Case Reports

Primary Pulmonary Valve Leiomyosarcoma in a 35-Year-Old Woman

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Primary cardiac leiomyosarcomas are rare, with a high incidence of local recurrence. Herein, we report the case of a 35-year-old woman who was admitted with right ventricular failure and suspected pulmonary embolism. Upon echocardiography, we detected a mass in the pulmonary trunk that involved the pulmonary valve and led to valvular stenosis.

The optimal protocol for treating these tumors is as yet unclear. Complete resection can rarely be achieved. However, palliative surgery is usually undertaken because many patients present with mechanical obstruction, such as significant pulmonary stenosis. ***(Tex Heart Inst J 2016;43(1):84-7)***

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Primary cardiac neoplasm is a rare condition with a prevalence of 0.001% to 0.03% in autopsy series.[1] More prevalent are metastases to the heart. Among the malignant primary tumors, angiosarcoma is most frequent, followed by rhabdomyosarcoma, mesothelioma, and fibrosarcoma.[2] Sarcoma is derived from the Greek for "fleshy tumor," although sarcomas include very heterogeneous subtypes.[3]

Primary cardiac leiomyosarcoma is a very rare tumor, found mostly in the left atrium and associated with poor outcomes. It constitutes less than 1% of malignant tumors and 8% of cardiac tumors.[4,5] The tumor grows rapidly and has high rates of distant metastasis and local recurrence after removal.[6] Therefore, the prognosis for primary cardiac leiomyosarcoma is poor: the mean survival period after diagnosis is 6 months.[7]

We describe a case of cardiac leiomyosarcoma with very rare involvement of the pulmonary valve (PV).

Case Report

In October 2013, a 35-year-old woman presented with exertional dyspnea. She had experienced a single episode of syncope with prolonged fever (temperature, 38.5 °C), chills, and night sweats. Two weeks before her admission, 4 hours of air travel had exacerbated her symptoms. The initial laboratory data showed leukocytosis (white blood cell count, 29,000/mm^3) with neutrophilia (86%). Her sedimentation rate was abnormally high (50 mm/hr). Both renal and liver functions were normal. The patient reported abdominal pain, nausea, and vomiting. Abdominal ultrasonography showed mild ascites, hepatic congestion, wall-thickening of the gall bladder, and mild pleural effusion. After her admission to an emergency department, an initial diagnosis of cholecystitis led to an urgent laparotomy. No abnormal findings were detected during surgery.

When the patient was studied paraclinically, her cutaneous tuberculin test was negative. The urine and blood cultures were also negative for bacteria. Her serum pro-brain natriuretic peptide and D-dimer levels were 1,545 and 523 ng/mL, respectively. All rheumatologic findings were within the normal range. Her heart size was normal on a chest radiograph. A small wedge-shaped area was noted in the parenchyma of the right lung.

Because a systolic ejection murmur was heard in the left sternal border, echocardiography was performed. Severe right ventricular (RV) enlargement, with moderate dysfunction, was detected. A homogenous mass in the RV outflow tract extended to the main pulmonary trunk, causing mild obstruction (estimated peak pressure gradient, 35 mmHg). The results of a perfusion lung scan and pulmonary computed tomographic angiography suggested pulmonary emboli. Moreover, multiple segmental

defects seen in the right lung were reported as highly probable for pulmonary emboli.

Doppler ultrasonography of both legs was negative for deep vein thrombosis. Anticoagulation therapy was initiated, and the patient was discharged from the hospital after adjustment of her warfarin dose.

One week later, the patient was admitted to our hospital with ongoing fever and chills, accompanied by dyspnea. On physical examination, a grade 3/6 systolic murmur was apparent in the left sternal border. Her lungs were clear, and there was no peripheral edema.

Transthoracic echocardiography revealed a bulky, hyperechoic, well-defined mass (Fig. 1) in the main pulmonary artery and proximal right branch, extending downward into the subpulmonic region. The PV itself could not be well distinguished from the mass. The mass had an obstructive effect at the level of the PV, thereby causing a substantial systolic peak pressure gradient of 57 mmHg. The pulmonary artery pressure was estimated to be 45 to 50 mmHg, in consideration of the proximal obstruction and tricuspid regurgitation peak velocity. The RV was severely enlarged and exhibited reduced function. Severe tricuspid regurgitation was seen to be secondary to annular dilation.

At this point, the patient was scheduled for cardiac surgery, which she refused. Subsequently, she underwent surgery in an emergency setting because of sudden loss of consciousness, subsequent convulsive movements, and cardiac arrest. After successful resuscitation and a subsequent midline sternotomy, a large gelatinous mass was seen in the pulmonary trunk, extending into the right branch. The PV, buried within the mass, had been surgically bisected (Fig. 2). Faint blood flow (via the PV) was noted through the mass. The tumor extended into the RV outflow tract. Some layered clot was noted overlying the mass. Radical resection, PV replacement, and trunk reconstruction were performed with use of a biologic prosthesis and pericardial patch.

Histopathologic photomicrographs of the mass (Fig. 3) showed that the tumor consisted of sheets and bundles of spindle and epithelioid cells with large vesiculated nuclei that suggested sarcoma. The cells were haphazardly arranged; some had large nucleoli with mitotic figures. There were also large areas of neoplastic necrosis. In immunohistochemical study, neoplastic cells were strongly positive for smooth-muscle actin, desmin, and vimentin, and negative for myogenin.

The patient's prolonged fever and dyspnea subsided after surgery. No residual mass was detected in the early

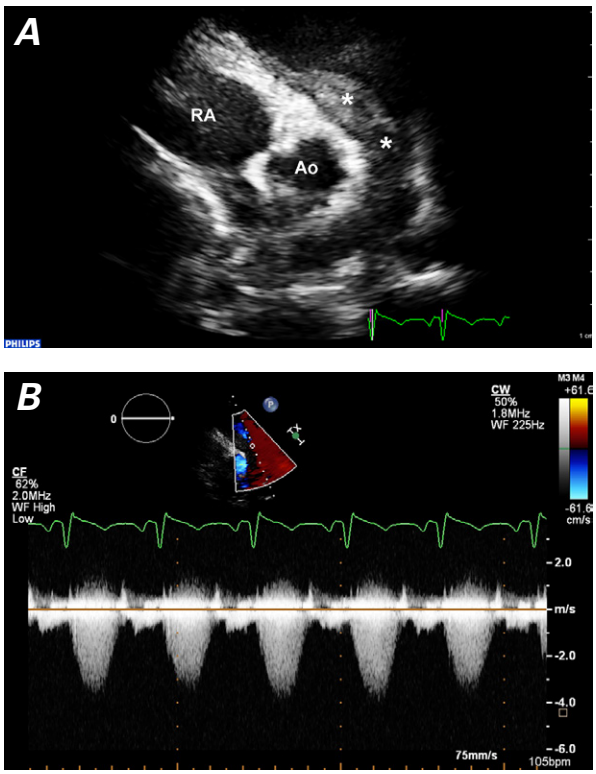

Fig. 1 ***A****) Transthoracic echocardiogram (parasternal short-axis view) shows the hypoechoic mass (asterisks) in the main pulmonary artery; the pulmonary valve cannot be differentiated from the mass.* ***B****) This Doppler study shows the mass occupying the pulmonary inflow tract, resulting in moderate stenosis (peak pressure gradient, 57 mmHg).*

Ao = aortic valve; RA = right atrium

Figure 1A is from: Poorzand H, Shabestari MM, Vakilian F, Teshnizi MA, Allahyari A. A rare case of cardiac leiomyosarcoma originated from pulmonary valve. In: Case-Based Session: Cases from Outside Europe. Eur Heart J Cardiovasc Imaging 2014;15(Suppl 2):ii148-ii150.

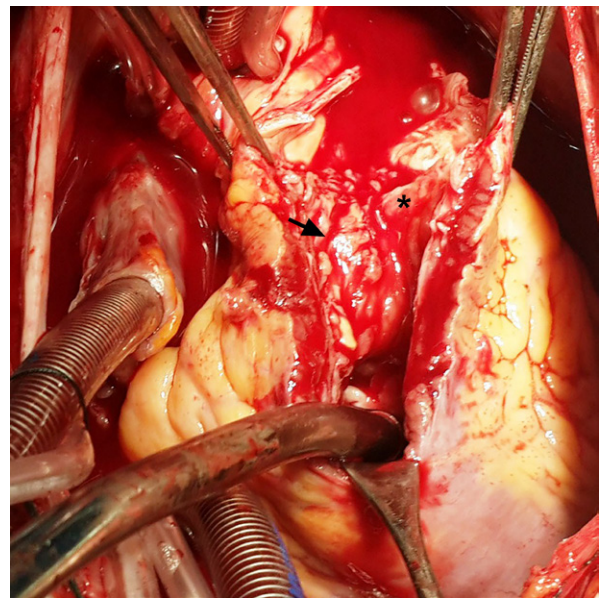

Fig. 2 *Intraoperative photograph of the large mass (arrow) involving the valve, with extension into the main pulmonary artery and right ventricular outflow tract. The asterisk denotes the bisected pulmonary valve.*

postoperative echocardiographic studies. She was discharged from the hospital in favorable condition and was referred to our oncology group for further study and therapy. Computed tomograms of the chest, abdomen, and pelvis did not show any distant metastasis. Adjuvant chemotherapy with gemcitabine and docetaxel was started. After 3 courses of treatment, echocardiography was performed to evaluate the patient's response to chemotherapy. Tumor recurrence was detected in the RV outflow tract, with extension toward the tricuspid valve (Fig. 4). Thereafter, the chemotherapeutic regimen was changed to ifosfamide and doxorubicin. The patient was asymptomatic during the follow-up period. At around the 4th month after the initiation of the 2nd chemotherapeutic regimen, the mass had decreased significantly in size.

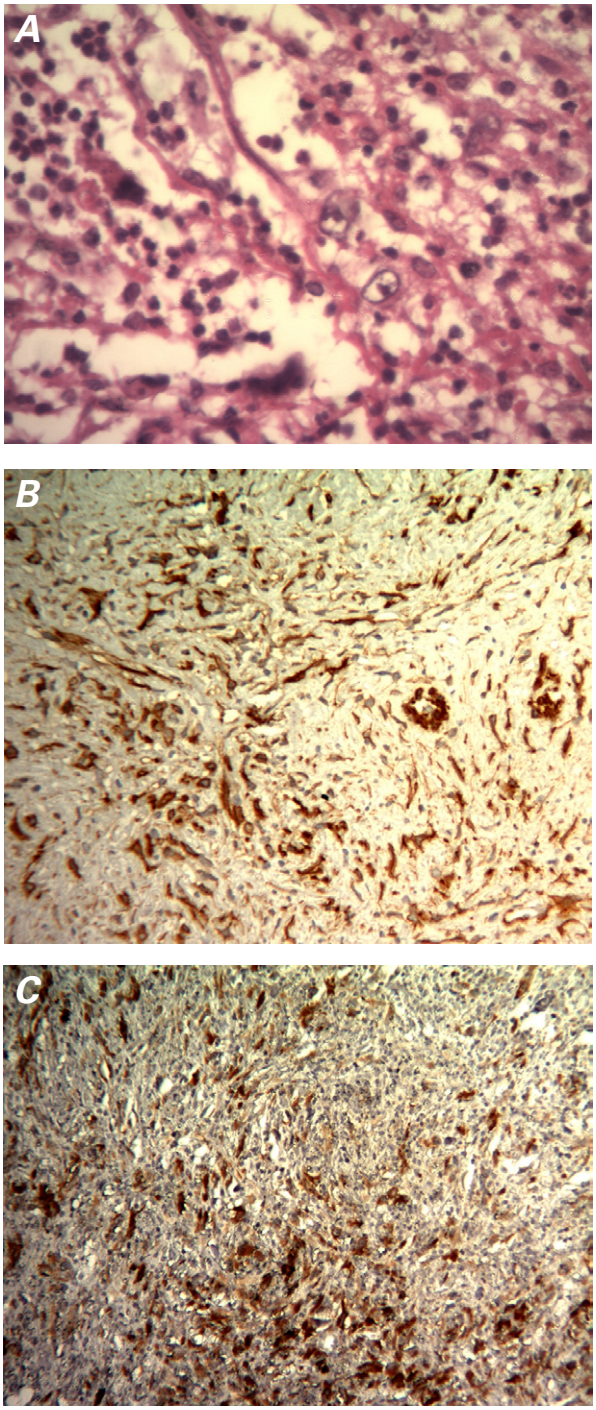

Fig. 3 *Photomicrographs of the resected mass.* ***A****) Hematoxylin & eosin stains show a sarcomatous lesion with prominent inflammatory reaction and spindle and epithelioid neoplastic cells (some with large nucleoli) in the background (orig. ×400).* ***B****) Immunohistochemical stains show strong and diffuse cytoplasmic immunoreactivity with smooth-muscle actin (orig. ×100), and* ***C****) strong and diffuse cytoplasmic positivity for desmin (orig. ×100).*

Discussion

Leiomyosarcoma is a malignant mesenchymal tumor with histologic and immunophenotypical evidence of smooth-muscle differentiation. In the heart, it is mostly found in the left atrium, often involving the pulmonary veins. Metastatic presentation of leiomyosarcoma in the heart is very rare.[8]

There is a wide age and size range for cardiac leiomyosarcoma, and a slight female predilection. The exact oncogenesis is not known. Because of delayed presentation, there is sometimes a systemic spread at the time of diagnosis.[4] As a result, management of this condition is difficult and subject to controversy. Typical clinical presentations of leiomyosarcoma include dyspnea, pericardial effusion, chest pain, atrial arrhythmias, and heart failure.[6]

This patient presented with constitutional symptoms and dyspnea. The condition was at first misdiagnosed as pulmonary thromboembolism, in consideration of her history of air travel, the subsequent dyspnea, and the perfusion defects upon imaging.

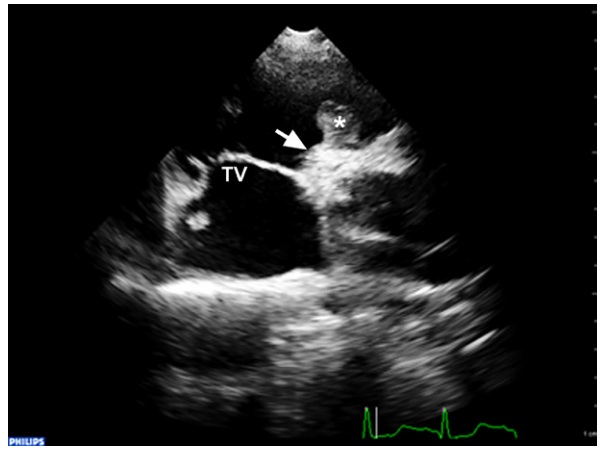

Fig. 4 *Transthoracic echocardiogram (parasternal off-axis view) shows recurrence of the tumor (asterisk) in the right ventricular outflow tract (arrow), extending to the level of the tricuspid valve annulus (TV).*

Echocardiographic imaging, enabling the identification of tumors as small as 3 mm, is the most sensitive imaging technique for the evaluation of cardiac masses.[6] Yet the results are not always straightforward. When the hypoechoic appearance of the mass in such clinical settings raises the suspicion of thrombus formation, it seems logical to initiate anticoagulation therapy.[9] However, soft-tissue characterization remains limited in comparison with that achieved by computed tomography and magnetic resonance imaging.[7] Macroscopically, the tumor appears to be a gelatinous mass, which is multiple in up to 30% of the cases.[3] It is recommended that further investigation be undertaken in patients who do not respond to initial anticoagulation,[5] as was true of our patient.

Leiomyosarcoma has a high rate of local recurrence, and metastases have been described after radical surgical extirpation.[10] Local recurrence was found in our patient after mass resection, but metastasis was not detected during the early follow-up period.

The optimal protocol and treatment efficacy are as yet unclear. Complete resection of these tumors can rarely be achieved; however, palliative surgery is usually undertaken, because many patients present with mechanical obstruction, such as significant mitral[11] or pulmonary stenosis (the latter was found in our patient).

Adjunctive chemotherapy, radiation therapy, or both are sometimes used.[12] Leiomyosarcoma has low radiosensitivity, and the efficacy of chemotherapy is still unknown.[13] Tumor shrinkage can be achieved by chemotherapy before surgery in nonemergency settings, but we had to perform surgery in the emergency setting because of cardiac arrest. The average survival time without operation is 6 to 12 months; surgery extends survival to 24 months. A vigorous attempt at tumor clearance, followed by adjuvant multimodal therapy and a tumor-monitoring program, might improve prospects.[11] Because of the tendency of leiomyosarcomas to recur, cardiac transplantation is not a realistic option.[12]

Conclusion

Pulmonary valve sarcoma, a rare disease with confusing clinical findings, is usually treated as pulmonary embolism before diagnosis. The role of histologic classification in prognosis and treatment is yet to be elucidated. Although surgery remains the only possibility for cure, adjuvant therapeutic methods should be studied further. Increased clinical awareness and improved diagnostic and therapeutic methods should give us greater hope for prolonged survival in such patients.

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