A 56-year-old woman with a history of Wolff-Parkinson-White syndrome and widely metastatic ovarian carcinoma presented with new atrial fibrillation with rapid ventricular response. Her medical history was significant for high-grade serous ovarian cancer metastatic to lungs, liver, spleen, and lymph nodes.

Metastasis to the heart is not as infrequent as one might suspect. Although primary cardiac tumors are rare (generally between 0.01% and 0.1% on postmortem analysis), the frequency of secondary metastatic tumors to the pericardium, myocardium, great vessels, or coronary arteries is between 0.7% and 3.5% at autopsy in the general population and up to 9.1% in patients with known malignancies.1-5 Moreover, the risk of cardiac metastasis rises with metastatic disease burden; 14.2% of patients with multiple distant metastases were found to have cardiac involvement.1 The incidence of cardiac metastases has increased over the last 30 years, perhaps attributable to increased life expectancy in oncologic patients benefitting from advances in cancer diagnosis and management.1,4,5

Although any type of tumor can affect the heart, the probability of cardiac involvement is a function of anatomic considerations, stage of disease, and individual tumor and host biology. Primary lung cancer represents 36% to 39% of cardiac metastases, followed by breast cancer (10%–12%) and hematologic malignancies (10%–21%).1,4,6 These numbers reflect the high prevalence of these tumors in the general population and their aggressive nature; in contrast, prostate cancer, although more prevalent in men than any of the above tumors, rarely metastasizes to the heart. Pleural mesothelioma and melanoma have an unusual proclivity to involve the heart, with estimates of 28% to 56% of patients with metastatic melanoma having some cardiac involvement.1,7 Other tumors with high rates of cardiac metastasis include ovarian, gastric, renal, and pancreatic carcinomas.1,4,6

Myriad Clinical Presentations

The clinical manifestations of cardiac metastases are nonspecific and depend on their location and tumor burden.1,4,5 Most cardiac metastases are clinically silent and are diagnosed only postmortem.1,4,5,8 When cardiac metastases manifest clinically, they can be difficult to distinguish from other causes of cardiovascular disease, with the most common symptoms and signs including dyspnea, palpitations, atrial flutter or fibrillation, lower-extremity edema, and chest pain.1 Cardiac metastasis may also present with dramatic, life-threatening manifestations, including cardiac tamponade from pericardial involvement.

Tumors can reach the heart via 4 pathways: hematogenous spread, lymphatic spread, transvenous extension, and direct extension. Spread by the hematogenous route generally gives rise to myocardial or endocardial metastasis and is common with melanoma (Figure 1A), lymphoma, and sarcoma, whereas spread by the lymphatic route will often result in pericardial and epicardial tumor involvement, as with many epithelial tumors such as lung (Figure 1B) and breast. Certain tumors such as renal cell carcinoma and hepatocellular carcinoma can extend into the inferior vena cava and grow into the right atrium via transvenous extension. Locally aggressive mediastinal and pleural tumors such as mesothelioma can directly invade the pericardial sac.

The pericardium is the most frequently involved site of cardiac metastasis, comprising 64% to 69% of all
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Cardiac metastases in 2 recent large case series.1,6 Tumor metastasis to the pericardium may initially result in pericarditis, with subsequent development of serosanguineous or hemorrhagic malignant pericardial effusions.5,9,10 Depending on their size and rate of accumulation, malignant pericardial effusions may be symptomatic or silent.5,9,10 Slow accumulation of pericardial effusions is unlikely to cause hemodynamic compromise, even with up to 2 L pericardial fluid. However, rapid accumulation of even small volumes from 100 to 200 mL can quickly result in cardiac tamponade, necessitating immediate pericardiocentesis to avert hemodynamic collapse.5,9,10 Although less common than pericardial effusions, deposits of pericardial metastases may also compromise cardiac output via constrictive physiology.11 Cardiac involvement (25%–34%) and myocardial involvement (29%–32%) represent the second and third most common sites of cardiac metastasis (Figure 1D).1,6 Depending on their location, epicardial or myocardial metastases may result in a variety of life-threatening complications. Disruption of the cardiac conduction system by cardiac metastases can lead to lethal arrhythmias, including atrial fibrillation with rapid ventricular response, complete atrioventricular block, or ventricular fibrillation.1,5,11 Even in the absence of coronary artery involvement, metastases to the myocardium and pericardium can sometimes mimic acute coronary syndromes, presenting with chest pain, elevated cardiac biomarkers, and ST- and T-wave abnormalities compatible with symptomatic coronary artery disease.12 Cardiac output may also be directly compromised by replacement of the myocardium by tumor cells, resulting in congestive heart failure.1,5 Rarely, deeply infiltrating myocardial metastases have even resulted in cardiac rupture, cardiac tamponade, and sudden death.5

Endocardial and intracavitary metastases are rare, making up 3% to 5% of cardiac metastases on autopsy.1,6 However, such intracavitary metastases can have dramatic clinical consequences. Cardiogenic shock has been documented from right ventricular outflow tract obstruction (Figure 1E).13 Cardiac metastasis can also cause symptomatic left ventricular outflow tract obstruction, a phenomenon usually observed in hypertrophic obstructive cardiomyopathy. Right heart failure may be seen from right atrial metastatic obstruction of right ventricular inflow. Cardioembolic complications of tumor emboli can include stroke from left-sided cardiac metastasis or pulmonary emboli from right-sided cardiac metastasis. In addition, metastatic involvement of the coronary arteries may result in angina or even myocardial infarction. Myocardial ischemia can be caused by neoplasm-induced coronary embolism, perivascular compression of the coronary arteries, or frank invasion of the coronary arteries.1,5

Involvement of the superior or inferior vena cava can be a prelude to cardiac metastasis. In particular, renal cell and hepatocellular carcinomas may spread via an endovascular route from the inferior vena cava to the right atrium, with potential hemodynamic and embolic consequences as described above.1,3 Superior vena cava involvement can result in superior vena cava syndrome, an oncologic

Figure 1. Metastatic tumors involving the heart and pericardium. A, Photomicrograph of metastatic melanoma involving the myocardium resulting in destruction of cardiac myocytes. Hematoxylin and eosin stain, x200 magnification. B, Photomicrograph of metastatic lung adenocarcinoma involving the epicardial lymphatics. Hematoxylin and eosin stain, x100 magnification. C, Gross photograph of a metastatic renal collecting duct carcinoma filling the pericardial space and encasing the heart, resulting in constrictive physiology. D, Gross photograph of a T-cell lymphoma involving the myocardium in the area of the anterior right ventricle and anterior interventricular septum, resulting in arrhythmias. E, Gross photograph of a large endocardial metastasis from a malignant peripheral nerve sheath tumor involving the endocardium in a patient with neurofibromatosis type 1 filling the right ventricle and resulting in right ventricular outflow tract obstruction.
Cardiac Metastasis

Potential Clinical Manifestations of Cardiac Metastasis

<table>
<thead>
<tr>
<th>Pericardial metastasis</th>
<th>Epidocardial and myocardial metastasis</th>
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<tbody>
<tr>
<td>Pericarditis, pericardial effusions, and cardiac tamponade</td>
<td>Atrial and ventricular arrhythmias and conduction disturbances, including atrial fibrillation with RVR, atrial flutter, complete AV block, PVCs, and ventricular fibrillation</td>
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<tr>
<td>Pericardial adherences and constrictive pericarditis</td>
<td>CHF with systolic or diastolic dysfunction</td>
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<td></td>
<td>Myocardial ischemia or infarction from perivascular coronary artery compression, tumor embolism, or coronary invasion</td>
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<td>Cardiac rupture</td>
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<td>Endocardial and intracavitary metastasis</td>
<td>Intracavitary obstruction, left and right heart failure, cardiogenic shock</td>
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<td>Pulmonary tumor emboli from right-sided metastasis</td>
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<td>Stroke from tumor emboli from left-sided metastasis</td>
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<td>Superior or inferior vena cava metastasis</td>
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<td>Inferior vena cava syndrome</td>
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<td>Right heart metastasis</td>
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AV indicates atrioventricular; CHF, congestive heart failure; PVC, premature ventricular contraction; and RVR, rapid ventricular response.

Detection and Characterization of Cardiac Metastasis

The possibility of cardiac metastasis should be considered in any patient with a malignancy and new cardiac symptoms, particularly with distant metastases or thoracic involvement. Physical examination may reveal various hints of cardiac metastases, from distant heart sounds suggesting a malignant pericardial effusion to new murmurs from intracardiac masses or a pericardial friction rub from pericarditis. ECG can be a useful, albeit nonspecific tool, with the most common abnormalities being nonspecific ST-T wave changes and new atrial arrhythmias. ECG findings of myocardial ischemia or injury, particularly localized and prolonged ST elevation, in the absence of ischemic symptoms have a high specificity for cardiac metastasis in patients with malignancy. Low-voltage and electric alternans may indicate the presence of a pericardial effusion.

Imaging studies are essential for the diagnosis of cardiac metastasis. Chest x-ray may demonstrate cardiomegaly ("water bottle" sign) from a pericardial effusion. Echocardiography is the initial imaging modality to detect pericardial effusions and to assess for the presence and clinical consequences of any cardiac metastasis. For many tumors, echocardiography can provide information on the location, size, and mobility of cardiac masses. For many tumors, echocardiography can provide information on the location, size, and mobility of cardiac masses. The use of echocardiographic contrast perfusion imaging may aid in the differentiation of some tumors from clot. Although it remains an essential imaging modality for the evaluation for cardiac metastasis, echocardiography has limitations, including decreased image quality in individuals with poor acoustic windows (eg, obesity) and limited evaluation of extracardiac structures. Cardiac magnetic resonance imaging (CMR), computed tomography (CT), and positron emission tomography can provide additional noninvasive characterization of cardiac metastases. CMR can acquire multiphase cardiac images with superb tissue characterization. Consequently, CMR may identify intramyocardial masses not readily visible on echocardiography or CT. Moreover, an assessment of perfusion after administration of gadolinium can be useful in differentiating malignant from benign cardiac masses, whereas late-enhancement techniques with long inversion recovery can be helpful in the identification of thrombus. Because CMR visualizes extracardiac structures, this modality is useful for identifying direct extension of tumor from the mediastinum. An additional technique (ie, tagging) can help to identify adhesions of the pericardium and to assess whether a mass has independent motion from adjacent cardiac structures.

Cardiac CT provides superb spatial resolution, although it has a lower contrast resolution than CMR. Like CMR, CT can identify direct tumor extension from adjacent mediastinal structures. The administration of intravenous contrast is needed to identify intracardiac tumors because they are often identified by filling defects (Figure 2). Because cardiac CT can visualize the coronary arteries, this imaging test should be considered when involvement of the coronary arteries is suspected, although it is notable that a slow heart rate is required for optimal imaging.

18F-fluorodeoxyglucose (FDG) positron emission tomography/CT can identify tumors that exhibit increased metabolism using glucose, thereby helping to differentiate some malignant tumors from benign ones. In many cases, proper dietary preparation is required to suppress FDG uptake from the normal myocardium. A particular challenge for FDG imaging of the myocardium is that increased uptake of FDG may be a nonspecific finding, which, depending on the clinical context, could represent hibernating myocardium, cardiac sarcoidosis, or a normal variant. An advantage of
Cardiac metastases, various techniques sometimes necessary to identify cardiac disease. The management of cardiac metastases depends on the clinical presentation.

Although clinical diagnosis of cardiac metastasis can sometimes be made on imaging, tissue histology remains the most definitive method for differentiating neoplastic from nonneoplastic masses and for planning definitive or palliative therapy. Although exploratory thoracotomy and open biopsy is sometimes necessary to identify cardiac metastases, various techniques for obtaining tumor cells do not require thoracic surgery. Malignant cells can be identified in the majority of malignant pericardial effusions drained by pericardiocentesis, and the cytology of malignant cells has an extraordinarily high correlation with the histological diagnosis. Another approach to more definitively obtain tissue is endomyocardial biopsy. Endomyocardial biopsy is useful especially for right-sided cardiac masses showing infiltration or obstruction.

**Outcome and Management of Cardiac Metastasis**
The management of cardiac metastases depends on the clinical presentation. Cardiac tamponade requires immediate pericardiocentesis, ideally performed with fluoroscopy or echocardiography guidance, although blind subxiphoid pericardiocentesis can be lifesaving in cases of imminent hemodynamic collapse. More definitive therapeutic options for malignant pericardial effusions include subxiphoid or transthoracic pericardial windows and percutaneous tube pericardiotomy. Metastasis-induced arrhythmias can sometimes be transiently managed by the use of antiarrhythmic medications or, in some cases, by radiofrequency ablation, although involvement of the conduction system may make arrhythmias difficult to control.

Cardiac metastases are most often found in patients with multiple metastases and a profound burden of disseminated disease. Therefore, the most important goals of intervention should include palliation of symptoms and prevention or delay of symptom recurrence. Surgical resection is generally reserved for cases in which prognosis is otherwise good, for patients in whom complete resection is technically feasible, or for specific cases of intracardiac obstruction. Intracardiac obstruction by cardiac metastases may necessitate surgery, although outcomes may be poor if ventricular function has been irreversibly compromised. Radiotherapy and chemotherapy can also be useful tools for the treatment of certain cardiac metastases. It is therefore important to involve a multidisciplinary team in the evaluation and management of the patient with cardiac metastasis.

**Conclusions**
Cardiac metastases are surprisingly common. Although often clinically silent, they should always be considered in any individual with new cardiac symptoms and known malignancy. The clinical sequelae of cardiac metastases are varied and numerous, and depend on the anatomic localization of tumor involvement. Most cardiac metastases are associated with widely metastatic disease and thoracic involvement, although certain tumors such as melanoma are particularly prone to cardiac metastasis. Echocardiography is the initial imaging test for the detection of cardiac metastasis, although CMR, cardiac CT, and positron emission tomography/CT may help further characterize and delineate the extent of both cardiac and extracardiac disease. Treatment of cardiac metastases depends on their immediate cardiac complications, as well as the clinical context, prognosis, and functional status of the patient.

**Case Resolution**
The patient’s atrial fibrillation was refractory to antiarrhythmic therapy. In the setting of her tachycardia, she exhibited worsening hemodynamic instability and required transfer to the intensive care unit, where multiple cardioversions were performed. Ultimately, her family elected to focus care on comfort measures only, and she died peacefully. Autopsy demonstrated metastatic tumor involving the pericardial space, epicardial surface of the heart, and lymphatics, with focal invasion into the left and right atrial myocardium, likely accounting for the arrhythmias and lack of efficacy of antiarrhythmic therapy.
Disclosures

None.

References

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