

Left Ventricular Metastases from Penile Squamous Cell Carcinoma



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INTRODUCTION

Cancer of the penis is rare in the United States but much more common in Asia, Africa, and Latin America. Squamous cell carcinoma is the most frequent histologic type. The mode of spread is initially through lymphatics to local, regional, and distant lymph nodes, whereas distant metastases occur late in the natural history of the disease; intracardiac involvement is extremely rare and not well documented in vivo. We report the case of a 66-year-old man with metastatic squamous cell carcinoma of the penis who was found to have left ventricular metastases and a large pericardial effusion on transthoracic echocardiography (TTE). Identification of cardiac metastases relies on multimodal noninvasive imaging. Transthoracic echocardiography with and without ultrasound-enhancing agents remains the preferred initial imaging modality when cardiac involvement is suspected. Transesophageal echocardiography (TEE), cardiac computed tomography (CT), and cardiovascular magnetic resonance (CMR) can provide additional information for tumor staging and tissue characterization. Myocardial infiltration by malignancy often leads to potentially life-threatening complications, such as cardiac tamponade, ventricular arrhythmias, and myocardial rupture.

CASE PRESENTATION

A 66-year-old man with no significant medical history presented to the emergency department complaining of penile pain and swelling and was diagnosed with balanoposthitis with phimosis. He was treated with a course of oral antibiotics, topical steroids, and antifungals. Two weeks later he presented again to our emergency department with worsening swelling, difficulty urinating, and a new ulceration on the left side of the penis. Physical exam was notable for markedly indurated glans and foreskin as well as a large left inguinal lymph node. Biopsy of the node revealed a poorly differentiated, keratinizing squamous cell carcinoma. The patient did not return for follow-up appointment.

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Two months later he was admitted to our hospital for worsening penile and inguinal pain, swelling, and hematuria. Review of systems was significant for fatigue, unintentional weight loss, persistent cough, and severe stabbing right-sided chest pain. Vital signs on admission were blood pressure 116/55 mm Hg, pulse 100 beats/minute, respiratory rate 20/minute, and SpO₂ 95% on room air. On examination, the patient had decreased breath sounds at the right base, bibasilar crackles, a swollen, extremely tender penis with an ulcerated sore, and a large, well circumscribed left inguinal lymph node. Notable laboratory studies included a white blood cell count of $13.1 \times 10^3/\text{mL}$ and an elevated serum calcium concentration of 13.2 mg/dL. Chest radiography (CXR) revealed bilateral ground glass opacities and a right pleural effusion. Contrast-enhanced CT of the chest, which was obtained to evaluate the abnormal CXR findings, revealed multiple pulmonary cavitory lesions and solid nodules, mediastinal lymphadenopathy, a large right pleural effusion with numerous metastatic lesions, and left ventricular hypodense masses with peripheral enhancement (Figure 1).

Electrocardiogram showed sinus rhythm with premature ventricular contractions and nonspecific repolarization abnormalities. Subsequently, the patient had intermittent episodes of atrial flutter and fibrillation with rapid ventricular response. In view of the cardiac findings noted on the chest CT, a TTE was obtained, which showed normal biventricular systolic function, large masses in the left ventricular lateral wall and apex, and a small pericardial effusion (<1 cm echo-free end-diastolic space; Figures 2 and 3).

Pleural fluid from diagnostic thoracentesis revealed no cytologic or immunophenotypic evidence of malignancy. Flexible bronchoscopy and endobronchial ultrasound showed a partially obstructing tumor in the bronchus intermedius, as well as tumor infiltration of all distal airways of the right lung. Endobronchial biopsy revealed moderately to poorly differentiated keratinizing squamous cell carcinoma with extensive tumor necrosis.

The patient was treated with a course of palliative chemotherapy consisting of paclitaxel, ifosfamide, and cisplatin followed by radiation therapy.

A repeat TTE was performed due to an episode of severe hypotension and was directly compared with the prior study obtained 3 weeks earlier. The visually estimated left ventricular ejection fraction was 50%, and two large echodense masses measuring 3.2×2.7 cm and 2.7×2.6 cm were again seen in the left ventricular anterior wall, lateral wall, and apex and were unchanged in appearance (Figure 4). A new, large (2.6 cm echo-free end-diastolic space) circumferential pericardial effusion was seen, associated with systolic inversion of the right atrium and exaggerated respirophasic variation of the mitral inflow, suggestive of early cardiac tamponade (Figures 4 and 5, Videos 1-4). In view of these echocardiographic findings and the unstable hemodynamic state, a pericardiocentesis was performed, and 600 mL of serosanguinous fluid was drained. The pericardial fluid was inadvertently not sent for cytologic exam.

VIDEO HIGHLIGHTS

Video 1: Parasternal short-axis view of the TTE showing left ventricular mass in the lateral wall (*asterisk*). A circumferential pericardial effusion is also seen.

Video 2: Apical four-chamber view of the TTE revealing masses in the apex and lateral wall of the left ventricle, with loss of the distinct endomyocardial delineation due to malignant tumor infiltration, as well as a large circumferential pericardial effusion.

Video 3: Apical two-chamber view of the TTE revealing tumor infiltrating the anterior wall of the left ventricle resulting in a regional wall motion abnormality. The pericardial effusion is again demonstrated here.

Video 4: Subcostal view of the TTE revealing a large pericardial effusion with systolic inversion of the right atrium. In the setting of hemodynamic compromise, this was assumed to represent an early sign of cardiac tamponade requiring urgent pericardiocentesis.

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Frequent episodes of atrial flutter and fibrillation as well as frequent premature ventricular contractions were controlled with amiodarone and metoprolol. Hospital course was complicated by numerous infectious and urologic issues, and the patient was eventually discharged to hospice. A pre-discharge echocardiogram, obtained to assess for recurrent pericardial effusion, revealed stable cardiac masses and a small amount of echogenic material in the pericardial space but no hemodynamically significant pericardial fluid.

DISCUSSION

This report presents the case of a 66-year-old man with a recently diagnosed metastatic squamous cell carcinoma of the penis with intracardiac masses localized to the left ventricle and a large pericardial effusion causing cardiac tamponade. The differential diagnosis of intracardiac masses is wide (Table 1). Every cardiac mass should be evaluated in its clinical context, with particular attention to patient age, sex, cardiac rhythm, presence of valve disease or prosthetic valves, and history of cardiomyopathy or malignancy. The differential can then be narrowed based on the mass location. It is important to emphasize that mural thrombi account for the majority of ventricular masses, followed by fibromas and metastatic disease.¹

Primary cardiac tumors are rare and are found in only 0.001%-0.05% of unselected autopsies.² Approximately 90% of primary



Figure 1 Contrast-enhanced CT of the chest, obtained to better assess abnormal findings noted on CXR, showing intracardiac left ventricular hypodense masses (*arrows*) and right-sided pleural effusion (*asterisk*) in the axial (**A**, **B**), coronal (**C**), and sagittal planes (**D**).

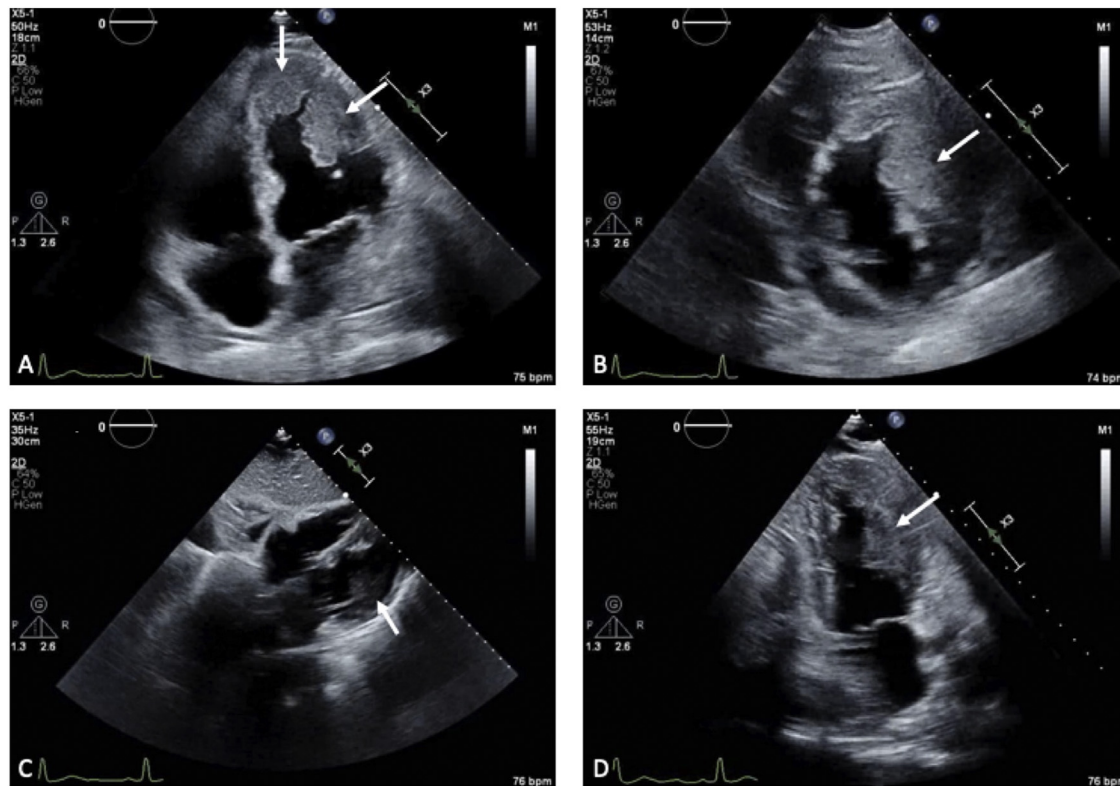


Figure 2 Baseline two-dimensional TTE apical four-chamber (A), parasternal short-axis (B), subcostal (C), and apical two-chamber (D) views, all obtained during systole and demonstrating large left ventricular masses (arrows) with loss of the distinct endomyocardial delineation due to tumor infiltration.

cardiac tumors excised surgically are benign, more frequently myxomas, papillary fibroelastomas, fibromas, and lipomas¹; 10% are malignant, with the vast majority being undifferentiated sarcomas.³

Metastatic cardiac tumors are much more frequent, being diagnosed at autopsy in 0.7%-3.5% of patients in the general population and up to 9.1% in patients with known malignancies.⁴ Lung cancer is

the most common cause of cardiac metastases, followed by mesothelioma, breast cancer, melanoma, and hematologic malignancies. Tumor spread occurs via four different pathways: hematogenous, lymphatic, transvenous extension, and direct extension. In a large autopsy series of 622 cases of cardiac metastases,⁵ two-thirds affected the pericardium, one-third affected the epicardium or myocardium, and a very small percentage affected the endocardium.

Clinical presentation of cardiac metastases is extremely variable, depending on tumor location and size, and in many cases cardiac involvement is clinically silent. Chest pain, dyspnea, edema, and palpitations are the most common symptoms. Serious, life-threatening complications such as atrial and ventricular arrhythmias, complete heart block, pulmonary emboli, pericardial effusion with or without tamponade, and even myocardial rupture can occur.

Identification of cardiac metastases relies on multimodal noninvasive imaging. Transthoracic echocardiography with and without ultrasound-enhancing agents remains the initial test of choice. In particular, contrast perfusion echocardiography helps to differentiate malignant masses with neovascularity, which demonstrate enhancement relative to the adjacent myocardium, from cardiac thrombi or less malignant tumors, which do not enhance or enhance to a lesser degree than the adjacent myocardium, respectively.⁶ Transesophageal echocardiography provides increased spatial resolution and can therefore identify smaller lesions compared with TTE. Cardiac CT adds useful information for tumor staging or evaluation of pulmonary symptoms. Finally, CMR can provide additional tissue characterization such as degree of vascularity and fibrosis. In our case, the appearance of the cardiac masses on chest CT and loss of the distinct endomyocardial

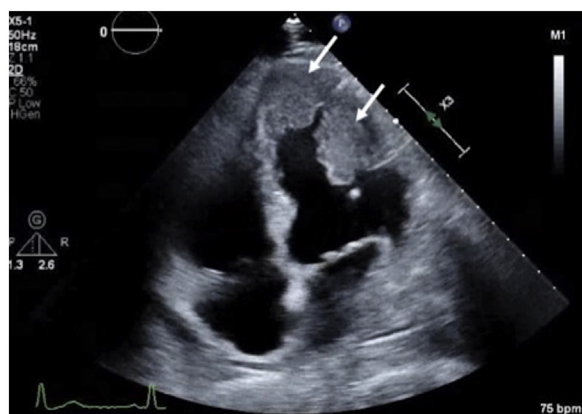


Figure 3 Transthoracic echocardiogram apical four-chamber view, systolic frame, demonstrating large left ventricular masses (arrows) with loss of the distinct endomyocardial delineation due to tumor infiltration and a small pericardial effusion adjacent to the right atrium.

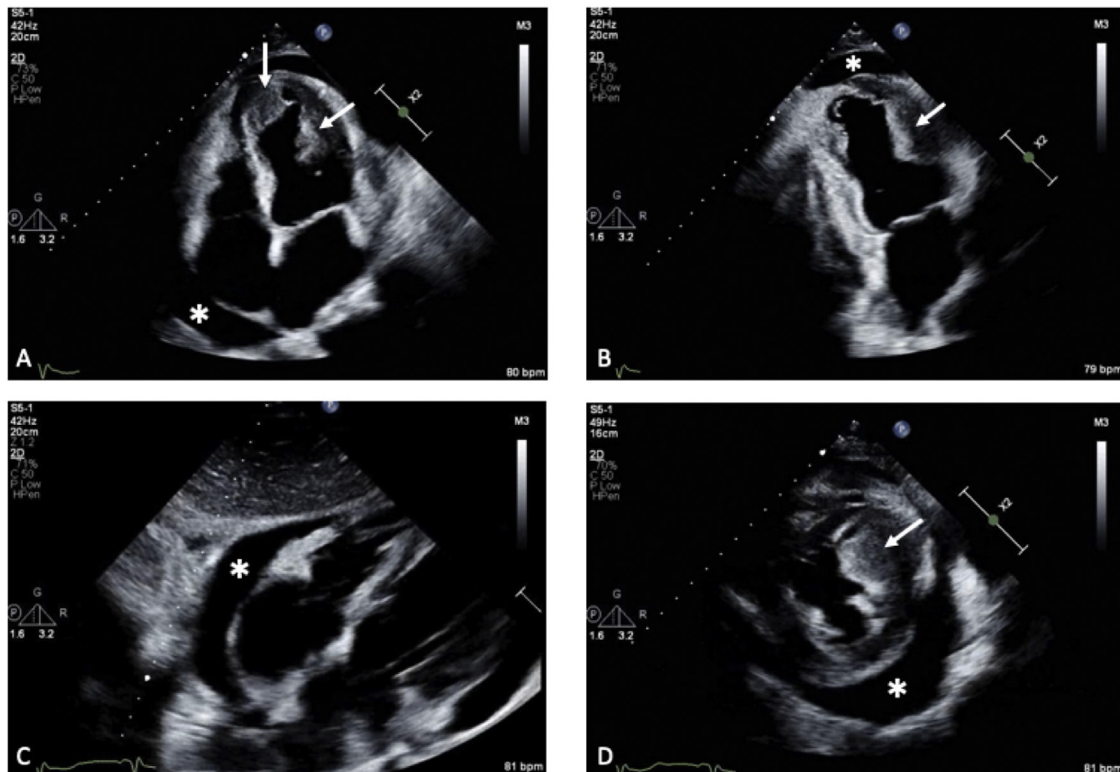


Figure 4 Follow up (three weeks later) two-dimensional TTE images showing left ventricular masses and pericardial effusion: **(A)** apical four-chamber view, systolic frame, showing lateral wall and apex infiltrated by tumor (*arrows*) and pericardial effusion (*asterisk*), **(B)** apical two-chamber view, systolic frame, showing mass infiltrating the anterior wall of the left ventricle (*arrow*), **(C)** subcostal view showing a large pericardial effusion adjacent to the right atrium and right ventricle (*asterisk*), and **(D)** parasternal short-axis view showing tumor mass infiltrating the anterior and anterolateral walls of the left ventricle (*arrow*) as well as a large pericardial effusion (*asterisk*).

delineation due to tumor infiltration on TTE were sufficient to establish a diagnosis of metastatic disease in the right clinical setting. Penile cancer is rare in the United States and in other developed nations. The American Cancer Society estimates that there will be 2,210 new cases in 2021 and approximately 460 deaths.⁷ In contrast, this cancer is much more common in Asia, Africa, and Latin America, where it may represent up to 10% of cancers in male patients. The vast majority of cancers of the penis are squamous cell carcinomas. The prognosis of patients with distant metastases is extremely poor, with a 5-year survival rate of only 9%.⁷

The risk of distant metastases is low and tends to occur late in the course of the disease, which makes our case even more unusual. Metastatic disease at presentation is seen, in fact, in less than 5% of patients with cancer of the penis.⁸ The mode of spread is initially through lymphatics to local, regional, and distant lymph nodes, whereas distant metastases occur late in the natural history of the disease; intracardiac involvement is extremely rare and not well documented in vivo. An extensive review of the literature revealed only 10 cases of cardiac metastases, the majority being found only during postmortem examination. Rippenrop *et al.*⁸ reported on 4,124 autopsies performed at their institution on patients with various malignancies; 217 were found to have cardiac involvement, only three of which were secondary to penile cancer. In contrast, cardiac involvement was more frequent in a series from Memorial Sloan Kettering reported by Chaux and colleagues,⁹ being found at autopsy in five out of 10 patients who died from metastatic squamous cell carcinoma of the penis. The report

by Siqueira¹⁰ describes a patient with no echocardiographic evidence of cardiac metastases but with right atrial and ventricular infiltration by squamous cell carcinoma at autopsy. Finally, Portero *et al.*¹¹ describe a patient who died from metastatic penile cancer in which the TTE showed a mass in the left atrium, subsequently proven at autopsy to be metastatic disease.

CONCLUSION

We describe a rare case of left ventricular intracardiac metastases from a squamous cell carcinoma of the penis that was complicated by hypercalcemia, atrial and ventricular arrhythmias, and cardiac tamponade. While multimodal imaging is often necessary in the workup of cardiac masses, in this case TTE proved sufficient to establish a diagnosis of metastatic disease.

We suggest that patients with advanced cancer of the penis be closely monitored for the development of cardiac involvement and its life-threatening complications.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.case.2022.01.009>.

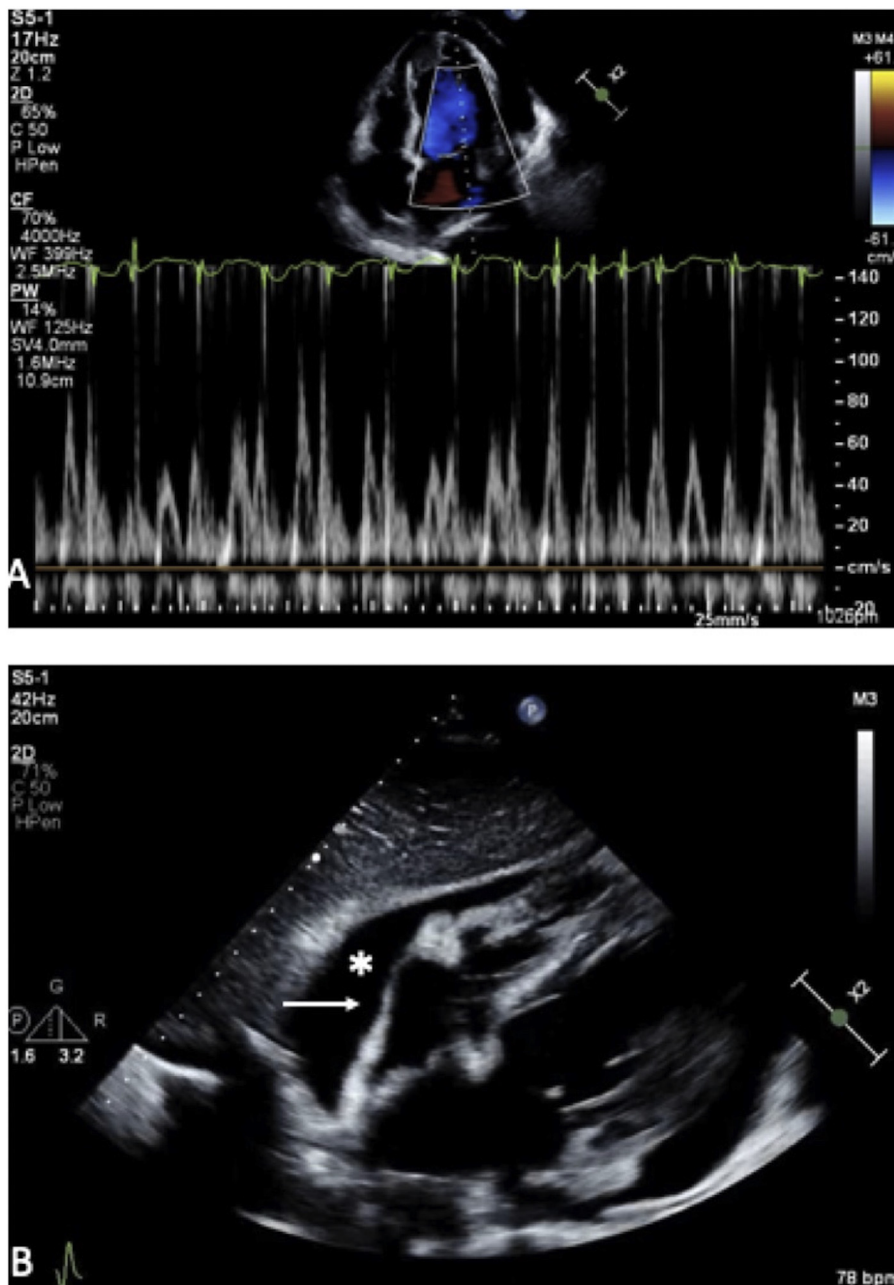


Figure 5 Transthoracic echocardiogram pulsed-wave Doppler obtained in the apical four- chamber view across the mitral inflow demonstrating exaggerated respirophasic variation **(A)**. Two-dimensional TTE image in the subcostal view demonstrates large pericardial effusion (*asterisk*) with systolic inversion of the right atrium (*arrow*) **(B)**.

Table 1 Differential diagnosis of cardiac masses

	Common	Uncommon
Primary malignant tumors	Angiosarcoma, undifferentiated sarcoma	Leiomyosarcoma, rhabdomyosarcoma
Primary benign tumors	Myxoma, papillary fibroelastoma, rhabdomyoma	Hemangioma, lipoma
Metastatic	Lung, breast, melanoma, hematologic	Colon, genitourinary, thyroid
Non-neoplastic	Thrombus, vegetation	Infiltrative disorder, calcified masses

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