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Case Report

Cytomegalovirus (CMV) colitis associated with chemotherapy and molecular targeted therapy for gynecologic cancer: A case report of ovarian cancer

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Cytomegalovirus (CMV) colitis associated with chemotherapy for gynecologic cancer is rare. We report a case of CMV colitis linked to treatment with paclitaxel/carboplatin (TC) and bevacizumab (BEV) for ovarian cancer. Our patient was a 59-year-old woman who completed one course of TC chemotherapy and one course of TC + BEV as neoadjuvant chemotherapy for advanced ovarian cancer. On the 7th day of TC + BEV therapy, she visited our hospital for continuous diarrhea, abdominal pain, and melena. Grade 4 neutropenia and fever were also detected. She was diagnosed as CMV colitis via colonoscopy and histopathological examination. This is the first case report of CMV colitis complicated by chemotherapy-induced febrile neutropenia during the treatment for gynecologic cancer.

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Introduction

Most cases of cytomegalovirus (CMV) infection are subclinical infections in childhood. CMV is reactivated in the immunosuppressed state. Graft-versus-host disease, systemic corticosteroid therapy, and HIV infection are risk factors for CMV infection. CMV colitis linked to chemotherapy is rare, and no cases of CMV colitis linked to gynecologic cancer have been reported. We report a case of CMV colitis associated with first-line chemotherapy with paclitaxel/carboplatin (TC) and bevacizumab (BEV) for ovarian cancer. Only one course of TC and one course of TC + BEV were administered to this patient. This is the first case report of CMV colitis complicated by chemotherapy-induced febrile neutropenia during the treatment for gynecologic cancer.

Case report: A 59-year-old nulliparous woman was hospitalized in the emergency department of Nagasaki University Hospital. She experienced breathing difficulty during exercise for 1 month and underwent examination by her family doctor. A pelvic tumor with pleural effusion was suspected on computed tomography, and she was admitted to our hospital. She underwent thoracentesis, and 1,000 mL of pleural effusion were removed (cytology of the pleural effusion was negative). She had normal findings on Pap smear; however, a pelvic tumor, with solid component in its wall, measured 30 × 25 mm^2, was detected via ultrasonography. Her serum CA125 concentration was 2,032 U/mL. She underwent laparotomy, and she was diagnosed with stage IIIC ovarian cancer (high-grade serous carcinoma, pT3cpNXpM0) on the basis of the pathology of the disseminated lesions. On the 15th postoperative day, she started TC chemotherapy (paclitaxel, 180 mg/m^2; carboplatin, AUC = 6, monthly). Intravenous drip infusion of the 16.5mg of dexamethasone was used at the first day of monthly TC chemotherapy. TC + BEV therapy was started on the 36th postoperative day (bevacizumab, 15 mg/kg).

On the 5th day of TC + BEV chemotherapy, melena and diarrhea were detected, and the patient was admitted to our hospital for diarrhea, melena and fever on the 7th day. Her

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complete blood count findings were as follows: leukocytes, 1,000/μL (seg 28.0%, lymph 65%, mono 5.0%, eosino 2.0%, baso 0%); hemoglobin, 11.5 g/dL; and platelets, 203×10^9/L. She was diagnosed with febrile neutropenia and hospitalized in the emergency department of our hospital. She was treated with antibiotics (Cefepime Dihydrochloride Hydrate 2g infusion every 12 hours) for 5 days and granulocyte colony stimulating factor (G-CSF) 75μg was also used for 5 days (subcutaneous injection). On the 10th day of TC + BEV chemotherapy, leukocytes was 1,000/μL and neutrophil count recovered to 33.0%（hemoglobin, 9.2 g/dL; and platelets, 167×10^9/L）and fever was not detected. In the treatment of advanced ovarian cancer with TC+BEV chemotherapy, intestinal perforation is reported as the BEV-related toxicities (5). However, the absence of abdominal tenderness or free air on abdominal X-ray indicated the absence of intestinal perforation. Multiple ulcers from the ascending colon to the descending colon were detected during colonoscopy (Figure 1a). Although the CMV antigen C7-HRP (pp65 antigen) was not detected, the pathological diagnosis was CMV colitis because cytomegalic inclusion bodies were detected in the intestinal stroma via histopathological examination of the ulcer (Figure 1b). The patient received ganciclovir for 23 days（GCV 580mg/day for 7days and 290mg/day for 16days）. Twenty-four days after administration of ganciclovir, multiple ulcers of the colon disappeared on colonoscopy.

She restarted treatment with TC chemotherapy without BEV (paclitaxel, 150 mg/m^2; carboplatin, AUC = 5, monthly) after the confirmation of improvement of CMV colitis via colonoscopy (Figure 2a, b). After six courses of TC chemotherapy, the patient underwent interval debulking surgery, and relapse of CMV colitis was not detected during the first treatment.

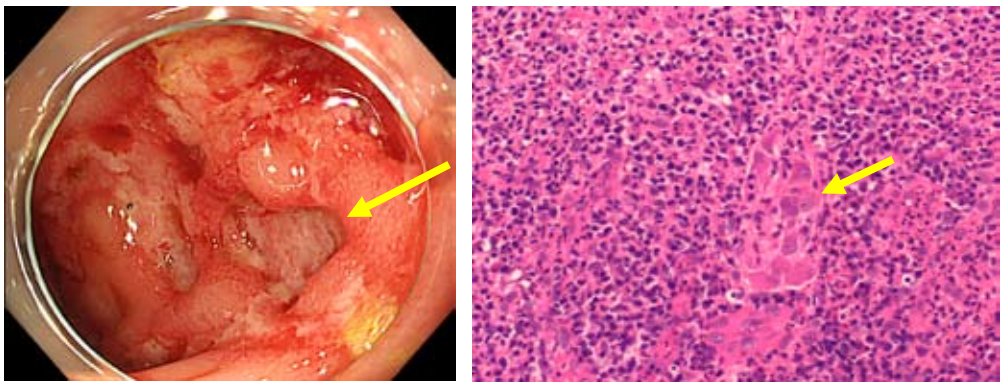

Figure 1. The findings of colonoscopy and pathology.
(a): Colonoscopy showd multiple ulcers from the ascending to descending colon
(b): Histopathological examination of the ulcer shows cytomegalic inclusion bodies indicating cytomegalovirus colitis

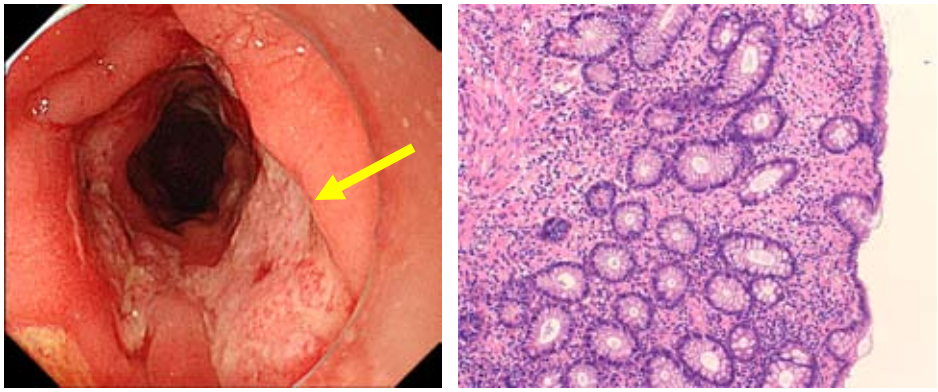

Figure 2. The findings of colonoscopy and pathology after treatment with ganciclovir for cytomegalovirus (CMV) colitis.
(a): The multiple ulcers from the ascending to descending colon were improved on colonoscopy.
(b): The improvement of CMV colitis was confirmed via histopathological examination.

Discussion:

The background of CMV infection as an opportunistic infection in adults

In Japan, approximately 70% of people experience CMV infection in childhood (1). The infection routes include saliva, urine, maternal-fetal transfusion, sexual intercourse, and transfusion. Although most people have latent CMV infection, the infection can become overt under immunosuppression. For example, CMV retinitis, pneumonia, and colitis can be found in immunosuppressed patients (patients receiving treatment with steroids or chemotherapeutic agents). CMV colitis is rare in immunocompetent patients (2, 3). Galiatsatos et al. reviewed the literature, identifying 44 immunocompetent patients with CMV colitis; however, they reported that most of these patients had comorbidities that would be expected to affect immune function (e.g., pregnancy, malignant disease) (3). Furthermore, they reported that there was a trend toward worsened survival in the patients with immune-modulating disease, compared to those with diseases not affecting immunity (the mortality rate was 56.3% versus 22.2%) (3).

Our case involved a patient with CMV colitis associated with treatment with only two courses of TC and one course of BEV chemotherapy for ovarian cancer. She had not taken chemotherapy or immunosuppressive agents before the diagnosis of ovarian carcinoma.

Risk factors for FN in patients receiving chemotherapy include older age, poor performance status (PS), HIV infection, the presence of advanced cancer, and presence of an open wound after a recent operation (4). Our patient was a table tennis player, and her PS was 0 at the diagnosis of ovarian cancer. She did not have HIV infection. Her risk factors for FN were an open wound and advanced cancer. It was possible that CMV colitis occurred in the immunosuppressed state induced by chemotherapy that was started early after surgery for advanced ovarian cancer and usage of dexamethasone at the TC chemotherapy.

The diagnosis of CMV colitis

In the diagnosis of CMV colitis, serology is useful for establishing evidence of previous CMV infection (CMV IgG) (2). The detection of CMV antigen (pp65.C7-HRP), polymerase chain reaction (PCR) detection of CMV DNA, and hematoxylin and eosin (H&E) staining are used to diagnosis CMV colitis. PCR detection of CMV DNA from the blood has replaced the pp65 antigen detection test. However, viremia does not always persist in patients with opportunistic CMV infection, and some patients have negative results for PCR and the pp65 antigen test. In these patients, the detection of owl's eye inclusion bodies via H&E staining is useful for diagnosing CMV colitis. Our patient was negative for pp65 antigen, but she was diagnosed with CMV colitis via H&E staining.

We rarely observe opportunistic infection in patients undergoing first-line chemotherapy for gynecologic cancers. However, CMV colitis arose in our patient after only two courses of TC and one course of BEV. If patients exhibit continuous diarrhea, fever, and/or melena during treatment with chemotherapy, we need to perform colonoscopy, and it is necessary to avoid the aimless administration of antidiarrheal agents and antibiotics.

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References

1) Zouketsusaibouisyoku guideline: Cytomegalovirus infection pp7-8, 2011
2) Goodman AL, Murray CD, Watkins J, Griffiths PD, Webster DP. CMV in the gut: a critical review of CMV detection in the immunocompetent host with colitis. Eur J Clin Microbiol Infect Dis 34:13-18, 2015
3) Galiatsatos P, Shrier I, Lamoureux E, Szilagyi A. Meta-analysis of Outcome of Cytomegalovirus Colitis in Immunocompetent Hosts. Dig Dis Sci 50:609-616:2005
4) Smith T J, Khatcheressian J, Lyman G.H et al. 2006 Update of Recommendations for the Use of White Blood Cell Growth Factors: An Evidence-Based Clinical Practice Guideline. J Clin Oncol 24: 3187-3205, 2006
5) M W. Saif & R. Mehra. Incidence and management of bevacizumab-related toxicities in colorectal cancer. Expert Opin. Drug Saf 5: 553-566, 2006.