Pneumatosis Cystoides Intestinalis after Chemotherapy for Hematological Malignancies: Report of 4 Cases

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Pneumatosis cystoides intestinalis (PCI) is known to be a relatively rare condition which is characterized by gas cysts in the gastrointestinal mucosa. We treated four cases of PCI accompanied by hematological malignancies during chemotherapy treatment. All cases suffered from abdominal discomfort. Abdominal X-ray films revealed gas cysts in the intestine. PCI was observed during leukocytopenic states, and three cases had septicemia. Etoposide was administered to three cases, and prednisolone to all cases. It is considered that PCI sometimes occurs in patients with hematological malignancies during a period of leukocytopenia, and may be caused by intestinal mucosal damage due to myelosuppressive agents and immunosuppression from prednisolone.

(Key words: PCI, leukemia, lymphoma, chemotherapy)

Introduction

Pneumatosis cystoides intestinalis (PCI) is a relatively rare condition characterized by multiple intramural gases existing in any part of the gastrointestinal tract, which is seen in association with various disorders. It is found incidentally during abdominal X-ray or endoscopic examinations in patients with mild abdominal symptoms. Usually it is not associated with peritonitis, and is a benign and self-limited condition (1, 2). The mechanism and etiology of PCI are not fully understood, although mechanical and bacterial factors may be involved (1, 2). Here we report four cases of PCI observed during chemotherapy treatment for hematological malignancies.

Case Report

Case 1

A 51-year-old Japanese man had been suffering from generalized erythema without pain or itching since March 1992. He was admitted to Niigata University Hospital on November 27 of the same year. Skin biopsy revealed many atypical lymphocytes with convoluted nucleus in the subcutaneous layer. These cells had T cell surface markers (CD3, CD4, CD25, and HLA-DR) as evidenced by immunohistological staining, and serum HTLV-1 antibody was negative. He was diagnosed as having malignant lymphoma of the skin. Ultraviolet therapy was ineffective for his erythema. From January 1993, highly intensive chemotherapy, MNCOP-V therapy (methotrexate with leukovorine rescue, mithoxantrone, cyclophosphamide, vincristine, prednisolone and etoposide) was started (Fig. 1). His erythema subsided during six courses of chemotherapy. At the fourth course of this regimen, 100 mg of etoposide was administered intravenously, and marked leukocytopenia (white blood cell count; WBC 400/µl) was observed (Fig. 1). Then, granulocyte colony stimulating factor (G-CSF) was infused. He suffered from septicemia and vague abdominal discomfort. Abdominal X-ray examination revealed multiple cystic lucencies overlying the total colon and free air under the bilateral diaphragma, indicating the presence of PCI (Fig. 2). No sign of peritonitis was observed. He was treated with face mask oxygen inhalation (5 l/min, 5 hours daily), parental nutrition and antibiotics. Serial abdominal X-ray films showed that pneumatosis was gradually reduced. Although erythema recurred after cessation of prednisolone, while body electron irradiation was effective. A skin biopsy was performed after irradiation therapy showed a small amount of lymphoma cells under the subcutaneous layer. He was discharged without any symptoms on July 16, 1993.

Case 2

A 42-year-old woman was admitted to our hospital due to a palpable mass lesion of the genital region in June 1992. Her...
PCI in Hematological Malignancies

Case 1 (51 y.o M) Malignant lymphoma of the skin: Pneumatosis cystoides intestinalis

Chemotherapy

- PSL: prednisolone
- CPM: cyclophosphamide
- MIT: mitoxantrone
- VCR: vincristine
- VP-16: etoposide
- MTX: methotrexate
- TPN: total parental nutrition
- PIPC: piperacillin sodium
- WBC: white blood cell count

Fig. 1. Clinical course of Case 1 with PCI. PSL: prednisolone, CPM: cyclophosphamide, MIT: mitoxantrone, VCR: vincristine, VP-16: etoposide, MTX: methotrexate, TPN: total parental nutrition, PIPC: piperacillin sodium, WBC: white blood cell count.

Fig. 2. Abdominal X-ray film of Case 1 showing large intramural gas in the intestinal mucosa and free air under the bilateral diaphragma.

Fig. 3. Abdominal X-ray film of Case 2.

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CD33. She was diagnosed as having acute myeloblastic leukemia (AML, M1). She was treated with BHAC-DMP (behenyl cytosine arabinoside, daunorubicin, 6-mercaptopurine, and prednisolone) as induction therapy. Septicemia by during a period of severe granulocytopenia occurred. She felt abdominal fullness and slight tenderness of the abdomen. Abdominal X-ray film showed multiple gas cysts in the ascending colon and free air under the diaphragm (Fig. 3). Oxygen inhalation was initiated, and PCI subsided gradually. She recovered from septicemia following the normalization of the granulocyte count. At that time, blastic cells were still found in the peripheral blood and bone marrow. Complete remission could not be achieved after acquisition with daily administration of cytosine arabinoside and etoposide. She died of infectious pericarditis on December 1, 1992.

Case 3

A 58-year-old woman with malignant lymphoma, of a diffuse mixed B cell type, initially diagnosed in 1990, was admitted to our hospital because of the rapid growth of a left lower abdominal mass on October 23, 1992. She was diagnosed as having recurrent malignant lymphoma, stage IIIA. MNCOP-V treatment (same as in Case 1) was started. After four courses of the regimen, including three days infusion of 95 mg etoposide, WBC was decreased to less than 1,000/µL. She felt slight abdominal fullness on December 10. Abdominal X-ray film showed the accumulation of intramural gas cysts in the total colon and terminal ileum, indicating the PCI (Fig. 4). PCI subsided rapidly following oxygen therapy and parental nutrition for one week. However, after the eighth course of the regimen, including the next three days infusion of 100 mg etoposide, PCI recurred. MNCOP-V regimen was finished, but the tumor mass was not reduced. Then, she was treated with salvage therapies.

Case 4

A 74-year-old man was admitted to our hospital due to the second relapse of AML (M2) on November 24, 1992. On admission, pancytopenia was severe, and fever continued. A small dose of cytosine arabinoside (20 mg/day) and G-CSF (75 µg/day) were administered. Although the high fever was controlled with prednisolone, peripheral blast cells were not decreased. Additional etoposide and mitoxantrone infusion were also ineffective. Rapid leukocytopenia was observed after mitoxantrone infusion. Septicemia occurred when WBC was less than 500/µL. At this time, he felt abdominal fullness, and abdominal X-ray film revealed PCI in the total colon (Fig. 5). Oxygen inhalation and parental nutrition were effective. These findings subsided gradually during two weeks' treatment. He died of pneumonia during a period of granulocytopenia on May 17, 1993.

Discussion

PCI is thought to be a rare condition characterized by the leakage of gas into the wall at any portion of the gastrointestinal mucosa. This condition was first described by DuVernoy in 1730 (2). Many etiologies for this disorder have been proposed, but these various theories share common concepts, that is, a mechanical theory and an infectious theory (1, 2).

The mechanical theory is widely accepted. A break of the intestinal mucosa permits air to pass, and under pressure, gases
in the lumen invade to the submucosa. Although PCI may occur in the absence of the primary disorder, it is usually associated with intestinal obstruction, inflammation, ulceration, diverticula, tumors, collagen disease, medical procedures such as endoscopy and operation, hypoxemia, chemoradiotherapy in malignancies (1, 2), and organ transplantation under immunosuppression (3–5).

Concerning the bacterial theory, Stevenson et al (6) reported that severe enterocolitis of the newborn caused the figure of PCI. In this situation, gas cysts may be formed by bacteria. In addition, Yale et al (7) reported that PCI can be made experimentally by injecting Clostridium perfringes into germ-free rats.

PCI occurs in patients with hematological malignancies as well (8–10). Myelosuppressive agents induce bone marrow suppression and granulocytopenia. Because intestinal mucosa is highly proliferative, it is supposed that mucosal damage occurs easily under chemotherapy. During combined chemotherapy including corticosteroids, corticosteroids may induce an atrophy of Payer’s patches in the intestine (11), resulting in the mucosal defects, and lowering the immune defense mechanisms.

In our four cases of PCI, all cases were treated with prednisolone, and were suffering from granulocytopenia. Septicemia occurred in three of these cases. The diagnosis of PCI was established by typical findings in abdominal X-ray films. No cases had a subinvasive procedure performed, such as barium enema or colonoscopy, since the rest of the intestine was important in these patients. In our cases, symptoms of PCI were quite obscure abdominal discomfort, slight abdominal pain and diarrhea which are nonspecific and frequently seen in other gastrointestinal diseases. Even when spontaneous pneumoperitoneum due to the rupture of subserosal cysts occurred, no sign of peritonitis was observed. Parental nutrition and inhaling oxygen were quite effective in the treatment of PCI and maintaining the rest of the intestine. It has been thought that inhaling oxygen by face mask or nasal catheter alters the composition of the cysts. A high concentration of oxygen in the cysts may reduce PCI, because the gas will subsequently be resolved into vessels (12). All cases showed a benign course, but PCI recurred in one case after oral intake during the administration of etoposide. Including this case, three of four cases received etoposide administration before the appearance of PCI. These findings suggest that intestinal mucosa may be highly sensitive to etoposide, triggering PCI by the mechanical theory. It is thus important to pay attention when etoposide is administered to these patients. From the viewpoint of the infectious theory, all cases were in immunosuppressive states. Therefore, the pathogenesis of PCI with hematological malignancies is likely multifactorial.

We conclude that PCI which is sometimes seen in patients with hematological malignancies during chemotherapy treatment is usually benign, and can be managed by inhaling oxygen and by parental nutrition.

References