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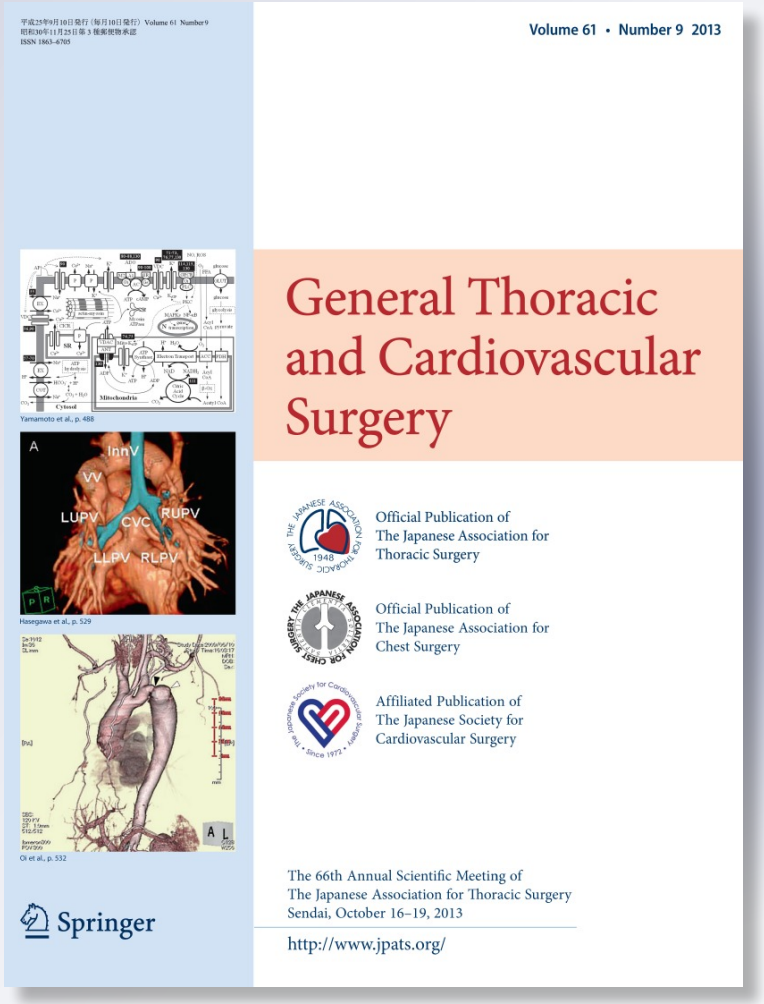
General Thoracic and Cardiovascular Surgery

ISSN 1863-6705
Volume 61
Number 9

Gen Thorac Cardiovasc Surg (2013)
61:534-537
DOI 10.1007/s11748-012-0192-2



Springer

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CASE REPORT

Leiomyosarcoma of the right inferior pulmonary vein: 2 years survival with multimodality therapy

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Received: 15 May 2012 / Accepted: 30 November 2012 / Published online: 10 December 2012

Abstract Primary leiomyosarcoma of the heart is an extremely rare and aggressive tumor. The authors report a case of a 29-year-old man with a leiomyosarcoma of the right inferior pulmonary vein who underwent surgery, chemotherapy, and radiotherapy. The patient experienced two local recurrences and he finally died 2 years after onset of symptoms because of multiple distal metastases.

Keywords: Cardiac tumors · Sarcoma · Pulmonary vein · Chemotherapy

Introduction

Leiomyosarcomas represent a minority of primary cardiac tumors and are associated with a poor outcome because of local recurrence and distal metastases. No consensus exists regarding the best operative strategy. We report a case of a 29-year-old man with a leiomyosarcoma of the right inferior pulmonary vein treated with a multimodality therapy including surgery, chemotherapy, and radiotherapy with a 2 years survival after onset of symptoms.

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Case report

A 29-year-old man was hospitalized for a chest radiography evidence of pneumopathy and treated with antibiotics; after a month he experienced a relapse of the respiratory symptoms with cough, hemoptysis, and crescendo dyspnea. A thoracic computed tomography (CT) was then performed showing a voluminous mass in the left atrium extended into the right inferior pulmonary vein, associated to bilateral pleural effusion and alveolar-interstitial syndrome consistent with cardiogenic pulmonary edema and right basal pulmonary embolism. Echocardiography confirmed the presence of a 54 mm diameter mass in the left atrium extending into the right inferior pulmonary vein and also obstructing the mitral valve (mean gradient 28 mmHg; ejection fraction (EF) 65 %). The patient was referred to our service for treatment and underwent urgent surgery for respiratory distress aggravation. Surgery was performed through median sternotomy; cardiopulmonary bypass (CPB) was established with aortic and bi-caval cannulation. The left atrium was opened showing a voluminous, firm tumor adherent to the right inferior pulmonary vein from which it seemed to originate. The endocardium was thickened and the endocardial fibrosis extended up to mitral valve causing a severe stenosis. The tumor was excised and the right inferior pulmonary vein permeability was re-established; the endocardial thickening was removed, while mitral valve could not be preserved because of the absence of a surgical plane of cleavage between the endocardial fibrosis and the valve and a mechanical prosthetic valve was implanted. Early postoperative course was marked by a cardiogenic shock responsive to inotropes and a progressively regressed pulmonary edema. Postoperative thoracic CT was performed 9 days after surgery and revealed the persistence of the

tumor at the right inferior pulmonary vein and the presence of an osteolytic lesion at the left transverse apophysis of the 9th thoracic vertebra (T9). The 18F-fluorodeoxyglucose positron emission tomography (PET) objectified an intense fixation (Standardized uptake value (SUV) max 16,5) on the residual lesion of the right inferior pulmonary vein, but did not reveal any other sites of fixation, even at T9; bone biopsy at T9 resulted negative too. Cerebral CT did not show any cerebral lesion. Interdisciplinary staff meeting suggested chemotherapy with adriamycin and ifosfamide; 40 days after the first operation and before chemotherapy cycle beginning the patient had acute pulmonary edema due to a complete left atrium obstruction by the tumor as highlighted by a new thoracic CT. The patient underwent redo surgery through right antero-lateral thoracotomy. A voluminous pulmonary mass belonging to right inferior pulmonary lobe was detected, still detachable from middle pulmonary lobe. Firstly inferior lobe artery and bronchus were ligated. After CPB establishment with right femoral artery and bicaval cannulation, left atrium was opened showing a tumor adherent to the circumference of right inferior pulmonary vein which resulted very dilated. The tumor was removed en bloc with the left atrial wall adjacent to right inferior pulmonary vein and the right inferior pulmonary lobe (Fig. 1). Left atrium was closed using a dacron patch (Hémapatch®). Postoperative course was uneventful. PET evaluation after 3 courses of chemotherapy with adriamycin and ifosfamide revealed the persistence of a cardiac hypermetabolic lesion; thoracic, abdominal, and cerebral CT only showed left atrial posterior wall thickening; no metastatic lesion was detected. Three months after the end of 6 courses of chemotherapy the patient presented with dyspnea and hemoptysis; CT detected a 40 mm diameter mass in the left atrium near the valvular prosthesis. The transesophageal echocardiography confirmed the presence of the mass adherent to the prosthesis (mean gradient 25 mmHg, pulmonary artery pressure 70 mmHg, EF 50 %). The patient underwent resternotomy 9 months after the first surgery; dense adhesions from previous cardiac surgery made the usual left atrial approach difficult so a transseptal approach to the mitral valve was performed. The mass, originating from the posterior left atrial wall 1 cm above the orifice of the left superior pulmonary vein, was excised and the left atrial wall was reconstructed with a pericardial patch. Postoperative course was marked by complete atrioventricular block requiring permanent pacing. A new chemotherapy course with gemcitabine and paclitaxel was then beginning. A scalp nodule appeared and the biopsy showed an undifferentiated sarcoma likely a chondrosarcoma. Local radiotherapy was then started. Unfortunately new adrenal and vertebral metastatic lesions appeared and the patient finally died 2 years after onset of symptoms.

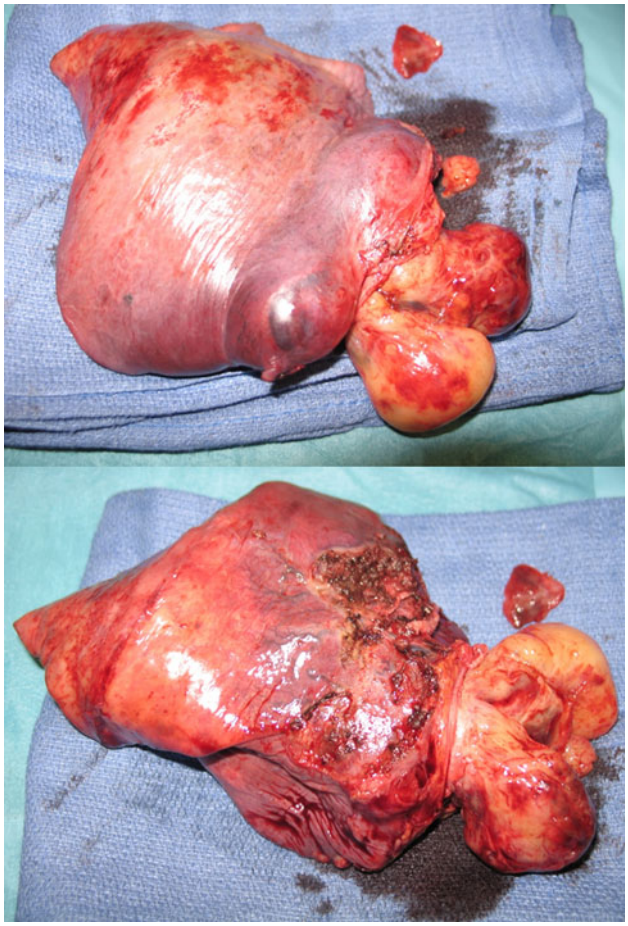

Fig. 1 View of the tumor recurrence that was removed en bloc with the *left* atrial wall adjacent to *right inferior* pulmonary vein and the *right inferior* pulmonary lobe

Histology

The excised tumor was 6 × 5 × 5 cm in dimension, 83 gr in weight, whitish in color, with necrotic and hemorrhagic areas up to 20 % of its volume. It was attached but not infiltrating the left atrial wall, which was fibrotic and thickened; conversely the tumor was firmly adherent and not detachable from the right inferior pulmonary vein. The excision margins of the surgical specimen were not clear of disease. Histologically the tumor consisted of densely packed fusiform cells sometimes arranged in a whirl-like pattern, with eosinophilic cytoplasm and hyperchromatic nuclei (Fig. 2). The index of mitotic activity was more than 35/10 consecutive HPF (high power fields). The interstitial matrix presented several necrotic foci up to 20 % of the tumor volume. The tumor was separated from the atrial wall by means of a fibro-edematosus tissue that did not go beyond the fibrosa layer of the endocardium. On the contrary, the tumor was in contact with the resection edge of the right inferior pulmonary vein and originated from the vessel wall that was entirely destructed.

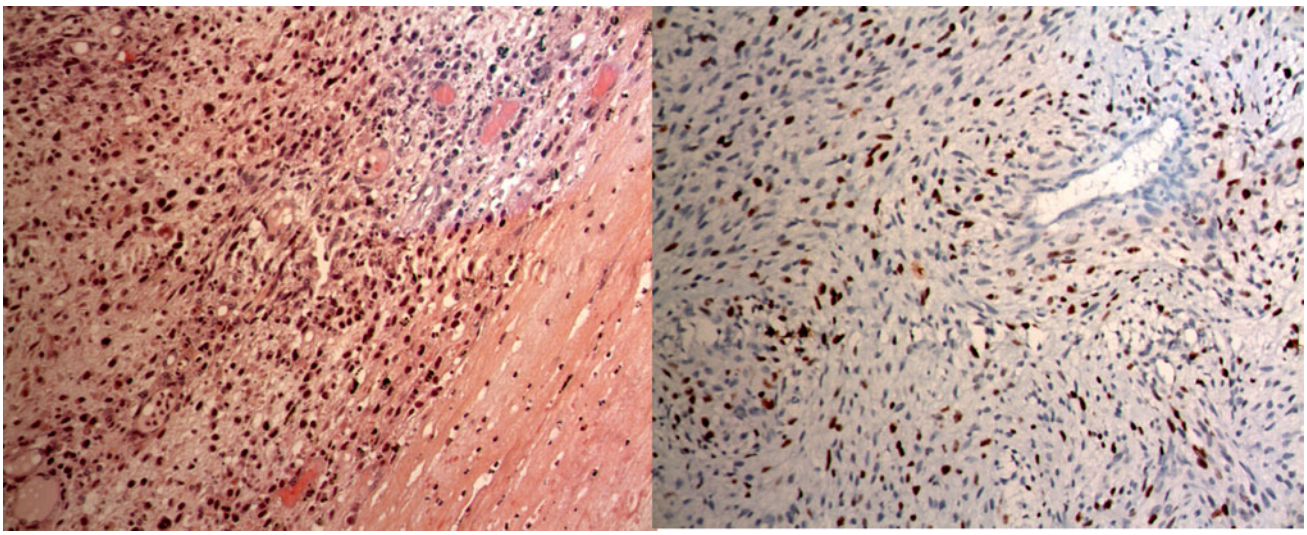

Fig. 2 *Right*: photomicrograph of the tumor section, showing the bundles of fusiform cells (hematoxylin and eosin stain, original magnification ×20); *left*: Ki67 staining (original magnification ×20)

Immunohistochemically the tumor cells showed a wide intracellular positive stain for vimentine, desmin, smooth muscle actine, and caldesmon. There was no immunoreactivity for vascular markers such as CD31 and CD34. Ki67 proliferation marker was present in 40 % of cells (Fig. 2). These morphological features were consistent with a diagnosis of a high grade leiomyosarcoma arising from the right inferior pulmonary vein with positive resection margins and the absence of tumoral infiltration of the left atrial wall.

The specimen obtained at the time of the right inferior lobectomy extended to the left atrium was 15 × 12 × 10 cm in dimension and 380 gr in weight. The tumor measured 7 × 5 × 4 cm and presented wide necrotic areas; it originated from the right inferior pulmonary vein and protruded into its lumen, and extended into the left atrium but still respecting the left atrial wall. The pulmonary parenchyma presented a sub-pleural whitish nodule in the basal pyramid measuring 0.5 cm in diameter and located at 5 cm from the primary tumor. Both the primary tumor and the satellite nodule presented the same histological features of the first specimen; of note there were no lymphatic metastasis.

The third specimen was 5 × 4 × 3 cm in dimension and 90 gr in weight and contained a 4 × 4 × 1.5 cm tumor implanted on the left atrial wall. Histologically the tumor consisted of both epithelioid and fusiform cells, with eosinophilic cytoplasm and hypercromatic nuclei; necrotic areas represented 60 % of the tumor volume.

Discussion

Primary cardiac tumors are extremely rare with an incidence ranging from 0.001 to 0.03 % at autopsy, while cardiac metastases occur 20–40 times more frequently than primary neoplasms [1]. Three-quarters of the primary cardiac tumors are benign and nearly half the benign heart tumors are myxomas [1]. Sarcomas, usually angiosarcomas, represent the most frequent malignant heart tumors accounting for 90–95 % of all malignant heart tumors, followed by lymphomas [2]; leiomyosarcoma accounts for about 9 % of all primary malignant heart tumors [2]. Vascular leiomyosarcoma represents only 2 % of soft tissue leiomyosarcomas; these rare tumors mainly derive from smooth muscle cells of vessel walls with predominant localization in the inferior vena cava and less frequently in the pulmonary arteries [3]. Pulmonary vein leiomyosarcoma is an extremely rare tumor first described at autopsy by Kidd and coll. in 1961 [4]; previously only 4 cases of sarcomas arising from of the pulmonary vein and filling the left atrium have been reported at autopsy [4].

Less than 20 cases of surgically treated cases of pulmonary vein leiomyosarcomas have been reported since 1989 [3, 5–13]. This entity shows no sex predilection, the mean age of presentation is 48 years (range 23–74) and symptoms are unspecific and consist of dyspnea, hemoptysis, cough, palpitations, and chest pain. Usually leiomyosarcomas of the pulmonary vein enter the left atrium and can involve the mitral valve causing obstructing symptoms. These tumors are very aggressive with a high risk to develop local and distal recurrences; metastases have been described at liver [9], scalp [9], and axillary lymph node [10]. Echocardiography and CT are useful to define the sites and the extent of involvement which determine the therapeutic approach. No consensus exists regarding the best operative strategy; however, wide surgical resection remains the cornerstone for treatment of this tumor with variable outcomes in literature [14]; additionally given the likely inadequacy of surgical margins and the

risk of metastases, adjuvant chemotherapy is the preferred post surgical treatment modality [14]. Mean survival for most cardiac sarcomas is about 9–11 months [14] and patients who underwent a complete resection show a better survival compared with patients who did not [15]. Therefore, total surgical resection with CPB and the addition of chemotherapy should offer these patients significant palliation and an opportuny for increased length of survival.

Conclusions

We present a case of leiomyosarcoma of the pulmonary vein and to our knowledge this is the fourth case report in a patient younger than 30 years [3, 9, 11]; additionally 2 years or more survival after the diagnosis of this aggressive tumor has been documented only in 4 patients who underwent surgery included this case [10, 11]. Despite rare frequency, accumulation of cases and longer follow-up are required to assess the definitive therapy other than surgical excision and prognostic factors of this rare entity.

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