-SPOT test for tuberculosis. <sup>1</sup> The routine blood examination showed a minimum hemoglobin concentration of 121 g/L.

### *Imaging examinations*

MRI examination of the pelvic cavity showed no obvious tumor recurrence or metastasis. <sup>1</sup> The walls of the rectum were significantly thickened and swollen, which was considered to have occurred after radiotherapy (Figure 1A). A colonoscopy was

also performed and revealed a giant ulcer (ulceration area > 2.0 cm<sup>2</sup>) covered with necrotic tissue and patchy telangiectasias in the rectum (Figure 2A). The colonoscopy diagnosis was radiation proctitis. Biopsies also confirmed changes consistent with radiation-induced proctitis and ruled out malignant lesions.

### **FINAL DIAGNOSIS**

<sup>1</sup>Based on the above examination results and after the exclusion of diseases, the patient was diagnosed with hemorrhagic CRP. <sup>1</sup>According to the toxicity grade of the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer[15], the patient experienced grade 2 radiation proctitis. Regarding the specific Vienna rectoscopy score criteria[16], the patient had <sup>9</sup>Grade 3 congested mucosa, Grade 3 telangiectasia, Grade 3 ulcerations, no stricture, and no necrosis.

### **TREATMENT**

After performing a comprehensive assessment and obtaining the patient's willingness, she underwent a conservative CHM regimen. A volume of 150 mL of modified Gegen Qinlian decoction (GQD) (Table 1) was used as a retention enema by injection into the rectum in the evening each day for 1 month.

### **OUTCOME AND FOLLOW-UP**

One week after she received retention enema treatment, the frequency of her diarrhea reduced to 2–3 times a day. Her symptoms of rectal tenesmus gradually subsided. On follow-up colonoscopy 1 month later, the rectal mucosal ulcer had healed, but patchy telangiectasias still existed (Figure 2B). However, due to the inconvenience of retention enema every day, the patient was thereafter prescribed oral administration of modified GQD instead of enema (Table 2). The decoction was administered at a dose of 150 mL each time, 3 times per day for 5 mo. On follow-up colonoscopy in April 2022, the rectal mucosal ulcer and patchy telangiectasias were almost healed, with an almost normal vascular pattern (Figure 2C). The MRI examination showed that the thickening and

swelling of the intestinal wall were markedly improved (Figure 1B & 1C). The frequency of her diarrhea reduced to 1–2 times a day. Her symptoms of rectal tenesmus and signs of mild pain in her lower abdomen disappeared. Her tongue was thin and light red, with thin and white coating. Her pulse was thready and moderate. During the period of treatment, no adverse reactions were reported, such as liver or renal function injury. A timeline with relevant data from the treatment period is shown in Supplemental Table 1.

## **DISCUSSION**

Treatment of CRP mainly consists of medical treatment, interventional treatment, and surgical treatment[8]. Endoscopy with ablation remains the preferred interventional treatment for CRP. Among the available medical treatments, sucalfate enemas are the most popular option. Other medical treatments include antibiotics, 5-aminosalicylic acid derivatives, probiotics, antioxidants, short-chain fatty acids, formalin instillation, and hyperbaric oxygen therapy. Unfortunately, there are no large, multicenter, randomized clinical trials evaluating the treatment options for CRP. Currently, clinical data on available treatment strategies are mostly from case reports or small studies[10,17]. According to the severity of disease, medical therapies are often used for mild diarrhea, cramping, or bleeding; endoscopic therapy for rectal bleeding; and surgical therapy for more severe cases, such as refractory bleeding and pain, strictures leading to intestinal obstruction, extremely deep ulcer, and fistulas.

Sucalfate retention enemas have been reported to be effective in the treatment of hemorrhagic CRP[18,19]. Other enemas, such as aminosalicylate, steroid, and short-chain fatty acid enemas, have not been shown to yield a sustainable effect on hemorrhagic proctitis[20]. Formalin (formaldehyde 4%–10%) can chemically cauterize telangiectasias and ulcerations and is often considered the most effective topical treatment of hemorrhagic proctitis. However, because of its corrosive nature, local morbidity was not negligible, particularly with respect to anal incontinence[21].



Argon plasma coagulation (APC) plays the most important role in the endoscopic treatment of hemorrhagic CRP[22]. Similar to formalin, it may require more than one treatment course. The associated prognostic factors were endoscopic features prior to APC, including the presence of telangiectasias on more than 50% of the surface area and ulcerations greater than 1 cm<sup>2</sup>. Zhong *et al* demonstrated that APC may be risky, with 13.3% of patients developing rectal fistulas. The only risk factor identified was an ulceration area greater than 1 cm<sup>2</sup>[23].

Our patient's first colonoscopy showed a very deep ulcer (ulceration area > 2 cm<sup>2</sup>) covered with necrotic tissue and patchy telangiectasias in the rectum. Based on her endoscopic characteristics and chief complaints, we diagnosed her with qi deficiency and damp heat syndrome and prescribed her with the CHM formula. The CHM formula was modified from GQD, which is a traditional Chinese herbal formula used to treat acute enteritis, chronic diarrhea, and bacterial dysentery[24,25]. It has been reported that GQD can alleviate DSS-induced ulcerative colitis by suppressing IL-6/JAK2/STAT3 signaling to restore Treg and Th17-cell homeostasis in colonic tissue[26].

Considering the presence of telangiectasias and ulceration, we added charcoal medicines, such as Diyu (*Radix Sanguisorbae*, charred), Oujie (*Nodus Nelumbinis Rhizomatis*, charred), and egg yolk oil, to control hemorrhagic proctitis. Charcoal medicines refer to a type of medicine carbonized under the guidance of TCM theory with some unique clinical effects[27]. In ancient times, charcoal medicines were used for the clinical treatment of hemoptysis, hematemesis, and hemorrhage[28]. In recent years, researchers have found that carbon dots are the material basis for the activity of charcoal-processed drugs[29]. They may exert different effects on stanching bleeding by stimulating the extrinsic blood coagulation pathway, activating the fibrinogen system and mitigating inflammatory responses by reducing the serum concentrations of tumor necrosis factor- $\alpha$ , interleukin-6, and interleukin-1 $\beta$  in hemorrhagic or infectious diseases[30,31].

In the first month of treatment, modified GQD was used for retention enema. In the second stage of treatment, given the patient's compliance, we changed our treatment strategy to using modified GQD as an oral administration, which was more convenient. Eventually, the patient achieved remarkable remission in both her clinical symptoms and imaging examinations. During the 3-month follow-up visits, the patient felt well.

### **CONCLUSION**

Modified GQD may be an effective, safe, and applicable approach to treat hemorrhagic CRP patients with giant ulcers. Further well-designed, high-quality clinical studies, such as randomized controlled trials, are needed to investigate the role of modified GQD in hemorrhagic CRP patients with giant ulcers.

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