Intravascular Synovial Sarcoma of the Pulmonary Artery with Massive Pleural Effusion: Report of a Case with a Favorable Response to Ifosfamide Chemotherapy and Palliative Radiation Therapy

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Abstract

Synovial sarcoma (SS) commonly arises in the para-articular soft tissue; however, very few cases of intravascular SS have so far been reported. We herein describe a case of pulmonary artery SS with massive pleural effusion. A biopsy of the pleural lesions showed uniform short spindle cell proliferation, while the SYT-SSX fusion gene, which is preceded by chromosomal translocation t(X;18)(p11;q11), was detected using reverse transcription-polymerase chain reaction. Treatment with ifosfamide chemotherapy and palliative radiation therapy was effective in reducing the growth of the tumor in the pulmonary artery and pleural lesions, indicating that this regimen may be useful for the treatment of unresectable SS in the pulmonary artery.

Key words: intravascular synovial sarcoma, pulmonary artery, pleura, ifosfamide, radiotherapy

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Introduction

Synovial sarcoma (SS) accounts for 1.6-15% of soft tissue sarcomas and most commonly arises in the deep soft tissue of the lower and upper extremities (1). SS occurs at equal frequencies in both sexes, and more than 50% of patients are teenagers or young adults. Histologically, SS is biphasic or monophasic. Varying proportions of epithelial and spindle cell components are present in biphasic SS, whereas only monotonous short spindle cells are detected in monophasic SS. On molecular analyses, SS has a specific chromosomal translocation t(X;18)(p11;q11), which leads to the formation of a SYT-SSX fusion gene. Intravascular SS (IVSS) of the pulmonary artery is extremely rare, with only three cases having been reported to date (2-4). The principal curative therapy for SS is complete surgical resection of the tumor tissue. However, the efficacy of chemotherapy and radiotherapy in treating unresectable IVSS remains undefined. We herein report a case of unresectable IVSS of the pulmonary artery with massive pleural effusion in which therapy with ifosfamide chemotherapy and palliative radiation was effective.

Case Report

A 23-year-old woman who had never smoked and had no remarkable previous history presented with a cough and right chest pain. A physical examination indicated a systolic murmur at the left sternal border and diminished breath sounds over the right lung. A chest radiograph disclosed a large amount of right pleural effusion, and an echocar-
diagnostic examination showed a tumor extending from the right pulmonary artery to the pulmonary trunk (Fig. 1A), which was subsequently confirmed on contrast-enhanced computed tomography (CECT). In addition, CECT revealed scattered lesions in the right pleura (Fig. 1B, C), and positron emission tomography (PET)-computed tomography (CT) showed an increased 2-deoxy-2\(^{18}\)F-fluoro-D-glucose uptake in the lesions (Fig. 1D). No other tumors were detected on whole-body PET-CT or brain magnetic resonance imaging. A biopsy of the pleural tumors demonstrated proliferation of uniform short spindle cells with ovoid vesicular nuclei and mitoses of up to seven mitotic bodies in a 2-mm\(^2\) area (Fig. 2A, B). An immunohistochemical analysis of the tumor cells revealed a positive expression for AE1/AE3 (Fig. 2C), vimentin, S100, CD56, CD99 and BCL-2. In contrast, staining for CAM5.2, epithelial membrane antigen, CD34, CD31, desmin, smooth muscle actin, p63 and CD21 was negative. The SYT-SSX fusion gene was detected using reverse transcription-polymerase chain reaction (Fig. 2D), and a pathological examination showed the tumor to be SS, although no malignant cells were detected in the pleural effusion. Palliative radiation therapy (54 Gy in 27 fractions over 41 days) was administered to the mediastinum in order to prevent pulmonary trunk obstruction. Ifosfamide (10 g/m\(^3\)) was also administered via continuous infusion over five days every three to four weeks due to the rapid progression of the pleural lesions despite performing thoracic drainage and pleurodesis. Chemotherapy and radiation therapy were effective in reducing both tumor growth and the pleural effusion (Fig. 3). The tumor has remained well controlled with ifosfamide chemotherapy for one year.

**Discussion**

The English language literature includes three cases of IVSS of the pulmonary artery: Schmid et al. (2) reported pulmonary tumor embolism associated with primary renal SS; Dusemund et al. (3) reported IVSS metastasis in the pulmonary artery from SS of the kidney; and Guo et al. (4) reported pulmonary artery obstruction caused by primary cardiac SS. Treatment in all of these cases included surgical resection. To the best of our knowledge, the current report is the first of a patient with unresectable IVSS of the pulmonary artery who was treated with and responded favorably to ifosfamide chemotherapy and radiation therapy.

The CECT and PET-CT findings in this case were suggestive of a tumor in the pulmonary artery rather than thrombosis due to the uptake on PET-CT, which initially indicated a diagnosis of pulmonary artery intimal sarcoma (5). However, the histopathology, immunohistochemistry and molecular genetics were indicative of SS, leading to the diagnosis of IVSS. Other possible diagnoses were spindle cell carcinoma, leiomyosarcoma, malignant peripheral nerve sheath tumor and malignant solitary fibrous tumor. However, each of these conditions was excluded based on the results of the pathological examination. The role of chemotherapy and radiotherapy in the treatment of IVSS remains undefined. Rosen et al. (6) previously reported that high-dose ifosfamide chemotherapy is effective against metastatic SSs. In that study, among 13 patients who received ifosfamide...
Figure 2. Histopathology findings. (A) Low-power image of a Hematoxylin and Eosin (H&E) staining section from the pleura, showing spindle cell proliferation with a fascicular pattern (magnification: ×100); (B) High-power image of an H&E staining section showing uniform short spindle cells with ovoid vesicular nuclei (magnification: ×400); (C) Immunohistochemical analysis showing focal AE1/AE3 positivity (magnification: ×100); (D) Reverse transcription-polymerase chain reaction analysis of the tumor specimen, revealing a SYT-SSX fusion gene which is lead by chromosomal translocation t(X; 18) (p11; q11).

Figure 3. Clinical course. (A) A chest radiograph before chemotherapy and radiotherapy showing a large amount of right pleural effusion; (B) A chest radiograph 9 months after chemotherapy and radiotherapy revealing improvement in the effusion; (C-D) A chest contrast-enhanced computed tomography image 10 months after chemotherapy and radiotherapy revealing regression of the effusion and a well-enhanced right pulmonary artery and trunk, indicating tumor regression (arrows).
chemotherapy, nine showed a partial response and four showed a complete response. Ifosfamide was also administered as adjuvant chemotherapy in all three previously reported patients with IVSS treated with surgical resection (7-9). In the present case of unresectable SS, the administration of ifosfamide chemotherapy plus palliative radiation therapy was effective. Tseng et al. (10) previously documented the complete regression of intimal sarcoma of the pulmonary artery following chemoradiotherapy, and treatment with radiotherapy effectively improved the right pulmonary artery obstruction in our case as well. Furthermore, Koray et al. (11) previously demonstrated the complete regression of pulmonary synovial sarcoma after chemoradiotherapy. Therefore, the use of ifosfamide chemotherapy in combination with radiotherapy may be recommended in cases of unresectable SS of the pulmonary artery. The current patient was considered to have primary IVSS with multiple pleural metastases, as the pleural tumors were widely scattered and the tumor in the pulmonary artery was very large. However, Baccari-Ezzine et al. (12) reported a case of intracardiac metastasis at the apex of the right ventricle from primary SS in the lungs. Although primary pleural SS is rare, this condition has been documented (13, 14); therefore, it is possible that our patient had primary pleural SS with intravascular metastasis.

In summary, we herein reported a case of SS with severe obstruction of the pulmonary artery in which unresectable lesions in the pulmonary artery and right pleura were effectively treated with ifosfamide chemotherapy and palliative radiation therapy. This case suggests that a diagnosis of SS should be considered in patients with pulmonary artery tumors and that combination therapy consisting of ifosfamide chemotherapy and radiotherapy may be useful for treating unresectable disease.

The authors state that they have no Conflict of Interest (COI).

References