

Myocardial Metastasis of Cutaneous Squamous Cell Carcinoma in a Burn Patient



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INTRODUCTION

Cardiac squamous cell carcinoma (SCC) is a rare entity of metastatic origin. Presentation can vary from cough to cardiac tamponade depending on location, degree of invasion, and disruption of function. Detailed visualization of the tumor is important for acute medical management, as well as interventional planning. Here we present a case of an SCC invading the right ventricular outflow tract (RVOT) of a patient with a massive cutaneous lesion.

CASE PRESENTATION

A 33-year-old Filipino man who had received burns to his torso and legs 23 years prior presented with a large and painful wound on his back. The wound began as a small lesion approximately 2 years prior but was not brought to medical attention because of limited health-care coverage. The patient reported associated symptoms including occasional fevers, decreased appetite, and weight loss of 10–15 lb over the course of 2 months. He denied nausea, vomiting, bowel irregularity, abdominal pain, chest pain, and shortness of breath. His surgical history was notable for several excisions and skin grafts of the areas scarred by the initial accident. On physical examination there was a 30 × 30-cm ulcerative and fungating mass (Figure 1) extending from the midline of the back to the left flank. On palpation of the mass there was tenderness and purulent discharge with a foul smell. There was no surrounding erythema, cellulitis, or crepitus. Admission vital signs revealed tachycardia (111 beats/min) without fever (36.5°C) or respiratory distress (oxygen saturation 99% on room air). Initial laboratory assessment revealed hypokalemia (3.2 mmol/L), hypomagnesemia (1.4 mg/dL), hypercalcemia (12.6 mg/dL; ionized calcium 1.72 mmol/L), leukocytosis (37,800 white blood cells/ μ L) with a neutrophilic predominance (84%), anemia (7.2 g/dL), and a high platelet count (600,000/ μ L). Although findings on urinalysis and chest radiography were negative, noncontrast computed tomography of the chest revealed lymphadenopathy and a pulmonary nodule.

The patient was admitted to general surgery to undergo a wedge biopsy of the mass before surgical excision (Figure 2) was attempted.

The pathology report revealed moderate to poorly differentiated invasive SCC, likely a Marjolin's transformation. A Marjolin's ulcer is an ulcerating, poorly differentiated SCC that can present decades after trauma to the skin (commonly with burns).¹

During the subsequent 2 weeks of his admission, the patient exhibited remitting fevers. Several cultures for microorganisms were negative, and both the fever and leukocytosis were refractory to antibiotics. Furthermore, given the biopsy and computed tomographic results, metastatic disease was a significant diagnostic consideration. Transthoracic echocardiography revealed an echo-dense mass (Figure 3) measuring 3.3 × 3.3 cm and occupying the RVOT. To assist in differentiation of possible thrombus from tumor, myocardial perfusion echocardiography was used, which revealed partial vascularity within the lesion (Figures 4 and 5, Video 1). Upper and lower extremity duplexes were negative for deep venous thrombosis, and although contrast-enhanced computed tomography was negative for a pulmonary embolism, it was significant for a left axillary lymph node that had increased in size from 6.0 mm–1.9 cm, and a left upper lobe pulmonary nodule that increased from 3.0–7.0 mm (within a 23-day interval). Subsequent transesophageal echocardiography confirmed the presence of a round, immobile, broad-based, echogenic mass measuring 3.3 × 2.1 × 2.8 cm (Figure 6, Videos 2 and 3). The mass was attached to the anterior RVOT without obstruction (Figure 7, Video 4), visualized caudal to the pulmonic valve and evidently infiltrating the myocardium. An endomyocardial biopsy was performed via right heart catheterization (Figures 8 and 9) under the guidance of three-dimensional transesophageal echocardiography and fluoroscopy, with specimens confirming the diagnosis of metastatic SCC (Figure 10).

After workup of the cardiac mass was complete, it was decided that the patient was to undergo outpatient chemotherapeutic efforts to reduce the tumor burden before surgical excision and reconstruction of the right ventricle. However, within a few weeks the patient was readmitted to the hospital requiring invasive mechanical ventilation and chest tube drainage of bilateral pleural effusions. Repeat imaging revealed diffuse metastasis to the bone, lung, and liver. Upon extubation and stabilization, he and his family opted for palliative care.

DISCUSSION

The presenting symptom of a cardiac neoplasm can vary greatly with location and size due to structural and functional disruption of cardiopulmonary physiology. This is also true of metastatic SCC (Figure 11), with which some patients are asymptomatic and others can experience myocardial infarction. Recently, Yoshihiro *et al*² reported a case of metastatic thyroid SCC (with confirmed cardiac metastasis) that presented with disseminated intravascular coagulopathy, which significantly improved after initiation of chemotherapy. Our patient did not present with any cardiac concerns, and the clinical constellation was well accounted for by the primary diagnosis of invasive SCC. However, in the context of a young patient with a limited

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Keywords: Metastasis, Squamous cell, Cancer, Cutaneous, Echocardiography
Conflicts of interest: The authors report no actual or potential conflicts of interest relative to this document.

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2468-6441

<https://doi.org/10.1016/j.case.2018.09.004>



Figure 1 Mass before excision. Large ulcerative fungating mass measuring about 30 × 30 cm, extending from the left back to left flank.



Figure 2 Patient's back after excision. After wide-margin excision of the mass, with exposed muscle. Subsequent biopsy confirmed margins were negative for malignancy.

history, chronically exposed skin lesion, undulating fever, and leukocytosis, it was prudent to rule out an underlying cardiac cause such as endocarditis.³

Although vegetations were not seen, a mass was found within the RVOT. With the aid of myocardial perfusion echocardiography, a contrast agent composed of air-filled microbubbles revealed partial vascularity within the lesion.⁴ These microbubbles are typically <10 μm in size and can permeate vessels of a greater diameter. Upon administration of the contrast agent, microbubbles can be seen throughout the chambers with heterogeneous echogenicity within the lesion. A burst of high-intensity ultrasound destabilizes the structure of the microbubbles, and they rupture, resulting in a loss of echogenicity immediately following the flash. The redemonstration of heterogeneous echoes within a few cardiac cycles relates a degree of vascularity suggestive of a neoplastic process.

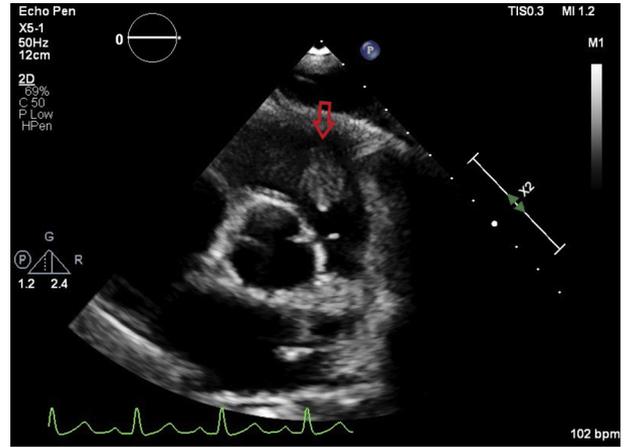


Figure 3 Transthoracic echocardiography of tumor in the RVOT. Parasternal short-axis view of the RVOT reveals a large, nonobstructive mass (red arrow) occupying the RVOT caudal to the pulmonic valve.

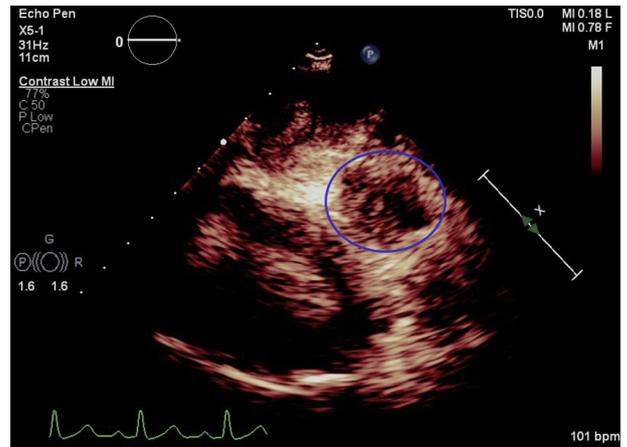


Figure 4 Myocardial perfusion echocardiography using a low mechanical index, real-time harmonic imaging, and Definity contrast, before high-power flash still frames, revealing patchy perfusion and establishing vascularity of the mass (blue circle).

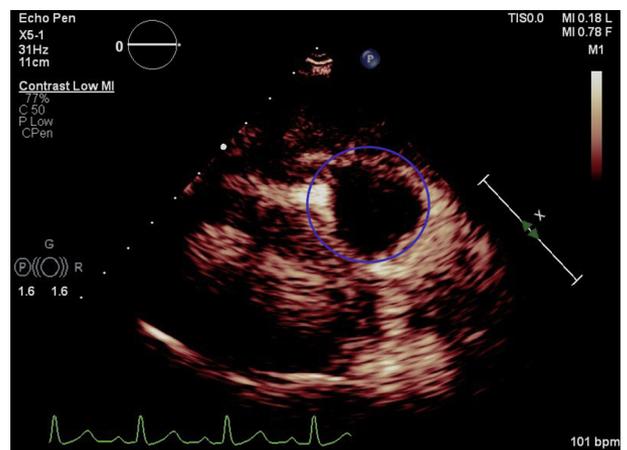


Figure 5 Myocardial perfusion echocardiography using a low mechanical index, real-time harmonic imaging, and Definity contrast, after high-power flash still frames, revealing patchy perfusion and establishing vascularity of the mass (blue circle).

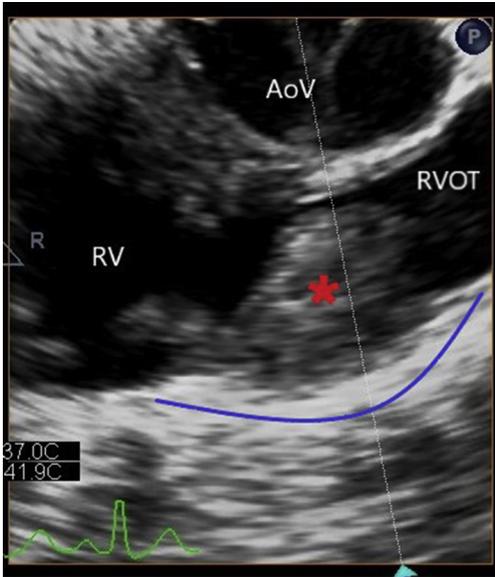


Figure 6 Transesophageal echocardiography of tumor in the right ventricular outflow tract (RVOT) reveals tumor (red asterisk) in the RVOT, with infiltration of the anterior right ventricular free wall (blue curved line). AoV, Aortic valve; RV, right ventricle.

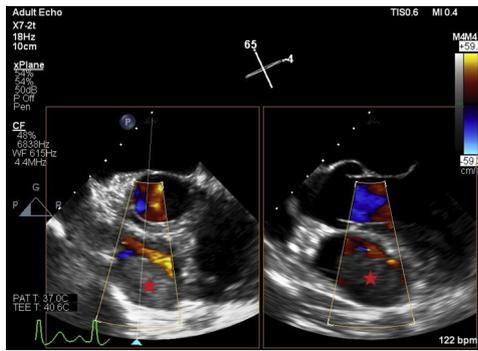


Figure 7 Transesophageal echocardiographic color Doppler still frames in systole, biplanar view, showing laminar blood flow across the RVOT, consistent with the nonobstructive nature of the mass (red star).

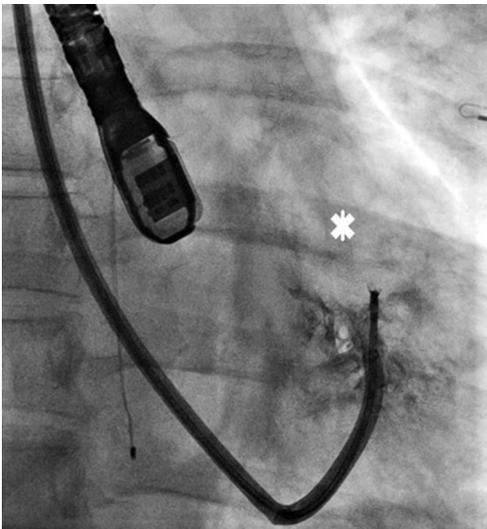


Figure 8 Intraprocedural fluoroscopic images: anteroposterior projection delineating tumor mass (asterisk) and location of biopsy site.

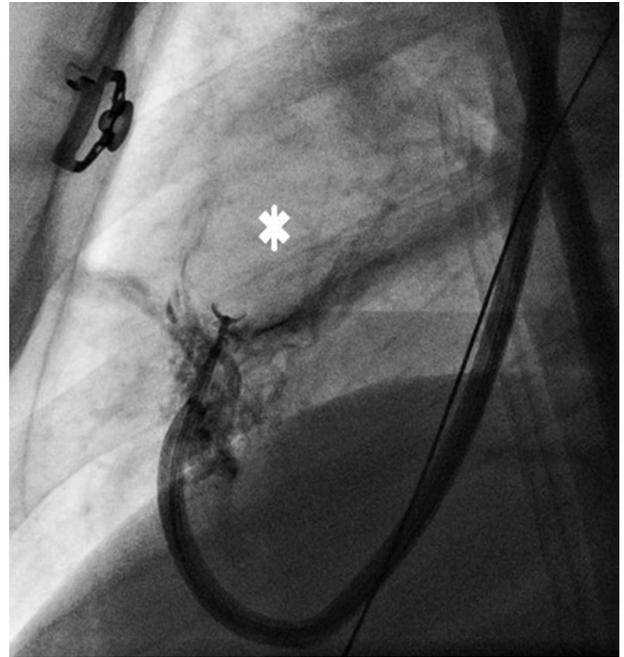


Figure 9 Intraprocedural fluoroscopic images: lateral projection delineating tumor mass (asterisk) and location of biopsy site.

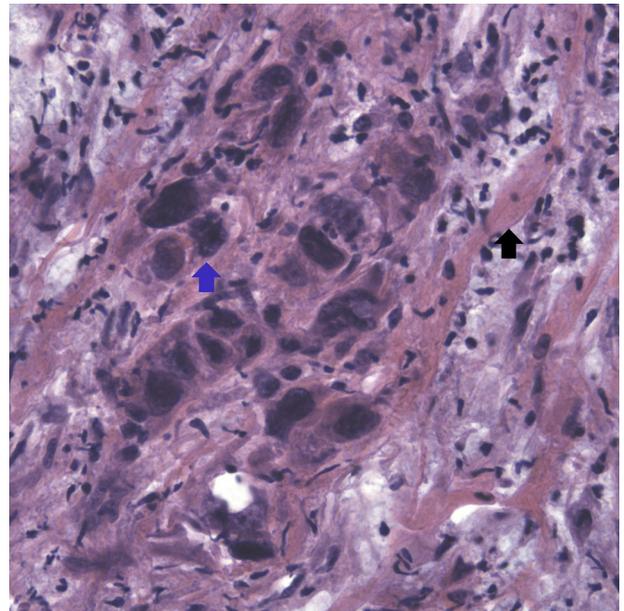


Figure 10 Endomyocardial mass biopsy. Histopathology showing normal myocardium (black arrow) infiltrated by highly malignant neoplasm. The cells show markedly enlarged nuclei with open, hyperchromatic chromatin consistent with metastatic SCC (blue arrow), confirmed by Hematoxylin and Eosin and cy-tokeratin immunostaining.

There were several clinical challenges associated with this case, concerning both the malignancy and the functional recovery of the heart. The first consideration was whether the mass altered right ventricular output. Once this was deemed stable, the next step was to determine the optimal medical-oncologic route of minimizing tumor burden

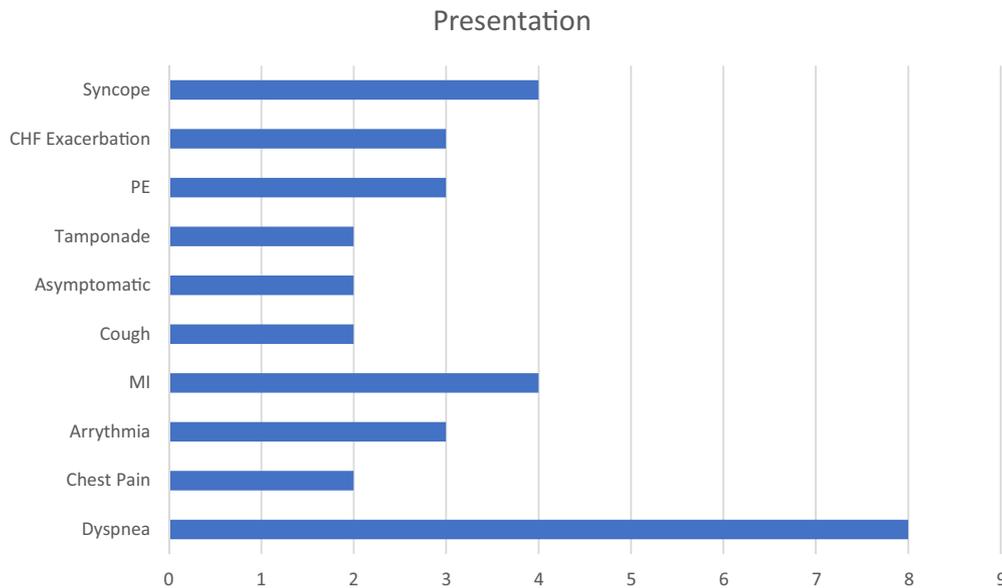


Figure 11 Most common presenting symptoms of patients with reported metastatic SCC, adapted from supplemental data. *CHF*, Congestive heart failure; *MI*, myocardial infarction; *PE*, pulmonary embolism.

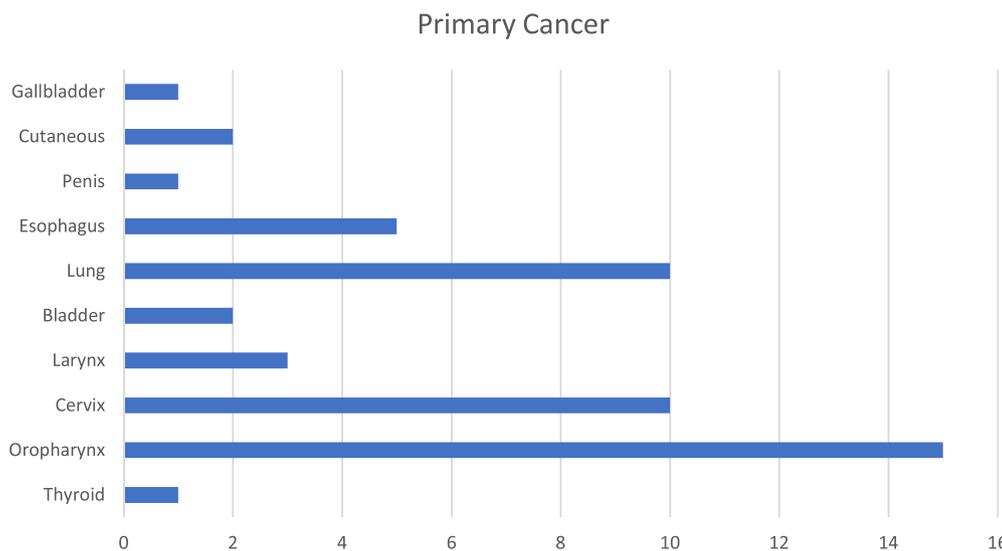


Figure 12 Primary site of malignancy in cases with cardiac metastasis of SCC, adapted from supplemental data.

preoperatively. The final decision concerned surgical intervention. Reconstruction of ventricles has been relatively well documented in patients who have congestive heart failure and post-myocardial infarction complications,^{5,6} with several techniques that have been developed with and without the use of grafts. Reconstruction of the RVOT has the added challenge of possible valvular involvement and the decision to resect or spare the pulmonic valve depending on tumor invasion. Unfortunately, the literature on reconstructive efforts in these cases is limited. One reason may be that in cases of advanced malignancy, surgical intervention is warranted to reverse disruption of cardiopulmonary physiology, rather than conferring a mortality or quality-of-life benefit as it relates to malignancy. Another possibility (one that is applicable to this case) is that early

management efforts focus on medical therapy for malignancy, such that only survivors progress to surgical management.

Tumors of the heart (both primary and secondary) are rare. Although most primary cardiac neoplasms are benign,⁷ metastatic neoplasms occur at an incidence orders of magnitude greater⁸ and are associated with poorer prognoses. Metastasis is most common from the lung and esophagus, typically (62%–81%) invading the pericardium.⁹ Metastasis into the myocardium is far less common and usually associated with melanoma or lymphoma, suggesting a hematogenous mode of spread.¹⁰ Rarer still is myocardial metastasis of SCC. There have been about 50 cases indexed by PubMed in the past 60 years (supplemental data), with the most common primary lesion originating from the oropharynx, lung, and cervix (Figure 12)

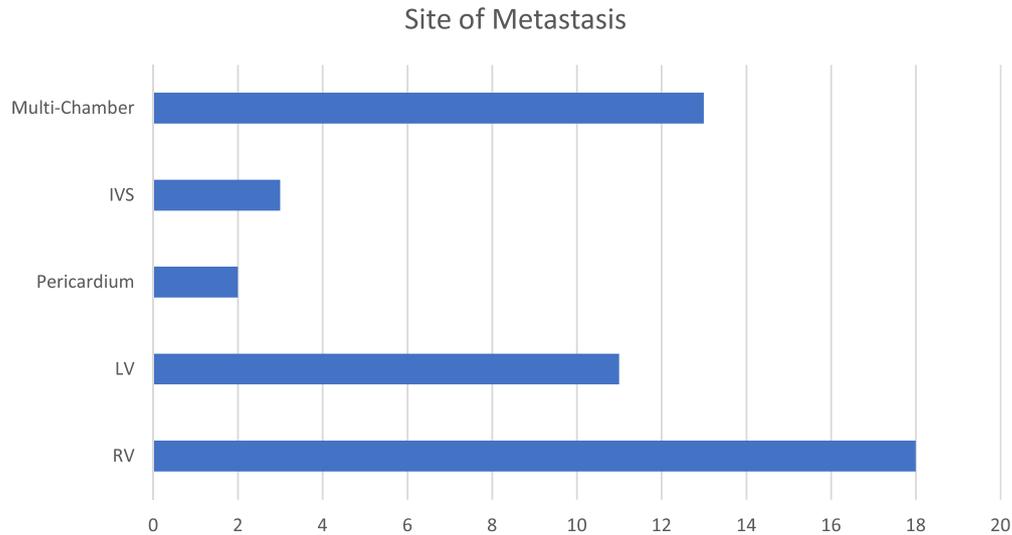


Figure 13 Site of cardiac metastasis in patients with primary SCC, adapted from supplemental data. Multichamber designates any combination of cardiac chambers, as well as extension into vasculature carrying blood into and out of the heart. *IVS*, Intraventricular septum; *LV*, left ventricle; *RV*, right ventricle.

and invading the ventricle or a combination of intracardiac sites (Figure 13). Within the above literature search, there is only a single confirmed case of cutaneous SCC with metastasis to the heart, found in a renal transplantation patient.¹¹ To the best of our knowledge, this is the first documented case of a Marjolin's ulcer with myocardial metastasis.

CONCLUSION

Cardiac metastasis of SCC is a rare entity, with consequent limited literature on optimal management strategies. Given the advanced stage at time of diagnosis, and likely aggressive nature of malignancy, prognosis is usually poor. The diagnosis of neoplasm can be made with confidence using noninvasive modalities such as transthoracic echocardiography with the aid of a contrast agent. However, biopsy is the gold standard for characterizing the tissue. Major obstacles include effective medical management of malignancy and optimal surgical excision and reconstruction of the affected site.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2018.09.004>.

REFERENCES

1. Esther RJ, Lamps L, Schwartz HS. Marjolin ulcers: secondary carcinomas in chronic wounds. *J South Orthop Assoc* 1999;8:181-7.
2. Yoshihiro T, Tsuchihashi K, Kusaba H, Nakashima T, Obara T, Nio K, et al. Cardiac metastasis of squamous cell carcinoma of the thyroid gland with severe disseminated intravascular coagulation: a case report. *Mol Clin Oncol* 2017;6:91-5.
3. Wang A, Gaca JG, Chu VH. Management considerations in infective endocarditis: a review. *JAMA* 2018;320:72-83.
4. Barletta G, Del Bene MR. Myocardial perfusion echocardiography and coronary microvascular dysfunction. *World J Cardiol* 2015;7:861-74.
5. Ruzza A, Czer LSC, Arabia F, Vespignani R, Esmailian F, Cheng W, et al. Left ventricular reconstruction for postinfarction left ventricular aneurysm: review of surgical techniques. *Tex Heart Inst J* 2017;44:326-35.
6. Skoglund K, Eriksson P, Svensson G, Dellborg M. Homograft reconstruction of the right ventricular outflow tract in adults with congenital heart disease: a systematic review. *Interact Cardiovasc Thorac Surg* 2016;22:57-62.
7. Yuda S, Nakatani S, Yutani C, Yamagishi M, Kitamura S, Miyatake K. Trends in the clinical and morphological characteristics of cardiac myxoma: 20-year experience of a single tertiary referral center in Japan. *Circ J* 2002;66:1008-13.
8. Chiles C, Woodard PK, Gutierrez FR, Link KM. Metastatic involvement of the heart and pericardium: CT and MR imaging. *Radiographics* 2001;21:439-49.
9. Lam KY, Dickens P, Chan AC. Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med* 1993;117:1027-31.
10. MacGee W. Metastatic and invasive tumours involving the heart in a geriatric population: a necropsy study. *Virchows Arch A Pathol Anat Histopathol* 1991;419:183-9.
11. Mackenzie KA, Simcock JW, Lainchbury JG, Currie MJ, Lynn KL. Myocardial metastasis of cutaneous squamous cell carcinoma in a renal transplant recipient. *Transplant Proc* 2009;41:4414-5.