

Case Report

Pneumothorax during Pazopanib Treatment in Patients with Soft-Tissue Sarcoma: Two Case Reports and a Review of the Literature

Yoshiro Nakahara^{a, b} Tomoya Fukui^a Ken Katono^a Yuuki Nishizawa^b
Yusuke Okuma^b Masachika Ikegami^d 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; ^dDepartment of Orthopaedic Surgery and Musculoskeletal Oncology, Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, Japan

Keywords

Pneumothorax · Soft-tissue sarcoma · Pazopanib

Abstract

Pazopanib, a multitargeting tyrosine kinase inhibitor, has single-agent activity in patients with advanced soft-tissue sarcoma. Herein, we describe 2 cases of pneumothorax that occurred during pazopanib treatment in patients with soft-tissue sarcoma. These 2 patients had multiple lung metastases. According to previous reports and our past experience, the risk of pneumothorax may be higher in patients with multiple lung metastases. Although a causal

relationship is uncertain, the risk of pneumothorax when prescribing pazopanib for these patients should be considered.

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Introduction

Soft-tissue sarcomas are rare cancers that account for 1% of all adult cancers [1]. Pazopanib, a multitargeting tyrosine kinase inhibitor, was approved for patients with advanced soft-tissue sarcoma. Pneumothorax was reported in the preapproval clinical trial of pazopanib as an adverse event [2]. Although the frequency of this complication was low, many questions remain regarding the causal relationship between the two as well as regarding the mechanism. In this study, we reviewed 2 cases of pneumothorax that occurred in patients with soft-tissue sarcoma during pazopanib treatment.

Case Reports

Case 1

A 63-year-old male presented with malignant fibrous histiocytoma originating from the left femur. The primary tumor was resected. One year after the operation, multiple lung metastases and a metastasis to the right pleura emerged. The patient was treated with gemcitabine plus docetaxel. He attained a partial response and continued this treatment for 1 year. However, multiple lung metastases and the metastasis to the right pleura progressed, and multiple liver metastases and peritoneum dissemination emerged. He was started on pazopanib treatment. After approximately 4.5 months of pazopanib treatment (132 days), a left hemopneumothorax was found by chest X-ray (Fig. 1). Thoracic cavity drainage and pleurodesis with autologous blood were performed; however, the patient did not recover from the pneumothorax and died from disease progression 34 days after occurrence.

Case 2

An 81-year-old female presented with a spindle cell and pleomorphic sarcoma from the left femur. The sarcoma was resected and she was treated with postoperative radiation therapy. However, the sarcoma recurred with multiple lung metastases and she was started on pazopanib treatment (600 mg/day). On the fourth day of pazopanib treatment, hemoptysis and dyspnea were noted, and bilateral pneumothorax was found by chest X-ray (Fig. 2). Pazopanib treatment was stopped, and thoracic cavity drainage was performed for the left and right pneumothorax without any treatment. The patient recovered from the pneumothorax and was discharged from hospital. She was observed without any chemotherapy. Three months later, she died of disease progression without recurrence of the pneumothorax.

Discussion

We have described 2 cases of pneumothorax that occurred in patients with soft-tissue sarcoma during pazopanib treatment. In the preapproval clinical trial of pazopanib for metastatic soft-tissue sarcoma, the frequency of pneumothorax during pazopanib treatment was reported to be 2.1% [2]. A case series reported by Hoag et al. [3] demonstrated that pneumo-

thorax sometimes occurs in patients with sarcoma as part of the natural history of the disease. Moreover, no pneumothorax was reported in the clinical trial of pazopanib for renal cell carcinoma treatment [4, 5]. Therefore, the causal relationship between pazopanib and pneumothorax remains uncertain.

The mechanism of secondary pneumothorax from lung metastases is unclear, although several theories have been proposed, including tumor necrosis, check valve, and tumor embolus [6]. Angiogenesis inhibitors are known to cause tumor necrosis and cavitations in lung lesions [7], which may possibly be the cause of pneumothorax during pazopanib treatment. Pneumothorax during bevacizumab treatment, another angiogenesis inhibitor, is a frequent occurrence [8, 9]. Moreover, pneumothorax during sunitinib, another multitargeting tyrosine kinase inhibitor treatment, has also been reported [10].

We have treated 16 patients with soft-tissue sarcoma with pazopanib, and 2 of these patients (12.5%) experienced pneumothorax complications. Similarly, Nakano et al. [11] reported that the frequency of pneumothorax in patients with soft-tissue sarcoma during pazopanib treatment was 9.4%. These frequencies are higher than that reported in the preapproval clinical trial of pazopanib.

The above-mentioned case series reported by Hoag et al. [3] also found chest radiograph findings in patients with sarcoma who experienced pneumothorax. Multiple nodules (in 48.4% of cases) and cavitory or cystic lesions (in 25.8% of cases) were the most common radiographic findings, with pleural abnormalities seen in 11.7% of cases. Our 2 cases reported here had multiple lung metastases. Moreover, 2 of 4 patients (50%) in our institute with multiple lung metastases were complicated by pneumothorax. Because pazopanib treatment is recommended for treatment of more advanced disease (e.g., multiple lung metastases), it might be expected that the frequency of pneumothorax in our institute may be higher than in previous reports.

The pneumothorax in case 2 was bilateral, and the above-mentioned case series also reported that 41.6% of the cases of pneumothoraxes in patients with sarcoma were bilateral on initial presentation [3].

According to that case series, 45.7% of the pneumothoraxes in patients with sarcoma recurred, and the outcomes of these patients were not positive; the 1-year mortality after pneumothorax was 75% [3]. In the present study, case 1 did not recover from the pneumothorax and died 34 days after occurrence.

In conclusion, herein we report 2 cases of pneumothorax that occurred during pazopanib treatment in patients with soft-tissue sarcoma. Although a causal relationship is uncertain, it is possible that the pneumothorax occurred as a result of the pazopanib treatment. According to a previous report [11] and our experience, the risk of pneumothorax may be higher in patients with multiple lung metastases, and the prognosis of patients with sarcoma who experience pneumothorax is poor. These risks should be considered when pazopanib is prescribed for the treatment of sarcoma.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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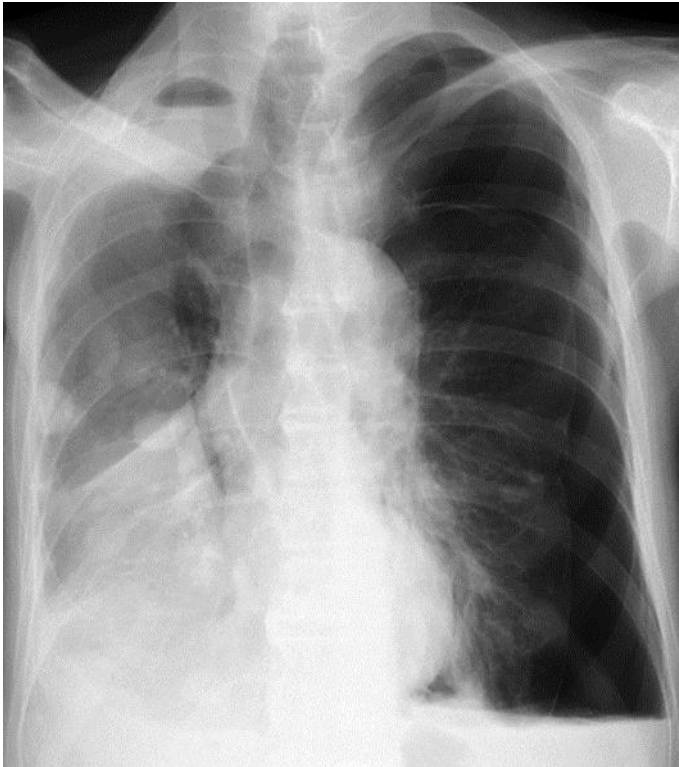


Fig. 1. Chest X-ray demonstrating multiple lung metastases of sarcoma and a metastasis to the right pleura and left hemopneumothorax.

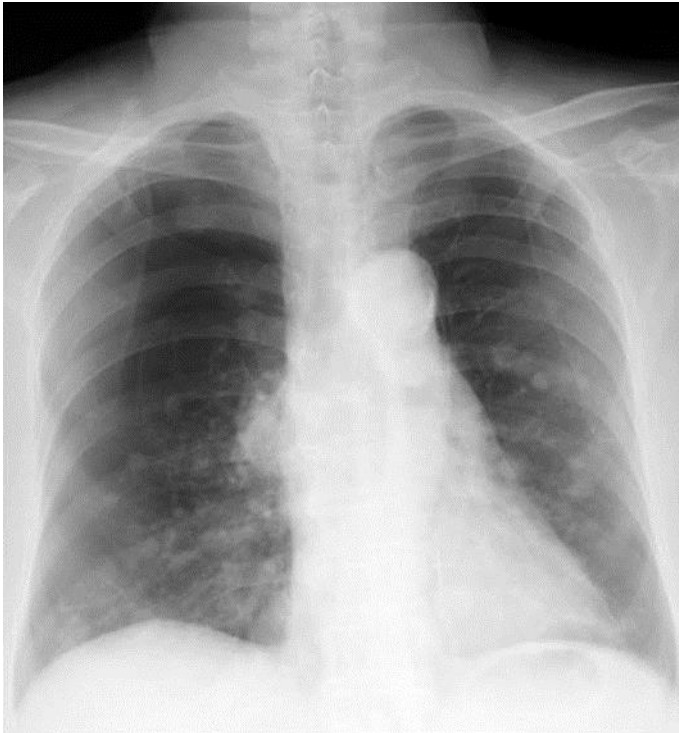


Fig. 2. Chest X-ray demonstrating multiple lung metastases of sarcoma and bilateral pneumothorax.