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A Rare Case of Diffuse Large B Cell Lymphoma Presenting as a Cardiac Mass

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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This case was presented at the 2018 Society of General Internal Medicine (SGIM) annual conference in Denver, Colorado
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Conflict of interest: None declared

Patient: Female, 57-year-old
Final Diagnosis: Mediastinal diffuse large B cell lymphoma infiltrating the heart as a right atrial cardiac mass
Symptoms: Cough • dyspnea • fatigue • weight loss
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Rare disease

Background: Primary mediastinal diffuse large B cell lymphoma (DLBCL) presenting as a large intracardiac tumor is extremely rare and has not been significantly reported in the literature. Cardiac lymphoma consists of 2 subtypes: mediastinal DLBCL invading the heart and primary cardiac lymphoma. Both subtypes have a poor prognosis and are treated similarly. Mediastinal DLBCL is a life-threatening condition that, if diagnosed early, has a better survival rate. This is a rare case of a mediastinal DLBCL invading the right atrium as a large intracardiac mass, causing partial obstruction of the tricuspid valve without hemodynamic compromise.

Case Report: A 57-year-old female presented with unintentional weight loss, fatigue, exertional dyspnea, and cough for 8 weeks. Transesophageal echocardiogram showed a mass (3.5×3.5 cm) in the posterior wall of the right atrium partially obstructing the tricuspid valve. Biopsy revealed DLBCL. Given new-onset lymphoma, a human immunodeficiency virus (HIV) test was done and came back positive. CD4 count was 100 cells/mm^3. Chemotherapy was initiated with rituximab, cyclophosphamide, epirubicin, vincristine, and prednisone (R-CHOP). Highly active anti-retroviral (HAART) therapy was started for HIV. After treatment with R-CHOP and HAART, the patient had complete resolution of the mass and symptoms on follow-up imaging and evaluation at 6 months.

Conclusions: Mediastinal DLBCL invading the heart is a life-threatening form of non-Hodgkin's lymphoma (NHL) and early diagnosis and treatment is critical as prognosis is poor especially if diagnosed in later stages of the disease. Testing for HIV is important as 5% of HIV patients are susceptible to developing NHL.

MeSH Keywords: Lymphoma, AIDS-Related • Lymphoma, B-Cell • Lymphoma, Large B-Cell, Diffuse

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/917159

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Background

Primary mediastinal diffuse large B cell lymphoma (DLBCL) is a rare and rapidly progressive malignancy [1]. It constitutes 2% to 4% of non-Hodgkin's lymphoma (NHL) and the prognosis differs between these 2 malignancies. Primary cardiac lymphoma (PCL) is a very rare malignancy that is confined to the heart and pericardium and accounts for 1.3% to 3% of all primary cardiac tumors. In contrast, cardiac metastases from any histologic tumor types are 20- to 40 times more common [2]. Although it has been reported that lymphomas have cardiac metastases in 8.7% to 27% of cases, a mediastinal DLBCL infiltrating the heart and presenting as a large intracardiac mass is extremely rare [1,3]. This presentation was seen in our patient.

Case Report

A 57-year-old African-American female presented with an 8-week history of 30-pound unintentional weight loss, fatigue, productive cough with yellow sputum and exertional dyspnea. Her vital signs were stable and within normal limits. Physical examination was unremarkable, without lymphadenopathy. No heart murmurs were auscultated, and the lungs were clear to auscultation bilaterally. Laboratory studies revealed white blood cell count of 9.0 10^9/L, hemoglobin of 8.6 g/dL, mean corpuscular volume of 81.0 fL, red blood cell distribution width of 16.9%. All measured electrolytes, renal and function, coagulation studies and troponin levels were unremarkable. Electrocardiogram showed Q waves in V1 with low voltage QRS complexes and nonspecific ST changes suggestive of infiltrative disease. Chest x-ray showed no cardiomegaly, pleural effusion, or pulmonary vascular congestion. CT chest with contrast showed a large (7.4×4.7×4.5 cm) right atrial mass communicating directly with the posterior mediastinum and extending to the esophagus, with associated hilar and mediastinal lymphadenopathy (Figures 1–3). Initially a transthoracic echocardiogram (TTE) was done and did not show any masses or abnormality. The initial TTE was read as normal. Due to high clinical suspicion of a cardiac mass and given the patient's presenting

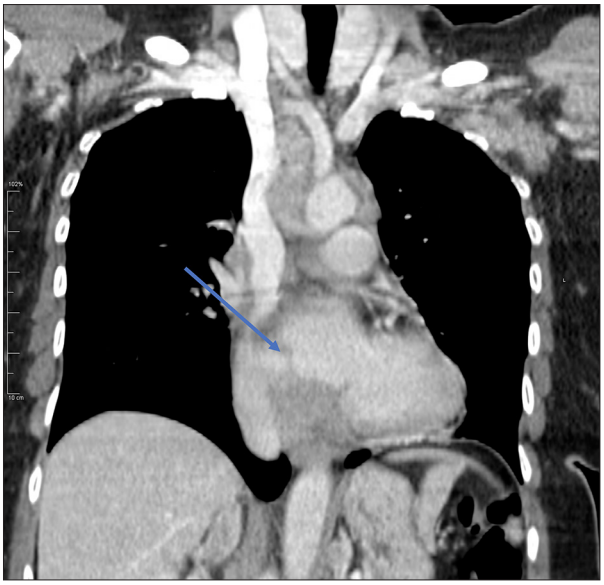

Figure 1. Computed tomography scan showing coronal view of right atrial mass (arrow).

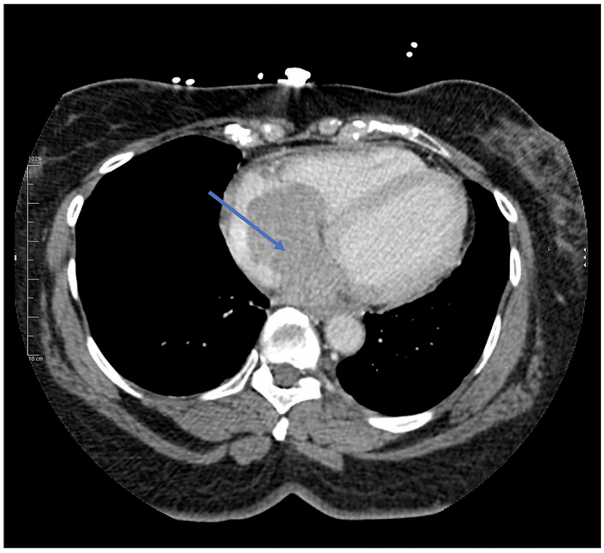

Figure 2. Computed tomography scan with transverse view. There is a right atrial mass with partial obstruction of the tricuspid valve (arrow).

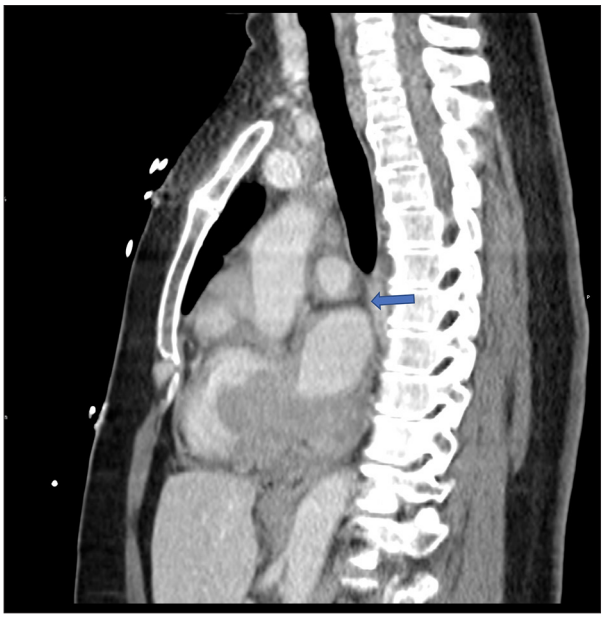

Figure 3. Computed tomography with sagittal view. There is posterior mediastinal involvement with no radiographic evidence of a fat plane separating the intracardiac mass and the esophagus (arrow).

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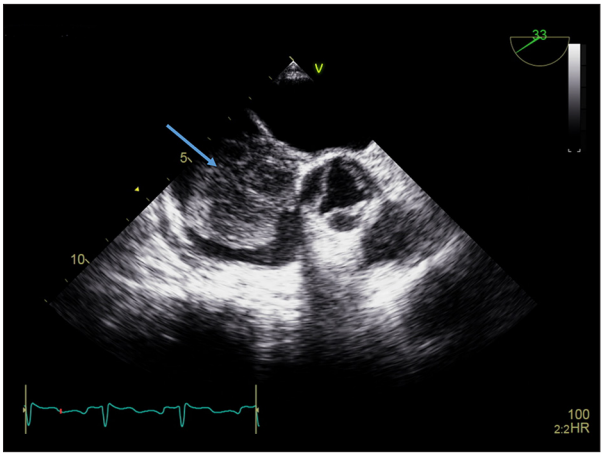

Figure 4. Transesophageal echogram (TEE) parasternal short view. There is a right atrial mass (arrow) with partial obstruction of the tricuspid valve with involvement of the aortic annulus. The mass is described as slightly lobulated and rounded, attached to the posterior wall of the right atrial and slightly to the septum with a wide base. The tumor is almost filling the whole right atrial cavity.

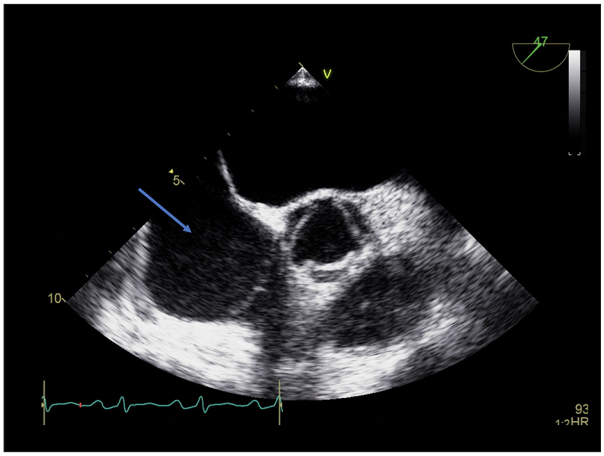

Figure 5. Transesophageal echogram (TEE) parasternal short view. There is resolution of the right atrial mass with fully intact tricuspid and aortic valves (arrow). The right atrial was noted to be slightly dilated. This was done after 6 weeks of rituximab, cyclophosphamide, epirubicin, vincristine, and prednisone (R-CHOP) alone.

symptoms, a transesophageal echo (TEE) was done and confirmed a mass (3.5×3.5 cm) in the posterior wall of the right atrium that was partially obstructing the tricuspid valve involving the inter-atrial septum without any pericardial effusion (Figure 4). There were no hemodynamic complications from obstruction of the tumor. A sternotomy was subsequently performed. Upon entrance to the pericardial cavity, the heart appeared to have a very whitish, thickened wall. A hard mass was palpated on the RV outflow tract. There were enlarged lymph nodes on the right side of the aorta. The mass was palpated, and the posterior right atrium was densely thickened. The mass appeared to be extending into the posterior mediastinum and, because of this, resection was not pursued due to extent of tumor. A biopsy of multiple mediastinal lymph nodes and the mass confirmed DLBCL. In contrast, a bone marrow biopsy did not show any evidence of lymphoma with normal trilinear hematopoiesis. The patient was subsequently diagnosed with mediastinal DLBCL (stage II BE) extending into the right atrium. The patient was found to be syphilis and human immunodeficiency virus (HIV) positive, with CD4 count of 100 cells/mm^3. Hepatitis B and C and tuberculous testing were negative.

Highly active antiretroviral therapy (HAART) therapy and 6 cycles of chemotherapy with rituximab, cyclophosphamide, epirubicin, vincristine, and prednisone (R-CHOP) were completed, with complete resolution of the mass on subsequent Positron emission tomography-computed tomography (PET/CT) imaging (Figure 5). The patient was followed up for 6 months after the last cycle of chemotherapy and found to be completely asymptomatic.

The patient's initial presenting symptoms of dyspnea with exertion, fatigue, and weight loss may be explained by her anemia and new diagnosis of HIV. Baseline hemoglobin was not available. Her cough may be due to compressive symptoms caused by the heart mass. Interestingly, she was found to be hemodynamically stable throughout her hospitalization even with her significant TEE findings. However, cardiac tumors are also known to be the great mimickers with non-specific symptoms and diagnostic findings. Symptoms can vary and the differential diagnosis can be broad. Diagnosis can also be difficult because cardiac masses on imaging can mimic other tumors like myxomas, angiosarcomas, or rhabdomyomas.

Discussion

Non-Hodgkin's lymphoma (NHL) is one of the acquired immune deficiency syndrome (AIDS)-defining illnesses and can be the initial presentation in 5% of patients with new onset NHL. The mediastinum is a rare primary site for AIDS-related NHL. The mediastinum can be extra-nodal but this such presentation is suggestive of advanced AIDS [4]. Patients who are HIV seropositive have a 200 times higher lifetime risk of developing NHL [4].

Differential diagnosis of a right atrial intracardiac mass should include atrial myxoma, rhabdomyosarcoma, atrial thrombus, and lymphoma. Some other conditions such as pseudomass partial hypertrophy of the heart can mimic cardiac tumors, especially when the clinical investigation includes only TTE. Given the rarity of primary cardiac tumors, patients presenting with an intracardiac mass and associated mediastinal

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lymphadenopathy should be evaluated for direct extension of the mediastinal lymphoma. Although there are multiple proposed mechanisms of lymphoma metastasis to the heart, direct extension and infiltration of the mediastinal DCLBL into the right atrium likely explained the intracardiac mass in our patient [5]. Interestingly, as NHL tumors respond well to chemotherapy, a diagnostic lymph node biopsy is preferred over invasive surgical intervention. Although in our patient there was a high initial clinical suspicion of sarcoma, less invasive techniques could have been used prior to performing a sternotomy. For example, a mediastinal lymph node biopsy may have been performed which would have likely confirmed the diagnosis of malignant lymphoma without the need for sternotomy.

Signs and symptoms may be non-specific and include dyspnea, arrhythmias, pericardial tamponade or effusion, left ventricle or right ventricle outflow tract obstruction, tumor embolization, and valvular heart disease [3]. Other findings may include superior vena cava syndrome, peripheral embolization, and an intracardiac thrombus [6]. However, intracardiac tumors originating from lymphomas are usually not discovered until autopsy.

As part of the initial workup of an intracardiac mass, it is important to highlight that a cardiac TTE is the initial imaging test. However, a TTE may underestimate the size and extent of the mass or not detect a mass as observed in our case. Initially, the TTE did not show a mass. The TTE images were revisited and after changes to the contrast settings in the reading software, a hypoechoic mass was seen that was initially missed by the interpreter. TEE has better sensitivity and diagnostic value for intracardiac masses than TTE [2]. When suspecting an intracardiac mass with negative TTE findings, the next step should be a TEE as this test has better diagnostic value. Chest X-ray may demonstrate cardiomegaly and signs of heart failure, which are non-specific findings [7]. Subsequent CT and magnetic resonance imaging will help determine size, spread of tumor, mediastinal involvement, and blood flow obstruction [3]. A PET/CT is also completed for staging and prognostication.

Tissue biopsy is essential in making the diagnosis given the broad differential of intracardiac masses. In the past, thoracotomy was done for tissue biopsy however less invasive tests are now used. These include TEE with biopsy, percutaneous intracardiac biopsy with combined fluoroscopy, endomyocardial biopsy, and pericardial fluid testing [3]. Pericardial fluid cytological testing may be used if pericardial effusion is present [6].

The treatment of relatively aggressive mediastinal DLBCL is similar to PCL; however, the former has a very poor prognosis due the rapid progression and invasion of the cancer. Patients with mediastinal DLBCL infiltrating the heart and PCL are usually diagnosed at a late stage of the disease which correlates to a poor prognosis [8]. As first line treatment in patients diagnosed with DLBCL, a chemotherapy regimen with R-CHOP has shown good response rates. Though this patient was 57 years old, fertility preservation should be addressed in younger patients before initiation of chemotherapy. Patients with previous infection to hepatitis B virus (hepatitis surface antigen negative and core antibody positive) treated with R-CHOP have a chance of reinfection by the virus [9]. Antiviral prophylaxis or regular hepatitis B virus DNA surveillance and antiviral therapy if there is reinfection should be done [9].

Intracardiac DLBCL tumors localized to the heart are also treated with radiotherapy. PCL may be surgically resected if localized to the heart. Early diagnosis of mediastinal DLBCL infiltrating the heart is critical as it is only resectable at early stages of disease due to rapid growth and invasion [6]. Surgery allows time for chemotherapy to work especially if the patient has hemodynamic instability. Surgery can also be palliative to help correct hemodynamics and improve blood flow to the lungs in the case of right ventricle outflow obstruction [10].

Post treatment surveillance should include FDG-PET/CT scanning [9]. About 30% of cases involving DLBCL will relapse. Biopsy should be done if relapse is suspected [9]. Allogenic stem cell transplantation should be considered for patients with early relapse or refractory disease. Patients who are not able to tolerate intense chemotherapy during relapse may be considered for less toxic regimens like rituximab, gemcitabine, and oxaliplatin [9]. In patients with poor cardiac function, pixantrone which is a novel anthracycline, may be used due to less cardiotoxicity [9]. Our patient was lost to follow up after 6 months.

Current guidelines recommend routine follow up in patients with DLBCL for 2 years after treatment. Patients who are found to have no evidence of relapse at 2 years have a life expectancy similar to the general population. Regular history and physical examinations as well as complete blood counts are needed. Physical examinations need to emphasize the possible extent of secondary tumors and assess for complications from chemotherapy. CT scans up to 2 years post treatment are also recommended. Regular surveillance with PET scans is not recommended [9].

Patients with DLBCL are more likely to be immunosuppressed due to HIV, Epstein-Barr virus (EBV), and transplant recipients. EBV and HIV testing should be done as part of the initial workup. Studies from patients in North America and Europe show complete remission rates of 48% to 63% and 1-year overall survival of 60% to 80% with CHOP and HAART [4]. Rituximab has been studied and a clinical trial published in 2005 showed no statistical significance in progression-free survival and overall survival due to treatment related adverse events however more studies are needed [9]. Treatment of DLBCL in

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HIV patients depends on results of phase 2 clinical trials, retrospective studies, and specialist-based recommendations [9].

Prognosis of DLBCL involving the heart is very poor with a 10% survival rate in 9 to 12 months without treatment [6]. Although mediastinal DLBCL has a high risk of mortality if untreated, treatment may be curable with intense chemotherapy [11]. There are various prognostic factors affecting survival rate. These include bone marrow and extra-nodal involvement as well as extent of disease. Survival even with treatment can be as low as 8 months in AIDS-associated NHL depending on these prognostic factors [11]. In addition, several studies have shown that low CD4 counts correlate with a worse prognosis. However, there has been a substantial increase in survival post-HAART era [4].

Conclusions

Mediastinal DLBCL infiltrating the heart is an aggressive form of NHL and early diagnosis and treatment is crucial as prognosis can be very poor especially in later stages of the disease. HIV testing is important in a patient who presents with NHL as immunocompromised patients are more susceptible to the disease. Furthermore, it is important to differentiate PCL from mediastinal DLBCL as the prognosis differs. Both can be treated with surgery. Mediastinal DLBCL infiltrating the heart is only resectable in early stages of the disease and early treatment with R-CHOP is important in management. Even with treatment, mortality is high. Our patient was treated successfully with chemotherapy alone showing complete resolution of the mass on subsequent TTE at 6 months after diagnosis.

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Conflict of interest

None.

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