

Pneumatosis cystoides intestinalis after fluorouracil chemotherapy for rectal cancer

Kenji Mimatsu, Takatsugu Oida, Atsushi Kawasaki, Hisao Kano, Youichi Kuboi, Osamu Aramaki, Sadao Amano

Kenji Mimatsu, Takatsugu Oida, Atsushi Kawasaki, Hisao Kano, Youichi Kuboi, Osamu Aramaki, Department of Surgery, Social Insurance Yokohama Central Hospital, Kanagawa 231-8553, Japan

Sadao Amano, Department of Surgery, Nihon University School of Medicine, Tokyo 173-0032, Japan

Author contributions: Mimatsu K, Oida T, Kawasaki A, Kano H, Kuboi Y and Aramaki O carried out the operation and were consultant overseeing the patient's care; Mimatsu K wrote the manuscript; Amano S was responsible for drafting the manuscript and revising it critically.

Correspondence to: Kenji Mimatsu, MD, Department of Surgery, Social Insurance Yokohama Central Hospital, 268 Yamashita-cho Naka-ku Yokohama, Kanagawa 231-8553, Japan. mimatsu.kenji@yokochu.jp

Telephone: +81-45-6411921 Fax: +81-45-6719872

Received: February 20, 2008 Revised: April 30, 2008

Accepted: May 6, 2008

Published online: May 28, 2008

Havana City, Cuba

Mimatsu K, Oida T, Kawasaki A, Kano H, Kuboi Y, Aramaki O, Amano S. Pneumatosis cystoides intestinalis after fluorouracil chemotherapy for rectal cancer. *World J Gastroenterol* 2008; 14(20): 3273-3275 Available from: URL: <http://www.wjgnet.com/1007-9327/14/3273.asp> DOI: <http://dx.doi.org/10.3748/wjg.14.3273>

INTRODUCTION

Fluorouracil (FU) is one of the most commonly used chemotherapeutic agents in clinical oncology regimens. With regard to colorectal cancer, treatment involving FU with leucovorin (LV) can improve the survival, tumor response and quality of life^[1] of patients. We report a case of pneumatosis cystoides intestinalis (PCI) in a patient who received adjuvant chemotherapy with 5-FU and 1-LV^[2]. To our knowledge, FU-related or FU-induced PCI has not been reported previously. This case will add to the reported series of patients with FU-induced small bowel toxicity^[3,4] and chemotherapy-related PCI^[5-9].

CASE REPORT

A 76-year-old male underwent anterior resection for stage III rectal cancer. He received an adjuvant chemotherapy protocol comprising intravenous bolus injection of 600 mg/m² 5-FU at 1 h after the initiation of 2 h-long 250 mg/m² 1-LV infusion, once a week for 6 wk, followed by 2 wk of rest^[2]. After 1 cycle of this treatment, the patient presented with diarrhea and abdominal pain. Although his abdomen was distended, he did not exhibit any peritoneal signs. He was afebrile and had no neutropenia. His stool culture was negative. An abdominal radiogram revealed the presence of free air under the diaphragm and intramural gas in the entire intestine (Figure 1). Abdominal computed tomography (CT) revealed the presence of free air in the intestinal wall, retroperitoneal space (Figure 2A), and falciform ligament (Figure 2B). Since bowel perforation was strongly suspected, an emergency operation was performed. Laparotomy revealed pneumatosis of the intestine (Figure 3) and colon, and pneumoretroperitoneum without evidence of perforation. Therefore, gastrostomy was performed to reduce the pressure in the bowel. PCI was

Abstract

Pneumatosis cystoides intestinalis (PCI) is a relatively rare condition characterized by intraluminal gas in the gastrointestinal tract. Several chemotherapeutic agents have been reported to be associated with PCI, although fluorouracil-related PCI is extremely rare. We report a case of a 76-year old man who received adjuvant chemotherapy for rectal cancer with fluorouracil (FU) and leucovorin (LV). After 1 cycle of the treatment, he presented with diarrhea and abdominal pain. Abdominal radiogram revealed the presence of free air under the diaphragm and intramural gas in the intestine. Laparotomy was performed, showing a suspected diagnosis of perforation in the gastrointestinal tract. Intraoperative findings revealed pneumatosis of the intestine without evidence of perforation. He was treated supportively and his symptoms improved. In conclusion, we should consider the possibility of PCI occurring in patients with malignancies during chemotherapy treatment.

© 2008 The WJG Press. All rights reserved.

Key words: Pneumatosis cystoides intestinalis; Chemotherapy; Fluorouracil; Colorectal cancer

Peer reviewer: Damian Casadesus Rodriguez, MD, PhD, Calixto Garcia University Hospital, J and University, Vedado,



Figure 1 Abdominal radiogram showing intraluminal gases in the entire small intestine and free air under the diaphragm.

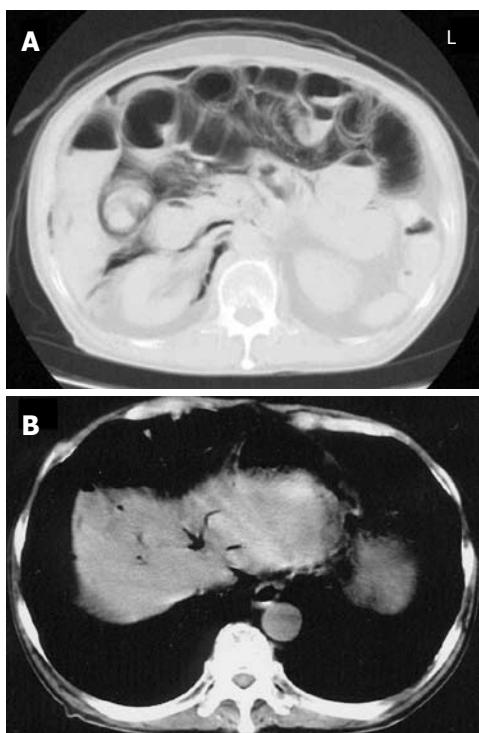


Figure 2 Abdominal CT scan showing excessive intraluminal gases in the entire small intestine and free air in the retroperitoneal space (A), and free air in the falciform ligament (B).

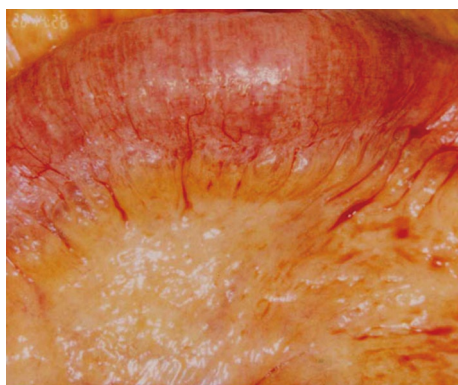


Figure 3 Expanded intraluminal air spaces in the small intestine and mesentery during intra-operation.

disappeared within 2 wk after parenteral nutrition, antibiotic treatment and oxygen therapy. Enema showed no

incidence of anastomotic stenosis and he administered oral uracil-ftorafur, and no recurrence of PCI was observed during the 1-year follow-up.

DISCUSSION

PCI is relatively rare condition characterized by multiple intraluminal gases existing in any part of the gastrointestinal tract. The mechanism and etiology of PCI are not fully understood. According to most hypotheses, mechanical and bacterial factors are the predominant causes for PCI^[10-12]. However, in this present case, no mechanical or bacterial factors, including bowel ischemia, bowel obstruction^[13,14], inflammatory bowel disease and infectious colitis, for the gas production in the intestinal wall were observed.

Several chemotherapeutic agents have been reported to be associated with PCI, including cyclophosphamide, cytarabine, vincristine, doxorubicin, daunorubicin, etoposide, docetaxel, irinotecan and cisplatin^[5-9]. Although fluorouracil-related PCI has not been previously described, the cytotoxic effect of chemotherapy on the epithelial bowel can also play a role in the pathogenesis of PCI^[7]. Because the intestinal mucosa is highly proliferative, mucosal damage occurs easily during chemotherapy^[6]. Moreover, the chemotherapeutic agent might interfere with the mucosal integrity of the intestinal tract, resulting in extensive intramural air^[8]. Tamura *et al*^[15] reported that PCI following chemotherapy might be due to depletion of submucosal lymphoid tissue or leukemic infiltrates, such as denuded Peyer's patches producing mucosal defects, thereby permitting entry of gas into the bowel wall. It was reported that chemotherapy-related PCI occurs due to immunosuppressive treatment for hematological malignancies^[5,6]. Neutropenia is an important factor for the development of PCI^[5-9]. However, the current patient did not suffer from neutropenia before or when PCI was diagnosed.

Several studies have reported severe erosion and superficial ulceration in the ileum after chemotherapy comprising 5-FU and LV in colon cancer patients^[5,4]. The mechanisms are thought to be multifactorial, including alteration in the local mucosal blood flow and thrombogenic and vasospastic effects of 5-FU on the vascular epithelium^[5]. The mechanism underlying 5-FU-induced PCI is thought to be multifactorial, including bowel toxicity caused by 5-FU itself.

In conclusion, although PCI is a rare complication of chemotherapy, the possibility of PCI occurring in patients undergoing chemotherapy should be kept in mind.

ACKNOWLEDGMENTS

The written consent was obtained from the patient for publication of this case report.

REFERENCES

- 1 Poon MA, O'Connell MJ, Wieand HS, Krook JE, Gerstner JB, Tschetter LK, Levitt R, Kardinal CG, Mailliard JA.

- Biochemical modulation of fluorouracil with leucovorin: confirmatory evidence of improved therapeutic efficacy in advanced colorectal cancer. *J Clin Oncol* 1991; **9**: 1967-1972
- 2 **Yoshino M**, Ota K, Kurihara M, Akazawa S, Tominaga T, Sasaki T, Konishi T, Kodaira S, Kumai K, Sugano K. [Late phase II trial of high-dose l-leucovorin and 5-fluorouracil in advanced colorectal carcinoma. l-Leucovorin and 5-FU Study Group (Japan Eastern Group)] *Gan To Kagaku Ryoho* 1995; **22**: 785-792
 - 3 **Fata F**, Ron IG, Kemeny N, O'Reilly E, Klimstra D, Kelsen DP. 5-fluorouracil-induced small bowel toxicity in patients with colorectal carcinoma. *Cancer* 1999; **86**: 1129-1134
 - 4 **Bucaloiu ID**, Dubagunta S, Pachipala KK, Kamal N, Fata F. Small-cell cancers, and an unusual reaction to chemotherapy: Case 4. Fluorouracil-related small bowel vasculitis. *J Clin Oncol* 2003; **21**: 2442-2443
 - 5 **Galm O**, Fabry U, Adam G, Osieka R. Pneumatosis intestinalis following cytotoxic or immunosuppressive treatment. *Digestion* 2001; **64**: 128-132
 - 6 **Hashimoto S**, Saitoh H, Wada K, Kobayashi T, Furushima H, Kawai H, Shinbo T, Funakoshi K, Takahashi H, Shibata A. Pneumatosis cystoides intestinalis after chemotherapy for hematological malignancies: report of 4 cases. *Intern Med* 1995; **34**: 212-215
 - 7 **Candelaria M**, Bournon-Cuellar R, Zubieta JL, Noel-Ettiene LM, Sanchez-Sanchez JM. Gastrointestinal pneumatosis after docetaxel chemotherapy. *J Clin Gastroenterol* 2002; **34**: 444-445
 - 8 **Shih IL**, Lu YS, Wang HP, Liu KL. Pneumatosis coli after etoposide chemotherapy for breast cancer. *J Clin Oncol* 2007; **25**: 1623-1625
 - 9 **Kung D**, Ruan DT, Chan RK, Ericsson ML, Saund MS. Pneumatosis intestinalis and portal venous gas without bowel ischemia in a patient treated with irinotecan and cisplatin. *Dig Dis Sci* 2008; **53**: 217-219
 - 10 **Heng Y**, Schuffler MD, Haggitt RC, Rohrmann CA. Pneumatosis intestinalis: a review. *Am J Gastroenterol* 1995; **90**: 1747-1758
 - 11 **Shindelman LE**, Geller SA, Wisch N, Bauer JJ. Pneumatosis cystoides intestinalis: a complication of systemic chemotherapy. *Am J Gastroenterol* 1981; **75**: 270-274
 - 12 **Rogy MA**, Mirza DF, Kovats E, Rauhs R. Pneumatosis cystoides intestinalis (PCI). *Int J Colorectal Dis* 1990; **5**: 120-124
 - 13 **Horiuchi A**, Akamatsu T, Mukawa K, Ochi Y, Arakura N, Kiyosawa K. Case report: Pneumatosis cystoides intestinalis associated with post-surgical bowel anastomosis: a report of three cases and review of the Japanese literature. *J Gastroenterol Hepatol* 1998; **13**: 534-537
 - 14 **Knechtle SJ**, Davidoff AM, Rice RP. Pneumatosis intestinalis. Surgical management and clinical outcome. *Ann Surg* 1990; **212**: 160-165
 - 15 **Tamura N**, Kojo H, Miyoshi Y, Fukumoto S, Hirayama C. Pneumatosis cystoides intestinalis: Report of 3 cases with special reference to its non-surgical treatment. *Z Gastroenterol* 1980; **18**: 617-624

S- Editor Li DL L- Editor Wang XL E- Editor Liu Y