Cardiac Lymphoma Presenting with Recurrent STEMI

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ABSTRACT: The incidence of primary cardiac tumors is exceedingly rare, whereas secondary cardiac tumors are more common in the global population. Cardiac involvement is seen in approximately 18% of patients with non-Hodgkin's lymphoma at the time of autopsy. Clinical manifestations of cardiac involvement are subtle and often go unrecognized until advanced stages of the disease. We present a rare case of metastatic cardiac lymphoma that presented as an ST-segment elevation myocardial infarction complicated by left ventricular free wall rupture and cardiogenic shock due to transmural myocardial necrosis from malignant cell infiltration.

BACKGROUND

Primary cardiac tumors are rare and usually benign. In the general population, primary cardiac tumors make up only 2% of all cardiac tumors, and 25% of those are diagnosed as malignant. Of those malignant tumors, 5% are classified as lymphomas.[2] Secondary malignant cardiac tumors are seen in up to 9% of patients with a known disseminated primary malignancy.[3] In patients with known lymphoma, cardiac metastasis has been reported in up to 25%.[4,5] Cardiac lymphoma is an infiltrative disease that can be intramural, pericardial, or epicardial in location. Depending on the underlying anatomic site, clinical complications may present as chest pain, heart failure, conduction abnormalities, pericardial effusions, superior vena cava syndrome, or restrictive cardiomyopathy.[6,7] Echocardiography and cardiac magnetic resonance imaging (cMRI) are useful in identifying cardiac metastases, with conclusive diagnosis made on biopsy or autopsy. Treatment includes chemotherapy variably combined with radiation therapy, although the prognosis remains poor. Surgery is performed for palliation in selected cases to relieve blood flow obstruction when present.[8]

We present a challenging case of undiagnosed metastatic lymphoma with cardiac involvement presenting as recurrent ST-segment elevated myocardial infarction (STEMI). While there are few published case reports of cardiac lymphoma presenting as STEMI, left ventricular (LV) free wall rupture is a uniquely rare complication.[9,10]

CASE REPORT

A 67-year-old man with a history of schizophrenia, hypertension, and coronary artery disease (CAD) presented to the hospital with progressive dyspnea over the course of 2 weeks. He had undergone a previous percutaneous coronary intervention (PCI) to the left anterior descending artery (LAD) at age 57. In the emergency department, the patient was found to have subtle 1-mm ST-segment elevation on electrocardiogram (ECG) in leads I, aVL, and V3-V6. Laboratory evaluation showed an elevated troponin at 0.26 ng/mL and a pro-brain natriuretic peptide (pro-BNP) level of 2,140 ng/L. While coronary angiography did not reveal a culprit lesion causing the STEMI, it did identify a 70% lesion with thrombolysis in myocardial infarction (TIMI) III flow in the proximal LAD. Interestingly, ST-segment changes on the ECG resolved during the angiography. The LAD was further assessed by optical coherence tomography (OCT), which demonstrated the presence of a fibroatherosclerotic lesion (Figure 1) in the proximal LAD causing significant luminal narrowing that was successfully treated with PCI. Additionally, there was evidence of 70% stenosis in the proximal left circumflex artery (LCx); due to ongoing chest pain, PCI of the LCx was also performed. Left ventricular end diastolic pressure was elevated at 26 mm Hg. The patient was subsequently admitted for post-PCI care and diuresis. The troponin level peaked at 0.31 ng/mL. Transthoracic echocardiogram (TTE) showed an LV ejection fraction of 45%, concentric LV hypertrophy with mild global hypokinesis, and moderate hypokinesis of the inferior wall.

The following day, the patient's condition worsened with development of cardiogenic shock that required inotropic support. Two days later, the patient developed acute chest pain, diaphoresis, and shortness of breath, and his troponin level was found to be elevated to 4.91 ng/mL; ECG demonstrated 4-mm ST-segment elevation in leads I, aVL and V4-V6 (Figure 2). Emergent coronary angiography showed unchanged coronary anatomy with patent stents. During angiography, both chest pain and ECG changes resolved. Endomyocardial biopsy from the left ventricle was also performed. The patient remained in cardiogenic shock on inotropic support. Three days later, the patient again developed acute chest pain and ST-segment

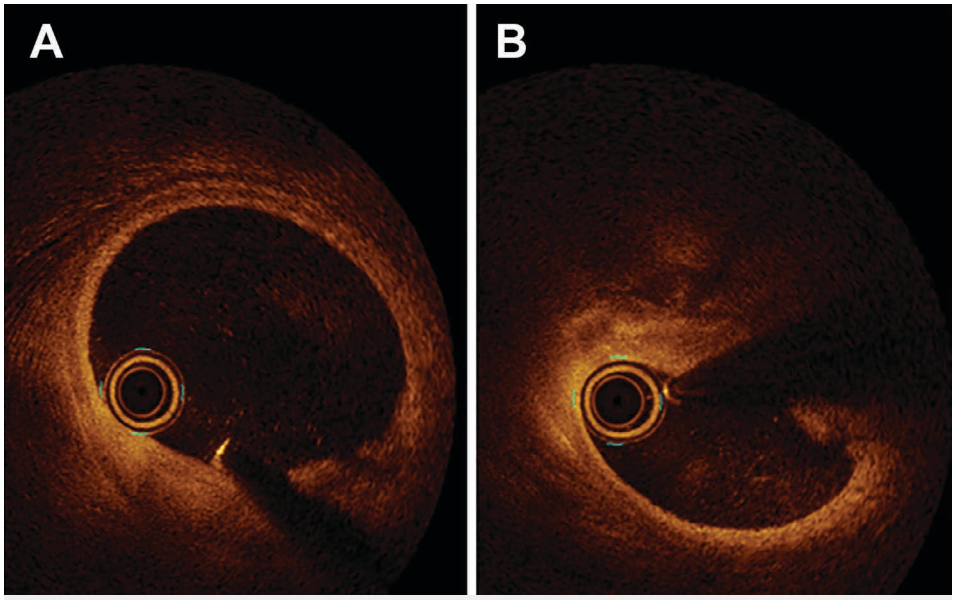

Figure 1.
(A) Optical coherence tomography showing left anterior descending artery normal segment compared to (B) the area of stenosis with fibroatherosclerotic lesion.

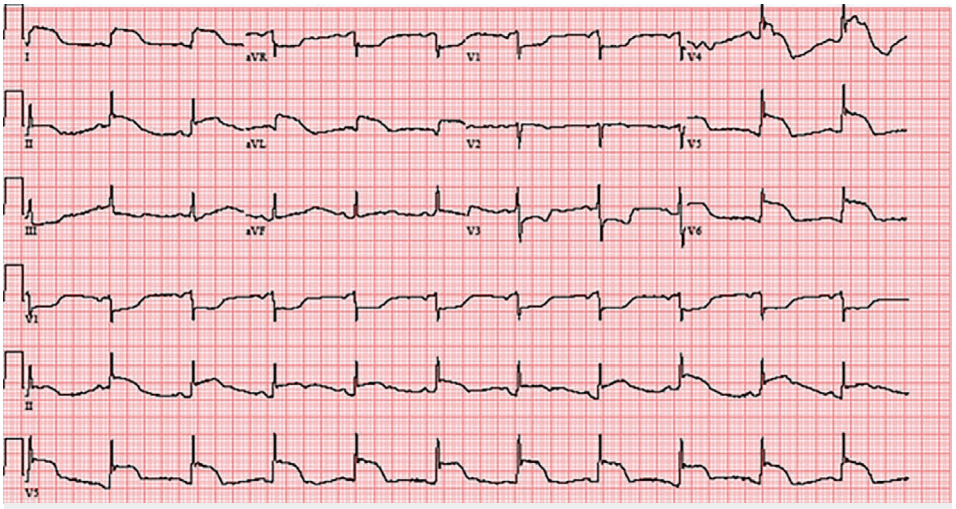

Figure 2.
Electrocardiogram showing profound ST-segment elevation in leads 1, aVL, and V4-V6.

elevation in the same leads I, aVL and V4-V6 on ECG. The concern for acute stent thrombosis was low given the recently identified cause of myocardial injury, and repeat coronary angiography was not performed. A repeat TTE with contrast revealed a new small pericardial effusion with a contained extravasation of contrast into the pericardium, consistent with an LV free wall rupture with containment via the pericardium (Figure 3). Due to his hemodynamic instability, the patient was deemed to be a high-risk candidate for open heart surgery, percutaneous repair, or use of mechanical circulatory support. After discussion with the family and patient, hospice care was pursued. The patient died a few hours after withdrawal of inotropic support. Endocardial biopsy did not show any evidence of amyloid or iron deposition, absent granulomas, viral inclusions or significant inflammation. Moderately increased fibrosis was seen between the myocytes. The autopsy report revealed the patient had aggressive Epstein-Barr virus encoded small RNAs with positive natural killer (NK)-cell lymphoma with multiorgan system involvement, including the right lung, liver, bilateral kidneys, distal esophagus, and the transmural involvement of myocardium of both right and left ventricles.

DISCUSSION

Cardiac metastasis is most commonly seen with primary malignancies of the lung, breast, esophagus, melanoma, and hematologic malignancies.[3,11] Cardiac involvement of a malignant lymphoma is usually a late manifestation of the disease and is a negative prognostic indicator for survival.[1] Metastatic cardiac lymphoma is challenging to diagnose due to the nonspecific symptoms in its early stages.[12] Clinical complications occur as a result of tumor cell infiltration and disruption of the myocardial infrastructure, including pericardial effusions, cardiac tamponade, arrhythmias, heart failure, coronary artery infiltration, and pulmonary embolism.[13] Dyspnea from congestive heart failure is the most commonly reported clinical symptom at presentation, followed by chest pain from direct infiltration of coronary arteries[4] and constitutional symptoms. The associated cardiac arrhythmias that have been described include atrioventricular blocks,[14] left and right bundle branch blocks, and ventricular arrhythmias.[15]

Cardiac lymphoma is an infiltrative process, and diffuse cardiac involvement has been reported in a few cases.[16] Myocardial cell necrosis and replacement

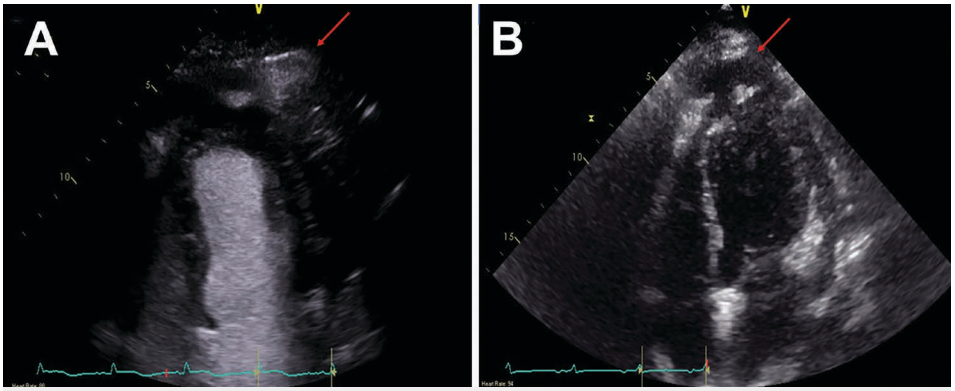

Figure 3.
Transthoracic echocardiogram depicting apical four-chamber view with (A) and without (B) contrast demonstrating pericardial effusion with contained extravasation of contrast into the pericardium consistent with a left ventricular apical wall rupture with containment via the pericardium.

with lymphoma cells that lack intercellular cohesion[17] can predispose a patient with transmural involvement to myocardial rupture. Although myocardial rupture is most commonly seen in the setting of transmural myocardial infarction,[18] it also has been reported in a few cases with myocardial infiltration from lymphoma.[17] Clinical presentation is consistent with recurrent chest pain and persistent or recurrent ST-segment elevation on ECG.[19] The other differentials for recurrent ST-segment elevation include recurrent episodes of transient myocardial ischemia as compared to persistent ST-segment elevation, which is most commonly seen in LV free wall aneurysm, early repolarization syndrome, and pericarditis. The sequela of myocardial rupture includes cardiac tamponade or pseudoaneurysm formation with containment by an organized thrombus or pericardium.[19] In these cases, the diagnosis is made with echocardiographic imaging and the definite treatment is surgical repair.

Its widespread availability and ease of use make TTE the first-line imaging modality for diagnosing cardiac metastasis[3,20] because it allows for identification of mass location and noninvasive hemodynamic assessment. cMRI is the preferred imaging modality for cardiac metastases[21] due to its improved spatial and soft-tissue resolution; it has the advantage of tissue characterization that can help differentiate between types of cardiac tumors and classify benign versus malignant lesions. cMRI has proven to be superior to TTE in the diagnosis of infiltrative cardiomyopathies due to its high resolution.[22] Contrast-enhanced cMRI and echocardiography can assist in mass differentiation (ie, thrombus versus tumor), although cMRI is more sensitive.[23] The early use of cMRI can provide much needed information that can be used in multidisciplinary discussion and establishment of a treatment plan. The time required for cMRI in the critically ill still limits its use, as was the case in the presented patient. In such patients, myocardial biopsy, although invasive, can be a rapid way to achieve diagnosis and in some cases may alter the treatment.[24]

The management of cardiac metastasis is challenging and often comes with a grave prognosis. Limited treatment options include palliative chemotherapy combined with radiotherapy. Surgical intervention is often not feasible due to the inoperable nature of the metastatic lesions. Additionally, there is unclear evidence on the mortality benefit of surgical intervention in malignant cases.

CONCLUSION

In this unique case, lymphoma metastasis to the myocardium mimicked acute coronary syndrome, yet the underlying etiology of this patient's symptoms was transmural malignant cell infiltration of the myocardium leading to LV free wall rupture contained within the pericardium and cardiogenic shock. Although PCI was successfully performed, the presence of CAD in this case may have been benign. This case demonstrates a rare etiology of recurrent STEMI and emphasizes the importance of developing a broad differential in ACS, particularly in cases where a clear culprit lesion is not identified. Cardiac metastases should be considered in all patients with known malignancy presenting with new cardiovascular symptoms.

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Conflict of Interest Disclosure:
The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

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cardiac lymphoma, ST-segment elevation, cardiogenic shock, left ventricular free wall rupture, coronary artery disease

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