Bilateral pneumothorax after bevacizumab-containing chemotherapy in fibrosarcoma

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ABSTRACT Bevacizumab-containing therapies can improve outcomes in patients with sarcoma. Bevacizumab had several notable adverse effects including bowel perforation but bilateral pneumothorax had never been reported in the available English literature. We reported a 23-year-old male with poorly differentiated fibrosarcoma who had spontaneous bilateral spontaneous pneumothorax (SP) after the third cycle of bevacizumab-containing chemotherapy. His bilateral pneumothorax resolved after closed drainage of pleural cavity with a small caliber catheter. The mechanism of pneumothorax developed after bevacizumab therapy was not clear. In patients who had chest discomfort after bevacizumab-containing therapy, pneumothorax should never be overlooked as one of the differential diagnoses.

KEY WORDS Pneumothorax; fibrosarcoma; bevacizumab; chemotherapy; small caliber catheter

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Introduction

Bevacizumab is a monoclonal antibody that binds and inactivates all isoforms of VEGF to inhibit angiogenesis and tumor growth and proliferation. It can improve outcomes in patients with sarcoma (1). Bevacizumab has several notable adverse effects including bleeding, hypertension, heart failure, proteinuria, thromboembolism and gastrointestinal (GI) perforation, an uncommon but serious adverse effect (2-4). However, bilateral SP occurring after bevacizumab-containing chemotherapy had never been reported in the literature. Herein, we present a case of bilateral pneumothorax occurring after bevacizumab-containing chemotherapy.

Case report

A 23-year-old man had a complaint of swelling and intermittent pain in the right thigh for two months before admission to the Surgical Department of our hospital. Physical examination showed significant swelling of the right thigh. Whole body PET/CT (Figure 1) demonstrated a large heterogeneous lesion located in the right iliac foss and no evidence of lung metastasis. Right inguinal lymph node biopsy was low-grade fibrosarcoma. Bevacizumab (5 mg/kg) and DP (docetaxol 75 mg/m^2, cisplatin 75 mg/m^2) every 21days were prescribed as first-line chemotherapy. The right thigh swelling was better than before. The patient had sudden-onset chest pain and dyspnea 13 days after the third cycle of Bevacizumab plus DP (day 55 after initial chemotherapy). Physical examination showed decreased breath sounds of the chest. Compared with the previous chest radiograph (Figure 2), a bilateral pneumothorax was disclosed (Figure 3). The pneumothorax resolved completely after chest tube drainage. The chest tube was removed 3 days later. In the fourth chemotherapy, bevacizumab was not used and pneumothorax was not occurred. However, in the fifth chemotherapy, we add the bevacizumab again, chest radiograph showed right pneumothorax a week later after bevacizumab (Figure 4). The pneumothorax resolved completely after chest tube drainage. The chest tube was removed 7 days later and the follow-up radiograph did not show recurrence of the pneumothorax. At the same time, we never use the bevacizumab again.

Discussion

Bevacizumab has several notable adverse effects including bleeding, hypertension, heart failure, proteinuria,

No potential conflict of interest.

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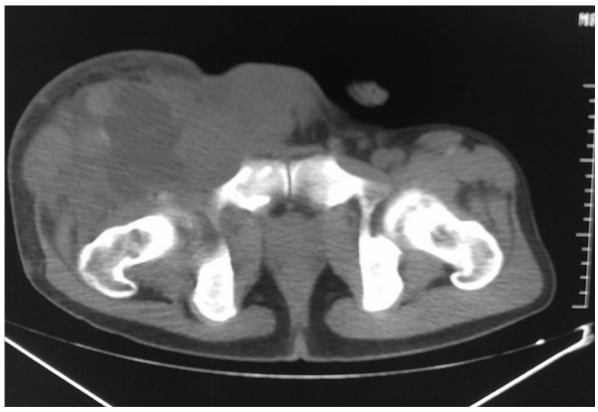

Figure 1. Whole body PET/CT demonstrated a large heterogeneous lesion located in the right iliac foss.

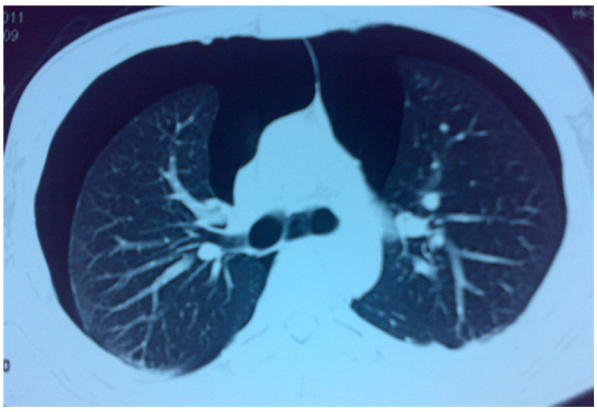

Figure 3. Chest CT shows bilateral pneumothorax after three cycles of bevacizumab containing chemotherapy.

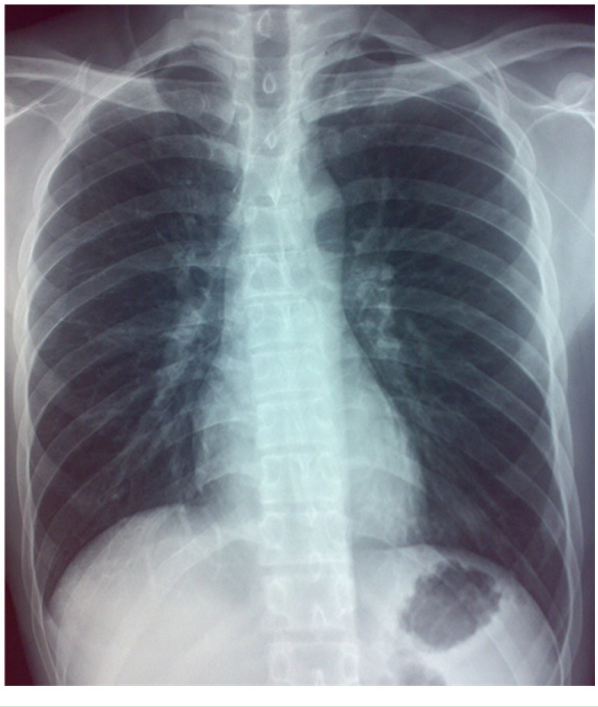

Figure 2. Chest radiography before treatment shows no lung metastases.

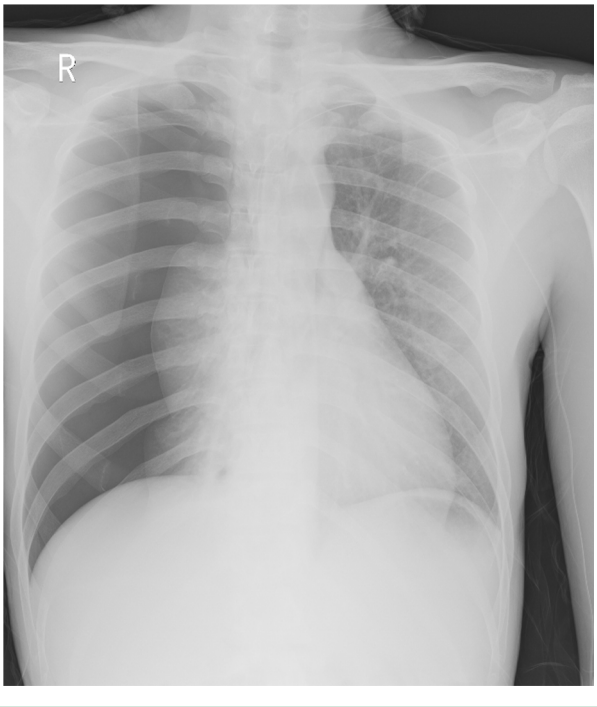

Figure 4. Chest radiography shows right pneumothorax after the fifth chemotherapy.

thromboembolism and gastrointestinal (GI) perforation and so on, but secondary SP especial bilateral SP after bevacizumab-containing therapies is a rare. Sarcomas appear to be the malignancy most often associated with SP (5,6). There were some sarcoma patients with bilateral SP during chemotherapy where pulmonary metastases were not detectable. This suggests that SP was either a coincidence or rather a complication of very small metastases adjacent to the pleura (7,8). In this case, when we used bevacizumab, SP was occurred, and when we did not use bevacizumab, there was not SP. On this basis of the above, we speculate that the pneumothorax in our patient was likely an adverse effect of the bevacizumab.

The risk factors for bevacizumab associated pneumothorax are unclear. In this case, metastatic lesions could not be noted in the initial chest radiography and CT, we presume that micrometastases were occurred before it could be detected by

imaging studies. Several theories regarding possible mechanisms of the bilateral penumothourax in sarcomas have been put forward. First, the rupture of a subpleural bleb in a patient with an underlying chronic pulmonary disease is possible. Second, tumor nodules may act as ball valves to produce a partial bronchiolar obstruction and hyperinflation of alveoli. The rupture of an emphysematous bulla in an overexpanded portion of the lung produces a pneumothorax (9).

Early detection of lung metastases is difficult, and Furrer *et al*. suggested that imaging studies such as chest radiography and CT are suboptimal for detecting micro-lesions and that sometimes pneumothorax could be the first and only evidence for metastases (10).

The pneumothorax after bevacizumab therapy was easily treated with a small caliber chest tube. A small caliber chest tube is considered as effective in management of an uncomplicated pneumothorax as a large caliber chest tube (11), and it can avoid a large wound and decrease the risk of bleeding from a large caliber chest tube, which is especially important due to the concerns of bleeding and delayed wound healing with bevacizumab therapy.

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