Primary Cardiac Lymphoma in a Patient With Well-Controlled Human Immunodeficiency Virus

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INTRODUCTION

Primary cardiac lymphoma (PCL) is defined as an extranodal lymphoma wherein the primary lesion arises from the heart. A minority of cardiac tumors are malignant, and only about 2% of those tumors are PCL.[1] Here we present a case of B-cell PCL in a patient with well-controlled HIV. The objectives of this case are to highlight the role of multimodal imaging in establishing the diagnosis and describe the successful management of this rare disease.

CASE PRESENTATION

A 62-year-old woman presented to the emergency department with worsening dyspnea on exertion and bilateral lower extremity edema. The patient had a history of hypertension and human immunodeficiency virus (HIV) and was on highly active antiretroviral therapy. The last CD4 count was 584 with undetectable viral load. The patient was afebrile. Blood pressure was 144/80 mm Hg; heart rate, 97 beats/minute; respiratory rate, 25 breaths/minute; and oxygen saturation, 100% on room air. Cardiopulmonary exam showed normal jugular venous pulsation, a regular rhythm, no murmurs, bibasilar crackles, a nondistended abdomen, and 2+ pitting edema of the bilateral lower extremities.

Electrocardiogram on admission showed low voltages. Chest x-ray showed mild pulmonary edema and a right pleural effusion. A transthoracic echocardiogram (TTE) demonstrated normal left ventricular systolic function, a 5.2 × 2.8 cm mass within the right atrium that appeared to prolapse through the tricuspid valve, and a large pericardial effusion with mild right ventricular diastolic compression in the basal portion, suggesting early cardiac tamponade (Figure 1, Video 1). The patient underwent urgent pericardiocentesis with nearly 800 mL of exudative fluid drained. The fluid had an elevated adenosine deaminase level of 103 units/L. Cardiovascular magnetic resonance imaging (CMR) further characterized this mass as complex with 3 components. Postcontrast early sequence and delayed enhancement images showed heterogenous enhancement of the masses. One component was along the posterior aspect of the right atrium possibly extending into the left atrium with involvement of the intrathoracic inferior vena cava (Figure 2A). This component demonstrated high T2 signal. A second mobile lesion herniated into the right ventricle through the tricuspid valve and demonstrated intermediate T2 signal (Figure 2B). A third component involved the right anterior atrium and ventricular wall with encasement of the right coronary artery (Figure 2C). T1 postcontrast images demonstrated enhancement of the right ventricular free wall and mass. These findings were also seen with transesophageal echocardiogram (Figure 3, Videos 2-4). Tricuspid inflow velocity was obtained with continuous-wave Doppler and indicated no significant obstruction (Figure 4). Computed tomography (CT) imaging of the neck, chest, abdomen, and pelvis did not reveal any evidence of a primary malignancy elsewhere. A magnetic resonance image of the brain was also unremarkable. Considering the extensive imaging findings and history of HIV, PCL was thought to be the most probable diagnosis.

VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiogram in the 4-chamber view showing a large pericardial effusion and mass that appeared to prolapse through the tricuspid valve.

Video 2: Two-dimensional transesophageal echocardiogram, midesophageal window, x plane view transecting the midsection of the right atrial mass. This video demonstrates 2 simultaneous views of the large right atrial mass attached to the inferolateral wall of the right atrium.

Video 3: Intraoperative transesophageal echocardiogram in the midesophageal 4-chamber view at 2° showing a complex right atrial mass almost extending into the right ventricle and prolapsing into the tricuspid valve.

Video 4: Single-beat three-dimensional intraoperative transesophageal echocardiogram showing the mobile right atrial mass from the right atrial perspective.

Video 5: Transthoracic echocardiogram in the apical 4-chamber view, right ventricle–focused, 8 months postsurgery and after chemotherapy demonstrating resolution of the cardiac mass, mildly reduced right ventricular systolic function (tricuspid annular plane systolic excursion 15 mm), and a thinner right ventricular wall when compared to Video 1.

View the video content online at www.cvcasejournal.com.

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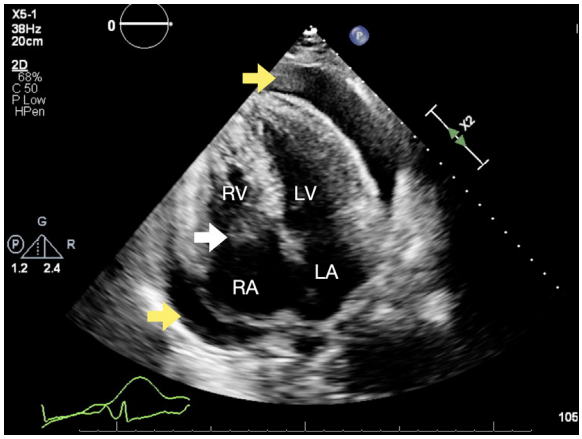

Figure 1 Transthoracic echocardiogram in the apical 4-chamber view during systole showing a large pericardial effusion *(yellow arrows)* and mass near the tricuspid valve *(white arrow)*. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

Given the hemodynamic compromise, our patient underwent early surgical debulking of the cardiac mass (Figure 5). Histopathologic assessment was consistent with high-grade B-cell lymphoma with Burkitt-like features (Figure 6). Immunohistochemical studies were positive for CD20, CD10, BCL6, and c-MYC. Further staging with a bone marrow biopsy and lumbar puncture did not show any evidence of lymphoma, although an elevated white blood cell count (75/mm^3) in the cerebrospinal fluid was suggestive of possible central nervous system involvement. Positron emission tomography (PET)-CT confirmed cardiac isolation of the tumor (Figure 7).

The patient was started on R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) and intrathecal methotrexate and cytarabine. Flow cytometry and cytology of the cerebrospinal fluid eventually came back negative for malignancy. The patient's chemotherapy regimen was escalated to R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin). The patient received 5 cycles of R-EPOCH for a total of 6 cycles of systemic chemotherapy. The patient received 2 cycles of prophylactic intrathecal chemotherapy before refusing further lumbar punctures. A PET-CT done after completion of chemotherapy 6 months later showed complete remission. Furthermore, posttreatment TTE showed resolution of the cardiac mass (Video 5). The patient remains in complete remission and has been doing well 14 months since the diagnosis of PCL.

DISCUSSION

The differential diagnosis of a cardiac mass can be categorized as either neoplastic or nonneoplastic. The former can be further characterized as either benign or malignant. Common benign cardiac tumors include myxomas, lipomas, fibromas, teratomas, and rhabdomyomas. Malignant cardiac tumors most commonly are metastatic from another primary source but also include sarcomas and PCLs.

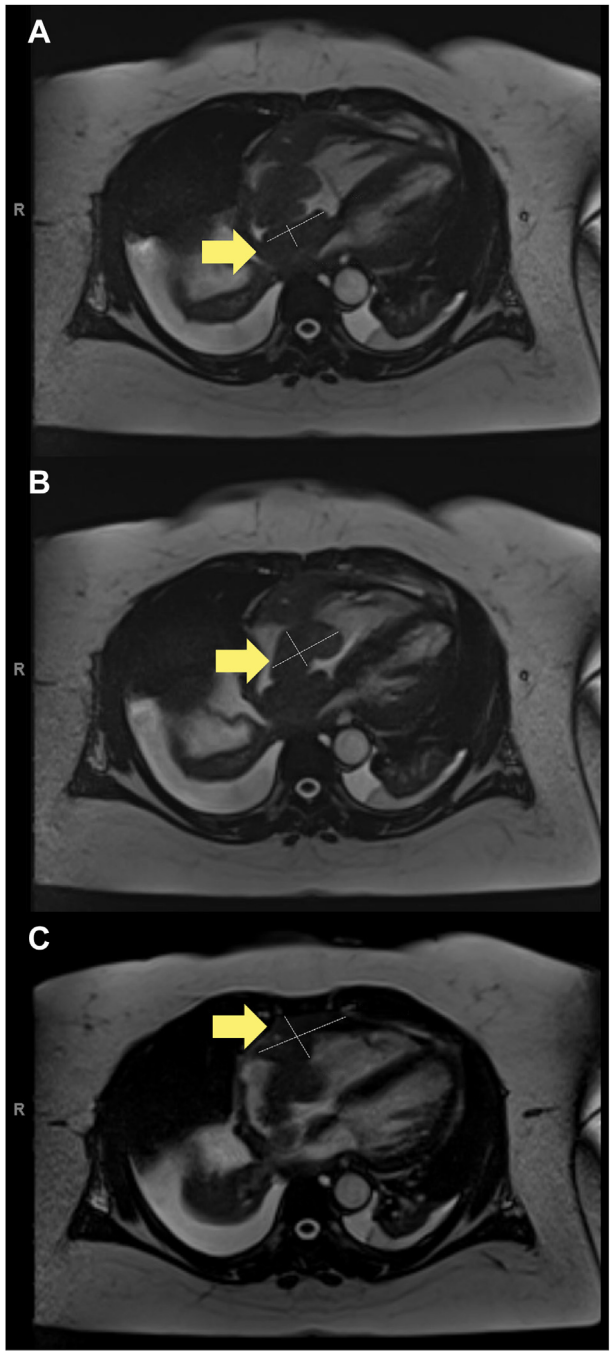

Figure 2 Short-axis T2-weighted CMR demonstrating several filling defects within the right atrium. **(A)** One component measured approximately 4.4 × 1.9 cm and is centered along the posterior wall of the right atrium and intra-atrial septum *(arrow)*. **(B)** A second component of the atrial filling defect is a lobulated mass and on axial dimensions measured approximately 5.0 × 2.8 cm *(arrow)*. **(C)** Separate to these 2 structures is a mass-like thickening of the right atrium and ventricular anterior free wall. On axial dimensions, this component measures approximately 6.2 × 3.0 cm *(arrow)*.

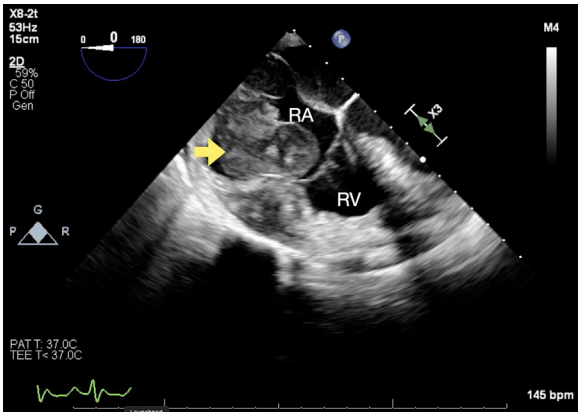

Figure 3 Transesophageal echocardiogram in the midesophageal 4-chamber view at 0° during systole showing a large multilobulated and heterogeneous mass *(arrow)* within the right atrium. *RA*, Right atrium; *RV*, right ventricle.

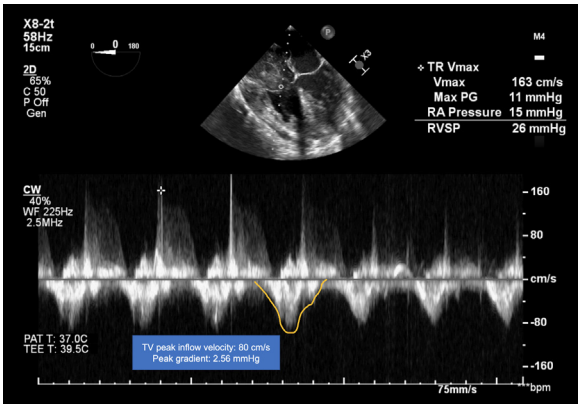

Figure 4 Transesophageal echocardiogram in the midesophageal 4-chamber view at 0°. The tricuspid inflow velocity obtained with continuous-wave Doppler was 80 cm/sec with a gradient of 2.6 mm Hg, indicating no significant obstruction.

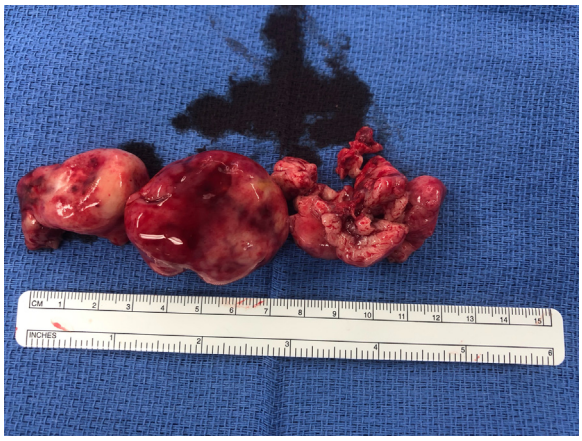

Figure 5 Gross specimen that was surgically excised.

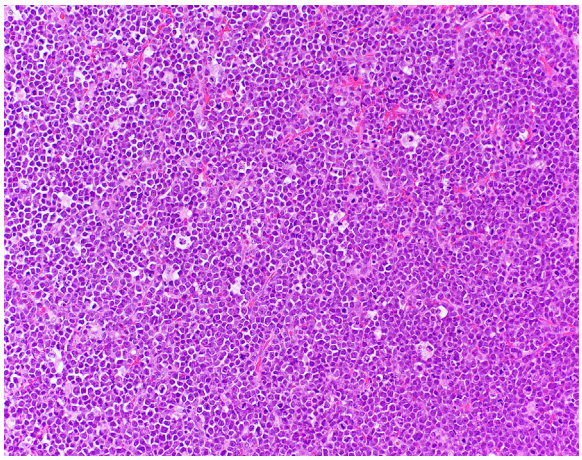

Figure 6 Hematoxylin and eosin stain showing diffuse infiltrate of small to intermediate atypical lymphocytes with prominent "starry sky" pattern due to numerous tingible body macrophages.

Nonneoplastic cardiac masses include intracardiac thrombi and valvular vegetations.

The largest review of PCL to date reports a total of 197 cases from 1949 to 2009. These cases were composed of individuals that were both immunocompetent and immunocompromised primarily from HIV. Irrespective of HIV status, diffuse large B-cell lymphoma was the predominant type of PCL, with fewer cases of Burkett lymphoma, T-cell lymphoma, and small lymphoblastic lymphoma reported. The median age at time of diagnosis was 64 years old with a male-to-female ratio of 1.94.[2] Right-sided heart involvement continues to be the most common,[2] although additional case reports describe involvement of solely the left atrium and left ventricle,[3] right and left atrium sparing either ventricle,[4] or the pericardial sac.[5,6] Presenting signs or symptoms are heterogenous, but most commonly involve dyspnea, pericardial effusion with or without tamponade, arrhythmia, or heart failure. The mean survival among those diagnosed with PCL is 12 months, which is reduced to 6 months among those with extracardiac disease and 3.5 months if immunocompromised.[2]

Immunocompromise is a risk factor for PCL.[2] The incidence of B-cell lymphomas in HIV patients has significantly decreased in the United States since the advent of highly active antiretroviral therapy. However, HIV infection causes chronic antigenic stimulation, inflammation, and cytokine dysregulation, even in those with preserved CD4 counts and undetectable viral loads, contributing to an increased risk of lymphoma and other malignancies in these patients.[7] Our patient is part of the increasing proportion of non-Hodgkin lymphoma occurring in patients with higher CD4 counts and undetectable HIV RNA levels.[8]

The workup of PCL requires multimodality imaging. A TTE showed a large cardiac mass with a pericardial effusion but could not delineate the composition of the mass. As such, echocardiography is best suited to capture hemodynamic consequences. To better characterize the mass, we used CMR, which revealed the tumor's extension into neighboring structures. PET-CT imaging was obtained after surgical resection but prior to chemotherapy initiation, which was done to not only confirm cardiac isolation but also to help distinguish

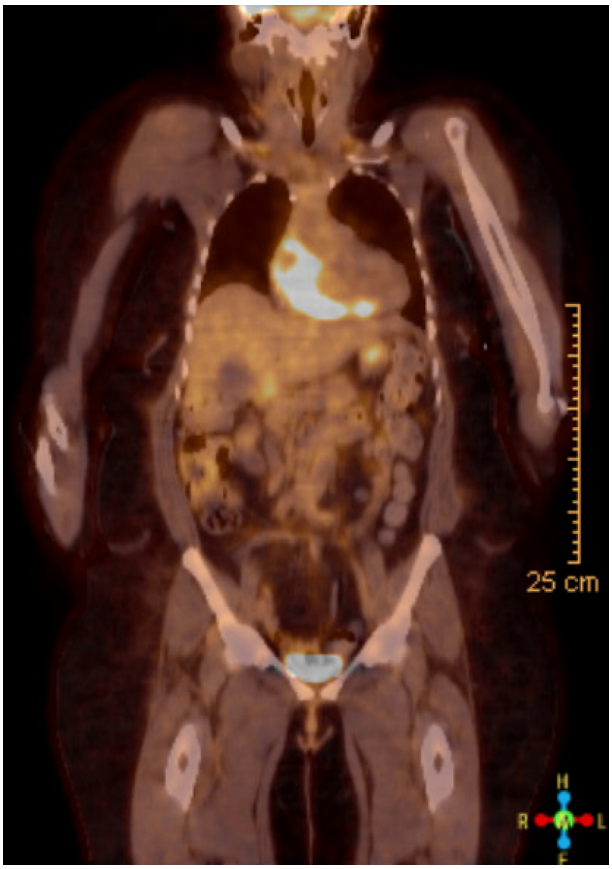

Figure 7 PET-CT was performed from the skull base to mid thighs. The patient was intravenously injected with 18F-FDG via the right antecubital vein. There was increased FDG activity inseparable from the right atrium, extending to the base of the left ventricle and left atrium; FDG activity was also seen in mediastinal and hilar lymph nodes but was thought to be reactive. There were no suspicious FDG avid lymph nodes below the diaphragm.

between a malignant versus benign tumor, the latter being associated with lower fluorodeoxyglucose avidity.[9]

A biopsy is needed for histologic diagnosis but is not always possible. Pericardial fluid cytology can help establish a diagnosis without tissue sampling in patients with a pericardial effusion. With our patient, pericardial fluid cytology resulted after surgical resection and was suspicious for a B-cell lymphoproliferative process; however, flow cytometry showed no immunophenotypic evidence of lymphoma.

All patients should receive a course of systemic chemotherapy, but not all undergo surgical resection. Surgical resection is indicated in the setting of hemodynamic compromise. Our patient had a large cardiac mass with multiple components, one of which herniated through the tricuspid valve and was initially thought to cause obstruction, while also preventing inflow from the inferior vena cava. For this, the patient first underwent surgical debulking, followed by chemotherapy. The majority of patients receive an anthracycline-containing regimen, primarily with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), for 6 cycles.[2] However, if patients have reduced cardiac function at baseline, they can receive an anthracycline-free regimen with R-CEOP (rituximab, cyclophosphamide, etoposide, vincristine, and prednisone).[10] In cases with central nervous system involvement, intrathecal chemotherapy is also administered.[5] Of note, our patient's tumor extended into the right ventricular free wall. As a tumor regresses with chemotherapy, the infiltrated myocardium becomes thinned (Video 5) and thus vulnerable to spontaneous hemopericardium and free wall rupture. In addition, coronary involvement can lead to myocardial ischemia or infarction.

CONCLUSION

We diagnosed a complicated and rare case of primary cardiac B-cell lymphoma in a patient with well-controlled HIV. Multimodal imaging led to a diagnosis that was later confirmed by tissue sampling. Echocardiography captured the hemodynamic compromise necessitating surgical resection. Our patient responded remarkably well to treatment without complications and remains in complete remission more than 1 year after diagnosis.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

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DISCLOSURE STATEMENT

The authors have nothing to disclose.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2022.09.003.

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