Cardiac Recurrence of Diffuse Large B-cell Lymphoma More Than a Decade After Attaining Complete Remission

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Conflict of interest: None declared

Patient: Female, 79
Final Diagnosis: Cardiac recurrence of DLBCL
Symptoms: Cardiogenic shock
Medication: —
Clinical Procedure: Biopsy specimen
Specialty: Cardiology/Hematology

Objective: Unusual clinical course
Background: Although diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma in adults, isolated cardiac recurrence of DLBCL which can cause fatal heart failure via various mechanisms is extremely rare. Furthermore, the frequency of recurrence of DLBCL more than 5 years after attaining complete remission is as low as 3.6%. The rate of complete remission and partial remission of DLBCL that have recurred 5 or more years after attaining the initial remission are reported to be 61% and 29%, respectively.

Case Report: A 79-year-old female with a history of DLBCL at the age of 63 years was transferred to our hospital because of cardiogenic shock. Although cardiac tamponade was suspected, her hemodynamics did not improve with pericardiocentesis. Thoracotomy showed an elastic to hard tumor occupying most of the right ventricular wall. Cytological examination of the pericardial effusion and histological examination of a biopsy of the tumor yielded a diagnosis of DLBCL; this information was available only post mortem. Immunostaining of a biopsy specimen suggested that her cardiac tumor was a recurrence of her lymphoma diagnosed 16 years previously. Bone marrow aspiration was not performed; no recurrences were detected in any other site. This patient thus appeared to have an isolated cardiac recurrence of DLBCL.

Conclusions: When managing a patient with a cardiac tumor and a past history of DLBCL, albeit more than a decade previously, establishing a histological diagnosis as early as possible would facilitate possible successful treatment and a good prognosis.

MeSH Keywords: Cardiac Tamponade • Heart Neoplasms • Lymphoma, Large B-Cell, Diffuse • Recurrence • Shock, Cardiogenic

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/910787

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Diffuse large B-cell lymphoma (DLBCL) is the commonest subtype of non-Hodgkin lymphoma in adults [1]. The standard regimen of rituximab and anthracyclines achieves complete remission (CR) in 76–78% of patients [2]. The frequency of recurrence more than 5 years after attaining complete remission is as low as 3.6%. Seventy-three percent of recurrences occur in extranodal sites, such as bone marrow, bone, skin, and sinuses. The 3-year survival rate after recurrence and treatment with autologous stem-cell transplantation is reportedly 83% [3]. We here report a rare case of fatal cardiac recurrence of DLBCL 16 years after achieving complete remission, indicating the importance of making a diagnosis as quickly as possible to maximize the chance of preventing death from this serious condition.

Case Report

A 79-year-old female with a history of stage 1 DLBCL in a left submandibular lymph node who had achieved CR with radiation therapy at the age of 63 years was transferred to our hospital because of cardiogenic shock. She did not have history of smoking, alcohol consumption, or allergies. She had been monitored carefully with neck ultrasonography annually until the age of 76 years with no evidence of local recurrence. She had developed a cough at 3 days prior to admission and dyspnea on the following day. Diuretic and antibiotic medications prescribed by her family doctor at a small community hospital were ineffective. She was admitted to that hospital with a diagnosis of heart failure and pneumonia on the previous day. After administration of nitroglycerin she went into shock. Catecholamine administration was ineffective, and she was therefore transferred to the emergency department of our hospital.

On admission, she was in a coma with Glasgow Coma Scale, E1, V1, M1. She had a feeble radial artery pulse, unmeasurable blood pressure, and severe cold sweats. Physical examination revealed decreased breath sounds in the lower left lung field and mild lower extremity edema. Electrocardiography showed complete AV block and ST elevation in the inferior leads (II, III, aVf). Echocardiography revealed preserved left ventricular ejection fraction, thickening of the myocardium of the right ventricular (RV) wall, and a pericardial effusion. Laboratory tests showed a white blood cell count of 25.0×10^9/L, C-reactive protein concentration of 80.9 mg/L, and lactate dehydrogenase of 2628 IU/L (Table 1), and negative HCV antibody. Blood gas analysis showed lactate of 12.7 mmol/L. Her systolic blood pressure gradually increased, coming up to 100 mmHg with administration of fluids and vasopressor therapy. After intratracheal intubation, coronary angiography was performed. Although all coronary arteries showed some narrowing, the thrombolysis in myocardial infarction trial grade was only 3. Left ventriculography showed no evidence of asynergy. These findings excluded a diagnosis of acute coronary syndrome. Chest-abdominal computed tomography (CT) with contrast enhancement revealed an
area of low attenuation on the anterior surface of the pericardi-
um and of high attenuation suspected to denote slight extrav-
asation around the right coronary artery (Figure 1). However,
no extravasation from the right coronary artery was identified
on coronary angiography. There was neither obstruction nor
wall irregularity in the right coronary artery itself. There was
no evidence of hepatosplenomegaly or enlarged lymph nodes.
Her shock was therefore suspected to have been caused by
pericardial effusion and hematoma consequent to perfora-
tion of the right coronary artery. Removal of 180 mL of bloody
effusion by pericardiocentesis had a minimal effect on her hemody-
namic state, only increasing her blood pressure by 10 mm Hg.
Median sternotomy, performed to achieve further drainage and
make a definitive diagnosis, revealed an elastic to hard tumor
in most of the anterior RV wall with a small amount of serous
pericardial effusion (Figure 2). Direct echocardiography re-
vealed a mass with unclear boundaries in the anterior RV wall
(Figure 3) through which the right coronary artery was running.
Severe RV systolic dysfunction was also found. She was diag-
nosed as having untreated cardiogenic shock caused by RV
systolic dysfunction as a result of invasion of the RV wall by
some kind of malignancy. The chest was closed after obtaining
a biopsy from the tumor. Her blood pressure decreased grad-
ually, and she died 22 hours after admission. A post mortem
diagnosis of DLBCL was made on the basis of cytological ex-
amination of the pericardial effusion and pathological exami-
nation of the biopsy specimen (Figure 4).

Flow cytometry performed 16 years previously when diag-
nosing the original DLBCL had shown CD19 (+), CD20 (+),
CD10 (+), and IgG (+). In contrast, immunostaining of the bi-
opsy specimen of the current cardiac tumor revealed CD20 (+),
CD3 (–), suggesting that it was an isolated cardiac recurrence
of stage 1 DLBCL presenting 16 years after achieving CR [4].

This conclusion was not definitive, however, because evidence
of other recurrence had been sought only by whole body CT
and without bone marrow aspiration.
Our patient had a recurrence of DLBCL in the wall of the RV 16 years after achieving CR of stage 1 DLBCL; such recurrences are extremely rare. Annual ultrasonographic follow-up of the left submandibular and neck lymph nodes had been terminated with no evidence of recurrence 12 years after achieving CR. In the 1970s, it was believed that DLBCL did not recur more than 2 years after achieving CR [5]. However, several recurrences occurring more than 5 years after CR have since been reported [6]. The incidence of such recurrences is as low as 3.6% and the median time from CR to recurrence reportedly 7.4 years [3]. Up to 73% of recurrences of DLBCL occur in extranodal sites such as bone-marrow, bone, skin, and nasal sinuses [3].

According to autopsy data, 10% of patients with malignant lymphoma have cardiac involvement [7,8]. However, most cardiac DLBCL diagnosed in living patients and treated with salvage chemotherapy is either primary cardiac DLBCL or synchronous metastases from other sites found at the time of initial diagnosis. Thus, isolated cardiac recurrence of DLBCL is extremely rare [9,10]. We found only 1 case report of recurrence of DLBCL in the heart more than 2 years after attaining CR [11]. Furthermore, we were unable to find any reports of cardiac recurrence diagnosed more than a decade after attaining CR, as was the case with our patient. The rates of CR and partial remission of DLBCL that have recurred 5 or more years after attaining the initial remission are reportedly 61% and 29%, respectively [12]. Therefore, although very rare, physicians should consider DLBCL in the differential diagnosis of a cardiac tumor in a patient with a history if DLBCL because...
multimodality therapy of such tumors has a high probability of success.

The manifestations of cardiac tumors vary greatly according to their location. There are 4 possible mechanisms: the first is obstruction of intra-cardiac blood flow and functional failure of cardiac valves; the second is various types of arrhythmia induced by tumor invasion of the cardiac walls; the third is the presence of a large pericardial effusion; and the fourth is cerebral infarction caused by tumor emboli from the left side of the heart [13]. On admission to our hospital, our patient was in cardiogenic shock as a result of right-cardio circulatory failure and complete AV block; this presentation was compatible with the first and second possible aforementioned mechanisms.

In general, DLBCL is one of the most aggressive types of lymphoma and can progress extremely rapidly, as illustrated by a report of a patient with palpitations who had normal findings on echocardiography and examination by a cardiologist at 3 weeks prior to presenting with heart failure caused by an 8 cm mass in the right atrium and ventricle [14]. It is also well known that cardiac DLBCL can cause circulatory failure at an early stage [15,16]. There are a few published case reports of patients with acute right-sided heart failure who underwent emergency tumor excision by the Fontan procedure before successfully undergoing chemotherapy or who received chemotherapy with the support of arterio-venous extracorporeal membrane oxygenation (ECMO) [14,15,17,18]. Because invasive treatments such as surgical revascularization, tumor excision, and assisted circulation with ECMO must often be considered in patients with rapidly progressive cardiac failure, prompt diagnosis and swift decision-making about the appropriateness of such invasive procedures in an individual are essential.

When we performed thoracotomy on our patient, we concluded that her death would have been inevitable regardless of whether her tumor had been excised. In retrospect, however, we could have considered administering chemotherapy with ECMO support given the high reported rates of CR in DLBCLs overall of 76–78%, and in cardiac DLBCL of 59% [19].

Although cytological examination of pericardial fluid is the easiest means of diagnosing cardiac lymphoma, its sensitivity is only 67%. Thus, if the results are negative, further diagnostic approaches such as endomyocardial biopsy with or without of ultrasound guidance, including transesophageal echocardiography (TEE), or biopsy via mediastinoscopy or thoracotomy, are required [20]. Endomyocardial biopsy has been recommended as a standard procedure for diagnosing cardiac tumors, guidance with TEE whenever possible being advised [21]. Transvenous endomyocardial biopsy under TEE guidance is useful, simple, and safe [22–25] despite usually requiring local pharyngeal or general anesthesia. In contrast, the recently introduced procedure of transvenous biopsy via cardiac catheterization with the guidance of intracardiac echocardiography (ICE) does not require such anesthesia and can facilitate assessment of cardiac structure [26–30]. Physicians who are involved in diagnosing cardiac tumors should be well versed in use of ICE.

Conclusions

When managing a patient with a cardiac tumor and a past history of DLBCL, even when that DLBCL has been in CR for more than a decade, it is mandatory to make a histological diagnosis as early as possible because of the possibility of successful treatment and a good prognosis.

Acknowledgments

We thank Dr. Kenji Hirahara for useful advice and warm encouragement and Dr. Trish Reynolds, MBBS, FRACP, from Edanz Group for editing a draft of this manuscript.

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Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)]
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