

—Case Report—

INDUCTION OF DIFFUSE NECROTIZING ENTEROCOLITIS BY ANTICANCER CHEMOTHERAPY

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Summary

Fulminant, necrotizing colitis is a frequent, and generally fatal, complication of severe granulocytopenia, occurring during the treatment of hematological malignancies. In these cases, the patient complains of severe peritonitis, including nausea, vomiting, abdominal pain, diarrhea or melena, and a high temperature. Here, a rare case of anticancer chemotherapy-induced diffuse necrotizing enterocolitis throughout the entire intestinal tract is presented, which developed in a patient who did not have a hematologic malignancy but who had colon cancer, the only clinical symptom of which was watery stools, without any evidence of peritoneal irritation. Full attention should be paid to progressive diarrhea in patients with malignancies during anticancer chemotherapy.

Key Words: *Anticancer chemotherapy, Diffuse necrotizing enterocolitis, Watery stool.*

Introduction

Neutropenic enterocolitis, also known as typhilitis or ileocecal syndrome, is a recognized complication of the treatment of hematologic malignancies and is fatal. These findings are usually limited to the ileum, cecum and ascending colon, and symptoms include nausea, vomiting, abdominal pain, diarrhea or melena, and a high temperature¹. We report here a rare case of diffuse necrotizing enterocolitis throughout the entire intestinal tract, which developed in a patient who did not have a hematologic malignancy but who had colon cancer, the only clinical symptom of which was watery stools, without any evidence of peritoneal irritation.

Case Report

A 58-year old man presented with a change in bowel habit, intermittent constipation and intermittent, fresh, bloody stool. Barium enema revealed two ulcerative lesions in the sigmoid colon. Transcolonoscopic biopsies revealed moderately differentiated (oral lesion) and well differentiated (anal lesion) adenocarcinomas. A computed tomographic scan of the liver and a gallium scintigram of the liver demonstrated the presence of multiple metastatic lesions that extended into both the right and left lobes. Anterior resection of the sigmoid colon was performed and a sili-con catheter was inserted through the gastroduodenal artery into the hepatic artery for chemotherapy of the hepatic metastases.

Figure 1 shows the patient's clinical course. On the first postoperative day, a daily intra-hepato-arterial infusion of 5-fluorouracil (5-

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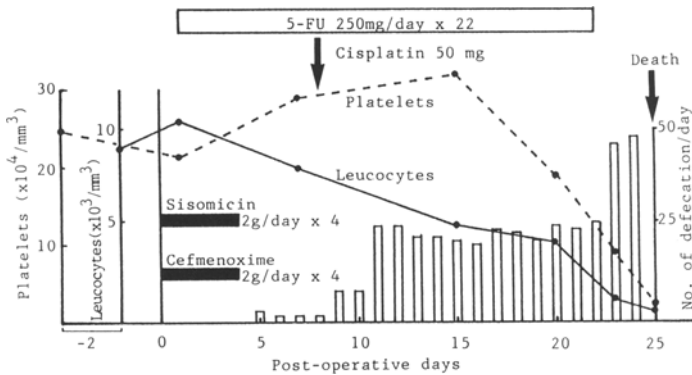


Fig. 1. Clinical course.

FU; 250 mg/day) was initiated. Cisplatin (50 mg) was administered on the 8th day through the catheter. On the 11th day, the patient began to pass watery stool more than 20 times per day, and continued to do so with increasing frequency until his death (25th day). Barium enema yielded the microcolon picture (22nd day); proctoscopy was considered but, because of the patient's critical condition, it could not be performed. No pathogenic microorganisms were detected in his stool culture on the 23rd day. In spite of the cessation of treatment with 5-FU and the aggressive replacement of fluid and nutrients, the frequency of elimination of watery stool increased, the patient died of a colitis-like syndrome with severe leucocytopenia and thrombocytopenia, on the 25th postoperative day. Throughout his postoperative clinical course, he did not have an elevated temperature, melena, vomiting, abdominal pain or evidence of peritoneal irritation.

Figure 2 shows the small intestine at autopsy. Diffuse enteritis, showing evidence of submucosal hemorrhage and necrosis, was observed both in the small and large intestines. The mesenteric arteries and veins did not contain thrombi or any other obstruction. Histologically, widespread intramural necrosis and hemorrhage were found in both the small

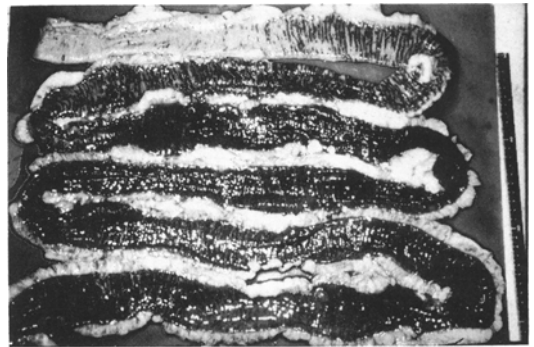


Fig. 2. Small intestine at autopsy, showing intramural necrotic and hemorrhagic findings. Sequence from top to bottom indicates upper jejunum to terminal ileum.

and large intestines, as shown in Fig. 3.

Discussion

Anticancer drugs of various types interfere at different points of the proliferative cycle of tumor cells and prevent further cell division. However, until now there have been no tumor-specific agents which influence the tumor cells selectively. In particular, normal tissue is also affected, especially tissue that normally manifests a high degree of proliferation. The rapidly proliferating epithelia of the gastrointestinal tract are particularly sensitive to anticancer drugs. Severe mucosal damage resulting in disorders such as glossitis, gingivi-

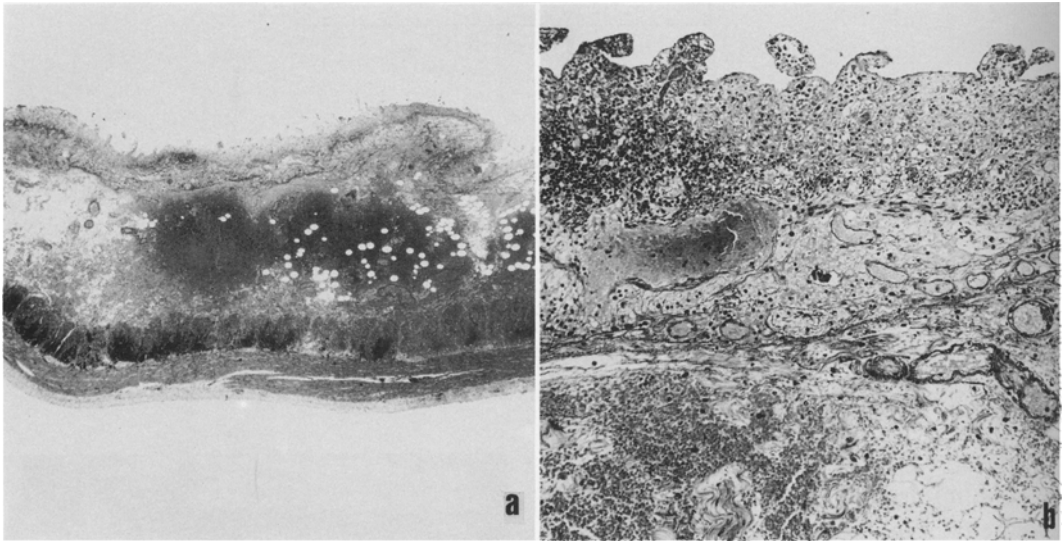


Fig. 3. Histologic findings of the small intestine, showing intramural necrosis and hemorrhage (a; HE $\times 20$, b; HE $\times 100$).

tis and ulcerating enteritis are not uncommon²).

In our case, intractable diarrhea was the only dominant clinical symptom and diffuse necrotizing enterocolitis was diagnosed at autopsy. Although we could not elucidate its pathogenesis, postoperative use of antibiotics³ was probably not the cause of this enterocolitis. At first, we thought that watery stool was due to cisplatin-induced colonic irritation since the frequency of diarrhea increased to 8 times per day on the day after the administration of cisplatin. We also thought that this diarrhea would not be a fatal complication at the time, given the patient's good general condition, absence of elevated temperature, melena and abdominal pain. Cisplatin was discontinued after the first administration, but administration of 5-FU was continued until the 22nd postoperative of day. On that day we obtained an abnormal microcolon picture and noted the rapid deterioration in the patient's general condition. We could not determine which drug had the greater influence on the

development of this complication, because intestinal toxicities of both cisplatin^{4,5} and 5-FU² have been reported.

Fulminant, localized, necrotizing colitis is a frequent, and generally fatal, complication of severe granulocytopenia, occurring during the treatment of hematological malignancies^{6,7}. The diagnosis has been recognized at autopsy in a series of patients, but there are recent reports^{7,8} of successful colonic resection. In these cases, the patient has complained of clinical symptoms of severe local or diffuse peritonitis. In our unusual case, although the patient did not show any signs of peritoneal irritation or peritonitis, diffuse necrotizing enterocolitis involving the entire length of the intestines was encountered at autopsy. We should have considered his illness more seriously and should have deleted all chemotherapeutic agents at the onset of his passing watery stool. Full attention should be paid to progressive diarrhea in patients with malignancies, during anticancer chemotherapy, especially when the diarrhea is associated with

leucocytopenia or neutrocytopenia^{7,9)}.

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