

# A case report of endoscopic therapy for radiation-induced hemorrhagic gastritis in patient with recurrent hepatocellular carcinoma

Ma Liang, MD<sup>a</sup>, Zhang Liwen, MD<sup>b</sup>, Dai Juan, MD<sup>a</sup>, Zhuang Yun, MD<sup>a</sup>, Ding Yanbo, MD<sup>a</sup>, Chen Jianping, MD, PhD<sup>a,\*</sup>

## Abstract

**Rationale:** Radiation-induced hemorrhagic gastritis is an infrequent cause of upper gastrointestinal bleeding and difficult to manage. The current standard treatment has not been well established.

**Patient concerns:** We described a 32-year-old male patient with hemorrhagic gastritis induced by external radiotherapy for hepatocellular carcinoma recurrence.

**Diagnoses:** The endoscopic examination showed a diffuse area of bleeding in the gastric antrum.

**Interventions:** After failure of conventional hemostasis treatment, we successfully stopped the hemorrhage with repeated endoscopic argon plasma coagulation (APC) combined with low-dose polyglycerol sclerotherapy.

**Outcomes:** The patient was followed up for 6 months to date without recurrence.

**Lessons:** Based on this case, we think that endoscopic APC combined with low-dose polidocanol sclerotherapy can be tried as a treatment for potentially life-threatening radiation-induced hemorrhagic gastritis.

**Abbreviations:** APC = argon plasma coagulation, HCC = hepatocellular carcinoma.

**Keywords:** argon plasma coagulation, polidocanol sclerotherapy, radiation-induced hemorrhagic gastritis

## 1. Introduction

Radiation-induced gastritis is a serious complication of radiation therapy for hepatocellular carcinoma (HCC) and can cause upper gastrointestinal bleeding.<sup>[1]</sup> Although a few instances of successful therapy for radiation-induced hemorrhagic gastritis have been reported,<sup>[2–4]</sup> the standard treatment method of this complication has not been established. In this case report, we encountered a

patient with hemorrhagic gastritis induced by external radiotherapy for HCC recurrence that was well-treated using endoscopic argon plasma coagulation (APC) combined with polidocanol sclerotherapy. After endoscopic therapy, bleeding and anemia associated with hemorrhagic gastritis gradually improved.

## 2. Case report

A 32-year-old man diagnosed with HCC received left hepatectomy in October 2016. Three courses of transcatheter arterial chemoembolization with oxaliplatin and 5-fluorouracil were administered from June 2017 to December 2017 for intrahepatic recurrence. In January 2018, he received Gamma Knife radiosurgery for the treatment of metastatic retroperitoneal lymph node. Three months after radiotherapy, the patient presented with hematemesis and melena. On April 11, 2018, the patient was recruited at the inpatient clinic of the Department of Gastroenterology, the First People's Hospital of Changzhou. His vital signs were quite unstable at the time of admission: heart rate was 86 beats/min, blood pressure was 105/66 mm Hg; and respiratory rate was 20 breaths/min. Laboratory evaluation revealed severe anemia with a hemoglobin level of 55 g/L. In addition, as listed in Table 1, other laboratory data, including coagulation function, liver function, and serum tumor markers, were normal. A contrast enhanced thoracic and abdominal computed tomography (CT) scan showed recurrent HCC with multiple lung and peritoneal lymph nodes metastasis (Fig. 1). On April 13, the 1st endoscopic examination showed diffuse edematous hyperemic mucosa with telangiectasis in the whole mucosa of the entire examined stomach. Multiple hemorrhagic patches with active oozing were visible over the antrum (Fig. 2A). Since the patient did not initially provide history of radiation

Editor: N/A.

ML, ZL, and DJ contributed equally to this study.

This study was supported by grants from the National Natural Science Foundation of China (no: 81700500), the Applied Basic Research Programs of Science, Technology Department of Changzhou city (CJ20160031), the Research Project of Jiangsu Province Commission of Health and Family Planning (no: H201547), the Major Scientific and Technological Project of Changzhou City Commission of Health and Family Planning (no: ZD201612), and the Scientific and Technological Project of NanJing Medical University (no: 2017NJMU042).

The authors have no conflicts of interest to disclose.

<sup>a</sup> Department of Digestive Disease, The First People's Hospital of Changzhou, The Third Affiliated Hospital of Soochow University, <sup>b</sup> Department of Pediatrics, the Second People's Hospital of Changzhou, Affiliate Hospital of NanJing Medical University, Changzhou, Jiangsu, China.

\* Correspondence: Chen Jianping, Department of Digestive Disease, The First People's Hospital of Changzhou, The Third Affiliated Hospital of Soochow University, Changzhou, Jiangsu 213003, China (e-mail: chenjianping123abc@163.com).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2018) 97:51(e13535)

Received: 15 August 2018 / Accepted: 12 November 2018

<http://dx.doi.org/10.1097/MD.0000000000013535>

| <b>Table 1</b>                                |              |                     |
|-----------------------------------------------|--------------|---------------------|
| <b>Laboratory observation upon admission.</b> |              |                     |
| <b>Characteristics</b>                        | <b>Index</b> | <b>Normal range</b> |
| Blood                                         |              |                     |
| WBC, $\times 10^9/L$                          | 1.69         | 4.0–10.0            |
| RBC ( $\times 10^{12}/L$ )                    | 1.83         | 3.5–5.5             |
| HB, g/L                                       | 55           | 120–155             |
| PLT, $\times 10^9/L$                          | 59           | 100–300             |
| Coagulation function                          |              |                     |
| PT, s                                         | 13.1         | 9.0–13.0            |
| APTT, s                                       | 29.2         | 19.0–34.5           |
| Liver function                                |              |                     |
| ALT, U/L                                      | 22           | 9–50                |
| AST, U/L                                      | 28           | 10–45               |
| $\gamma$ -GT, U/L                             | 41           | 10–60               |
| ALP, U/L                                      | 113          | 40–125              |
| TP, g/L                                       | 43.6         | 60–82               |
| ALB, g/L                                      | 23.7         | 35–55               |
| CHE, U/L                                      | 1635         | 3000–8000           |
| Serum tumor markers                           |              |                     |
| AFP, ng/mL                                    | 1210         | 0–8                 |
| CEA, ng/mL                                    | 0.69         | 0–5                 |
| CA199, U/mL                                   | 11.54        | 0–37                |
| CA125, U/mL                                   | 8.17         | 0–35                |

ALB=albumin, ALP=alkaline phosphatase, ALT=alanine transaminase, APTT=activated partial thromboplastin time, AST=aspartate aminotransferase, CHE=cholinesterase,  $\gamma$ -GT=glutamyl-transpetidase, PT=prothrombin time, TP=total protein.

therapy, the initial cause of bleeding was misdiagnosed as portal hypertensive gastropathy. He was treated by endoscopic APC and received octreotide acetate (3 mg q12 hours iv) and esomeprazole (20 mg q12 hours iv). However, upper gastrointestinal bleeding still occurred off and on, and anemic aggravation (Fig. 3). On April 17, the 2nd endoscopic examination still showed multiple hemorrhagic spot at antral mucosa. He was diagnosed as radiation-induced gastritis. Due to the inaccessibility of endoscopic APC treatment alone, he was treated with endoscopic APC combined with low-dose polidocanol sclerotherapy (Fig. 2B). Ten days after the 2nd endoscopic therapy, additional endoscopic APC treatment was performed for the

remaining telangiectasia (Fig. 2C). His tarry stool stopped after endoscopic therapy, and his hemoglobin levels improved to 105 g/L after multiple blood transfusions. No gastrointestinal bleeding recurred in a 6-month follow-up period.

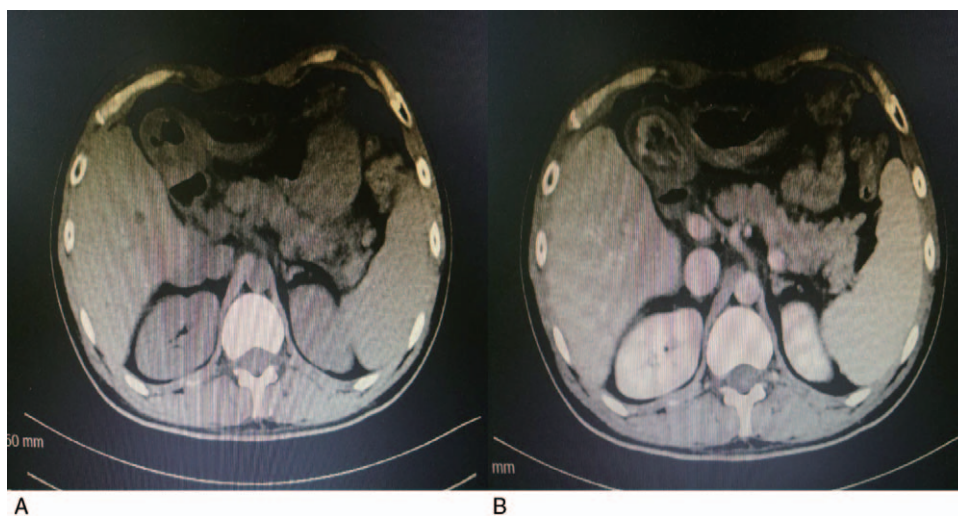
### 2.1. Ethic statement

Our institutional review board was waived due to the retrospective nature of the study. Informed consent was obtained from the patient's parents for the publication of this case report.

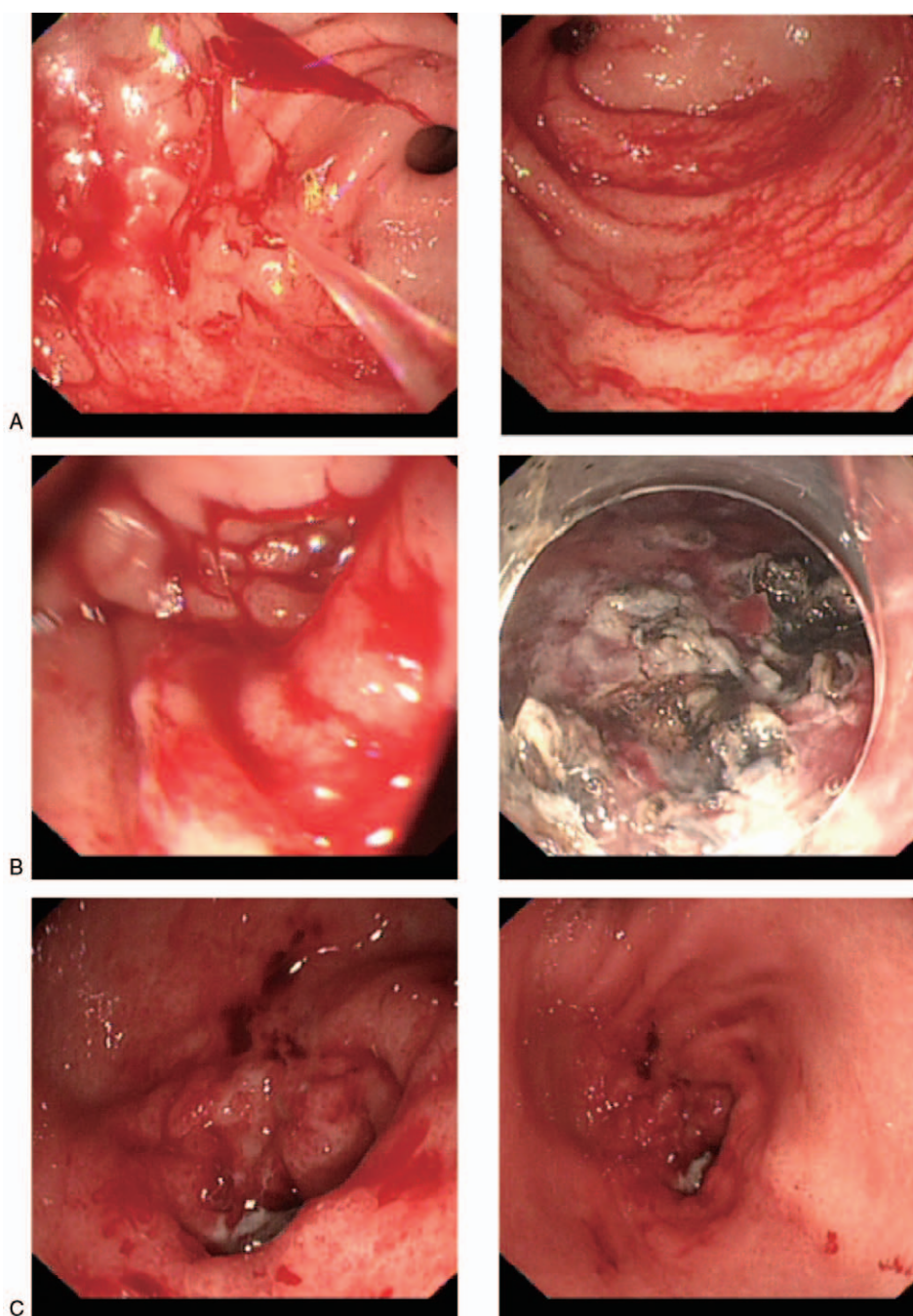
### 3. Discussion

In recent years, radiation therapy has been considered as an effective treatment for patients with HCC that cannot be surgically operated, particularly when combined with other treatment regimens, such as intra-arterial chemotherapy.<sup>[1,5]</sup> Among them, radiation-induced gastritis is the most serious complication and difficult to manage. Because stomach is a radiation-sensitive tissue with durability dosage of 45 Gy, patients with HCC are more vulnerable to gastroduodenal toxicity. Clinical research find that high daily fraction and a high total dose are the main risk factors in gastric injuries.<sup>[2,3]</sup> The main clinical manifestations of radiation gastritis are abdominal pain, bloating, anorexia, nausea, vomiting, and more serious cases can cause gastrointestinal bleeding. Clinical reports are mostly due to melena and hematemesis, and usually occur 2 to 3 months after initial radiotherapy.<sup>[4]</sup> The initial manifestation is acute inflammation of the common gastric mucosa. If injury progresses, vasculopathy may evolve to progressive obliterative endarteritis and endothelial proliferation, leading to mucosal ischemia, ulceration, and telangiectasias.<sup>[2–4]</sup> Typical features of endoscopic finding are the presence of telangiectasia and mucosal edema, and other manifestations of diffuse erythema of mucosa, shallow or deep ulcers and scar formation.

The refractory hemorrhage caused by radiation-induced gastritis is a diffuse process with multiple bleeding sites. The anti-secretory agents and blood transfusion therapy all yielded unsatisfactory control of bleeding. At present, successful treatment methods are only limited to case sharing, and the



**Figure 1.** Conventional and enhanced computed tomography (CT) images. Thoracic and abdominal contrast-enhanced CT showed: postoperative changes in liver cancer, multiple high-density shadows in the left lobe of the liver, cirrhosis, splenomegaly, multiple metastases in both lungs, and multiple lymph nodes in the abdominal cavity. (A) Conventional CT images. (B) Enhanced CT images.



**Figure 2.** Endoscopic appearance of antral mucosa before and after endoscopic treatment. (A) Multiple telangiectasias spontaneously bleeding at diffuse antral mucosa. (B) After endoscopic argon plasma coagulation (APC) and low-dose polidocanol sclerotherapy, multiple telangiectasias were replaced by superficial ulcers with blood clot; (C) Gastric sinus ulcer formation, a small amount of oozing blood on the anterior wall and the large curved side of the mucosa, no bleeding after APC hemostasis.

standard treatment method has not been established. The current main treatment options are as follows:

1. Glucocorticoid therapy: Many investigators have confirmed the value of glucocorticoid in treating many cases of radiation-induced gastritis.<sup>[1,6]</sup> Zhang et al<sup>[1]</sup> and Hyong et al<sup>[6]</sup> reported a patient with radiation-induced gastritis who was successfully treated with prednisolone. It is possible that prednisolone's anti-inflammatory functions is attributed to inhibit inflammation by a diverse array of mechanisms, including decreasing chemotaxis of

monocytes and neutrophils, inhibiting adhesive molecule synthesis, and decreasing eicosanoid production.<sup>[7]</sup> In addition, Kernstine et al<sup>[8]</sup> and Banerjee et al<sup>[9]</sup> reported that hyperbaric oxygen therapy can not only effectively control bleeding, but also reduce hormone dose in 2 cases with radiation-induced gastritis.

2. Endoscopic therapy: Thermal therapy is the cornerstone of endoscopic treatment of bleeding mucosal lesions of the gastrointestinal tract. A few instances of APC successful hemostasis of radiation-induced hemorrhagic gastritis, colitis, and proctitis have been reported.<sup>[2-4]</sup> In addition, Kantsevoy

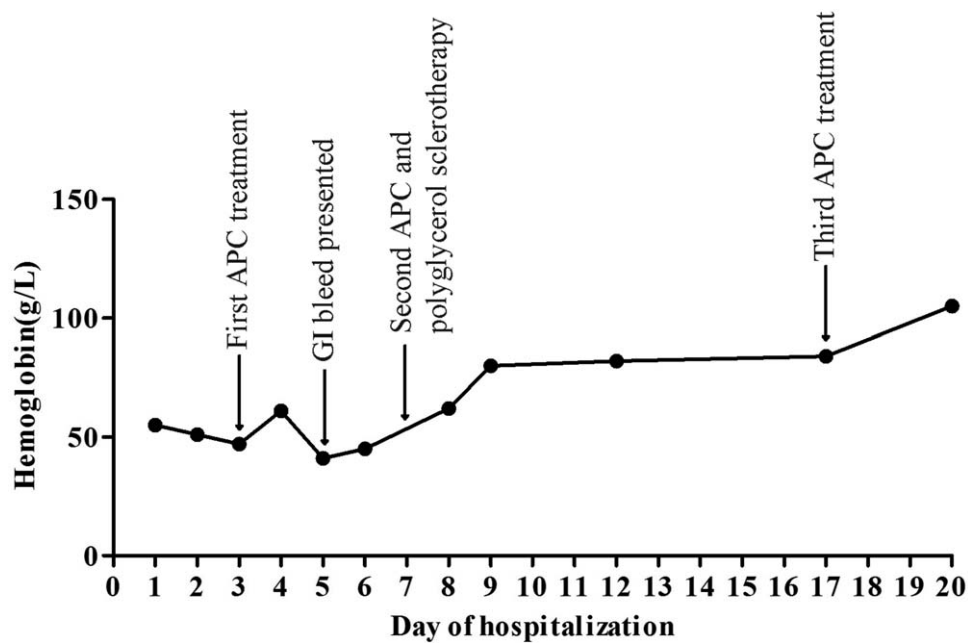


Figure 3. Patient's hemoglobin at baseline and after endoscopic treatment.

et al<sup>[10]</sup> reported that cryotherapy successfully treated radiation-induced gastritis. Staiano et al<sup>[11]</sup> also reported that a patient with radiation-induced gastritis who was successfully treated with endoscopic band ligation.

3. Surgical treatment: Surgery may be necessary if other treatment fails, but it is associated with a high mortality.

In our case, the present patient had ongoing gastric bleeding with symptomatic anemia requiring transfusions of multiple packed red blood cells because of the inability to maintain hemoglobin levels 8 g/dL. Therefore, we initially used endoscopic APC treatment, but the patient still had intermittent blackouts accompanied by a decrease in hemoglobin. It indicated that the treatment with endoscopic APC alone cannot achieve satisfactory efficacy for the extensive hemorrhage of the gastric mucosa. However, after the subsequent 2 treatment of endoscopic APC combined with low-dose polidocanol sclerotherapy, the bleeding never recurred in this patient until 6 months after follow-up.

#### 4. Conclusion

To our knowledge, the efficacy of endoscopic APC combined with low-dose polidocanol sclerotherapy in this location has not been reported. This report describes a further potential treatment modality for radiation-induced hemorrhagic gastritis. Because our observation is limited to 1 patient, more patients and longer follow-up are necessary to confirm the effectiveness of endoscopic APC combined with low-dose polidocanol sclerotherapy for radiation-induced gastritis.

#### Author contributions

**Conceptualization:** Chen Jianping.

**Formal analysis:** Dai Juan.

**Methodology:** Ding Yanbo.

**Project administration:** Zhuang Yun.

**Writing – original draft:** Ma Liang.

**Writing – review & editing:** Zhang Liwen.

chen Jianping orcid: 0000-0002-5505-4140.

#### References

- [1] Zhang L, Xie XY, Wang Y, et al. Treatment of radiation-induced hemorrhagic gastritis with prednisolone: a case report. *World J Gastroenterol* 2012;18:7402–4.
- [2] Shukuwa K, Kume K, Yamasaki M, et al. Argon plasma coagulation therapy for a hemorrhagic radiation-induced gastritis in patient with pancreatic cancer. *World J Gastroenterol* 2007;46:975–7.
- [3] Wada S, Tamada K, Tomiyama T, et al. Endoscopic hemostasis for radiation-induced gastritis using argon plasma coagulation. *J Gastroenterol Hepatol* 2003;18:1215–8.
- [4] Toyoda H, Jaramillo E, Mukai K, et al. Treatment of radiation-induced hemorrhagic duodenitis with argon plasma coagulation. *Endoscopy* 2004;36:192.
- [5] Vasileios T, Evaggelia P, Georgios P, et al. Subtotal gastrectomy for diffused hemorrhagic gastritis induced by radiation, following liver resection for hilar cholangiocarcinoma. A case report. *Int J Surg Case Rep* 2016;18:30–2.
- [6] Hyong GY, Hong YK, Do YK, et al. Successful treatment of intractable bleeding caused by radiation-induced hemorrhagic gastritis using oral prednisolone: a case report. *Cancer Res Treat* 2015;47:334–8.
- [7] Indaram AV, Visvalingam V, Locke M, et al. Mucosal cytokine production in radiation-induced proctosigmoiditis compared with inflammatory bowel disease. *Am J Gastroenterol* 2000;95:1221–5.
- [8] Kernstine KH, Greensmith JE, Johlin FC, et al. Hyperbaric oxygen treatment of hemorrhagic radiation-induced gastritis after esophagectomy. *Ann Thorac Surg* 2005;80:1115–7.
- [9] Banerjee N, Javed A, Deepak D, et al. Hyperbaric oxygen therapy: an adjuvant treatment modality for chemo-radiation induced hemorrhagic gastritis. *Trop Gastroenterol* 2011;32:248–50.
- [10] Kantsevov SV, Cruz-Correa MR, Vaughn CA, et al. Endoscopic cryotherapy for the treatment of bleeding mucosal vascular lesions of the GI tract: a pilot study. *Gastrointest Endosc* 2003;57:403–6.
- [11] Staiano T, Grassia R, Iiritano E, et al. Treatment of radiation-induced hemorrhagic gastritis with endoscopic band ligation. *Gastrointest Endosc* 2010;72:452–3.