

Case Report

Pneumothorax during Pemetrexed Treatment in a Patient with Non-Small Cell Lung Cancer: A Case Report and Literature Review

Yoshiro Nakahara^{a, b} Shinichiro Mikura^b Makoto Nagamata^b
Tomoya Fukui^a Jiichiro Sasaki^c Noriyuki Masuda^a

^aDepartment of Respiratory Medicine, Kitasato University School of Medicine, Sagamihara, Japan; ^bDepartment of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, Japan; ^cResearch and Development Center for New Medical Frontiers, Kitasato University School of Medicine, Sagamihara, Japan

Keywords

Pemetrexed · Pneumothorax · Non-small cell lung cancer

Abstract

Pemetrexed is a multitargeted antifolate that has demonstrated antitumor activity in non-small cell lung cancer. A 70-year-old male presented with a stage IV non-small cell lung cancer. The patient was treated with pemetrexed as third-line chemotherapy. However, a pneumothorax occurred 16 days after the administration of the second cycle of pemetrexed. The pneumothorax was slight and the patient was observed without undergoing any additional treatment. Twenty-four days after its initial occurrence, the pneumothorax had improved. This is the first case of pneumothorax that has been observed during pemetrexed treatment. Pneumothorax during chemotherapy is rare; however, it is a life-threatening complication and should not be overlooked.

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Introduction

Pemetrexed is a multitargeted antifolate that has demonstrated antitumor activity in non-small cell lung cancer. It has several notable adverse effects including myelosuppression, nausea, vomiting, diarrhea, and skin toxicity. However, the occurrence of pneumothorax during pemetrexed chemotherapy has not been previously reported [1]. Herein, we present a case of pneumothorax that was observed during pemetrexed chemotherapy.

Case Report

An asymptomatic 70-year-old man was referred to the Department of Respiratory Diseases because of abnormal shadows found during a chest computed tomography scan. The scan revealed bilateral infiltrative shadows in the lower lung lobes (Fig. 1). Transbronchial lung biopsy was performed and the patient was diagnosed with non-small cell lung cancer classified as stage IV (T3N3M1a). The patient was treated every 3 weeks with 3 cycles of first-line chemotherapy, including carboplatin (AUC 5) on day 1 and gemcitabine (1,000 mg/m²) on days 1 and 8. After 3 cycles of chemotherapy, the bilateral infiltrative shadows had progressed. Consequently, the patient was treated every 3 weeks with 3 cycles of docetaxel (60 mg/m²) monotherapy as second-line chemotherapy. However, after the third cycle, the infiltrative shadows had progressed again. Subsequently, the patient was treated with pemetrexed (500 mg/m²) as third-line chemotherapy, every 3 weeks. In the first cycle of the chemotherapy, there were no grade 3 or 4 adverse events. However, the patient experienced sudden onset of cough and dyspnea 16 days after the administration of the second cycle of pemetrexed. Physical examination showed decreased breathing sounds in the right chest, and a chest radiograph revealed a pneumothorax (Fig. 2, Fig. 3). Because the pneumothorax was slight, the patient was observed without any treatment, and pemetrexed therapy was stopped. The pneumothorax had improved 24 days after the occurrence of the pneumothorax (Fig. 4). However, the patient died 2 months after the occurrence of pneumothorax because of disease progression.

Discussion

Secondary spontaneous pneumothorax after chemotherapy is rare; however, well-documented occurrence is associated with primary or metastatic lung lesions. Lai et al. [2] reported that pneumothorax appeared in 18 out of 5,567 (0.32%) lung cancer patients, and 2 out of 18 patients experienced pneumothorax during chemotherapy. Maniwa et al. [3] reported that pneumothorax associated with the treatment for pulmonary malignancy (primary and metastatic) tends to require chest tube drainage over a long period, and sometimes requires surgical treatment; this is associated with increased perioperative morbidity and mortality because of the dense adhesions or anatomical changes in the thoracic cavity caused by treatment or the progression of the tumors [3].

Recently, molecular targeted therapies have also been linked with the occurrence of pneumothorax. Mori et al. [4] reported a case of simultaneous bilateral spontaneous pneumothorax that occurred during gefitinib treatment for lung adenocarcinoma with multiple lung metastases. A case of pneumothorax after bevacizumab-containing chemotherapy for colorectal cancer with lung metastases was reported by Yang et al. [5]. In addition, Gennatas

et al. [6] reported a case of pneumothorax during crizotinib therapy in a patient with anaplastic lymphoma kinase-rearranged lung adenocarcinoma. In contrast, pneumothorax during cytotoxic chemotherapy treatment is rare, and secondary spontaneous pneumothorax during pemetrexed has not been previously reported in the available literature.

The mechanism of secondary pneumothorax from pulmonary malignancy is unclear, although several theories have been proposed. The proposed mechanisms are as follows: accidental rupture of the subpleural bulla or bleb during chemotherapy; the formation of a bronchopleural fistula as a result of direct tumor invasion or necrosis of the peripheral tumor after effective chemotherapy; a check-valve mechanism associated with airway compression by the tumor; and an air leak caused by pulmonary infarction from tumor emboli [7].

In the present case, there was no clinical response to pemetrexed treatment, and tumor necrosis was not observed. Furthermore, neither progression of airway compression or signs of pulmonary infarction were observed. In addition, there were no subpleural bullae or blebs on chest computed tomography before pemetrexed treatment. We believe that the pneumothorax was possibly caused by the formation of a bronchopleural fistula as a result of direct tumor invasion of the peripheral tumor.

In summary, ours is the first reported case of pneumothorax to have occurred during pemetrexed treatment. Pneumothorax during chemotherapy is rare; however, it is a life-threatening complication that should not be overlooked. It is important to observe the patients' symptoms during chemotherapy treatment.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors state that they have no conflict of interest.

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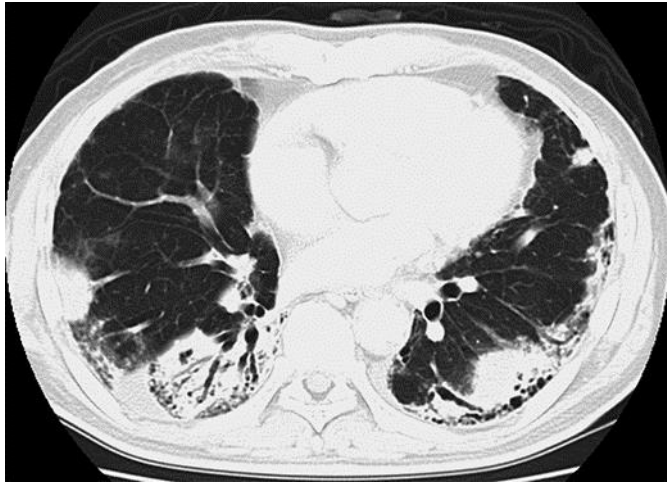


Fig. 1. Chest computed tomography demonstrating bilateral infiltrative shadows. These lesions were diagnosed as non-small cell lung cancer by transbronchial lung biopsy.

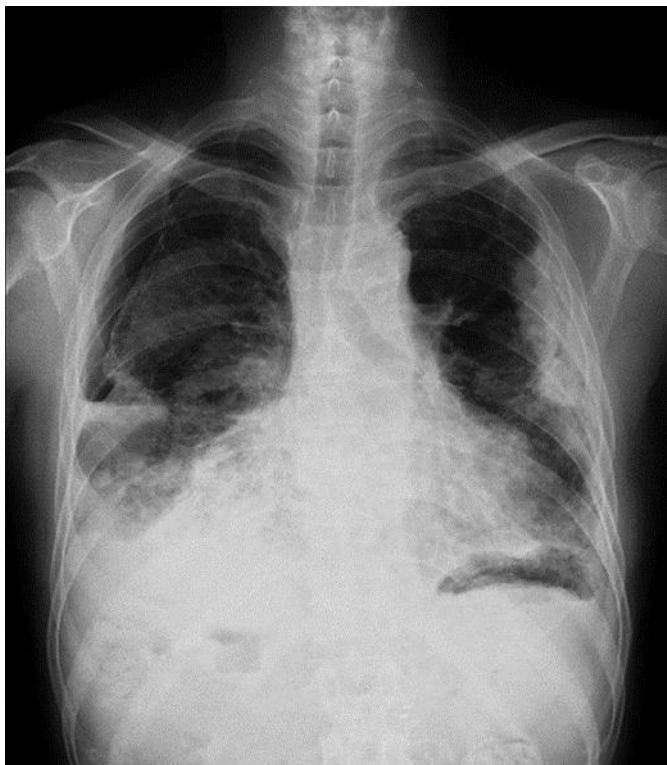


Fig. 2. Chest X-ray demonstrating right pneumothorax.

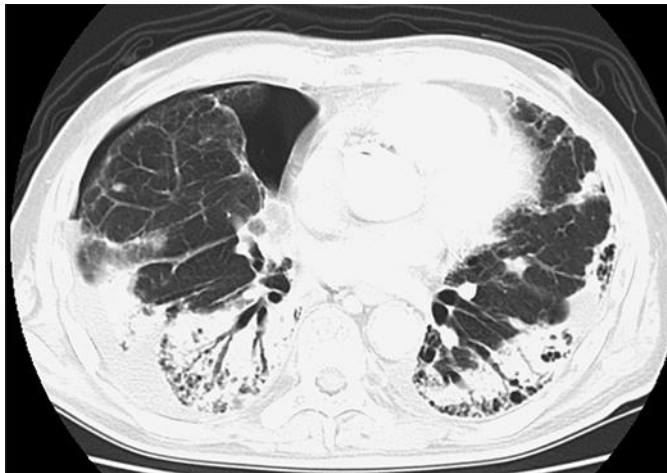


Fig. 3. Chest computed tomography demonstrating right pneumothorax, and bilateral infiltrative shadows had progressed.

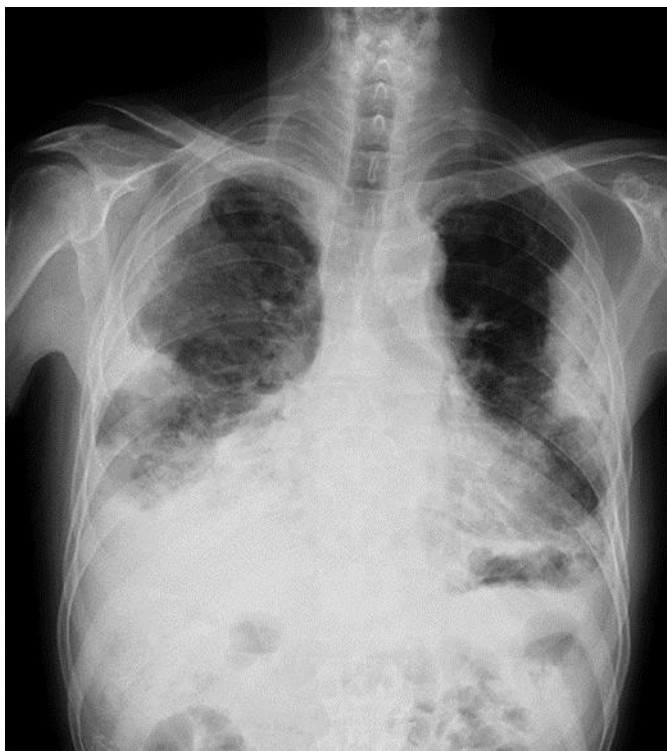


Fig. 4. The pneumothorax had improved 24 days after the occurrence of the pneumothorax.