

## Pseudomembranous Colitis: A Complicated Case with Transient Increase of Carcinoembryonic Antigen

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Pseudomembranous colitis (PMC) is a frequent cause of morbidity and mortality among hospitalized patients. Although diarrhea is the most common manifestation, PMC may be associated with intraperitoneal fluid accumulation in the severe cases. And a few cases showing both ascites and pleural effusion have been reported in patients with PMC. We report a case of PMC who showed elevated serum and ascites levels of carcinoembryonic antigen (CEA) with a normal CEA level in pleural effusion and who successfully recovered after oral administration of metronidazole. After treatment, the serum CEA level returned to the reference range. (**Ewha Med J 2015;38(1):54-58**)

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### Key Words

Pseudomembranous colitis; Ascites; Pleural effusion; Carcinoembryonic antigen

### Introduction

Pseudomembranous colitis (PMC) is a frequently severe and sometimes fatal iatrogenic form of inflammatory bowel disease that is associated with antibiotics in the vast majority of cases. The most common clinical features of PMC include watery diarrhea, abdominal pain and cramping, fever, leukocytosis, hypoalbuminemia, and hypovolemia [1]. Metronidazole and vancomycin were commonly used for PMC in clinical practice. Ascites associated with PMC is commonly reported, but PMC accompanied by ascites and pleural effusion has been rarely reported worldwide; only one case has been reported in South Korea [2-4]. Elevation in the carcinoembryonic antigen (CEA) level within ascites fluid has also been rarely reported in patients with PMC [4]. We herein report a case involving a patient with sigmoidoscopy-confirmed PMC who showed elevated serum and ascites CEA levels with a normal level in pleural effusion.

### Case

An 80-year-old male was admitted to our hospital with complaints of watery diarrhea, dyspnea, and abdominal distension. He had no recent travel history and had a medical history of hypertension. Eight days before admission, he fell down while walking, resulting in a laceration on his leg. He was admitted to a local hospital, and intravenous ceftriaxone of 2.0 g/day was initiated after the laceration was sutured. The patient developed diarrhea after 5 days of treatment. He was suspected to have acute gastroenteritis and was thus treated with scopolamine and continuous intravenous antibiotics. His diarrhea, dyspnea, and abdominal distension were aggravated ever since.

On physical examination, the patient's body temperature was 37.8°C, arterial pressure was 100/70 mmHg, pulse rate was 110 beats/min, and respiratory rate was 24 breaths/min. Lung auscultation revealed decreased sounds in both lower lobe fields, and heart auscultation revealed no murmur. The patient's abdo-

men was markedly distended, and his lower limbs were edematous. Other findings were not remarkable.

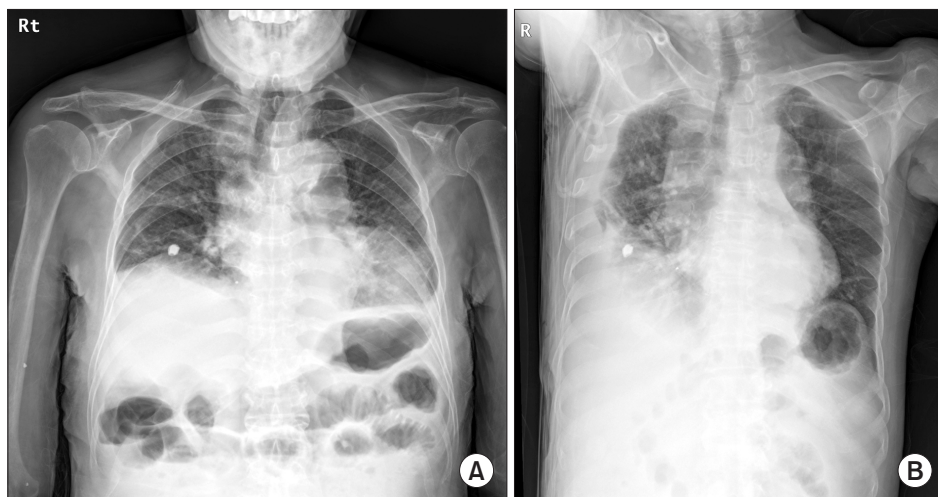
The laboratory test showed a white blood cell (WBC) count of  $15,320/\text{mm}^3$ , hemoglobin level of 11.1 g/dL, and platelet count of  $231,000/\text{mm}^3$ . The C-reactive protein (CRP) level was 115.9 mg/L (normal, approximately 5 mg/L), and the erythrocyte sedimentation rate (ESR) was 46 mm/hr (normal, approximately 15 mm/hr). Serum chemistry revealed a total protein level of 4.8 g/dL (normal range, 6.7 to 8.7 g/dL) and albumin level of 2.1 g/dL (normal range, 3.5 to 5.2 g/dL). The serum CEA level was 15.9 ng/mL (normal, approximately 5 ng/mL). A *Clostridium difficile* toxin enzyme-linked immunosorbent assay (ELISA) was performed twice and showed negative results in both instances.

Chest radiographs showed diffuse ground glass opacities, peribronchial infiltration in both lungs, and bilateral costophrenic angle blunting. Decubitus chest radiographs showed a moderate amount of bilateral pleural effusion (Fig. 1). Pleural fluid analy-

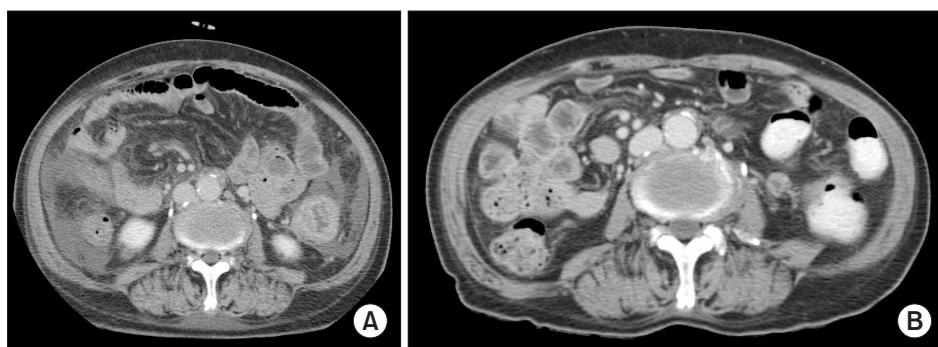
sis revealed a WBC count of  $230/\text{mm}^3$  (neutrophils, 3%), total protein level of 2.3 g/dL, albumin level of 0.1 g/dL, adenosine deaminase level of 10 U/L, lactate dehydrogenase level of 161 U/L, and CEA level of 4.3 ng/mL. The fluid was a transudate. A transthoracic echocardiogram showed no abnormal findings.

Abdominal computed tomography (CT) showed diffuse wall thickening of the colonic loops and a moderate amount of ascites (Fig. 2A). Ascites fluid analysis revealed a WBC count of  $6,880/\text{mm}^3$  (neutrophils, 85%), total protein level of 1.5 g/dL, albumin level of 1.3 g/dL, lactate dehydrogenase level of 185 U/L, adenosine deaminase level of 17.0 IU/L, and CEA level of 19.2 ng/mL. Gram staining and culture results were negative. Serum-ascites albumin gradient was 0.8 g/dL.

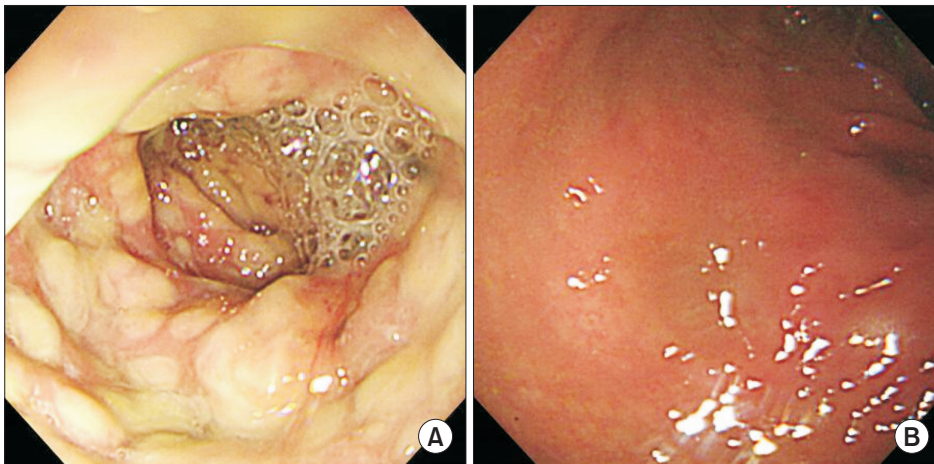
Flexible sigmoidoscopy showed multiple diffuse, yellowish plaques on edematous mucosa (Fig. 3A). The patient was diagnosed with PMC based on the typical sigmoidoscopic findings, and treatment with metronidazole was initiated (500 mg three times daily for 14 days). The diarrhea, abdominal pain, and



**Fig. 1.** Chest radiograph upon admission. (A) It shows diffuse ground glass opacities, peribronchial infiltrations in both lungs, and bilateral costophrenic angle blunting. (B) Right decubitus chest radiograph shows a moderate amount of pleural effusion.



**Fig. 2.** Abdominal computed tomography (CT). (A) It shows diffuse wall thickening of the colonic loops and a moderate amount of ascites. (B) Marked improvement in the diffuse wall thickening of the colonic loops and no ascites are present on day 21 of treatment.



**Fig. 3.** Endoscopic findings. (A) Flexible sigmoidoscopy shows multiple diffuse, yellowish plaques on edematous mucosa. (B) Colonoscopy shows the absence of both the mucosal edema and pseudomembrane on day 21 of treatment.

fever had resolved by day 5 of treatment. On day 14 of treatment, chest radiographs no longer showed diffuse ground glass opacities, peribronchial infiltration, or bilateral costophrenic angle blunting. On day 21 of treatment, the patient underwent a follow-up colonoscopy because of the elevated serum CEA level, and the previous lesions with pseudomembrane disappeared (Fig. 3B). Esophagogastroduodenoscopy showed no abnormal findings. The repeated abdominal CT showed marked improvement in the diffuse wall thickening of the colonic loops and no ascites (Fig. 2B). The follow-up laboratory test showed a WBC count of  $6,770/\text{mm}^3$ , hemoglobin level of 10.9 g/dL, platelet count of  $245,000/\text{mm}^3$ , and CRP level of 0.9 mg/L. The serum chemistry results showed a total protein level of 7.0 g/dL and albumin level of 3.2 g/dL. The serum CEA level had normalized at 4.6 ng/mL. The patient's symptoms resolved completely, and he was discharged from the hospital.

## Discussion

Disruption of the protective colonic flora by broad-spectrum antibiotics is the most common predisposing factor for the development of PMC. Various antibiotics may have distinct influences on not only the gut microbiota but also *C. difficile*. Severe PMC is characterized by abdominal pain, profuse diarrhea, and systemic symptoms such as fever, anorexia, nausea, and malaise. Leukocytosis, elevated CRP levels, and low albumin levels are frequently seen in patients with severe PMC [5].

*C. difficile*-associated disease is usually diagnosed following the demonstration of toxin A and/or B in stool samples. A number of studies have shown that for both assays, the false-

negative rates can be high (10~30%) [6]. Therefore, flexible sigmoidoscopy has been proposed in patients suspected to have *C. difficile*-associated diarrhea but who have negative stool test results for *C. difficile* toxins. In our patient, the ELISA results were twice negative for both toxins A and B.

Plain radiographic findings in patients with PMC vary depending on the severity and extent of disease. Colonic ileus, small bowel ileus, ascites, and nodular haustral thickening have been identified in patients with PMC. Common CT findings include wall thickening, low-attenuation mural thickening corresponding to mucosal and submucosal edema, the target sign, pericolonic stranding, and ascites [7].

Ascites is demonstrated by abdominal ultrasonography and CT in approximately 16% to 77% of patients with PMC [2]. Three possible mechanisms have been proposed for the pathogenesis of ascites in patients with PMC: hypoalbuminemia, transmural colonic inflammation with microperforation and infectious peritonitis, and toxin-mediated generation of cytokines that enhance vascular permeability [1].

Pleural effusion is rare in patients with PMC, and when present, seems to be associated with hypoalbuminemia. The presence of pleural effusion also reflects some extent of altered cardiac function, which contributes to the unfavorable outcome [8]. In this patient, the presence of hypoalbuminemia may explain the pathogenesis of the pleural effusion because of the normal N-terminal pro-brain natriuretic peptide level and transthoracic echocardiographic findings.

The serum level of CEA may be increased in patients with malignancies that secrete CEA into the circulation (gastrointestinal tract, colorectal, liver, lung, breast, ovarian, pancreatic, and

**Table 1.** Summary of cases reported previously and the present case of pseudomembranous colitis

Variable	Boaz et al. (2000) [3]	Kang et al. (2008) [4]	Present study
Patient (age/sex)	25/Female	64/Female	80/Male
Previous antibiotics	Clindamycin for dental infection (10 days) and ciprofloxacin after hospitalization (4 days)	Ceftriaxone for aneurysmal operation (11 days)	Ceftriaxone for wound management (8 days)
Laboratory finding			
WBC (/mm <sup>3</sup> )	34,800	11,210	15,320
Albumin (g/dL)	3.0	1.9	2.1
<i>C. difficile</i> toxin assay	Negative	Negative	Negative
Serum CEA (ng/mL)	ND	5.6	15.94 (4.68 after treatment)
Ascite fluid analysis			
WBC (/mm <sup>3</sup> )	34,000	800 (PMN, 30%)	6,800 (PMN, 85%)
Albumin (g/dL)	ND	1.8 (SAAG, 0.1)	1.3 (SAAG, 0.8)
CEA (ng/mL)	ND	70.1	19.21
Pleural fluid analysis	ND	Exudate	Transudate
Treatment	Oral vancomycin	Oral metronidazole	Oral metronidazole

WBC, white blood cell; CEA, carcinoembryonic antigen; *C. difficile*, *Clostridium difficile*; ND, no description; PMN, polymorphonuclear leukocyte; SAAG, serum ascites albumin gradient.

prostate cancers as well as medullary thyroid carcinoma) [9]. But these levels can also increase in smokers and patients with benign disease, including non-malignant liver disease (cirrhosis, hepatitis, alcoholic liver disease), chronic kidney disease, lung disease (pleural inflammation, pneumonia), and bowel inflammation (ulcerative colitis, diverticulitis). Benign diseases only rarely give rise to serum values >10 ng/mL [10]. Serum and ascites CEA levels should be examined in all patients with ascites. At an ascites CEA cut-off level of 10 ng/mL in one study, 50% of patients with cancer exhibited significantly elevated serum and ascites CEA levels; however, the serum CEA level was not increased in patients with benign disease [11]. Interestingly, the ascites and serum CEA levels were simultaneously elevated in the present case. Therefore, we evaluated the patient for a hidden malignancy by esophagogastroduodenoscopy, colonoscopy, and chest and abdominal CT. No findings led us to suspect the presence of malignancy.

Table 1 provides a summary of previously reported cases of PMC accompanied by ascites and pleural effusion. As in other cases, the present case was also accompanied by ascites and pleural effusion and showed improvement after treatment. Additionally, elevated serum CEA levels returned to the reference ranges after treatment.

In conclusion, the pleural effusion is synchronous with ascites

in the severe PMC. These abnormalities may be improved by treatment of PMC. Additionally, an elevated CEA level in the patients with severe bowel inflammation such as complicated PMC can be correlated with inflammation.

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