A Case of Intimal Sarcoma of the Pulmonary Artery Treated with Chemoradiotherapy

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Abstract

We report on a 45-year-old woman with intimal sarcoma of the pulmonary artery. She presented with a chief complaint of shortness of breath. Computed tomography (CT) of the chest showed an intraluminal hypoattenuated area extending from the main pulmonary artery into the right main pulmonary artery and bilateral lobar pulmonary arteries. She underwent resection of the lobulated mass from the pulmonary artery. The tumor was diagnosed as an intimal sarcoma. Although she received chemotherapy with amrubicin and carboplatin when the tumor recurred, the tumor enlarged. After radiotherapy was performed, CT of the chest showed shrinkage of the tumor and the regression of consolidation and ground-glass opacity. Radiotherapy and chemotherapy are treatment option for patients with pulmonary artery sarcoma.

Key words: intimal sarcoma, pulmonary artery, radiotherapy, chemotherapy, surgery, computed tomography

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Introduction

Intimal sarcoma of the pulmonary artery is rare (1). This tumor was first described at autopsy by Mandelstamm in 1923 (2). It is easily misdiagnosed as a chronic pulmonary embolism, mediastinal mass, or tumor emboli, leading to inappropriate treatment, such as prolonged anticoagulation or thrombolysis. The prognosis of pulmonary artery sarcoma is extremely poor, with a median survival time without surgical resection of only 1.5 months (3). Surgical resection decreases clinical symptoms and lengths survival (4). Chemotherapy and radiotherapy for pulmonary artery sarcoma remains controversial, although some studies have demonstrated their effectiveness (5, 6). We report on a 45-year-old woman with intimal sarcoma of the pulmonary artery that treatment with surgery, radiotherapy, and chemotherapy successfully lengthened survival.

Case Report

A 45-year-old woman presented with a chief complaint of shortness of breath, which had gradually worsened over the preceding 2 months. She had no significant past medical history. She had never smoked but sometimes drank alcohol. Physical examination revealed tachypnea (20 breaths per minute) and tachycardia (heart rate, 106 beats per minute). Blood pressure was 108/70 mm Hg, and body temperature was 36.2°C. Cardiac auscultation revealed no murmur, and pulmonary auscultation revealed no piping. The abdomen was flat and soft, and the legs showed no edema.

Analysis of arterial blood gas showed hypoxia and hypocapnia as follows: pH, 7.484; PaCO₂, 23.5 mmHg; PaO₂, 47.3 mmHg; base excess, -4.0 mmol/L, and oxygen saturation, 86%. Peripheral blood and chemistry profiles were within the normal ranges. Serum levels of tumor markers for lung carcinoma, such as carcinoembryonic antigen, cytokeratin 19 fragment, and pro-gastrin-releasing peptide, were within the normal ranges. Serum levels of human atrial
natriuretic peptide and brain natriuretic peptide were elevated to 220 pg/mL and 353 pg/mL, respectively. A chest X-ray film showed enlargement of the left main pulmonary artery (Fig. 1A). Contrast-enhanced computed tomography (CE-CT) of the chest showed an intraluminal hypoattenuated area extending from the main pulmonary artery into the right main pulmonary artery and the bilateral lobar pulmonary arteries, consolidation in the upper lobe of the right lung, and ground-glass opacity (GGO) in the lower lobes of the both lungs, most likely representing infarction (Fig. 1B). Abdominal and pelvic CE-CT showed no evidence of metastatic disease. A tumor of the pulmonary artery was diagnosed.

The patient underwent resection of a tumor of the pulmonary artery. Resection was performed with cardiopulmonary bypass. The opening of the main pulmonary artery and right pulmonary artery revealed a 3×3×2-cm lobulated mass that had attached to the intima of the main pulmonary artery and had extended through the lumens of both the right and left pulmonary arteries. The tumor was entirely removed without injury to the interventricular septum. The pulmonary artery was reconstructed with a pericardial patch.

The resected tumor included mucoid regions. The cytology of pericardial effusion was class II. Histological examination of the tumor revealed proliferation of spindle cells with pleomorphic nuclei in a myxoid and collagenized background (Fig. 2A). Specimens of the tumor were immunohistochemically positive for vimentin and were focally positive for alpha-smooth muscle actin and CD34 but were negative for desmin, cytokeratin, S-100 protein, and CD31 (Figs. 2B, 2C). On the basis of morphological and immunohistochemical findings, the tumor was diagnosed as an intimal sarcoma of the pulmonary artery.

CE-CT of the chest immediately after surgery did not show an obvious intraluminal hypoattenuated area in the pulmonary artery. However, 2 months after surgery, chest CE-CT showed an intraluminal hypoattenuated area along
the main pulmonary artery and bilateral lobar pulmonary arteries, consolidation in the upper lobe of the right lung, and GGO in the lower lobe of both lungs (Figs. 3A, 3B). Lung perfusion scintigraphy demonstrated diffusely reduced tracer uptake and multiple segmental defects in both right and left lungs (predominantly in the right lung). Cardiac ultrasonography revealed hypokinesis from the posterior to lateral left ventricle due to pressure from the tumor, a decreased ejection fraction of 55%, and right ventricular dilatation. Additionally, Doppler echocardiography demonstrated a maximum pressure gradient across the right ventricular outflow tract of 87 mmHg. We diagnosed local recurrence accompanied by pulmonary embolism.

Although the patient had received 2 courses of chemotherapy with carboplatin (with a target area under the concentration versus time curve of 4 mg min/mL using the Calvert formula on day 1) and amrubicin (30 mg/m² on days 1, 2, and 3) every 3 weeks, the tumor had enlarged slightly. After chemotherapy, the patient received radiotherapy that consisted of 53 Gy in initially 3 fractions of 3-Gy per fraction and 22 fractions of 2-Gy per fractions centered around the tumor. The tumor along the right main pulmonary artery and bilateral pulmonary lobar arteries shrank 60% in length compared with before radiotherapy, and CE-CT showed decreased consolidation and GGO (Figs. 3C, 3D). In addition, the maximum pressure gradient across the right ventricular outflow tract had decreased to 45 mmHg. Seven months after radiotherapy, chest CE-CT revealed an additional mass in the pericardium and metastases in the lower lobe of the right lung. Although we recommended chemotherapy with ifosfamide as second-line chemotherapy to the patient and her husband, they refused. We then recommended radiotherapy limited to the mass in the pericardium and the pulmonary metastases. Although the mass in the pericardium and the pulmonary metastases were treated with radiotherapy (45 Gy in 15 fractions of 3-Gy per fraction), the tumors enlarged, and the performance status of the patient worsened to 3. The patient died 16 months after surgery and 9 months after radiotherapy because of respiratory failure and heart failure due to tumor progression. Permission for an autopsy could not be obtained.

**Discussion**

We have reported on a 45-year old woman with intimal sarcoma of the pulmonary artery that treatment with surgery, radiotherapy, and chemotherapy successfully lengthened survival. Additionally, to our knowledge, this is the first case of intimal sarcoma of the pulmonary artery treated with a combination of amrubicin and carboplatin; unfortunately, this combination chemotherapy was not effective.

Pulmonary artery sarcoma is rare and has a poor prognosis, with median survival times of 1.5 months without surgical resection and 10 months with resection (4). Surgical resection offers the chance of longer survival in patients with pulmonary artery sarcoma (2). Therefore, surgical resection should be attempted for all cases diagnosed at an early stage, even if cure seems unlikely. However, establishing a definitive diagnosis of pulmonary artery sarcoma is difficult. These tumors have been misdiagnosed as chronic pulmonary
emboli and tumor emboli or have been diagnosed only at autopsy (7). Thus, to avoid inappropriate therapy, such as prolonged administration of anticoagulants or thrombolytic agents, pulmonary artery sarcoma should be considered when CT shows an intraluminal hypoattenuated area of the pulmonary artery.

Histologic examination shows that pulmonary artery sarcoma is most often undifferentiated (30%), with leiomyosarcoma being the next most common type (8). Intimal sarcomas of the pulmonary artery are usually poorly differentiated mesenchymal malignant tumors with fibroblastic and myofibroblastic differentiation and exhibit a variable immunohistochemical positivity for vimentin and alpha-smooth muscle actin but negativity for desmin (9). The present case was diagnosed as an intimal sarcoma of the pulmonary artery on the basis of immunohistochemical findings and the proliferation of spindle cells with pleomorphic nuclei in a myxoid and collagenized background. However, the histologic subclassification of the pulmonary artery sarcoma does not appear to be useful for selecting treatment (10). Therefore, the diagnosis as a pulmonary artery sarcoma seems to be the most appropriate basis for selecting treatment.

The roles of chemotherapy and radiotherapy in the treatment of pulmonary artery sarcoma remain undefined. However, some reports have shown that chemotherapy or radiotherapy is effective against pulmonary artery sarcoma (5, 6, 11). The addition to surgical treatment of chemotherapy or radiotherapy or both has lengthened survival times compared with surgery alone (12, 13). Moreover, patients with aortic sarcoma who receive aggressive surgical therapy and postoperative radiation combined with systemic chemotherapy survive longer than those with tumors who receive no treatment (11). Therefore, we believe chemotherapy or radiotherapy should be attempted in patients with pulmonary artery sarcoma that is unresectable or is recurrent after surgery.

Doxorubicin is one of the most effective agents for the treatment of soft-tissue sarcomas in adults. Some previous reports have shown that concomitant doxorubicin infusion and radiotherapy is effective against pulmonary artery sarcoma (6, 11). However, a standard chemotherapy regimen has not been established for pulmonary artery sarcoma. Amrubucin is a novel, totally synthesized anthracycline derivative that differs from doxorubicin by the amino group at the 9-position and by its unique sugar moiety (14). Amrubucin shows antitumor activity and is more potent than doxorubicin against several human tumor xenografts implanted in nude mice (15). In an experimental animal model, amrubucin did not cause chronic cardiotoxicity or exacerbate doxorubicin-induced cardiotoxicity in dogs (16). Furthermore, carboplatin had additive effects with doxorubicin in a human leukemia cell line (17). Thus, we chose the amrubucin and carboplatin as combination chemotherapeutic agents. In the future, a standard chemotherapy for pulmonary artery sarcoma should be established, although doing so is complicated by the small number of cases.

Ifosfamide is another principle cytotoxic agent for patients with soft-tissue sarcomas and has achieved response rates greater than 20% (18). Increasing the ifosfamide dosage from 5 g/m² to 14 mg/m² is associated with improved response rates (19). In addition, ifosfamide is beneficial for patients in whom treatment with doxorubicin-based regimens has failed (20). Therefore, we recommended chemotherapy with ifosfamide as second-line chemotherapy to the patient and her husband. However, they refused second-line chemotherapy.

In conclusion, radiotherapy and chemotherapy should be attempted in patients with pulmonary artery sarcoma that is unresectable or is recurrent after surgery, although the most effective way of prolonging survival has been surgical intervention. The survival of patients with pulmonary artery sarcoma can be prolonged if the tumors are diagnosed early and if multimodality treatment, including radical surgical resection and chemotherapy and radiotherapy, is performed.

References


