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Appendicitis complicated by appendiceal metastasis via peritoneal dissemination from lung cancer

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Keywords
appendicitis, bevacizumab, lung cancer, metastasis, peritoneal dissemination.

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Abstract

Peritoneal disseminations from lung cancer are difficult to detect during the patient's clinical course. Therefore, complications of this condition are unclear. We report a case in which peritoneal dissemination from lung cancer complicated appendicitis. A 74-year-old man with lung cancer who was receiving maintenance therapy presented at our hospital because of abdominal pain. It was the seventh day after the 14th cycle of maintenance therapy with bevacizumab. He was diagnosed with acute appendicitis. The resected appendix showed acute appendicitis complicated by appendiceal metastasis from lung cancer. Adenocarcinoma was observed predominantly in the serous membrane from the neck to the tail of the appendix. The distribution of the adenocarcinoma was diffuse. Peritoneal dissemination was considered the route of metastasis. He was admitted to the palliative care unit 10 months after appendectomy. Appendiceal metastasis via peritoneal dissemination from lung cancer complicated appendicitis in our patient who had been receiving bevacizumab.

Introduction

The appendix is an uncommon site of metastases for lung cancer. Only a few cases have been previously reported [1]. In almost all of these cases, hematogenous or lymphogenous metastasis from lung cancer caused appendicitis. However, no previous reports have demonstrated appendiceal metastasis via peritoneal dissemination from lung cancer.

We here report a case of appendiceal metastasis via peritoneal dissemination from lung cancer. Metastasis developed under maintenance therapy with bevacizumab and caused appendicitis.

Case Report

A 74-year-old man presented at our hospital because of chest pain. Chest radiography showed a left pleural effusion. Cytology from the pleural effusion confirmed lung adenocarcinoma (cTxN0M1a, stage IV). Molecular testing was negative for *EGFR* mutations and positive for *ALK* rearrangement. Other metastases were not detected. Carboplatin, paclitaxel, and bevacizumab therapy was started. The pleural effusion decreased after two cycles of chemotherapy. After six cycles of chemotherapy with the three drugs, maintenance therapy with bevacizumab was started. The treatment period of maintenance therapy was extended to 15 months. During maintenance therapy, no metastatic lesions were detected, and no signs suggestive of disease progression were observed.

Seven days after the last treatment with bevacizumab (the 14th cycle of maintenance therapy), the patient developed left abdominal pain. He presented at our hospital again. His anthropometric information and laboratory values were as follows: height, 158 cm; weight, 61 kg; blood pressure, 163/117 mmHg; pulse rate, 120/min, regular; body temperature, 37.5 °C; white blood cell count, 13,520/μL; and C-reactive protein level, 40.8 mg/dL. Abdominal computed tomography (CT) showed an enlarged appendix. He was diagnosed with acute appendicitis, and appendectomy was performed. The resected enlarged appendix was filled with mucus. Invasion with adenocarcinoma was detected (Fig. 1).

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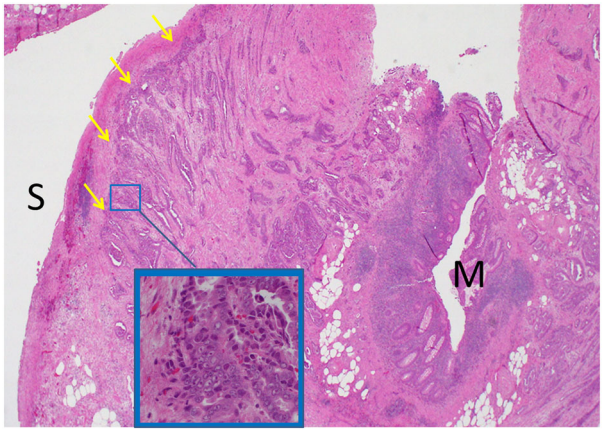

Figure 1. Histological findings of the resected appendix showing appendicitis complicated by a lung cancer metastasis. S indicates the serous membrane site, and M represents the mucosa site. Cancer cell distribution was observed predominantly in the serous membrane (yellow indicator) and was uniform from the neck to the tail of the appendix. The mucosa site was intact. Peritoneal dissemination was suggested as the route of metastasis.

Immunostaining showed positive staining for thyroid transcription factor-1 and cytokeratin (CK)-7 and negative staining for CK20. He was diagnosed with acute phlegmonous appendicitis complicated by appendiceal metastasis from lung cancer. Adenocarcinoma was observed predominantly in the serous membrane from the neck to the tail of the appendix (Fig. 1). Distribution of the cancer cells was diffuse. Peritoneal dissemination was suggested as the route of metastasis rather than the hematogenous or lymphogenous route. We reviewed the abdominal CT under maintenance therapy. Two months before the onset of appendicitis, small ascites and high-density lesions in the intestine were observed, although they were not detected before chemotherapy (Fig. 2a–b). After appendectomy, his abdominal pain disappeared, and oral food intake was restarted. He was discharged from our hospital 1 month after appendectomy. We discontinued chemotherapy and continued the best supportive care. Seven months post-appendectomy, treatment with crizotinib was started. He had no abdominal pain, although the left pleural effusion and ascites were increased (Fig. 2c). On the second day of treatment with crizotinib, dyspnea and hypoxia developed. We considered that the symptoms were an adverse reaction to crizotinib treatment. We discontinued treatment with crizotinib. Ten months after appendectomy, the patient was admitted to a palliative care unit.

Discussion

We discovered two important clinical findings. First, peritoneal dissemination from lung cancer can complicate appendicitis. Second, lung cancer metastases via peritoneal dissemination can slowly progress.

Peritoneal dissemination from lung cancer can complicate appendicitis. Although the appendix is an uncommon site of metastasis from lung cancer, several reports have been previously published [1]. Almost all of these cases had complicated appendicitis from stricture of the appendiceal lumen caused by hematogenous or lymphogenous metastasis to the appendix. In the present case, peritoneal dissemination was suggested as the route. This is the first report to describe that peritoneal dissemination of lung cancer can complicate appendicitis. We think that cancer invasion to the serous membrane triggered appendicitis. The present case developed appendicitis while undergoing treatment with bevacizumab. In patients receiving bevacizumab, intestinal perforation occasionally occurs, and this adverse event is suggested to result from cancer necrosis or impaired wound healing. Therefore, similar clinical conditions may have existed in the present case.

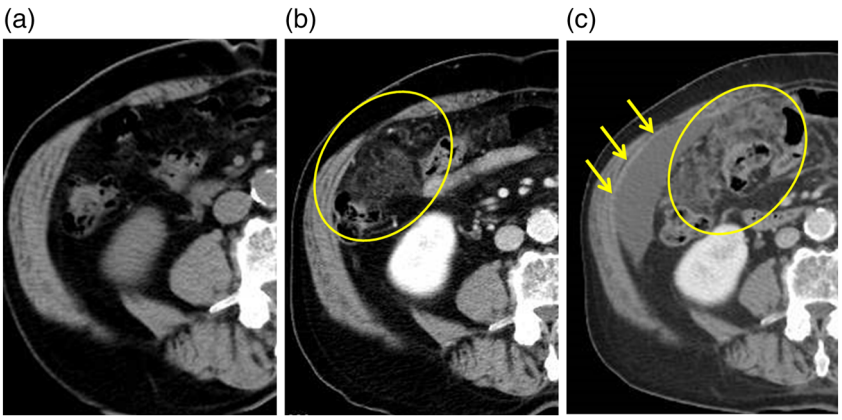

Figure 2. The time course of the abdominal computed tomography findings suggest that peritoneal dissemination was progressing slowly. (a) In May 2012, high-density lesions in the intestine were not observed before chemotherapy. (b) In November 2013, the patient was receiving bevacizumab, and 2 months before the onset of appendicitis, high-density lesions in the intestine (inside the yellow line) and small ascites (not shown) were observed. (c) In August 2014, 7 months after the onset of appendicitis, high-density lesions in the intestine (inside the yellow line) and the ascites (yellow indicator) were increased.

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The present patient showed neither abdominal symptoms nor obvious ascites while receiving bevacizumab, although he had complained of chest pain at the first visit [2]. The time course of the CT findings suggested that peritoneal dissemination slowly progressed while the patient received maintenance therapy with bevacizumab. Bevacizumab, which can inhibit the vascular endothelial growth factor (VEGF), may contribute to reducing the progression of peritoneal dissemination. VEGF enhances vascular permeability and angiogenesis in the abdominal wall and contributes to establishing peritoneal dissemination with malignant ascites. A high level of VEGF in malignant ascites was observed in ovarian cancer [3], although this was not confirmed in the present case.

Molecular-targeted drugs such as bevacizumab effectively improve the outcomes of lung cancer. As a result, treatment can continue in the long term, and disease progression becomes variable. Sato reported that only 0.77% of patients with advanced lung cancer developed peritoneal metastasis during their clinical course [4]. Besides, metastatic involvement of the peritoneum is seen in 2.7–16% of lung cancer autopsy findings [5]. These findings suggest that undiagnosed peritoneal dissemination in the clinical course of lung cancer can be present.

Peritoneal dissemination from lung cancer can complicate appendicitis. Further, lung cancer metastasis via peritoneal dissemination can slowly progress. Even though there are no abdominal symptoms, peritoneal dissemination can be present in some lung cancer patients receiving bevacizumab.

Disclosure Statements

No conflict of interest declared.

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

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