

Acute onset of ulcerative colitis during chemoradiotherapy for anaplastic lymphoma kinase-positive lung adenocarcinoma

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Keywords

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Abstract

We report a case of acute onset of ulcerative colitis (UC) during chemoradiotherapy in a patient with anaplastic lymphoma kinase (ALK)-positive lung adenocarcinoma. A 46-year-old male patient with an abnormal chest shadow was referred to our hospital. He was diagnosed with lung adenocarcinoma, clinical stage T1aN3M0 and stage IIIB. Concurrent chemoradiotherapy was selected for his initial therapy. After two cycles of cisplatin and vinorelbine administration, he experienced persistent diarrhoea and anorexia. Findings of the colonoscopy revealed a pancolitis type of UC. After discontinuation of chemotherapy, oral administration of mesalazine was initiated. The development of UC during chemotherapy is very rare and only a few case reports have been published. Although adverse events are rare, it is very important to assess the colitis precisely by performing a colonoscopy when protracted abdominal pain is experienced by the patient, along with diarrhoea or bloody stool during chemotherapy.

Introduction

Cytotoxic chemotherapy can cause various adverse effects involving the mucosa of the gastrointestinal tract. Ischaemic and pseudomembranous enterocolitis are well-known cytotoxic drug-induced enterocolitis [1,2]. Although drug-induced enterocolitis is a common phenomenon, ulcerative colitis (UC) is a very rare condition and only a few cases have been reported previously [3,4].

Here, we discuss a case of acute onset UC during chemoradiotherapy in a patient with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer.

Case Report

A 46-year-old male patient with an abnormal chest shadow was referred to our hospital. He had no obvious history of gastrointestinal diseases. Positron emission tomography-computed tomography (PET-CT) studies revealed a high uptake of fluorodeoxyglucose (FDG) in the

small nodules of the right upper lobe, and bilateral mediastinal and right hilar lymphadenopathy (Fig. 1A, B). Specimens obtained by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS TBNA) of the mediastinal lymph node showed adenocarcinoma harbouring the ALK fusion gene (Fig. 1C–E). The clinical stage of his carcinoma was T1aN3M0 and stage IIIB. Concurrent chemoradiotherapy was selected for his initial therapy. After two cycles of cisplatin and vinorelbine administration, he experienced persistent diarrhoea and anorexia. Supportive care using digestive drugs had poor efficacy for treating his symptoms. Results were negative for the presence of the *Clostridium difficile* (*C. difficile*) toxin and culture. Before consolidation chemotherapy, he underwent a complete colonoscopy, which revealed oedematous thickening of the bowel wall with ulceration and erythema (Fig. 2A–D). Findings of the colonoscopy suggested a pancolitis type of UC. Histopathology of the mucosa specimens showed distortion of the crypts with diffuse

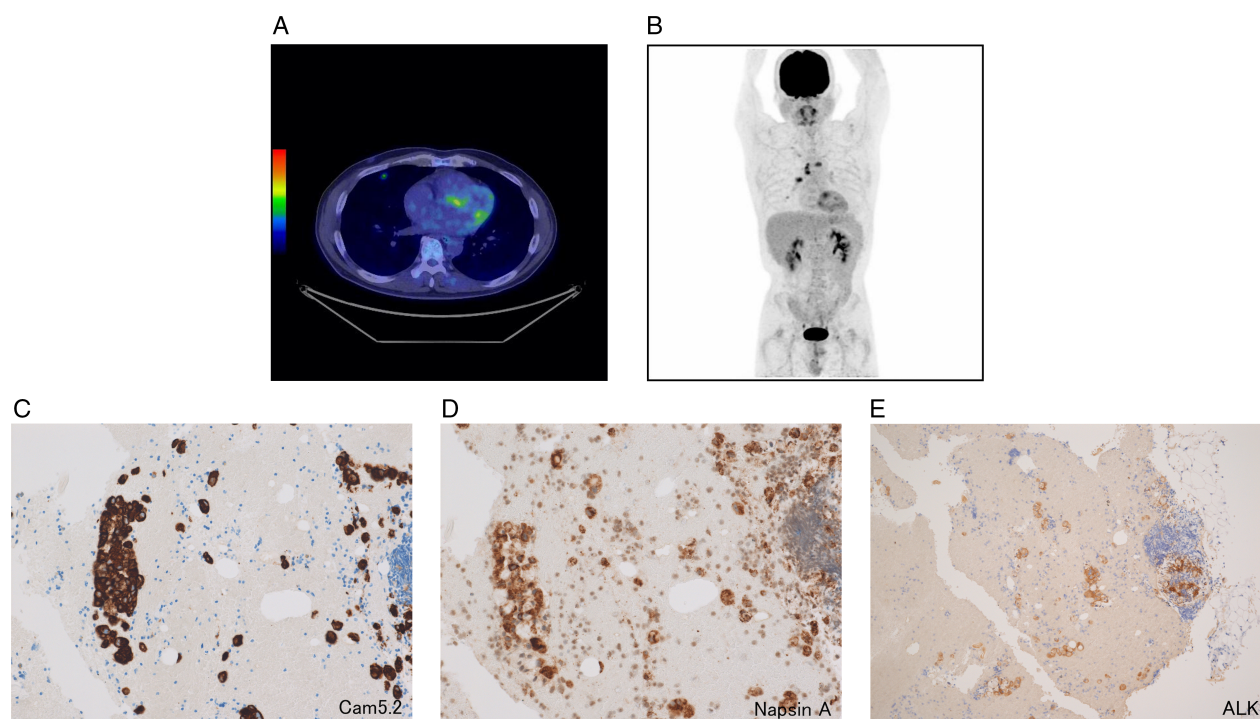


Figure 1. (A, B) Positron emission tomography-computed tomography scan imaging showed high uptake of fluorodeoxyglucose (FDG) in the small nodules of the right upper lobe, bilateral mediastinal and right hilar lymphadenopathy, and absence of FDG uptake in the bowels. (C–E) Specimens taken by endobronchial ultrasound-guided transbronchial needle aspiration showed the aggregation of atypical oval cell with abundant chromatin with positive-staining cam 5.2 (C, 200 \times) and napsin A (D, 200 \times), suggesting adenocarcinoma. Tumour tissue also showed positive staining of anaplastic lymphoma kinase immunohistochemistry (E, 200 \times).

infiltration of inflammatory cells (Fig. 2E). He was diagnosed clinically and pathologically with UC.

Although radiotherapy was continued, concurrent chemotherapy was discontinued after he was diagnosed with UC. The oral administration of mesalazine was initiated. After 2 months of administration of mesalazine, his digestive symptoms remitted and a second colonoscopy revealed that his UC improved. At the time of UC remission, his tumour slightly increased in size. Because his tumour harboured the ALK fusion gene, we administered an oral ALK inhibitor, alectinib as a second line therapy. We started with 300 mg/day of alectinib for the first 2 weeks and then dosed up to 600 mg/day. Administration of 600 mg/day has been effective in maintaining a response after the tumour recurrence.

Discussion

Chemotherapy-induced colitis is common with use of cytotoxic anticancer agents including fluoropyrimidines, irinotecan, methotrexate, docetaxel, vinorelbine and cisplatin [1,2]. Vinorelbine is also known to have venous toxicity and often causes cutaneous ulcers. Although various

mechanisms are proposed for chemotherapy-induced colitis, including increased intestinal permeability, early onset anticholinergic effects and mesenteric vascular insufficiency, precise mechanisms are different for every drug.

The colitis in patients receiving chemotherapeutic agents is usually divided into three types including: neutropenic colitis, ischaemic colitis and *C. difficile*-associated colitis [2]. In our case, there was no evidence of compromised neutropenic status during chemoradiotherapy. After diarrhoea occurred, we confirmed the negative results of the *C. difficile* toxin and culture. A high possibility of ischaemic colitis remained. We also obtained typical images of UC during the colonoscopy and the pathology of the intestinal mucosa indicated evidence of UC. UC as an adverse effect of cytotoxic chemotherapy is a very rare condition. Previously, only two case reports have demonstrated UC during cytotoxic chemotherapy. One case was a patient with lung cancer whose UC was induced by bevacizumab therapy and the other case was a patient with breast cancer whose UC was induced by the therapy of a combination of capecitabine and trastuzumab [3,4].

Although precise mechanisms underlying the causes of UC are unknown, some mechanisms were speculated. In

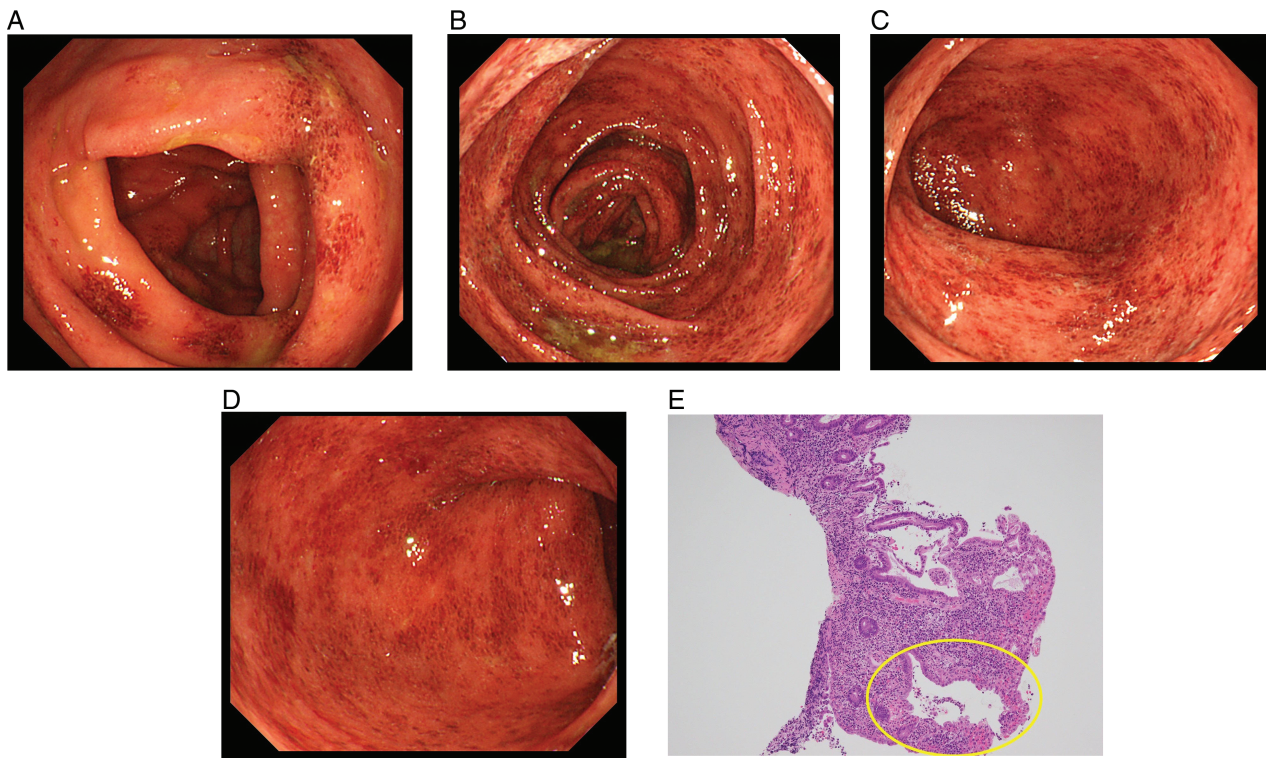


Figure 2. (A–D) Colonoscopy showed diffuse mucosal oedema, redness and petechial haemorrhagic lesions from hepatic flexure to rectum (200 \times , A, hepatic flexure; B, splenic flexure; C, sigmoid colon; D, rectum). (E) Biopsy specimens taken by colonoscopy revealed distortion of the architecture of colonic crypts including inflammatory cells (200 \times). Tissue also included crypt abscess (yellow circle).

patients receiving bevacizumab, anti-angiogenesis activity of bevacizumab may have played an important role [4]. Previously, therapy with a combination of docetaxel and vinorelbine for breast cancer was associated with exacerbation of intestinal toxicity [1]. In the present case, we also used cisplatin in addition to vinorelbine, and therefore, additive toxicity may have been induced. Intestinal mucosa vasculopathy associated with vinorelbine might affect the development of UC.

Although our patient did not have a colonoscopy before concurrent chemoradiotherapy, UC likely did not exist before the treatment for the following reasons. First, our patient had no history of abdominal pains, diarrhoea or bloody stool. A faecal occult blood test was also negative before the treatment. Because the UC of this patient was a pancolitis type, the patient was unlikely to remain free of symptoms. Second, baseline PET-CT apparently showed no FDG uptake in bowel, which can support the notion that there was no pre-existing UC. Third, previous reports suggested that cytotoxic chemotherapy can remit activity of UC [5]. If UC existed before the diagnosis of lung cancer, chemotherapy would have inhibited the symptoms.

In conclusion, we encountered a rare case of UC during chemoradiotherapy. Although this rare complication occurred in a patient with a rare type of lung cancer with ALK translocation, it is very important to assess the patient to determine the type of colitis by colonoscopy when the patient experiences protracted abdominal pain, diarrhoea or bloody stool during chemotherapy.

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Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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