

A Rare Case of Persistent Pneumothorax in Non-Small Cell Lung Cancer on Bevacizumab Therapy

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Abstract

Bevacizumab which is a humanized murine monoclonal antibody against vascular endothelial growth factor, given in combination with carboplatin and paclitaxel, was granted a labeling extension treatment of advanced-stage Non-Small Cell Lung Cancer (NSCLC). Common toxic effects include hypertension, proteinuria, and neutropenia. Rare complications include bleeding, particularly hemoptysis, and surgical wound dehiscence, but pneumothorax in NSCLC is rare. We report a case of persistent pneumothorax related to bevacizumab in a patient with NSCLC.

Keywords: Non-small cell lung cancer; Bevacizumab; Pneumothorax

Introduction

Bevacizumab is used as a standard regimen for chemotherapy in patients with Non-small cell lung cancer (NSCLC) [1,2]. Common toxic effects include hypertension, proteinuria, and neutropenia. However, pneumothorax occurring after Bevacizumab-containing chemotherapy in NSCLC has been rarely described [3].

Case Report

54-year-old man was admitted in March 2010 to our hospital because of dyspnea and right pleural effusion. He had smoked three packs of cigarettes per day for thirty four years. Chest X-ray showed right pleural effusion (Figure 1A). Chest CT disclosed right pleural effusion and bilateral diffuse Low Attenuation Area (LAA). To determine the cause of pleural effusion, thoracentesis was performed and showed exudative pleural effusion. Pleural fluid cytology was consistent with adenocarcinoma (Figure 1B). Epidermal Growth Factor Receptor mutation was negative. Diagnostic workup was performed, and finally he was diagnosed as advanced-stage NSCLC. To control malignant pleural effusion, chemical pleurodesis was performed. And then, he administered two cycles of Cisplatin (CDDP) with Pemetrexed as first-line chemotherapy. It was not effective so that second-line chemotherapy of Carboplatin (CBDCA), Paclitaxel (PTX) with Bevacizumab was administered and continued six cycles. Chest CT after second-line chemotherapy showed right pneumothorax with pleural

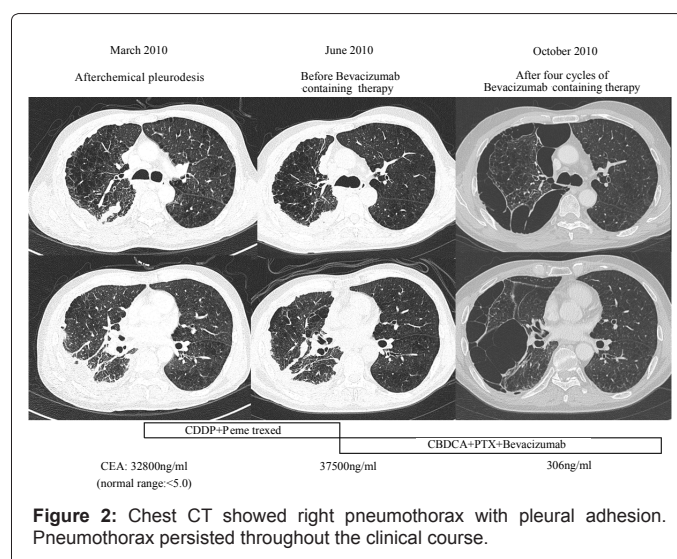


Figure 2: Chest CT showed right pneumothorax with pleural adhesion. Pneumothorax persisted throughout the clinical course.

adhesion (Figure 2). Nevertheless pneumothorax persisted throughout the clinical course; his condition was stable 28 months after diagnosis. As shown in Figure 2, pneumothorax with pleural adhesion persisted, but his respiratory failure did not worsened. Therefore, pneumothorax was not treated using chest tube or thoracoscopy. Carcinoembryonic Antigen (CEA) was gradually reduced after chemotherapy.

Discussion

Bevacizumab, which is a humanized monoclonal antibody against Vascular Endothelial Growth Factor (VEGF), is used as a standard regimen for chemotherapy in patients with NSCLC [1,2]. Common

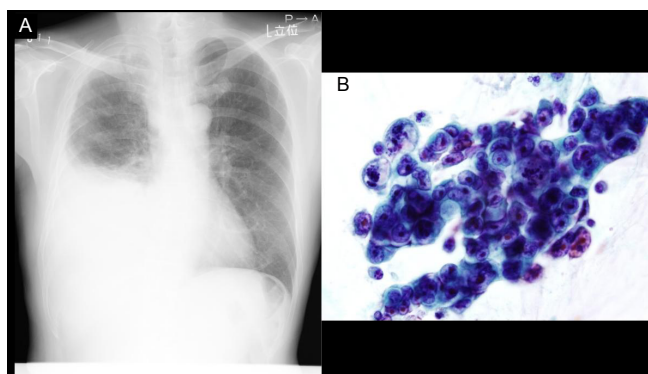


Figure 1: (A) Chest X-ray on admission demonstrates right pleural effusion (B) Pleural fluid cytology: There are clusters of tumor cells with high nuclear-cytoplasmic (N/C) ratio, granular chromatin and nucleoli (Papanicolaou stain; x400)

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toxic effects include hypertension, proteinuria, and neutropenia. Rare complications include bleeding, particularly hemoptysis, and surgical wound dehiscence. Pneumothorax related to bevacizumab has been rarely described [3]. To our knowledge, there are a few reports that pneumothorax occurring after Bevacizumab-containing chemotherapy. Yang et al. [4] reported a case of pneumothorax occurring after Bevacizumab-containing chemotherapy in colorectal cancer with lung metastases. They treated pneumothorax with small caliber chest tube and the tube was removed 5 days later. No recurrence was observed. They described that a small caliber chest tube was considered effective in management of uncomplicated pneumothorax. On the other hand, one patient died of recurrent bilateral pneumothoraces in phase II study of doxorubicin and bevacizumab for patients with metastatic soft tissue sarcomas [5]. Although pneumothorax resulting from treatment is a rare phenomenon [6], there was one case report of patients with lung metastases who developed recurrent pneumothoraces while receiving doxorubicin-based combination regimen [7]. Therefore, they speculated that recurrent pneumothoraces was treatment-related, but it was not clear whether doxorubicin or bevacizumab was main reason of pneumothoraces. Generally, several mechanisms of pneumothorax have been considered; Subpleural bulla rupture after chemotherapy, fistulas induced by tumor lysis due to chemotherapy, and air leak due to pulmonary infarction from tumor emboli. In our case, several reasons have been considered; first reason was rupture of bulla by diffuse LAA in both lungs, and second reason was subpleural bulla rupture and fistula formation after disappearing pleural dissemination by Bevacizumab-containing therapy. Furthermore VEGF is a strong player in lung structure maintenance [8,9] and it has been reported chronic blockade of VEGF receptors causes alveolar septal cell apoptosis and lung capillary loss [10]. Hence Bevacizumab may cause pneumothorax in some patient; careful follow up will be needed.

Conclusion

Pneumothorax in patients with NSCLC after Bevacizumab-

containing therapy is extremely rare. However, pneumothorax should not be overlooked because it is sometimes severe pulmonary complication, and should be considered in patients with NSCLC who have diffuse LAA or diagnosed as chronic obstructive pulmonary disease.

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