Thoracic Empyema Associated with Recurrent Colon Cancer

Report of a Case and Review of the Literature

Takuya Osada, M.D., Ph.D.,*† Hirokazu Nagawa, M.D., Ph.D.,*†
Tadahiko Masaki, M.D., Ph.D.,‡ Nelson H. Tsuno, M.D., Ph.D.,*†
Eiji Sunami, M.D., Ph.D.,* Toshiaki Watanabe, M.D., Ph.D.,*‡
Tetsuichiro Muto, M.D., Ph.D.,‡ Yoichi Shibata, M.D., Ph.D.,†

From the Departments of *Surgical Oncology and †Transfusion Medicine, Graduate School of Medicine, the University of Tokyo, ‡Second Department of Surgery, Kyorin University School of Medicine, and §Department of Surgery, Cancer Institute Hospital, Tokyo, Japan

Many types of infections associated with colorectal cancer have been reported. Here, we describe a rare case of thoracic empyema that was observed during immunotherapy for recurrent colon cancer. Culture of the pleural fluid yielded *Streptococcus bovis*, which is known to be associated with gastrointestinal lesions, especially colorectal malignancies. The possible correlation between these two clinical entities—empyema and colon cancer—is discussed.

*Key words: Thoracic empyema; Colorectal cancer; *Streptococcus bovis*; Immunotherapy*


Primary or secondary colorectal tumors cause many kinds of symptoms, including abdominal pain, fever, and constipation. Infections, although quite rare, can in some instances be the sole clue to the presence of malignancy.1 2 Many types of infections associated with colorectal cancer have been reported, including retroperitoneal abscess, hepatic abscess, nontraumatic gas gangrene, pulmonary microabscess, endocarditis, pericarditis, and meningitis.1-4 These infections are related to either invasion of tissues or organs that are in close proximity to the tumor, or may be secondary to distant seeding, arising through transient bacteremia caused by necrotic tumor tissue. In this report, we describe a rare case of thoracic empyema that occurred in a patient with recurrent colon cancer during the course of immunotherapy using dendritic cells (DCs).

REPORT OF A CASE

A 47-year-old male underwent left hemicolectomy with lymph node dissection for descending colon cancer on August 25, 1996. The tumor was histologically classified as well-differentiated adenocarcinoma, Dukes C, with no sign of vessel invasion. In July 1997, he was diagnosed as having local recurrence of the tumor with metastasis to the paraaortic lymph nodes and spleen by computed tomography (CT). Several courses of chemotherapy using 5-fluorouracil and leucovorin were administered from August 1997 to April 1998, but were judged to be ineffective, due possibly to acquisition of chemoresistance by the tumor cells. Therefore the patient chose to accept immunotherapy using dendritic cells on June 15, 1998, after informed consent had been obtained.

On June 29, leukapheresis was performed and DCs were isolated using density gradient centrifugation.5 After two days of culture, activated DCs were pulsed with autologous tumor lysate, washed intensively, and infused into the patient intravenously. Monocytes were cultured for six days in medium containing granulocyte-macrophage colony-stimulating factor and interleukin-4.6 The following week, these monocyte-derived DCs were pulsed with tumor lysate and inoculated into the patient as described above. We always checked the levels of endotoxin in the culture medium before DC inoculation. Leukaphereses were repeated five times biweekly during a period of 2.5 months.

During these treatments, the serum level of carcinoembryonic antigen stopped increasing and finally began to decrease (Fig. 1). Unfortunately, however, CT images obtained on September 7 indicated the presence of local tumor recurrence with peritoneal dissemination (Fig. 2A). Slight accumulation of effusion in the left pleural cavity was also observed (Fig. 2B). Thereafter, the patient developed progressive back pain and was slightly feverish. He suddenly

Address reprint requests to Dr. Osada: The Department of Surgical Oncology, Graduate School of Medicine, the University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.

291
developed dyspnea, and was readmitted to the University of Tokyo Hospital on September 16. The white blood cell count was 31,600/mm$^3$ on admission. On physical examination, respiratory sounds were clearly audible at the right chest wall but weak on the left. Chest x-ray films (Fig. 3) demonstrated further accumulation of effusion in the left pleural cavity and collapse of the left lobe. Puncture of the cavity yielded 1,500 ml of purulent and slightly bloody effusion. Bacterial culture of the fluid yielded Streptococcus bovis. Abdominal CT scan revealed no apparent abscess formation in the peritoneal cavity. Continuous drainage of the pleural effusion was done, and appropriate antibiotics were infused. Despite these intensive measures, the patient did not recover from the infection and died of respiratory failure on September 23. Autopsy was not performed.

**DISCUSSION**

Infections in patients with colorectal cancer have been reported, but clinically these are unusual. Such infections are related to the breakdown of normal mucosal barriers, and include endocarditis, pericarditis, pulmonary microabscess, meningitis, nontraumatic gas gangrene, hepatic abscess, and retroperitoneal abscess. Among these, thoracic empyema is quite rare, and to our knowledge only four cases have been reported (Table 1).$^1,7-9$ Empyema associated with colorectal cancer was firstly reported by Bentley and Lepper$^7$ in two patients, and it was caused by Clostridium perfringens infection. In the third case, reported by Panwalker,$^1$ laparotomy revealed a large perforated cecal adenocarcinoma and a retroperitoneal abscess tracking along the right paracolic gutter to the right side of the groin and the diaphragm. Cultures of pleural fluid and abscess fluid yielded...