

## MINI-FOCUS ISSUE ON CARDIO-ONCOLOGY

### CASE REPORT: CLINICAL CASE

# Primary Cardiac Lymphoma With Dramatic Response to Chemotherapy Diagnosed by Transvenous Biopsy



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#### ABSTRACT

Primary cardiac lymphoma is a rare disease with the potential to be fatal. This case reports a patient who developed primary cardiac lymphoma resulting in cardiac tamponade. Despite a compromised general condition, the lymphoma was diagnosed through a transvenous tumor biopsy. Chemotherapy led to significant improvement in the patient's condition. Malignant lymphoma can be treated with chemotherapy. Therefore, the performance of tumor biopsies even in patients with poor general condition enabled the initiation of treatment. (JACC Case Rep. 2024;29:102728) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

#### HISTORY OF PRESENTATION

A 53-year-old man presented with a 2-week history of palpitation and dyspnea. Physical examination was unremarkable. The electrocardiogram showed an incomplete right bundle branch block. Chest radiograph revealed cardiac enlargement and bilateral pleural effusions. Blood tests showed hemoglobin 13.1 g/dL, lactate dehydrogenase 358 U/L, and soluble interleukin-2 receptor 1,380 U/mL; human immunodeficiency virus antibody was negative. Thyroid

function was normal. Transthoracic echocardiogram (TTE) revealed a mobile and solid mass measuring 79 × 55 mm, occupying most of the right atrium (RA) (Figures 1A and 1B, Videos 1 and 2). Left ventricular systolic function was preserved with an ejection fraction of 75%. The cardiac-gated magnetic resonance imaging showed a multilobulated mass measuring approximately 80 mm, almost entirely occupying the RA with attachment to the lateral wall of the RA (Figure 2).

#### TAKE-HOME MESSAGE

- This report highlights the importance of tumor biopsy, even in cases of poor condition.

#### PAST MEDICAL HISTORY

The patient underwent an annual medical examination without any previous medical history or cardiovascular risk factors.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

Manuscript received June 17, 2024; revised manuscript received September 18, 2024, accepted September 26, 2024.

**ABBREVIATIONS  
AND ACRONYMS****<sup>18</sup>F** = fluorine-18**CR** = complete response**DA-EPOCH-R** = dose-adjusted etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin, and rituximab**DLBCL** = diffuse large B-cell lymphoma**FDG** = fluorodeoxyglucose**PET** = positron emission tomography**R-CHOP** = intravenous rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone**RA** = right atrium**TTE** = transthoracic echocardiogram**DIFFERENTIAL DIAGNOSIS**

Based on the clinical course, we considered the differential diagnosis of cardiac malignant tumors (eg, lymphoma, sarcoma).

**INVESTIGATIONS**

Fluorine-18 (<sup>18</sup>F)-fluorodeoxyglucose (FDG) positron emission tomography (PET) showed increased FDG avidity in the cardiac mass lesion (SUVmax [the maximum standardized uptake value] 23.62) and no lymph nodes and other organs (Figure 3). Coronary angiography showed no significant stenosis in the coronary arteries and no blood vessels feeding the tumor. Cardiac tamponade developed, and pericardiocentesis was performed. Pericardial effusion was exudative, and cytologic examination revealed the presence of atypical cells; however, no malignant cells were identified (class II). After that, the patient experienced worsening dyspnea. A transvenous biopsy of the RA mass was subsequently performed under TTE guidance (Figure 4, Video 3).

**MANAGEMENT**

B-cell lymphoma was diagnosed by flow cytometry of the mass biopsy, and the patient received chemotherapy with intravenous rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) immediately prior to pathologic diagnosis, given the patient's compromised general condition. Thereafter, the tumor tended to shrink, pericardial

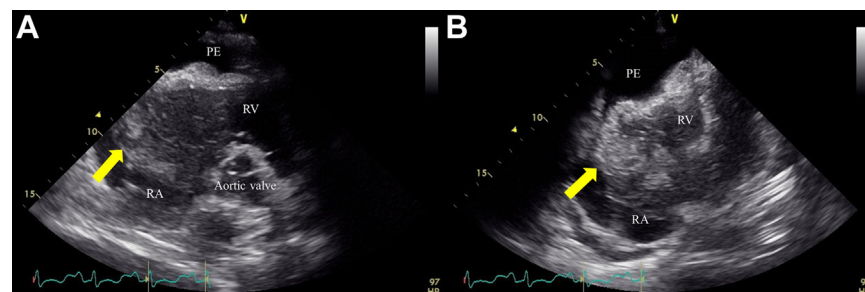
effusion disappeared, and symptoms improved. Pathologic examination showed diffuse proliferation of large lymphoid cells (Figure 5), and immunostaining revealed positivity for CD20 and negativity for CD3. Furthermore, these atypical cells were highly expressed for BCL2, BCL6, and MYC. Ki-67 labeling index was more than 95% for tumor cells. Finally, the diagnosis of diffuse large B-cell lymphoma (DLBCL) was made. Fluorescence in situ hybridization could not be performed due to insufficient sample materials. Considering DLBCL with high expression of MYC and BCL2, the patient received chemotherapy with dose-adjusted etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R) for 6 cycles.

**OUTCOME AND FOLLOW-UP**

The patient underwent cardiac TTE and <sup>18</sup>F-FDG PET after chemotherapy. TTE showed resolution of the pericardial effusion, preserved left ventricular systolic function (Figure 6A and 6B, Video 4), and the RA mass had shrunk in size (15 × 11 mm) (Figures 6C and 6D, Videos 5 and 6). The patient achieved complete response (CR) as confirmed by <sup>18</sup>F-FDG PET (Figure 6E).

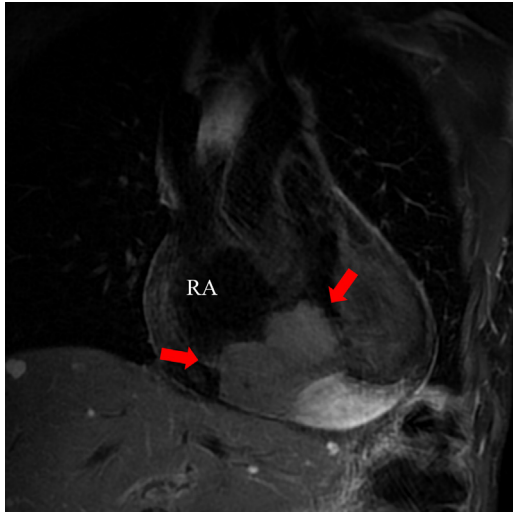
**DISCUSSION**

Primary cardiac lymphoma accounts for 1% of primary cardiac tumors and 0.5% of extranodal lymphomas.<sup>1</sup> Most commonly, the tumor is partially located within the RA of the heart and the most common subtype is DLBCL.<sup>2</sup> Dyspnea, arrhythmia, heart failure, and chest pain may be caused by tumor. In cases where the disease affects the pericardium, effusion or

**FIGURE 1** Transthoracic Echocardiogram

The images revealed a mobile mass occupying most of the right atrium (RA) and protruding into the right ventricle (RV) (arrows), with pericardial effusion (PE): (A) parasternal view and (B) apical view.

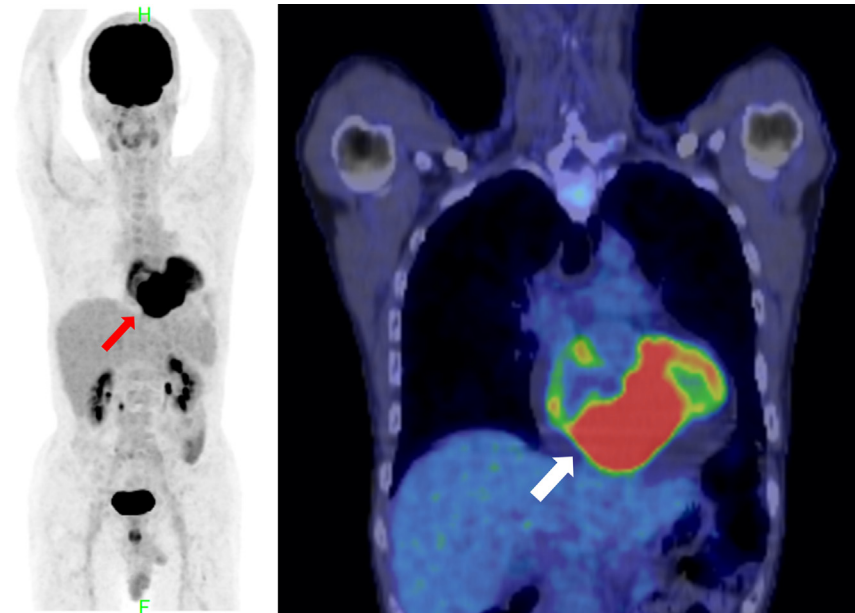
**FIGURE 2** Fat-Suppressed T2-Weighted Cardiac Magnetic Resonance Imaging



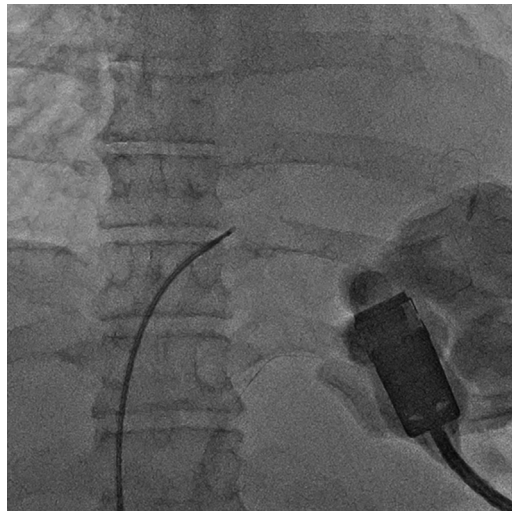
The images revealed a mass with irregular margins that was attached to the lateral wall of the right atrium (RA), infiltrating the myocardium and occupying almost the entire RA (arrows). It showed mild hyperintensity on fat-suppressed T2-weighted images.

hemorrhage may occur.<sup>2</sup> Primary cardiac lymphoma can be fatal if diagnosed late and generally has a poor prognosis. In this case, cardiac tamponade occurred and the course was acute, but transthoracic echocardiography-guided tumor biopsy was performed, leading to the diagnosis of DLBCL, and enabling treatment. Due to the patient's poor respiratory condition, we decided to perform biopsy under transthoracic echocardiography guidance instead of the generally considered biopsy under transesophageal echocardiography guidance. The biopsy was clearly visualized and successfully performed without any complications, despite the potential risks of cardiac tamponade and pulmonary embolism due to thrombus or tumor associated with transvenous biopsy. Surgical resection does not improve prognosis with primary cardiac lymphoma.<sup>3</sup> The standard treatment of DLBCL is chemotherapy with R-CHOP.<sup>4</sup> Double-hit lymphomas with translocations involving *MYC* and either *BCL2* or *BCL6*, and triple-hit lymphomas involving the translocation of *MYC*, *BCL2*, and *BCL6*, have a poor prognosis in DLBCL. R-CHOP therapy alone may prove inadequate in the treatment of these aggressive lymphomas.<sup>5</sup> Although DA-EPOCH-R therapy has demonstrated efficacy in treating primary mediastinal large B-cell lymphoma, a

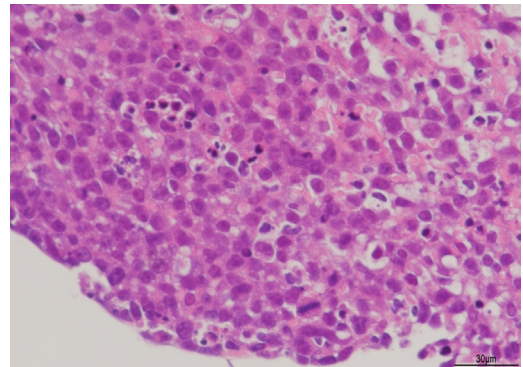
**FIGURE 3** Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography



Increased fluorodeoxyglucose avidity in the cardiac mass lesion (arrow) and no lymph nodes and other organs are shown.

**FIGURE 4** Radiograph Image at the Time of Biopsy

Biopsy was performed with the guidance of transthoracic echocardiography while confirming the location of the tumor with biopsy forceps.

**FIGURE 5** Pathologic Findings

This pathologic image was captured at 400× magnification. Hematoxylin and eosin stain shows diffuse and cohesive infiltrates of large atypical cells.

DLBCL subtype, it has not proven useful in treating DLBCL and is not a typical form of treatment.<sup>6,7</sup> Retrospective studies indicate that DA-EPOCH-R therapy is a valuable treatment option for double-hit lymphoma.<sup>8</sup> Although fluorescence in situ hybridization analysis was not conducted due to the limited sample size, high expression of MYC and BCL2 proteins led us to initiate DA-EPOCH-R therapy due to the aggressiveness of the lymphoma. Finally, the patient achieved CR. The median survival period for primary cardiac malignant lymphoma is 12 months, and factors associated with poor prognosis include immune status, left ventricular involvement, presence of extracardiac disease, and arrhythmia.<sup>9</sup> It has been suggested that cases lacking these poor prognostic factors or those treated with chemotherapy may have a better long-term prognosis. This case did

not exhibit such poor prognostic factors, and because chemotherapy led to CR, it was thought that long-term survival could be expected.

## CONCLUSIONS

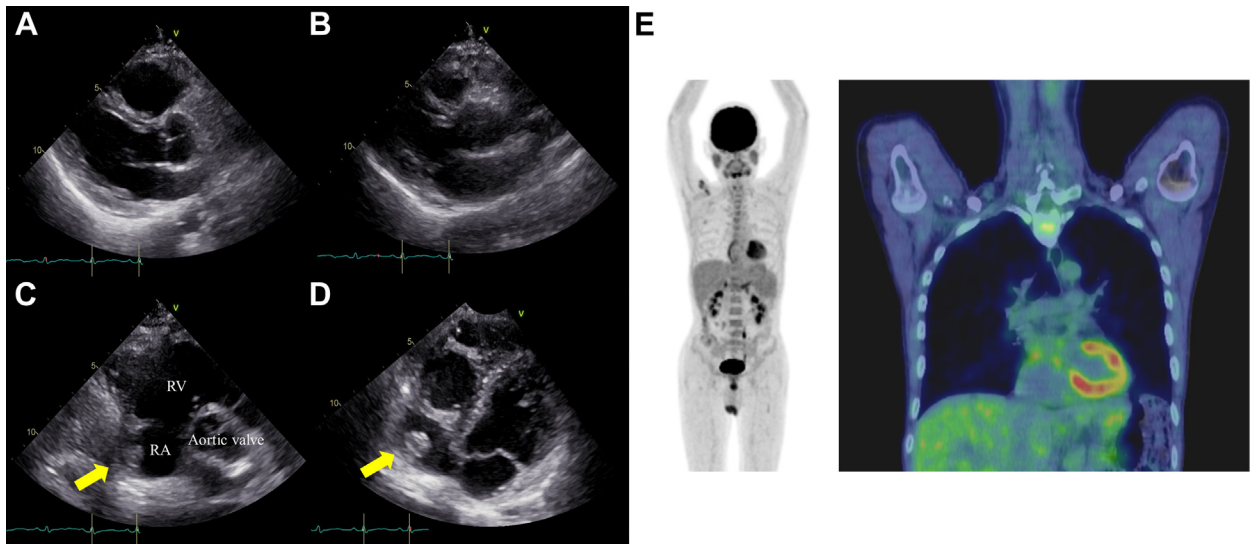
We experienced a case in which DLBCL caused by cardiac tamponade was diagnosed, treated, and improved. Early detection and intervention are critical for primary cardiac lymphoma, which carries a poor prognosis.

## FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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**FIGURE 6** Follow-Up Imaging



Transthoracic echocardiogram showed resolution of the pericardial effusion and preserved left ventricular systolic function (A: diastolic image, B: systolic image). The right atrial mass has shrunk in size (15 × 11 mm) (arrows). (C and D) Fluorine-18 fluorodeoxyglucose positron emission tomography showed only physiological uptake around the heart and within the myocardium (E). RA = right atrium; RV = right ventricle.

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**KEY WORDS** cancer, echocardiography, imaging, shortness of breath

**APPENDIX** For supplemental videos, please see the online version of this paper.