The first case of primary cardiac lymphoma, diffuse large B-cell type, successfully treated with EPOCH-R

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Case Report

Abstract

Primary cardiac lymphomas are rare non-Hodgkin lymphomas. They account for less than 1% of intrinsic cardiac tumors and extranodal Non-Hodgkin lymphomas. Currently, there are no formal established guidelines for the treatment of primary cardiac lymphomas. Diffuse large B cell lymphoma is the most common subtype known to afflict the heart. This case documents the successful treatment of primary cardiac diffuse large B-cell lymphoma in an elderly male with sarcoidosis. To our knowledge this is the first published case report illustrating the use of the EPOCH-R with a modest pre-phase cytoreduction consisting of steroids, cyclophosphamide and etoposide for this indication. This strategy prevented perforation of the tumor during therapy and decreased cardiotoxicity.

Keywords: PCL (Primary cardiac lymphoma), DLBCL (Diffuse large B cell lymphoma), EPOCH-R (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin).

Introduction

Primary cardiac lymphomas are rare non-Hodgkin lymphomas. They account for less than 1% of intrinsic cardiac tumors and extranodal Non-Hodgkin lymphomas.¹ Prior to advanced imaging techniques, primary cardiac tumors were largely observed post-mortem.² Patients with primary cardiac lymphoma (PCL) can present with a variety of manifestations including heart failure, chest pain, dyspnea, arrhythmias, and tamponade.² Presently, there are no formal established guidelines for treatment of primary cardiac lymphomas. This case documents the successful treatment of a diffuse large B-cell PCL in an elderly patient with sarcoidosis.

Case presentation

Our patient is a 72-year-old white man with past medical history significant for paroxysmal atrial fibrillation and sarcoidosis affecting the pulmonary, renal, and cutaneous systems who presented with two weeks of palpitations, dyspnea on exertion and lightheadedness. He was evaluated by his cardiologist who recommended an elective atrial fibrillation radiofrequency ablation (RFA). Prior to the planned procedure a transesophageal echocardiogram was performed which revealed a large tissue density within the pericardial space, adjacent to the free wall of the right ventricle and right atrium, and invading the myocardium with extension through the interatrial septum (Figure 1). The RFA was aborted and the patient was admitted for further evaluation of the new cardiac mass, initially suspected to be cardiac sarcoidosis.

Subsequent work up included a cardiac MRI, which displayed a dense 7.5 cm by 3.5 cm mass involving the right ventricle and right atrium, wrapping around the great vessels (Figure 2). Right heart cardiac catheterization with endomyocardial biopsy was performed which revealed clusters of large atypical B lymphoid cells with the following immunophenotype: CD30+, CD79a+, Pax5+, Alk 1+, CD138+, CD 10-, Bcl 2+, Bcl 6+, CD45+, focally CD20+, Ki67: 80-90% (Figure 3). These findings were consistent with diffuse large B cell lymphoma (DLBCL). His PET-CT demonstrated absence of extracardiac lesions, confirming the diagnosis of primary cardiac lymphoma (PCL) (Figure 4).

The patient began treatment with a EPOCH-R³ (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) modified chemotherapy based regimen which consisted of a pre-phase treatment with dexamethasone 12 mg once daily for four days, a cumulative dose of cyclophosphamide 600 mg/m² over five days and etoposide 50 mg/m² for three days. Doses of cyclophosphamide and etoposide were initiated at lower
doses and titrated upward to reach the target dose. This strategy was invoked based upon prior experiences and studies that suggest that a modest pre-phase cytoreduction reduces the risk of cardiac perforation. Rituximab was given on day six. He was also given granulocyte colony stimulating factor (GCSF).
Figure 2A: Cardiac MRI T1 weighted black blood image showing mass anterior to the right atrium and right ventricle within the pericardial space that is isointense to the muscles. Figure 2B: Cardiac MRI T2 weighted black blood image showing right heart hyperintense mass.

Figure 3: Hematoxylin and Eosin stain (H&E) 40x showing clusters of large atypical B lymphoid cells. Immunostains are positive for B cell markers CD79a, CD30 and Pax5.
Our patient was observed closely in the cardiac intensive care unit throughout the duration of chemotherapy due to the high risk of fatal arrhythmia, tamponade, perforation and heart failure. Interim restaging, confirmed complete remission of the intracardiac mass. His post chemotherapy TTE demonstrated a slight reduction in ejection fraction (Figure 1). He received a total of three cycles of EPOCH-R and remained hemodynamically stable within the hospital. No further chemotherapy was given due to a decline in the patient’s performance status.

Discussion

This case illustrates a patient with primary cardiac diffuse large B cell lymphoma who presented with cardiac manifestations. He was treated with a modified EPOCH-R regimen consisting of pre-phase therapy with dexamethasone, cyclophosphamide and etoposide for cytoreduction of the cardiac mass. Currently, there are no established guidelines for the treatment of primary cardiac lymphomas. Some patients have been treated with primary surgical interventions followed by chemotherapy while others with CHOP based chemotherapy strategies with or without radiation. In a systematic review of primary cardiac lymphoma cases, approximately 90% of patients were treated with chemotherapy and 28% with surgery. Surgery is indicated in the setting of severe hemodynamic instability.

Diffuse large B-cell lymphoma is the most common primary cardiac lymphoma described in the literature in both HIV and immunocompetent patients. The treatment of DLBCL of cardiac origin involves careful consideration of important treatment ramifications including perforation and arrhythmias. Other studies have reported successful use of a low-dose and slow increase of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) as well as a 50% dose reduction in the cyclophosphamide and doxorubicin administered during the first cycle to prevent perforation due to rapid tumor regression of the primary cardiac lymphoma. We have adopted a novel conservative gradual pre-phase treatment plan for patients with DLBCL PCL.

Doxorubicin is an excellent anti-neoplastic agent to be utilized in the treatment of cardiac DLBCL. Doxorubicin, while being cardiotoxic, is also the most important drug for this disease, hence the careful consideration of cardiac status is required before making a decision to
use an anthracycline.\textsuperscript{8,9} Patients with PCL may present with a mild compromise of their ejection fraction due to the lymphoma and not from intrinsic cardiomyopathy. This appears to improve after pre-treatment cytoreduction, making the decision to use an anthracycline easier. Furthermore, liposomal formulations of doxorubicin offer a higher area under the curve and are less cardiotoxic.\textsuperscript{9,10}

**Conclusion**

This is the first documented case of primary cardiac diffuse large B cell lymphoma successfully treated with EPOCH-R consisting of a modest pre-phase cytoreduction with steroids, cyclophosphamide and etoposide. This regimen reduces the risk of cardiac perforation in patients with relatively normal ejection fractions.

**Conflict of interest**

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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**References**