

## Thoracic Empyema Associated with Colorectal Cancer — A Case Report and Literature Review

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A previously healthy 31-year-old female was transferred to our hospital after laparoscopic drainage of an abdominal abscess. She was found to have a left-sided empyema, which grew *Bacteroides fragilis* on culture. She was then diagnosed with rectal adenocarcinoma that had perforated, accounting for the abdominal abscess. An unusual pathologic finding in the resected specimen was septic thrombi in the lumen of a small vein.

To our knowledge, only six other cases of empyema associated with colorectal cancer have been reported since the 1960s. Aside from the colo-pleural fistula in two of those cases, the route of pleural infection in the reported cases was not totally clear. The finding of septic thrombi in a small vein in our case is good evidence that *B. fragilis*, a normal flora in the colorectum, may enter the circulation causing bacteremia and empyema. Therefore, unusual infections with fecal flora may indicate the presence of a malignancy. (*Thorac Med* 2004; 19: 273-278)

Key words: thoracic empyema, colorectal cancer, *Bacteroides fragilis*

### Introduction

Colorectal cancer presents most commonly with rectal bleeding, altered bowel habits (narrowing, constipation, intermittent diarrhea, tenesmus), and abdominal pain, anemia, occult blood in the stool, or weight loss. However, infections are rare complications in colorectal cancer. In some instances, unusual infections may be the sole clue to the presence of the malignancy [1].

A variety of infections associated with colorectal cancer have been reported, frequently caused by *Streptococcus bovis*, and involving bacteremia, retroperitoneal abscess, hepatic abscess, non-traumatic gas gangrene, pulmonary microabscess, endocarditis, pericarditis, and meningitis [1-5].

*Bacteroides fragilis*, an important constituent of the normal flora of the colon, has also been implicated in infections associated with colon cancer [1,5-8]. We describe herein a rare case of thoracic empyema caused by *B. fragilis* in a patient with rectal carcinoma.

### Case Report

A 31-year-old female was referred to our hospital because of an abdominal abscess. The patient had been well until one month prior to this admission, when she began to have constipation with intermittent diarrhea. Three weeks before admission, the stool passage began turning bloody. Two weeks before admission, she developed severe

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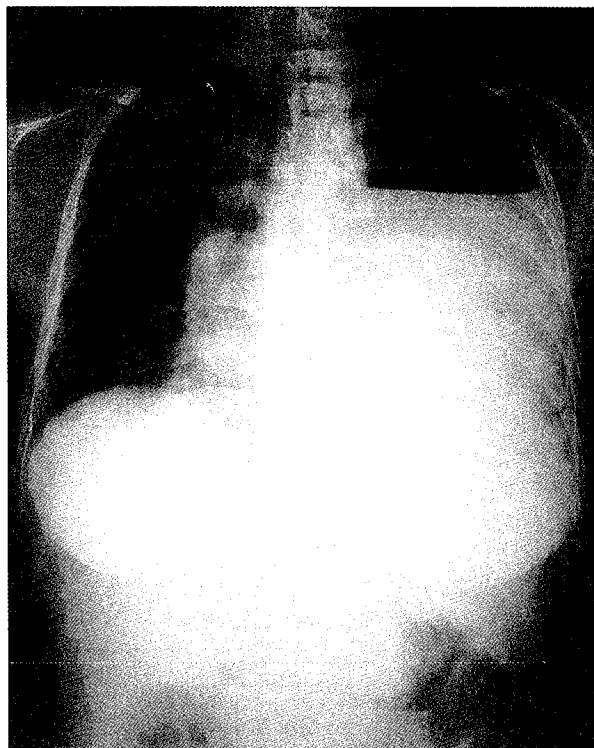
lower abdominal tenderness accompanied by fever. She went to a local hospital where the physical examination revealed abdominal rebounding tenderness. Laparoscopy was performed, revealing an abdominal abscess. The abscess was drained and she was given antibiotics for two weeks. Unfortunately, a spiking fever with leukocytosis persisted, and she was therefore referred to our hospital.

On admission, the patient recalled having constipation for a period of time, but was not particularly bothered by it. She was unmarried and had never been pregnant. She denied nausea, vomiting, cough, arthralgia, or bruising easily. There were no previous hospitalizations, recent travel, or family history of colon cancer.

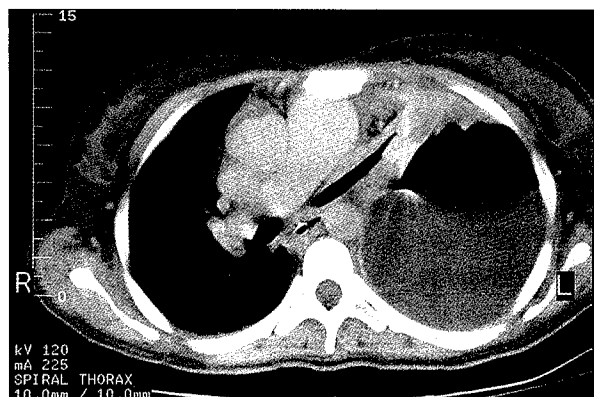
Her temperature was 38.0°C; pulse, 126 beats per minute; respiratory rate, 24 breaths per minute; and blood pressure, 100/70 mmHg. The patient was thin and appeared acutely ill. On chest auscultation, the breathing sounds were decreased in the lower two-thirds of the left hemithorax, with corresponding dullness to percussion in the same area. The abdomen was soft and mildly distended, without rebound tenderness or shifting dullness. There was a wound in the middle of the abdomen with purulent drainage. The remainder of the physical examination was normal.

Laboratory studies revealed the following: hematocrit, 29.4%; hemoglobin, 9.3 g/dl; white blood cell (WBC) count, 43,840/mm<sup>3</sup> (3% band forms, 81% neutrophils, 6% lymphocytes); platelet count, 572,000/mm<sup>3</sup>; glucose, 77 mg/dl; serum creatinine, 1.3 mg/dl; and aspartate aminotransferase (AST), 13 U/L. An electrocardiogram showed sinus tachycardia. A chest X-ray showed massive pleural effusion with an air-fluid level in the left chest (Figure 1). An abdominal plain radiograph showed a diffuse increase in bowel gas. The urine analysis was normal.

A chest computed tomography (CT) scan demonstrated massive left pleural effusion with an air-fluid level, passive atelectasis of the left lung, and a shift of the heart to the right. No mediastinal or hilar lymphadenopathy, pneumonia patch, or subphrenic abscess was seen (Figure 2). A thoracentesis



**Fig. 1.** Chest radiograph taken at admission shows massive pleural effusion with an air-fluid level in the left hemithorax.



**Fig. 2.** Chest CT demonstrates a shift of the heart to the right and atelectasis of the left lung, and massive pleural effusion with an air-fluid level in the left-side pleural cavity. The mediastinum and hilar region is free from lymphadenopathy.

was performed, and gray, turbid, foul-smelling, purulent fluid was aspirated. A chest tube was inserted and empiric therapy with antibiotics was initiated, using intravenous cefepime (1 g every 8 hours), amikacin (500 mg every 24 hours), and

metronidazole (500 mg every 6 hours). The patient's condition improved with this treatment, and the WBC count fell to  $1,2400/\text{mm}^3$  on the fourth hospital day. The pleural fluid culture yielded *Bacteroides fragilis*, and the cytology was negative for malignant cells. There was no evidence of liver abscess or ascites with abdominal ultrasound.

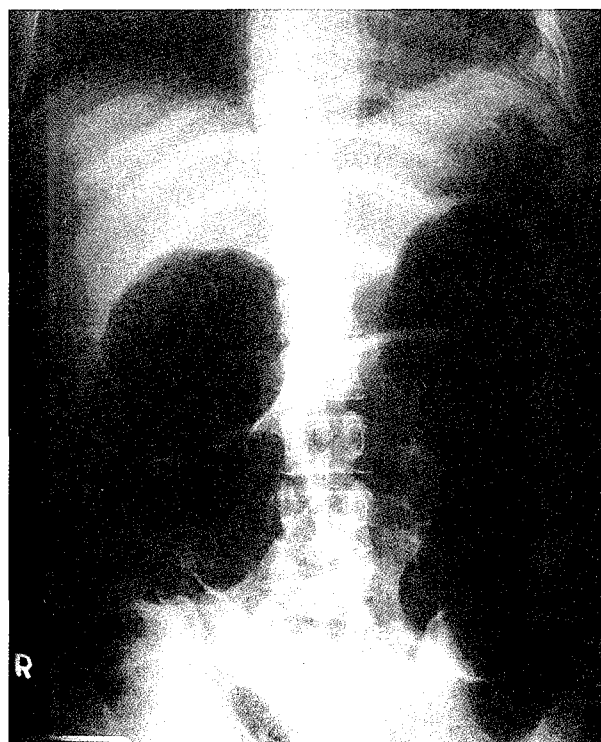
On the fifth hospital day, the patient had hematochezia and worsening abdominal distension. A follow-up series of radiographs follow-up showed a diffuse increase in bowel gas with dilatational bowel loops; the maximum diameter of the colon was about 6 to 7 cm (Figure 3). Colonoscopy revealed a rectal mass. A CT scan of the abdomen and pelvis showed a huge rectal mass with focal peritonitis in the pelvic cavity (Figure 4). The pathological examination of a trans-anal biopsy confirmed adenocarcinoma. The carcinoembryonic antigen (CEA) was as high as 30.61 ng/ml. On the twentieth hospital day, the patient underwent a radical pro-

ctectomy, colorectal anastomosis and lymph node dissection. The pathology showed a moderately differentiated adenocarcinoma, stage III (T4N1M0), with lymph node involvement, vascular invasion, and rectal perforation, in association with a pericolic abscess. A small vessel had septic thrombi in its lumen (Figure 5).

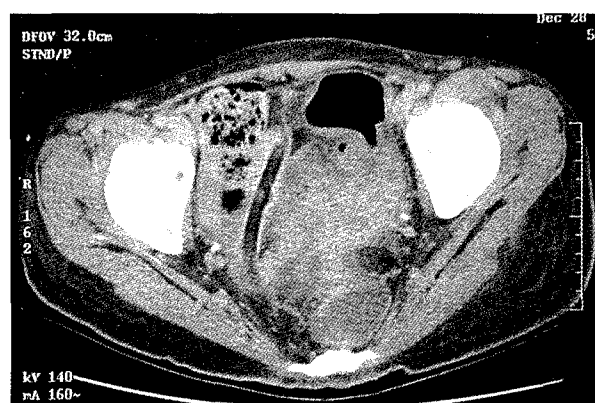
After surgery, the leukocytosis gradually resolved and the patient became afebrile. She was discharged in stable condition, and remained well one and half years after discharge, at which time her CEA was 2.37 ng/ml.

## Discussion

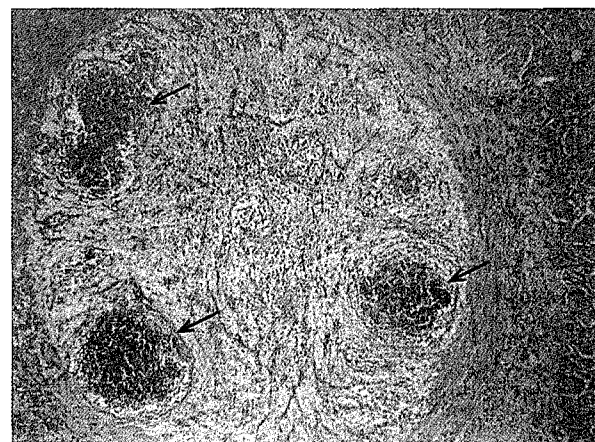
This case is unusual in that a patient with a



**Fig. 3.** Abdominal plain radiograph taken two weeks after admission reveals a diffuse increase in bowel gas with dilatational bowel loops. The maximum diameter of the colon is about 6 to 7cm.



**Fig. 4.** Abdominal CT reveals a huge rectal mass with central necrosis just above the bladder in the pelvic cavity.



**Fig. 5.** (H&E, 400X) A small vessel is occupied with septic thrombi (*arrowheads*) in its lumen.

previously undiagnosed colon cancer presented to us with empyema and an accumulation of fluid and gas in the left pleural space. There was an absence of pneumothorax and broncho-pleural fistula clinically, which indicated that the intrathoracic gas could have been produced by the anaerobic bacilli, *Bacteroides fragilis*. Her history of a change in bowel habits and the abdominal abscess should have been a clue to other intra-abdominal pathology, but it was only after drainage of the abdominal abscess and that empyema and adenocarcinoma of the colon were diagnosed.

It is not surprising, however, that the empyema itself did not suggest colorectal cancer. To our knowledge, only six other such cases have been reported (Table 1) [1,5,9-11]. Aside from the colo-pleural fistula in two of those cases, the route of pleural infection in the reported cases was not totally clear. Bacteremia and/or a direct extension of the intra-abdominal infection seemed likely. Our patient had a pathologically demonstrated perforation of her rectal carcinoma, which accounted for the original pericolonic abscess. There was no evidence of subphrenic abscess formation evaluated by laparoscopy, abdominal ultrasound, and abdominal CT. An interesting finding in the resected specimen was septic thrombi in the lumen of a small vein.

We think her infection might have spread to the pleural space by one of three pathways. The first is a direct spread from the intra-abdominal abscess. A second possibility is that the bacteria might have entered the circulation via the superior hemorr-

hoidal vein and inferior mesenteric vein, thence into the portal system and through the liver, with eventual entry into the systemic circulation. The final possible route is via the inferior and middle hemorrhoidal vein to the internal iliac vein, inferior vena cava, and then into the systemic circulation. The patient had no evidence of subphrenic or liver abscess, which might decrease the likelihood of the first or second route.

A shift in the relative proportions of organisms in the fecal flora in patients with colon cancer has been reported, notably an increase in *Bacteroides* species [6]. Of these species found in the feces of patients with colon cancer, *B. vulgatus* was the most frequent, and *B. fragilis* accounted for only 4% of the organisms. However, its relative frequency was 39% in lavage fluid and 42% in cultures of the colonic mucosa. This suggests that *B. fragilis* has an intimate association with the gut mucosa [7-8].

The *B. fragilis* group has special virulence factors, including an immunologically distinct capsule composed of two polysaccharides, which promotes various infections [12]. *B. fragilis* also has pili, which increase adherence to the intestinal epithelium and mucus to five-fold that of nonpiliated counterparts [13]. The *B. fragilis* group produces the short-chain fatty acid succinic acid, which inhibits phagocytosis [14], as well as a variety of enzymes and superoxide dismutase, which may contribute to tissue damage, enable the organism to escape host defenses, or defend against oxygen free radicals [15]. For these reasons, even though *B. fragilis* may

**Table 1.** Summary of reported cases of thoracic empyema associated with colorectal tumor

Authors	Age (yr) / Gender	Site of Colon Tumor	Site of Empyema	Bacterial Pathogens
Bentley and Lepper [9]	74 / M	Cecum and duodenum*	Right	<i>Escherichia coli</i> , <i>Clostridium perfringens</i>
Bentley and Lepper [9]	53 / M	Sigmoid	Right	<i>Clostridium perfringens</i>
Panwalker et al [1]	71 / M	Cecum	Right	<i>Escherichia coli</i> , <i>Bacteroides fragilis</i>
Ishiwa et al [10]	51 / F	Transverse*	Left	Not described
Teruuchi S et al [11]	63 / M	Transverse	Left	Not described
Takuya Osada et al [5]	47 / M	Descending	Left	<i>Streptococcus bovis</i>

\* Recurrent gastric cancer

account for only a small proportion of the fecal flora, it is the most important anaerobic organism encountered in clinical infection.

## Conclusion

The *B. fragilis* group is a quite small part of the normal flora. With its special virulence factors, it is an important pathogen of infections and correlates to colorectal cancer. Thoracic empyema is very rarely caused by *B. fragilis*, *S. bovis*, or *E. coli*. If this does happen, and is accompanied by colorectal symptoms, the chances of a colorectal malignancy are considerable.

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## 大腸直腸癌合併膿胸—病例報告及文獻回顧

劉景隆 李昭賢 吳健樑 陳培然

一位31歲先前健康的女性病患，此次因腹膿瘍經腹腔引流術後轉診入院接受治療。住院期間，發現左側膿胸，而肋膜積液細菌培養結果為鬆脆類桿菌 (*Bacteroides fragilis*) 感染。之後，病患確診為直腸腺癌合併腸破裂，因而造成腹膿瘍。另一個意外的病理發現，在一條小靜脈管徑內存在著散播性的微小膿瘍。

據我們所知，自1960年代以來，共有六例大腸直腸癌合併膿胸罕見病例之文獻記載。其中，除二例發現有大腸肋膜瘻管外，其餘四例的感染途徑並不十分清楚。在本篇報告中的一個意外發現，在一條小靜脈管徑內存在散播性的微小膿瘍，由此可以證明鬆脆類桿菌，一種大腸直腸正常內生菌，可以進入血液循環，造成菌血症和膿胸。因此，在一個不尋常的內生腸道菌感染，有可能存在著惡性腫瘤。(《胸腔醫學》2004; 19: 273-278)

關鍵詞：膿胸，大腸直腸癌，鬆脆類桿菌 (*Bacteroides fragilis*)