Respiratory Medicine Case Reports 15 (2015) 42–44

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Pneumothorax triggered by the combination of gefitinib and amrubicin and treated with endobronchial silicone spigots

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Keywords:
Pneumothorax
Gefitinib
Amrubicin
Endoscopic bronchial occlusion
EWS

A B S T R A C T

Pneumothorax is a rare complication in cancer chemotherapy. We report a case in which a male patient with advanced non-small cell lung cancer (NSCLC) developed repetitive pneumothorax after receiving a combination of the chemotherapeutic drugs gefitinib and amrubicin (GEF + AMR). Both episodes of pneumothorax occurred on the 3rd day of GEF + AMR administration. Tube thoracostomy was performed, but pulmonary air leaks persisted in the second pneumothorax. Whereas surgical intervention was not applicable because of poor respiratory reserve, the chest tube was successfully removed by endoscopic occlusion of bronchopleural fistula with endobronchial Watanabe spigots (EWSs), a type of silicone bronchial blocker.

Introduction

Although pneumothorax is a rare complication in cancer chemotherapy, it may be life-threatening when it occurs in patients with extensive pulmonary involvement of cancer. Herein, we report a case in which a lung cancer patient with extensive lung metastasis experienced two episodes of pneumothorax triggered by a specific combination of chemotherapeutic drugs. Although his 2nd pneumothorax was complicated by sustained air leaks, it was resolved by endobronchial occlusion with silicone bronchial blockers.

Case presentation

A 59-year old man was urgently admitted to our hospital because of sudden onset of dyspnea on the 3rd day of the 2nd administration of gefitinib (GEF) combined with amrubicin (AMR). Chest radiography and chest computed tomography (CT) scans revealed left-sided pneumothorax. He had undergone a right upper lobectomy for lung adenocarcinoma 8 years before, but had experienced disease recurrence one year later. Treatment with gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), had been initiated because his lung cancer carried a deletion in exon 19 of EGFR; this therapy had a remarkable effect. Thereafter, he had been treated with several lines of chemotherapy and radiation therapy for about 7 years. Further, he had undergone pleurodesis for right malignant pleural effusion. The combination of GEF and AMR (GEF + AMR) was initiated for the first time in April 2014 as the 12th line treatment. Stable disease was attained with slow decrement of the serum carcinoembryonic antigen (CEA) value, although he had poor respiratory reserve due to cancer spread in both lung.

After confirming the presence of pneumothorax, a chest drainage tube was inserted into the left thoracic cavity. The left lung was fully expanded rapidly by continuous aspiration, and the tube was successfully removed without pleurodesis. The patient was discharged and chemotherapy was restarted. The 3rd administration of GEF + AMR was initiated on the 47th day from the start of the 2nd administration. Once again, the patient was urgently admitted to our hospital on the 3rd day of the treatment, complaining of severe dyspnea. Arterial blood gas analysis revealed severe hypoxemia and hypercapnia despite breathing 10 L/min oxygen, indicating life-threatening hypoventilation (Table 1). Chest CT scans revealed left-sided pneumothorax (Fig. 1). A 12 Fr chest drainage tube was emergently inserted, and the arterial blood gas

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http://dx.doi.org/10.1016/j.rmcr.2015.02.007

Table 1
Arterial blood gas analysis.

O_2 (by mask)	On admission 10 L/min	After insertion of chest tube 6 L/min
pH	7.02	7.30
PaO_2 (mmHg)	66.3	81.0
$PaCO_2$ (mmHg)	100.0	45.5
HCO_3 (mmol/L)	24.7	21.5
SO_2 (%)	79.4	94.7

data improved rapidly. Although the drainage tube was changed to a 20 Fr double lumen Trochar catheter, the air leaks continued, resulting in collapse of the left lung when the chest tube was clamped. Since operative intervention for pneumothorax was inapplicable because of the patient's poor respiratory reserve, endobronchial approach was performed (Fig. 2). Firstly, an endobronchial Watanabe spigot (EWS) of 7-mm thickness was inserted into the left B5 by using a flexible bronchoscope under venous anesthesia after determining the bronchi responsible for the air leak by an occlusion test. Because of sustained air leak, an additional EWS of 7-mm thickness was inserted into the left B3 segmental bronchi, resulting in termination of the air leaks. After confirming full expansion of the left lung during clamping the tube, pleurodesis was performed with talc. Although air leak diminished, dyspnea and high fever developed. The chest X-ray image on the day 7 showed new consolidations in the left S3 and S5, suggesting diminished lung volume and obstructive pneumonia (Fig. 3). High fever and dyspnea resolved by antibiotics and the removal of the EWS in the left B5. The drainage tube was removed on the day 14. He was discharged on the 48th hospital day with support by 3 L/min oxygen.

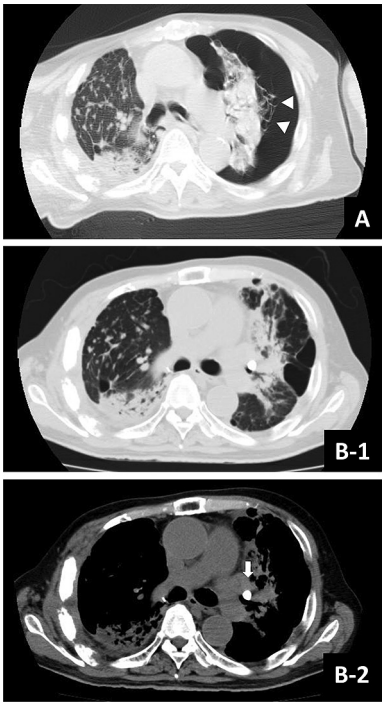

Fig. 1. CT images before and after insertion of EWSs Upper, the left lung was collapsed by the 2nd episode of pneumothorax. The bullous lesions are indicated by arrowheads. Middle, full expansion of the left lung under the clamp of the chest tube was attained by endoscopic occlusion of bronchopleural fistula by endobronchial Watanabe spigots (EWS). Lower, image showing an EWS in the left B3 (arrow).

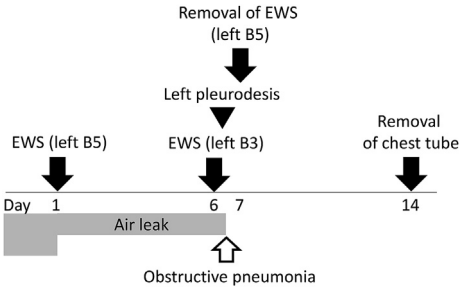

Fig. 2. Time course after the insertion of the first EWS An EWS was inserted into the left B5 on day 1. Because of sustained air leaks, an additional EWS was inserted into the left B3, followed by left pleurodesis. The EWS in the left B5 was removed on day 7 to resolve obstructive pneumonia. Since air leaks disappeared, the chest drainage tube was removed on day14.

Discussion

Pneumothorax is a rare complication of cancer chemotherapy, and it has been reported during the treatment of different types of cancer and with various drugs [1–6]. Lai et al. reported that 18 out of 5567 lung cancer patients (0.32%) experienced a pneumothorax but only two out of these 18 patients developed pneumothorax after chemotherapy (0.036%) [7]. Even in these two patients, it is unclear whether chemotherapy triggered pneumothorax. Pneumothorax was reported sporadically during treatment of lung cancer with an EGFR-TKI, whereas it was not reported with amrubicin [8–10]. In our patient, pneumothorax had not occurred during an approximate 7-year history of chemotherapy that included GEF alone, AMR alone and combination of GEF with various cytotoxic drugs such as pemetrexed, gemcitabine, docetaxel and nab-paclitaxel. Only the specific combination of GEF and AMR appears to have triggered pneumothorax. In addition, both episodes of pneumothorax occurred on the 3rd day of GEF + AMR treatment, suggesting a causative relationship between this combination of chemotherapeutic agents and pneumothorax. Several authors reported chemotherapy-induced pneumothorax when a dramatic response was induced with or without cavitation [6,11,12], but this was not the case with our patient. Although chest CT revealed bilateral extensive lung metastasis and multiple bullous lesions (Fig. 1), the precise mechanism of pneumothorax by GEF + AMR in our patient is not clear.

Occlusion of the bronchopleural fistula by transbronchial insertion of EWS is reportedly effective for persistent air leaks in pneumothorax in patients with poor respiratory reserve [13,14]. EWS was effective in our patient, resulting in termination of air leaks and full expansion of the left lung, although transient pneumonia developed and dyspnea deteriorated. This report may further the understanding of pneumothorax triggered by cancer chemotherapy and contribute to its treatment in patients with severe respiratory conditions.

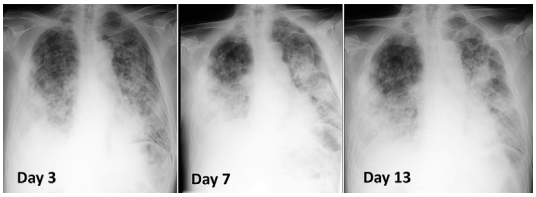

Fig. 3. Chest X-ray images after the insertion of the second EWS New consolidations were observed in the left S3 and S5 on the day 7. The consolidation in the left S3 and S5 were decreased in size by antibiotics and the removal of the EWS in the left B5. Dyspnea was resolved and high fever disappeared.

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