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Case Report
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Treatment of a Myocardial Infiltrating Mediastinal Diffuse Large B-cell Lymphoma: A Case Report

Hassane Abdallah[1,2], Gabriel Fortin[3], Hussam Achour[2], Pier-Alexandre Vasil[1] and Marianne Coutu[1]*

[1]Cardiac Surgery Department, University of Sherbrooke, Quebec, Canada

[2]Prince Sultan Cardiac Center, Al Hasa, Al Hofuf, Saudi Arabia

[3]Internal Medicine Department, University of Sherbrooke, Quebec, Canada

Abstract

Although primary cardiac lymphoma is rare and challenging to diagnose due to nonspecific symptoms, secondary infiltration is more common, usually from the adjacent lung, breast, esophagus or thymus. However, very few cases describing the treatment of a myocardial infiltrating lymphoma are found in the literature. We report the case of a 28-year-old immune competent woman who presented with rapidly progressing heart failure symptoms and ischemic changes on her electro cardiogram. Different modalities of cardiac imaging showed a large mass compressing and infiltrating the right side of her heart. A biopsy was done and revealed the diagnosis of a mediastinal B-cell lymphoma. She was treated accordingly with steroids and multi cycles of chemotherapy (R-EPOCH protocol), without any major adverse cardiac event. Although the risk of a myocardial rupture remains possible, we describe a case which demonstrates that a myocardial infiltrating lymphoma can safely be treated with standard chemotherapy regimens.

Keywords: Diffuse large B-cell lymphoma; Mediastinal lymphoma; Myocardial infiltration; Heart rupture

Abbreviations

DLBCL: Diffuse Large B-Cell Lymphoma; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography; R-EPOCH: Rituximab, Etoposide, Prednisone, Vincristine Sulfate, Cyclophosphamide, Hydroxydaunorubicin; STEMI: ST-Elevation Myocardial Infarction; NHL: Non-Hodgkin Lymphoma; PMBL: Primary Mediastinal B-Cell Lymphoma

Learning Objective

- To be aware of the possibility of heart infiltration by an adjacent lymphoma and to be able to diagnose it, considering that the clinical presentation may be unspecific.
- To acknowledge that the risk of cardiac rupture secondary to chemotherapy is smaller than the risk encountered by not treating the lymphoma.

Introduction

Lymphoma's involvement of the heart is uncommon. In very rare instances, it can be a primary cardiac lymphoma, with only a few cases being reported. Given the rarity of the primary type, the early diagnosis is often difficult to make. It is generally aggressive and nearly 80% of the tumor type is Diffuse Large B-Cell Type Lymphoma (DLBCL) and in some other rare cases, Burkitt lymphomas. A secondary cardiac lymphoma is more common. When it happens, it usually is secondary to a systemic malignancy. This means that the lymphoma may have originated from another part of the body, usually an adjacent organ.

However, there are many predisposing factors that may contribute to lymphoma formation and development, but no specific risk factors have been identified for lymphoma involving the heart.

The treatment options depend upon each individual case's specific circumstances. It varies from surgical therapy to radio and/or chemotherapy with or without supportive treatment.

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Correspondence:
Hassane Abdallah, Cardiac Surgery Department, 10550 Place de l'Acadie #318, H4N 0B3, Montreal, Quebec, Canada, Tel: 4389893555; E-mail: abdallahhassane@hotmail.com

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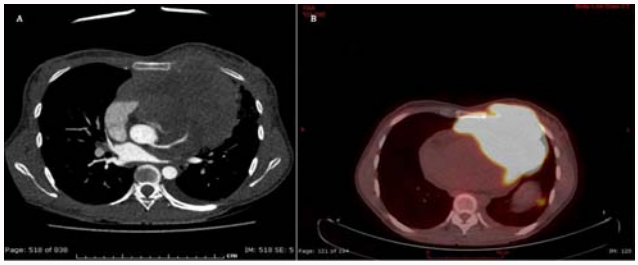

Figure 1: Initial imaging performed before any treatment attempted. A) Aortic CECT (Contrast-Enhanced CT-scan) shows a large heterogeneous invasive anterior mediastinal mass with pleural, anterior chest wall and pericardial invasion. Moreover, there is soft tissue infiltration surrounding the left coronary artery with wall irregularities; B) FDG-PET (Fluoro Desoxy Glucose-Positron Emission Tomography) scan shows the large hypermetabolic (SUV: 17) anterior mediastinal mass with evidence of chest wall & pericardial invasion.

Case Report

A 28-year-old non-smoker Caucasian woman, mother of three kids, who had no history of any chronic illness and denied excessive alcohol consumption, presented to the emergency department complaining of a progressive left shoulder and back pain, palpitations, fatigability, dyspnea on exertion, orthopnea and paroxysmal nocturnal dyspnea. All those symptoms developed over the last few months. She also described a swollen mass on her chest and another in her back that made it uncomfortable for her to lie on her back. She had no history of weight loss, but described occasional night sweats.

On clinical examination, she was fully conscious, alert and oriented. Her blood pressure was 138/90 millimeter of mercury (mmHg), heart rate 118 beats per minute, body temperature 36.4°C, respiratory rate 20 per minute, and oxygen saturation 100% on room air. An electrocardiogram was immediately done and revealed an ST-segment elevation in leads V2 through V4 with reciprocal ST depression in leads III and a VF. Aspirin, Ticagrelor and intravenous unfractionned heparin were started immediately. Laboratory results revealed a white blood cell count of 9.1 g/L, hemoglobin of 125 g/L and platelets of 414 g/L. Troponin I were equivocal (0.090 ng/mL, normal: <0.034), lactate deshydrogenase was 418 (elevated). The rest of the laboratory results were normal. The patient was transferred to the cardiac catheterization lab for emergency primary coronary angiography with possible angioplasty.

The coronary angiogram showed no atheromatous lesions of the coronaries, but it revealed a stiff left anterior descending artery that did not move in the images because of an anterolateral akinesia.

Echocardiography was performed, in an attempt to understand the cause of her symptoms and her unusual coronary angiogram findings. This exam revealed a massive anterior mediastinal mass that compressed most of the right ventricle and conusarteriosus as well as a part of the left ventricle. As there was no visible separation between the pericardium and myocardium in certain views, it was suspected that the tumor infiltrated the myocardium. Moreover, the interior of the left ventricle showed a small mass at the apex, but it was hard to know if it was a trabeculae, or the infiltration by the tumor. The compression of the heart by the tumor led to an anterolateral, apical and right ventricular hypokinesia and an acceleration of the pulmonary artery flow: the maximum and average gradients of the valve were respectively 42 mmHg and 27 mmHg, with the pulmonary artery systolic pressure estimated at 42 mmHg+15 mmHg (however

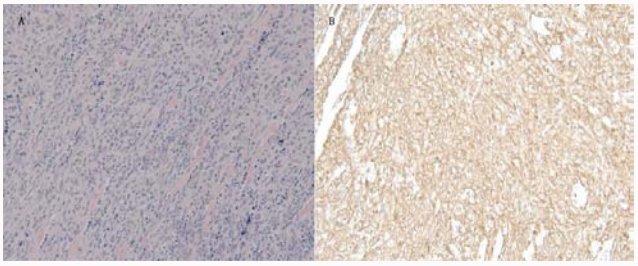

Figure 2: Pathology of the biopsied mass lesion. A) Hematoxylin and eosin stain (X20) of the left anterior hemithorax specimen showing a diffuse large cells lymphoma proliferation, dissociating the striated muscular fibers; B) Immunohistochemistry of the left anterior hemithorax specimen showing a CD20 positive proliferation.

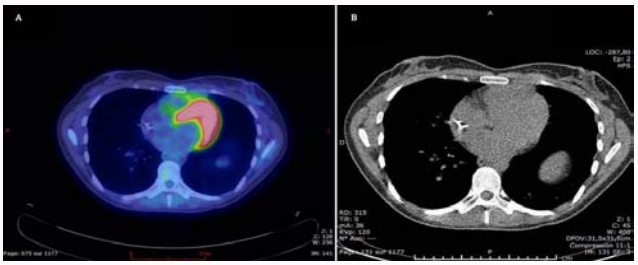

Figure 3: Imagining performed after chemotherapy. A) FDG-PET scan (obtained after five chemotherapy cycles) shows a complete remission with only a metabolically inactive anterior mediastinal lesion left; B) Low-Dose CT-scan (obtained after five chemotherapy cycles) shows the regression of the anterior mediastinal mass.

difficult to evaluate due to the presence of a very mild tricuspid regurgitation). Left ventricular ejection fraction was moderately reduced to 40% to 45%. The inferior vena cava was dilated and not compliant to respiratory variations. There was a 15 millimeters posterior pericardial effusion.

Cardiac ventriculogram, CT (Computed Tomography) scan, MRI (Magnetic Resonance Imagery) (Figure 1A) and PET (Positron Emission Tomography) scan were performed. All those imaging modalities confirmed the extension of the tumor transmurally, infiltrating the heart muscle (Figure 1B). The mass was extending to the anterior left hemithorax. A left pleural effusion was also present, as well as right hilar and paratracheal lymphadenopathies, a left lung nodule, abdominal lesions and a subcutaneous right hemithorax nodule. The Ann Arbor staging was determined as IV-X.

The mass measured 14.7 cm (transverse) by 8.7 cm (anteroposterior) by 17.2 cm (craniocaudal), infiltrating and compressing the right ventricle and especially the conus arteriosus. The aorta and pulmonary trunk were displaced by the tumor, but were still patent.

The general surgery team performed an excisional biopsy. They felt that the most accessible part of the tumor was located at the anterior left hemithorax. The biopsy was performed under local anesthesia in the OR, with a team of anesthesiologist and ENT surgeon available if there were any complications regarding her airway. The specimen was sent to our pathology department. It revealed that the mass was a non-germinal center DLBCL that originated from the mediastinum (Figure 2). The oncology team installed telemetry as a way to be warned of any complications and presented the patient to the cardiac surgery team in case of a cardiac rupture.

Seven days of supportive treatment with corticosteroids were instituted. The patient had a remarkable improvement in her clinical symptoms and signs. However, a follow-up echocardiography did not show any change on the tumor's effect to the heart.

Chemotherapy was then started with a dose-adjusted R-EPOCH protocol (Rituximab, Etoposide, Prednisone, Vincristine Sulfate, Cyclophosphamide, Hydroxydaunorubicin), according to the National Comprehensive Cancer Network guidelines [1]. Cycles were scheduled every 3 weeks.

The first three cycles were well tolerated and the cardiovascular symptoms resolved. Unfortunately, the patient developed a small bowel rupture, which was thought to be secondary to the high dosages of corticosteroids she was receiving. She underwent a successful surgery with no other complications thereafter.

The PET scan which was repeated before the fourth cycle showed marked regression in the mass's size to 5.2 cm (transverse) × 1.8 cm (anteroposterior) × 3.1 cm (craniocaudal). The previous cardiac infiltration was no longer noticeable (Figure 3A).

At latest follow-up, after 5 cycles of chemotherapy, the patient was back to her normal pre-diagnosis status. All of her cardiovascular symptoms had resolved, as well as the decline in her general status that was previously noted. There were no infectious complications and she had started back to work. Her PET scan showed a complete remission, with only an anterior mediastinal tissular lesion persisting that was metabolically inactive (Figure 3B).

Discussion

Symptoms of left heart failure, elevated pulmonary artery systolic pressure, decreased left ventricular ejection fraction and STEMI (ST Segment Elevation Myocardial Infarction) signs on the electrocardiogram can all be attributed to the compression of the heart by the tumor that was proven by different imaging modalities. Mediastinal tumors are a very rare cause for these clinical manifestations and would make an interesting discussion. However, the part that interests us the most for this report is the possibility of heart rupture caused by melting of the tumor after starting chemotherapy.

The most common subtype of Non-Hodgkin Lymphomas (NHL) is DLBCL [2]. However, Primary Mediastinal Large B cell Lymphoma (PMBL) accounts for only 2.4% of all NHL. These tumors are more frequent in women and tend to arise in the fourth decade [3]. Their usual invasive pattern is frequently causing an obstruction of the airways and/or a superior vena cava syndrome [4]. While small studies report up to a 48% rate of pericardial effusion associated with PMBL [5], documented myocardial infiltration is reported only anecdotally in the literature.

Some cases of heart rupture secondary to malignant infiltration have been described, however, they happened before chemotherapy could be started [6,7]. The reported cases of heart infiltration by DLBCL treated with chemotherapy showed remission without rupture [8-10]. We found no reports of rupture secondary to chemotherapy for an infiltrating heart tumor.

Our case seems to follow the few examples that have been reported, in that the chemotherapy reduced the mediastinal tumor dimensions without causing any major cardiac complications in spite of a transmural infiltration.

Interestingly, there are case reports that showed the use of cardiac surgery to remove a symptomatic tumor in the right atrium [11]. In order to relieve hypoxemia caused by the tumor's mass effect and a patent foramen ovale, the intraventricular mass was resected, but the infiltrating part of the tumor was left in place. Chemotherapy was started later and the patient went into remission. This seems to demonstrate that chemotherapy following heart surgery can be tolerated [12], but in our case, surgery was not indicated because corticosteroids reduced the tumor volume enough to relieve most of the symptoms.

Corticosteroids are often used to decrease multiple side effects of cancer, such as the loss of appetite or the diminished energy. In addition to these general benefits, steroids are part of virtually all lymphoma treatment regimens [1]. In fact, it is well known that lymphocytes are particularly sensible to these molecules, which induce their apoptosis by different cellular pathways that are not yet completely understood [13]. By this toxicity, they induce a reversal of most lymphomas, with a concomitant reduction of their mass effect. However, this effect is only temporary, and chemotherapy must always follow their initiation [14].

The limited literature shows that myocardial infiltration by a tumor can be treated with chemotherapy, and does not bear a major risk of complication secondary to the tumor melting. Based on the few cases found, we conclude that the untreated tumor puts the patient at greater risk of heart rupture than its treatment by chemotherapy. However, due to the dangerous implications of this complication and the limited data, it should still be anticipated. Cardiac surgery is possible for immediate relief of life-threatening conditions, but corticosteroids followed by chemotherapy are usually enough in the case of PMB.

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Conflict of Interest

The authors declare that they have no competing interests.

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