Colonoscopy for Frank Bloody Stools associated with Cancer Chemotherapy

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Diarrhea is a common complication of cancer chemotherapy, while bloody stool is rare. Pseudomembranous colitis has been reported as causing bloody diarrhea after chemotherapy. In this report, we describe nine consecutive patients who presented frank bloody stools within one month after cancer chemotherapy. Patients with a history of pelvic irradiation or with a previously identified colorectal tumor were excluded. Among nine patients, bleeding from tumor undetected before chemotherapy was seen in three, pseudomembranous colitis in four, ischemic colitis in one and methicillin-resistant Staphylococcus aureus enterocolitis in one. Of the three tumors, one was an adenomatous polyp and the other two were metastatic tumors. Two of the four patients with pseudomembranous colitis had not received antibiotics before the onset of colitis. Causes of bloody stools after chemotherapy were various and colonoscopy played an important role in diagnosis and prompt therapy.

Key Words: bloody stool – chemotherapy – pseudomembranous colitis – metastatic colorectal cancer – colonoscopy

INTRODUCTION

Diarrhea is a common complication of cancer chemotherapy, but bloody stool is rare. The causes of bloody stools after chemotherapy have not been well examined in consecutive cases.

Pseudomembranous colitis (PMC) has been reported in patients undergoing intensive chemotherapy (1), and is frequently accompanied by bloody diarrhea (1,2). PMC after cancer chemotherapy without the previous administration of antibiotics has aroused considerable interest (2–11). Ischemic colitis, which often presents bloody diarrhea, has also been noted as a serious complication of chemotherapy (1). Methicillin-resistant Staphylococcus aureus (MRSA) enterocolitis after chemotherapy has been reported from Japan (12).

In this report, we present nine patients who received colonoscopy for evaluation of frank bloody stools after cancer chemotherapy.

CASE REPORTS

Colonoscopic examinations which were requested for the evaluation of frank bloody stools within one month after cancer chemotherapy between 1990 and 1994 at the National Cancer Center Hospital were reviewed. Patients with a history of pelvic irradiation or patients with colorectal tumors that were identified before chemotherapy were excluded. Diagnosis was based on the patient's history, laboratory findings, endoscopic findings, biopsy interpretation, stool culture and Clostridium difficile toxin in the stool. C difficile toxin was detected using the latex agglutination test C.D. Check D-1 (Shionogi Pharmaceutical) (13). Diagnosis of PMC was based on the presence of pseudomembrane on colonoscopy and biopsy specimen (14), regardless of whether C difficile or its toxin was detected. MRSA enterocolitis was diagnosed based on stool culture for MRSA.

The clinicopathological features of these nine patients are summarized in Table 1.

CASE 1

A 40-yr-old man presented mild diarrhea and blood in the stool during chemotherapy for malignant lymphoma of the mediastinum. Colonoscopy revealed a bleeding adenomatous polyp in the sigmoid colon (Fig. 1), at which time the platelet count was reduced to 1.7 × 10^4/µl. After recovery of the platelet count, polypectomy was carried out and no bleeding was observed on further chemotherapy.

CASE 2

A 41-yr-old man was attacked by sudden massive anal bleeding 31 days after chemotherapy. Colonoscopy revealed a tumor of the transverse colon and the biopsy disclosed poorly differentiated adenocarcinoma metastatic from lung cancer. Resection of the transverse colon was then performed and no bleeding was observed on further chemotherapy.
Table 1. Cases with Bloody Stool within one month of previous cancer chemotherapy

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Neoplasm</th>
<th>Chemotherapy</th>
<th>BM (/day)</th>
<th>Nadir WBC (/µl)</th>
<th>Nadir platelet count (x10^4/µl)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>M</td>
<td>ML</td>
<td>VLB, AraC, CBDP, PDN</td>
<td>3</td>
<td>200</td>
<td>1.7</td>
<td>Bleeding polyp</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>M</td>
<td>Lung</td>
<td>CDDP, VDS, CPT-11</td>
<td>3</td>
<td>1500</td>
<td>13.0</td>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>M</td>
<td>Colon</td>
<td>5-FU (c.i.)</td>
<td>2</td>
<td>8000</td>
<td>38.9</td>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>M</td>
<td>Lung</td>
<td>CDDP, VP-16</td>
<td>7</td>
<td>1500</td>
<td>5.2</td>
<td>Ischemic colitis</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>M</td>
<td>Colon</td>
<td>5-FU derivative</td>
<td>6</td>
<td>500</td>
<td>8.7</td>
<td>MRSA enterocolitis</td>
</tr>
<tr>
<td>6</td>
<td>59</td>
<td>M</td>
<td>Colon</td>
<td>5-FU (c.i.)</td>
<td>14</td>
<td>6500</td>
<td>20.8</td>
<td>PMC</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>F</td>
<td>Ovary</td>
<td>CDDP, CPA, 8 VP-16</td>
<td>8</td>
<td>300</td>
<td>1.3</td>
<td>PMC</td>
</tr>
<tr>
<td>8</td>
<td>56</td>
<td>F</td>
<td>Ovary</td>
<td>CDDP, DOX, CPA</td>
<td>8</td>
<td>1700</td>
<td>4.7</td>
<td>PMC</td>
</tr>
<tr>
<td>9</td>
<td>68</td>
<td>M</td>
<td>H&amp;N</td>
<td>CPT-11</td>
<td>&gt;10</td>
<td>300</td>
<td>3.5</td>
<td>PMC</td>
</tr>
</tbody>
</table>

BM, maximal bowel movement; ML, malignant lymphoma; H&N, cancer of the head and neck; MRSA, methicillin-resistant Staphylococcus aureus; PMC, pseudomembranous colitis; c.i., continuous infusion. Chemotherapeutic agents: VLB, vinblastine sulfate; AraC, cytarabine; CBDP, carboplatin; PDN, prednisolone; CDDP, cisplatin; VDS, vindesine sulfate; CPT-11, irinotecan hydrochloride; 5-FU, fluorouracil; VP-16, etoposide; CPA, cyclophosphamide; DOX, doxorubicin hydrochloride.

**Figure 1.** Colonoscopic picture of bleeding colonic polyp (Case 1).

**Figure 2.** Colonoscopic picture of Case 4. Longitudinal ulcerations (↑) were seen in the sigmoid colon.

**CASE 3**

A 50-yr-old man complained of bloody stool during continuous infusion chemotherapy with fluorouracil on an outpatient basis. Sigmoidoscopy revealed a rectal tumor which was suspected of being an invasion of the recurrent colon cancer.

**CASE 4**

A 72-yr-old man suddenly presented left-sided abdominal pain with bloody diarrhea 15 days after chemotherapy. He had a history of ischemic colitis. Bloody diarrhea subsided spontaneously on the day after the onset. Colonoscopy revealed longitudinal ulcerations from the sigmoid to the descending colon (Fig. 2), compatible with ischemic colitis.

**CASE 5**

A 67-yr-old man was treated with a newly developed, orally administered fluoro-pyrimidine derivative. Diarrhea started the day after drug administration and did not respond to usual anti-diarrheal therapy. His condition gradually deteriorated to watery diarrhea with blood more than ten times a day. MRSA was cultured in the stool. Colonoscopy showed scattered redness and erosions mainly in the sigmoid colon without pseudomembrane.
Table 2. Cases of pseudomembranous colitis

<table>
<thead>
<tr>
<th>Case no.</th>
<th>CD toxin</th>
<th>Stool culture</th>
<th>Previous antibiotics</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>ND</td>
<td>Normal</td>
<td>None</td>
<td>SASP</td>
<td>Recovery</td>
</tr>
<tr>
<td>7</td>
<td>–</td>
<td>Normal</td>
<td>IPM, fluconazole</td>
<td>VCM</td>
<td>Recovery</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>Normal</td>
<td>None</td>
<td>VCM</td>
<td>Recovery</td>
</tr>
<tr>
<td>9</td>
<td>ND</td>
<td>Candida albicans</td>
<td>IPM, AMK</td>
<td>VCM, OFLX</td>
<td>Death</td>
</tr>
</tbody>
</table>

CD, Clostridium difficile; ND, not done; IPM, imipenem/cilastatin; AMK, amikacin sulfate; SASP, salazosulfapyridine; OFLX, ofloxacin; VCM, vancomycin hydrochloride

CASES 6–9

These four cases (Table 2) showed pseudomembrane endoscopically. Only one case had a positive result for C. difficile toxin in the stool, and none had a positive stool culture for C. difficile. Two of these PMC cases had not been previously treated with antibiotics.

CASE 6

Fresh bloody stool was noted on the day after onset of diarrhea during the continuous intravenous chemotherapy of fluorouracil. Although colonoscopy and biopsy confirmed the diagnosis of PMC, stool culture and toxin test were negative for C. difficile and Vancomycin (VCM) was not administered. It took 28 days before the cessation of diarrhea.

CASE 7

Diarrhea started on the 13th day after antineoplastic drug administration and bloody stool was seen two days later. VCM was soon administered and the symptoms stopped three days after VCM administration.

CASE 8

Diarrhea started on the 7th day of chemotherapy and toxin test was positive. Although this patient had recovered soon after VCM treatment, she had recurrent C. difficile colitis after chemotherapy two months later. VCM was effective in both episodes of colitis.

CASE 9

Diarrhea started on the day of antineoplastic chemotherapy and became intractable. Sigmoidoscopic examination was done on the 25th day of onset and the diagnosis of PMC was made. Although the patient received VCM and ofloxacin, his condition had already deteriorated with septicemia and he died on the 35th day of chemotherapy.

DISCUSSION

We investigated nine patients with frank bloody stools associated with cancer chemotherapy. Patients with a history of pelvic irradiation were excluded because radiation colitis is expected in such cases, and this would be unsuitable for examining the causes of bloody stools associated with cancer chemotherapy.

In our series, a bleeding colonic polyp and two metastatic cancers were detected. These lesions did not cause bleeding and were not identified before chemotherapy. A decrease in the platelet count due to chemotherapy may have induced bleeding from a preexisting colonic polyp in Case 1. Increased bowel movement may also cause bleeding from the tumor. Those cases in which bleeding was ascribed to a colorectal tumor could be distinguished from cases of enterocolitis by the severity of diarrhea. Patients who present bloody stool not associated with severe chemotherapy may suggest bleeding from a tumor in the large intestine.

Identification of the causes of colitis after antineoplastic chemotherapy is sometimes difficult (15). Dosik et al. described 26 patients with cancer who died from necrotizing colitis and showed three pathologic categories: PMC, agranulocytic colitis and ischemic colitis (1).

Agranulocytic colitis or neutropenic colitis is a segmental necrotizing and ulcerating colitis mainly affecting the cecum. It can arise in patients receiving aggressive chemotherapy especially for leukemia (16–18). In our series, there was no patient compatible with neutropenic colitis. However, awareness and early diagnosis of this complication is important, since it has a high mortality rate.

MRSA enterocolitis after chemotherapy has been reported in Japan (12). Although colonoscopic findings of MRSA enterocolitis have not been examined in detail, one report noted that it was not accompanied by pseudomembrane of the colon (19).

PMC after antimicrobial agents is associated with bloody diarrhea in 5–10% of cases (20), but all of the patients with PMC after cancer chemotherapy in Kamthan’s series presented bloody stools. (2). Frequency of bloody stools in PMC after cancer chemotherapy is unknown, but it could be higher than in usual PMC, because of a tendency to bleed as a hematological side effect. C. difficile and its toxins are considered the main cause of PMC (21). In our series, none of the subjects were positive for the stool culture for C. difficile. This result may be due to the failure to use an anaerobic transport device in our hospital. Although the latex agglutination test for C. difficile is rapid and simple, it has relatively poor sensitivity and specificity (22,23). Better results in the toxin test can be expected using the currently available cytotoxin assay or enzyme immunoassay (24). However, considering the importance of the prompt diagnosis and early treatment of PMC, endoscopy plays an important role in the diagnosis of severe chemotherapy-related diarrhea. Flexible sigmoidoscopy seems to be sufficient for this purpose, since 91% of patients with PMC were diagnosed using a 60-cm flexible sigmoidoscope (25).
Based on the present experience, we consider that although patients with bloody stools after chemotherapy are exhausted, endoscopy is an important diagnostic tool which enables the prompt administration of individualized treatment.

Acknowledgments

This work was supported in part by Grants-in-Aid for Cancer Research and the Comprehensive 10-year Strategy for Cancer Control from the Ministry of Health and Welfare of Japan.

References