Cardiac Metastasis: An Often Forgotten Cause of Congestive Heart Failure

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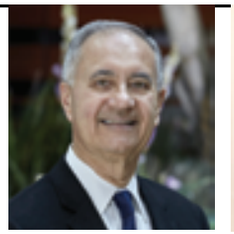
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Case Report

A 35-year-old man, previously healthy, presented to a community hospital with a 1-month history of malaise, significant weight loss, and epigastric pain. Prior to his presentation, he had several episodes of non-bloody emesis, melena and mild exertional dyspnea. There was no significant family history of malignancy. His examination at the time of presentation was unremarkable.

An initial ultrasound of the abdomen revealed multiple hypoechoic lesions suggestive of metastases. A computed tomography scan with contrast showed multiple hepatic, pancreatic, renal, adrenal, perirenal and omental lesions, discrete bony lytic lesions, several mediastinal masses, multiple pulmonary nodules and accentuation of interlobular septal lines consistent with either cardiac failure or lymphangitic tumour spread. A large filling defect in the left atrium measuring 4.5 × 6 cm immediately adjacent to the mitral valve was noted.

A computed tomography-guided core biopsy of the liver was performed showing spindle cell lesions with cytological atypia. Immunohistochemistry demonstrated immunoreactivity for CD117 suggestive of malignant gastrointestinal stromal tumour (GIST) (Figure 1).

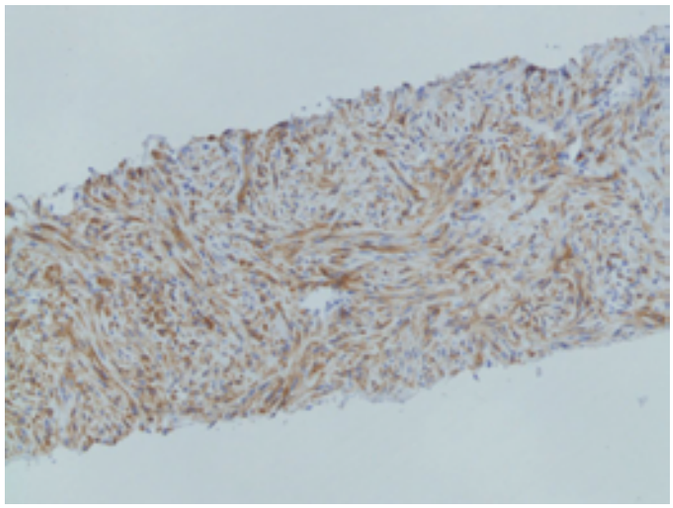
Figure 1. Computed tomography-image showing spindle cell lesions with cytological atypia. Immunohistochemistry demonstrated immunoreactivity for CD117 suggestive of malignant gastrointestinal stromal tumour.

The patient continued to develop increasing abdominal pain, nausea, hemoptysis, and episodes of desaturation. He was transferred to our tertiary care hospital for further evaluation and management.

Upon transfer, his initial examination revealed sinus tachycardia at 120–130 beats per minute. There were no murmurs on auscultation of the precordium but crackles were present at the lung bases and he experienced mild orthopnea. His abdomen was diffusely tender to palpation with no ascites or palpable masses. Serial chest radiography showed worsening airspace opacities with the appearance of pulmonary edema.

A transthoracic echocardiogram confirmed the presence of a left atrial mass directly adjacent to the anterior leaflet of the mitral valve (Figure 2), and extending posteriorly toward the pulmonary veins and filling most of the left atrium. The site of attachment was postulated to be the valve itself given that it moved with the mitral valve. Mitral inflow velocities were significantly elevated in keeping with severe obstruction. Right ventricular systolic pressure was

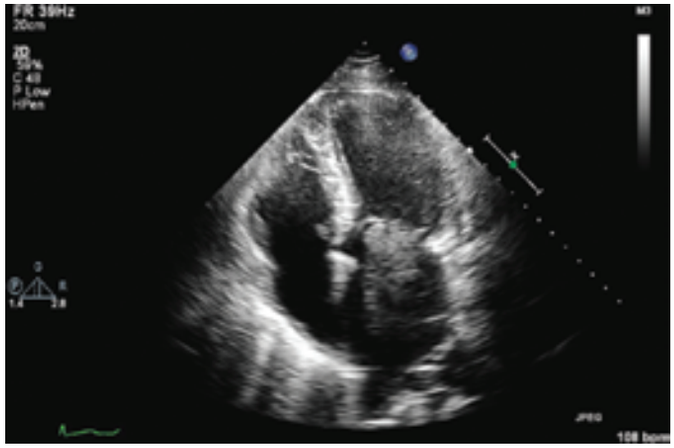

Figure 2. Image from a transthoracic echocardiogram confirmed the presence of a left atrial mass directly adjacent to the anterior leaflet of the mitral valve.

measured by Doppler to be 80–90 mmHg and moderate left atrial dilatation was noted.

Medical and radiation oncology were consulted for consideration of palliative therapies for the atrial mass. Chemotherapy with imatinib was not initiated due to the risk of transient tumour enlargement from intratumoral hemorrhage or myxoid degeneration, which could cause complete obstruction of the mitral valve. In spite of treatment with dexamethasone, aggressive intravenous diuresis, and 2 localized radiation treatments, the patient's dyspnea worsened and he required non-invasive positive pressure ventilation. Cardiac surgery for tumour resection was considered but given the poor prognosis from the extent of his intra-abdominal disease, the patient elected to continue with medical management only. On day 6 of admission, the patient's respiratory status deteriorated and he passed away.

Discussion

Cardiovascular disease was found by the Public Health Agency of Canada to be the most common reason for hospitalization in the country. Congestive heart failure forms a significant subset of this population, causing 54, 333 hospital admissions in Canada in 2005-2006.[1] In patients without a significant history of ischemic heart disease, a more extensive differential diagnosis for heart failure must be considered (Table 1).[2,3]

Table 1. Differential Diagnosis of Heart Failure

Decreased Left Ventricular Ejection Fraction	Preserved Left Ventricular Ejection Fraction
Ischemic cardiomyopathy	Diastolic heart failure
Myocarditis	• Hypertensive heart disease
Infiltrative cardiomyopathies	• Diabetic heart disease
• Amyloidosis	• Hypertrophic cardiomyopathy
• Sarcoidosis	• Infiltrative cardiomyopathies
• Eosinophilic myocarditis	Valvular heart disease
• Hemochromatosis	Right heart failure
Peripartum cardiomyopathy	• Pulmonary hypertension
Hypertensive heart disease	• Arrhythmogenic right ventricular cardiomyopathy
Human immunodeficiency virus-associated cardiomyopathy	• Right ventricular infarction
Giant cell myocarditis	Pericardial disease
Toxins (e.g., alcohol, doxorubicin, cyanide)	• Constrictive pericarditis
	• Pericardial effusion or tamponade
	High-output heart failure (e.g,. anemia, hyperthyroidism)
	Pulmonary vein stenosis

Adapted from Colucci 2013[2] and Zile and Gaasch 2013.[3]

Cardiac Metastases

Tumours of the heart are categorized as primary or secondary. Primary tumours have a prevalence of 0.02% in pooled autopsy studies,[2–4] and are often benign, the majority of them myxomas. Very rarely, primary malignant tumours such as sarcomas can arise. The vast majority of cardiac tumours are secondary, the result of metastases from elsewhere in the body. These occur either by retrograde lymphatic extension, transvenous spread, hematogenous spread, or direct invasion from adjacent structures. In autopsy studies, cardiac metastases were found in up to 25% of patients who had passed away from malignancy.[4]

Pooled data from 32 epidemiological studies have shown that bronchogenic carcinoma, hematological malignancies and breast cancer make up 2/3 of cases of cardiac metastases.[5] These are usually due to invasion of nearby cardiac structures or lymphatic spread through the mediastinal lymph nodes.

In an Italian post-mortem study, 2/3 of cardiac metastases involved the pericardium. Often, pericardial effusion is the first manifestation of cardiac involvement and may sometimes be the first sign of malignant tumour spread.[6]

While approximately 90% of cardiac metastases are asymptomatic, some have suggested that this is an overestimation as attention is commonly focused on symptom control of the primary malignancy.[5] Symptoms caused by cardiac tumours include dyspnea, cough, syncope, palpitations, and chest pain but vary depending on location, size, and etiology of the tumour. Complications of cardiac invasion by metastases include myxoid tumour degeneration and distal embolization, myocardial rupture from tumour infiltration, and fatal ventricular arrhythmias. The most common causes of death in cases of cardiac metastases are heart failure resulting from restrictive myocardial involvement, ventricular inflow or outflow obstruction, constrictive pericardial

involvement, or hemorrhagic pericardial effusion and subsequent tamponade.[4]

Electrocardiographic findings are typically non-specific and include ventricular and supraventricular tachyarrhythmias, conduction delays, and localized ST segment elevation indicative of myocardial tumour invasion. Pericarditis caused by tumour infiltration will usually appear as nonspecific ST segment deviations.

Echocardiography is the imagining modality of choice for initial evaluation of cardiac masses. It is often able to distinguish between benign and malignant tumours based on appearance. Benign myxomas are usually intracavitary pedunculated masses found in the left atrium attached to the interatrial septum.[4] In contrast, metastatic lesions are not commonly seen within the cardiac chambers due to the infrequency of endocardial involvement.[6] Those that are intracavitary will be wide-based, involve multiple cardiac structures, and show evidence of destruction of cardiac chambers. Pericardial tumours may form dense pericardial bands or project into the pericardial space in a cauliflower-like appearance with atypically-appearing, localized effusions. Pericardiocentesis with examination of fluid for cytology may be helpful, though if cellularity is poor, pericardial biopsy may be required. Large infiltrating tumours can cause wall motion abnormalities but are difficult to detect due to lack of echogenicity.[4]

Cardiac magnetic resonance imaging gives valuable additional soft tissue characterization of the tumour, with ability to measure flow velocities and extent of invasion of cardiac structures but its use is limited by availability. If etiology of the mass is unclear, biopsy under fluoroscopy is possible, taking care to avoid microembolization of the tumour. Pulmonary artery catheterization can be helpful in the hemodynamic monitoring of valvular obstruction caused by large tumours.[4]

Treatment of the cardiac tumour is dependent on the underlying malignancy with the goal of symptom palliation as the heart is seldom the sole site of metastasis. Radiation therapy for cardiac metastases was first reported in 1940 and should be considered as it has been observed to be quite successful in symptom management.[5] Catheter-directed instillation of radioisotopes or chemotherapy, especially in malignant pericardial effusion, has been attempted in many centres with success, though may be poorly tolerated due to side effects including pericardial sclerosis.[4] There is little recent literature surrounding surgical resection of cardiac tumours with most studies taking place in the 1980s. Mortality is high, estimated around 40% in this patient population.[5] Rates of recurrence after surgery are difficult to gauge as the primary metastatic process is most often a cause of death in the short-term. In a highly selective group of patients with good functional status, localized disease and longer life expectancy, resection of the cardiac tumour may be an option. Overall prognosis of symptomatic cardiac metastases is poor with a 5-year survival rate of 7%.[5]

Conclusion

We described a case of late-stage metastatic GIST with rapidly decompensating congestive heart failure due to a large left atrial metastasis obstructing the mitral valve. GIST is an uncommon malignancy with an annual Canadian incidence rate of 0.91/100 000 person-years.[7] It rarely metastasizes outside of the peritoneum and only one other case of GIST with a cardiac metastasis was found on review of the MEDLINE database, reported by Bashir et al.[8] Metastatic GIST is difficult to treat and a retrospective cohort study done by DeMatteo et al. observed a median survival time of 17-19 months for patients with metastatic disease.[9]

Cardiac metastases are relatively common in malignancy, particularly in bronchogenic carcinoma, hematological malignancies and breast cancer, but may be underdiagnosed due to their asymptomatic nature, non-specific symptoms or clinical focus on the primary neoplasm.[5] In cancer patients presenting with heart failure, after ischemic disease and chemotherapy-related toxicity has been ruled out, metastases to cardiac structures should be considered as a potential etiology. Echocardiography is a useful initial diagnostic tool in evaluating for cardiac masses. Localized radiation, chemotherapy, and in rare cases cardiac surgery have been proven effective in controlling symptoms and complications associated with cardiac tumours.

Key Points

- Cardiac tumours should be included in the differential diagnosis for congestive heart failure in patients in whom ischemic heart disease is not the primary etiology, especially in patients at risk for malignancy
- Transthoracic echocardiography should be used in the initial evaluation of these patients to investigate for presence of pericardial effusions or intracardiac masses
- Local radiation and chemotherapy has been used successfully for symptom palliation but cardiac metastases are generally a poor prognostic indicator

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References

1. Public Health Agency of Canada. Tracking heart disease and stroke in Canada. Ottawa: Author; 2009. Available at: http://www.phac-aspc.gc.ca/publicat/2009/cvd-avc/index-eng.php (accessed 2013 December 10).
2. Colucci WS. Evaluation of the patient with heart failure or cardiomyopathy. Philadelphia, PA: UpToDate; 2013. Available at: http://www.uptodate.com/contents/evaluation-of-the-patient-with-heart-failure-or-cardiomyopathy?source=search_result&search=heart+failure&selectedTitle=3%7E150#H5 (accessed 2013 May 8).
3. Zile MR, Gaasch WH. Clinical manifestations and diagnosis of diastolic heart failure. Philadelphia, PA: UpToDate; 2013. Available at: http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-diastolic-heart-failure?source=see_link (accessed 2014 January 4).
4. Reynan K, Kockeritz U, Strasser RH. Metastases to the heart. Ann Oncol 2004;15:375–81.
5. Al-Mamgani A, Baartman L, Baaijens M, et al. Cardiac metastases. Int J Clin Oncol 2008;13:369–72.
6. Bussani R, De-Giorgio F, Abbate A, et al. Cardiac metastases. J Clin Pathol 2007;60:27–34.
7. Yan BM, Kaplan GG, Urbanski S, et al. Epidemiology of gastrointestinal stromal tumours in a defined Canadian health region: a population-based study. Int J Surg Pathol 2008;16(3):241–50.
8. Bashir U, Khan H, Qureshi A, et al. gastrointestinal stromal tumour with skeletal muscle, adrenal and cardiac metastases: an unusual occurrence. Indian J Pathol Microbiol 2011;54(2):362.
9. DeMatteo RP, Lewis JJ, Leung D, et al. Two hundred gastrointestinal stromal tumours: recurrence patterns and prognostic factors for survival. Ann Surg 2000;231(1):51–58.