

## Case Report

# A Case of Unresectable Pulmonary Artery Intimal Sarcoma with Prolonged Survival by Chemotherapy

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## Keywords

Chemotherapy · Right heart failure · Pulmonary hypertension · Soft tissue sarcoma

## Abstract

Pulmonary artery intimal sarcoma is a rare malignant tumor. Due to its low prevalence, little is known about efficacious systemic chemotherapies in cases where the tumors are unresectable or metastatic. In addition, the location of the disease can contribute to poor survival regardless of the response to therapy, as the tumor's position can cause pulmonary artery hypertension either rapidly or chronically. We encountered a case of unresectable pulmonary artery intimal sarcoma with lung metastases. Treatment with several cytotoxic agents resulted in prolonged survival of 14.2 months. Here, we report the clinical course of this case and present a review of the relevant literature.

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## Introduction

Pulmonary artery intimal sarcoma is an extremely rare type of malignant tumor, which mimics pulmonary thromboembolism. The location of the tumor in the pulmonary artery is usually associated with the development of pulmonary hypertension, which can be life-

threatening. Due to its low incidence, the pathology and treatment strategies of pulmonary artery intimal sarcoma remain to be elucidated [1, 2]. Aggressive surgical approaches for locoregional pulmonary artery intimal sarcoma have led to improved patient survival with a median survival period of 17–26 months [3, 4, 5]. The prognosis of unresectable or metastatic disease has historically been extremely poor, with median survival of 1.5 months three decades ago [6]. However, due to advances in chemotherapy and radiotherapy, the survival of such patients with advanced pulmonary artery intimal sarcoma has improved markedly, ranging from 8 to 17 months [7, 8]. Doxorubicin-based chemotherapeutic regimens are commonly used in patients with unresectable pulmonary artery intimal sarcoma. Other drugs have also been reported to show some benefits in such cases. Here, we report a case of unresectable pulmonary artery intimal sarcoma treated with a total of four lines of chemotherapy, including paclitaxel as first-line therapy. Although these chemotherapies did not result in a substantial volumetric response as determined by imaging studies, the patient showed prolonged survival of 14.2 months with well-controlled pulmonary hypertension.

### Case Report

A 60-year-old woman had been consulting with a breast surgeon division regularly for the post-surgical follow-up of stage I left lobular breast carcinoma. She complained of progressive shortness of breath for a period of a few months. She was unable to walk long distances due to dyspnea. On arterial blood gas analysis, SaO<sub>2</sub> and PaO<sub>2</sub> were 89% and 55.9 mm Hg, respectively, when breathing room air. Chest radiography showed a growing abnormal shadow at the hilum of the left lung. As she had an allergy to contrast medium, magnetic resonance imaging (MRI) was performed, which revealed an obstruction in the pulmonary artery (Fig. 1a). The lesion appeared to stem from the pulmonary artery bifurcation and extended mainly into the right pulmonary artery. Her heart function parameters were within the normal limits on echocardiography, except that her pulmonary regurgitation end-diastolic pulmonary regurgitation pressure gradient (PrEDP) was slightly elevated at 10 mm Hg. A diagnosis of pulmonary artery intimal sarcoma was made following tissue sampling through an intravascular catheter. The histological type was undifferentiated pleomorphic sarcoma. Pathologically, tumor cells were negative for cytokeratin AE1/AE3, smooth muscle actin, desmin, caldesmon, S-100, and CD34 on immunohistochemical analysis. Fifty percent of the tumor cells were positive for Ki-67 (Fig. 2a). Her breast carcinoma cells had been positive for expression of estrogen receptor and progesterone receptor. However, the specimen from the pulmonary artery showed expression of neither of these receptors. Multiple nodular lesions in the lungs identified by computed tomography (CT) and MRI were then considered as metastases (Fig. 3a).

In our case, the patient showed poor ECOG Performance Status of 2 mainly due to exertional dyspnea. In addition, she was at risk of developing pulmonary hypertension as evidenced by echocardiography. Taking into consideration cardiotoxicity and tolerability, these conditions precluded the use of doxorubicin even as a single-agent for primary therapy. Paclitaxel was then chosen for the initial chemotherapy (80 mg/m<sup>2</sup> on days 1, 8, and 15 of a 28-day cycle). Following two cycles of treatment, MRI revealed shrinkage of the extended tumor tail in the right pulmonary artery (Fig. 1b). However, after three cycles, the tumor in the left pulmonary artery showed locoregional progression on following MRI (Fig. 1c). Most of the pulmonary metastases disappeared as evidenced by CT (Fig. 3b). Progression-free survival was 3.6 months. Doxorubicin was used as second-line chemotherapy (60 mg/m<sup>2</sup> on day 1 of a

21-day cycle). Prior to treatment, the patient's heart function was re-evaluated by echocardiography, and showed no changes from the status at onset. Doxorubicin was efficacious for 4.5 months, maintaining stable disease. After six cycles of doxorubicin, the tumor branching into the left pulmonary artery showed progression (Fig. 1d). She underwent third-line chemotherapy using gemcitabine (1,000 mg/m<sup>2</sup> on days 1 and 8 of a 21-day cycle, then the schedule was changed to biweekly at the same dose due to toxicity). After two cycles of gemcitabine, imaging examination revealed tumor progression. Subsequently, fourth-line chemotherapy using eribulin was started (1.4 mg/m<sup>2</sup> on days 1 and 15 of a 28-day cycle). However, after one and half cycles, the patient died of respiratory failure following disease progression. A month before her death, a surface skin nodule on the left chest was surgically resected, which was shown pathologically to be a skin metastasis of the sarcoma (Fig. 2b). Her overall survival period was 14.2 months after the initial chemotherapy.

## Discussion

Little is known about efficacious chemotherapy regimens in patients with unresectable or metastatic pulmonary artery intimal sarcoma. In general, doxorubicin-based regimens are recommended for the treatment of soft tissue sarcomas [9]. In addition, several cytotoxic agents were studied and reported to be useful for soft tissue sarcomas. Of these, paclitaxel has also been shown to be effective for soft tissue sarcoma [10, 11, 12]. We selected paclitaxel as the first-line chemotherapy in the present case because of her poor PS and increased risk of pulmonary hypertension due to preexisting severe pulmonary artery obstruction. Chemotherapy with paclitaxel showed slight tumor reduction in the pulmonary artery and disappearance of pulmonary metastasis, although radiographic changes were insufficient for the criteria of RECIST partial response. To our knowledge, there have been no previous case reports regarding efficacy of paclitaxel in patients with pulmonary intimal artery sarcoma. Our experience suggests that paclitaxel may be a useful alternative agent for treatment of patients with pulmonary intimal artery sarcoma. We subsequently administered three regimens of salvage chemotherapy including doxorubicin after relapse, which had little efficacy for disease control. However, the serial chemotherapeutic regimens used in our case may have contributed to her prolonged survival of 14.2 months. This survival period was comparable to the results reported in the literatures, such as 8–17 months in patients with advanced and metastatic pulmonary intimal artery sarcoma [7, 8].

With regard to other novel agents for pulmonary intimal artery sarcoma, Funatsu et al. described a case of pulmonary artery intimal sarcoma showing partial response to pazopanib [13], a multitarget tyrosine kinase inhibitor active in advanced or metastatic soft tissue sarcoma [14]. In addition, there have been case reports showing good response of pulmonary artery intimal sarcoma to vinorelbine-based regimens [15, 16]. These agents could have been alternative choices in our case. Further clinical experience is required to improve the outcome and understand the roles of systemic chemotherapies in patients with advanced and unresectable pulmonary artery intimal sarcoma.

In summary, first-line treatment with paclitaxel followed by several regimens commonly used for soft tissue sarcomas resulted in prolonged survival in our case of non-operable pulmonary intimal sarcoma. Therefore, chemotherapy can be one of the treatment options for patients with advanced and unresectable pulmonary artery intimal sarcoma.

### Statement of Ethics

Ethical approval was not relevant or applicable to this case report. Full informed consent to publish manuscript and images obtained from the patient.

### Disclosure Statement

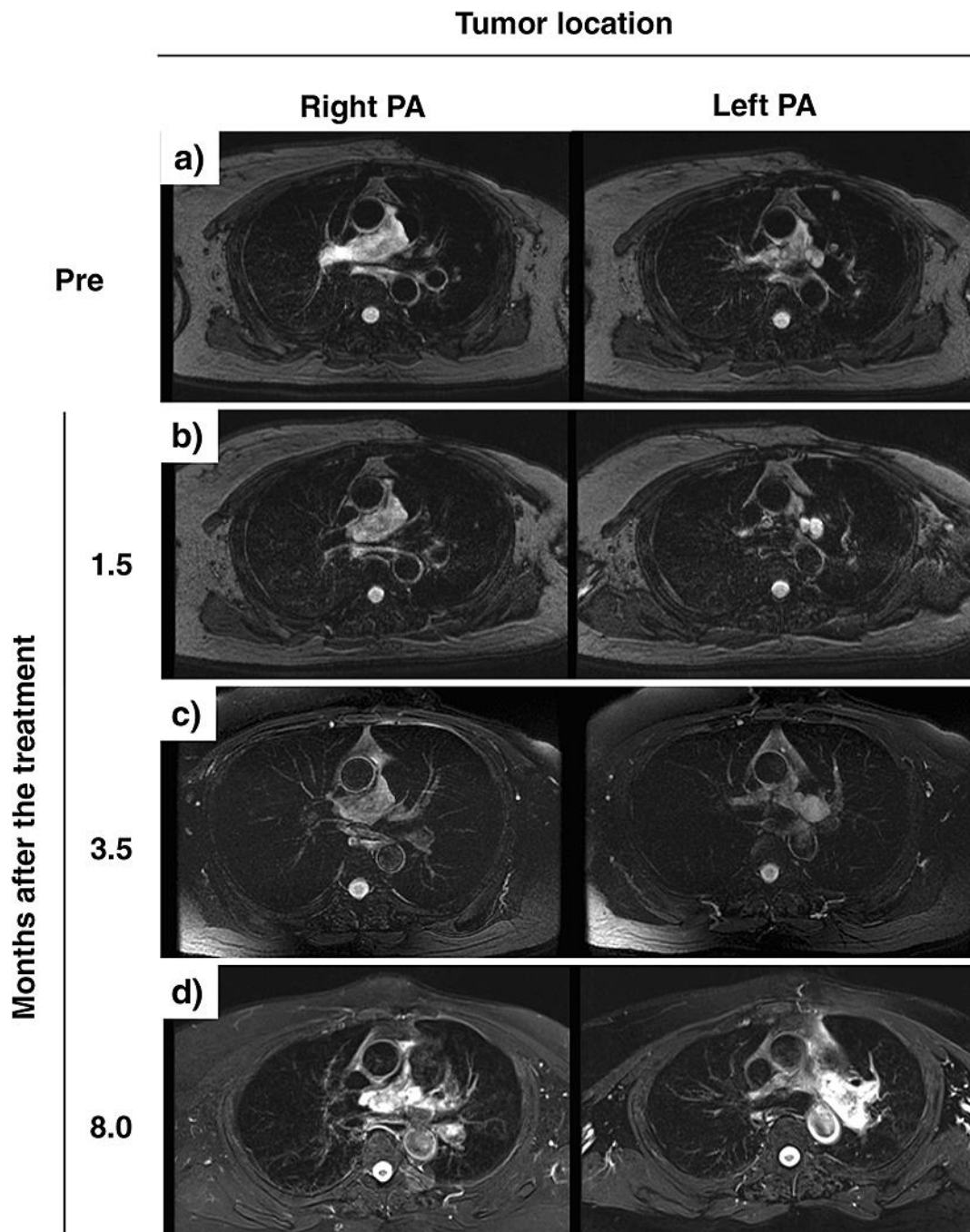
The authors declare no conflict of interests.

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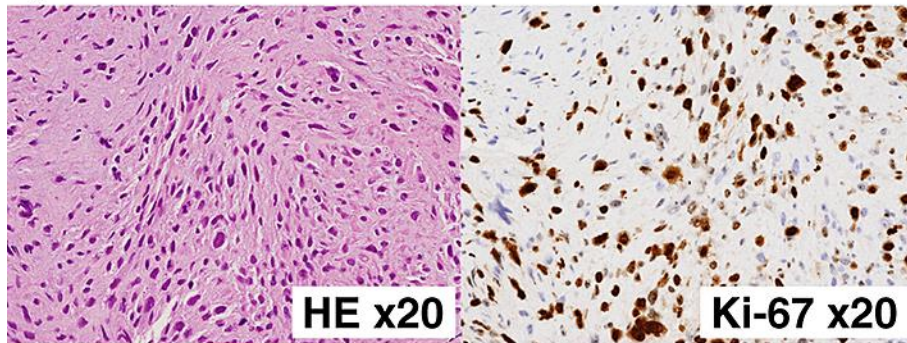
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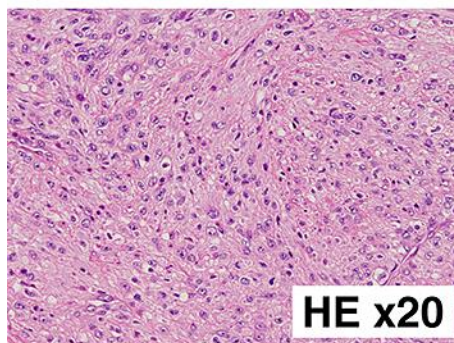
**Fig. 1.** Imaging studies by MRI. (a) MRI at onset showed a lesion in the main pulmonary artery extending to the right and left pulmonary arteries. (b) One and half cycles of first-line paclitaxel treatment resulted in shrinkage of the tumor tail extending to the right pulmonary artery. (c) At 3.5 months, the tumor in the left pulmonary artery showed progression. (d) At 8.0 months, the tumor in the left pulmonary artery showed further progression.



a)

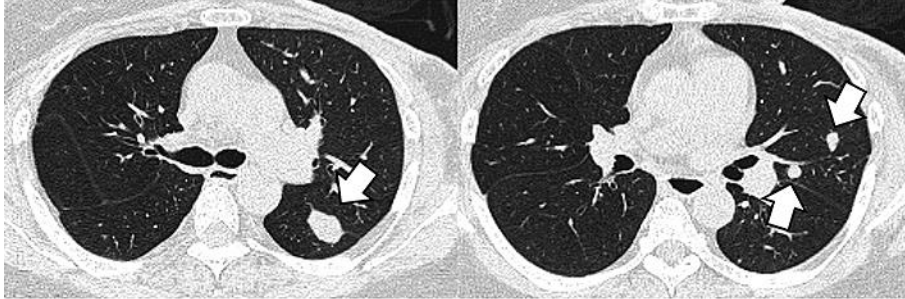


b)

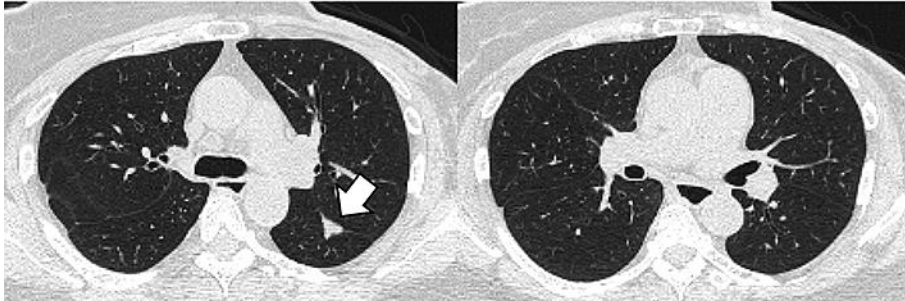


**Fig. 2.** Pathological studies. (a) Left–Histologically, the tumor cells showed a pattern of soft tissue sarcoma. On immunohistochemical analysis, they were negative for cytokeratin AE1/AE3, smooth muscle actin, desmin, caldesmon, S-100, and CD34. Right–Fifty percent of the tumor cells were positive for Ki-67. (b) Tumor cells in the skin nodule resected at 13 months after onset were histologically diagnosed as soft tissue sarcoma.

**a) Before the treatment**



**b) After paclitaxel (3.5 months)**



**Fig. 3.** Imaging studies by CT. (a) CT at onset showed multiple lung nodules (arrow). (b) After three cycles of first-line paclitaxel treatment, most of the lung nodules disappeared.