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Case Report

Primary cardiac MYC/BCL6 double hit non-Hodgkin lymphoma

Ombretta Annibali (MD)[a], Antonio Nenna (MD)[b,*], Raffaele Barbato (MD)[b], Massimo Chello (MD)[b], Pietro Sedati (MD)[c], Antonella Bianchi (MD)[d], Giuseppe Deda (MD)[d], Giuseppe Avvisati (MD)[a]

[a] Unit of Hematology, Stem Cell Transplantation, Department of Medicine, Università Campus Bio-Medico di Roma, Rome, Italy
[b] Unit of Heart Surgery, Department of Medicine, Università Campus Bio-Medico di Roma, Rome, Italy
[c] Unit of Anatomical Pathology, Department of Medicine, Università Campus Bio-Medico di Roma, Rome, Italy
[d] Unit of Diagnostic Imaging, Department of Medicine, Università Campus Bio-Medico di Roma, Rome, Italy

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ABSTRACT

Cardiac and pericardial involvement by malignant lymphoma is a rare condition. The present case report describes a case of primary cardiac MYC/BCL6 double hit non-Hodgkin lymphoma in the pericardium, and highlights the importance of a prompt diagnosis and aggressive pharmacologic treatment of this disease. In a symptomatic patient, a minimally invasive 3 cm sub-xiphoidal incision was performed under deep sedation with spontaneous ventilation to perform a pericardial biopsy. A 5 cm × 3 cm portion of pericardium was removed from above the right ventricle, thus ameliorating the extrinsic compression on the right chambers. The patient received 6 cycles of immuno-chemotherapy (rituximab plus cyclophosphamide, vincristine, and methylprednisolone), with no complications, achieving complete remission with no symptoms. Malignancies must be excluded in every case of acute pericardial disease with imaging techniques, and lymphomas should be always considered in the differential diagnosis of cardiac tumors. Complete surgical removal of the tumor is not necessary to achieve complete remission, and minimally invasive surgical approaches are an effective tool to confirm diagnosis and allow a precise histologic characterization.

<**Learning objective:** Primary MYC/BCL6 double hit non-Hodgkin lymphoma is a rare tumor of the pericardium, which requires prompt diagnosis and treatment. Minimally invasive surgical approaches are an effective tool to confirm diagnosis and allow a precise histologic characterization. Pericardial tumors should always be considered in the differential diagnosis of acute pericardial disease presenting with pericardial effusion. Double hit diffuse large B cell-lymphoma has a poor prognosis with standard chemotherapy and the treatment should be tailored according to the patient's comorbidities and performance status.>

Introduction

Cardiac and pericardial involvement by malignant lymphoma is a rare condition, representing approximately 1% of cardiac tumors and 0.5% of extra-nodal non-Hodgkin lymphoma, with diffuse large B cell lymphoma being the most common type [1]. Early symptoms are cardiac failure, syncope, arrhythmia, and pericardial effusion [2], but diagnosis is suspected with cardiac imaging and confirmed histologically. In addition to having a difficult diagnosis, prognosis is poor since patients usually die within a few months after diagnosis due to systemic involvement [3]. The present case report describes a case of primary cardiac MYC/BCL6 double hit non-Hodgkin lymphoma in the pericardium, and highlights the importance of a prompt diagnosis and aggressive pharmacologic treatment of this disease.

Case report

An 80-year-old man with a 3-month history of dyspnea was hospitalized because of chest pain and dyspnea with mild effort (New York Heart Association class III). Blood tests were unremarkable except for high levels of lactate dehydrogenase (1608 U/L) and C-reactive protein (193 mg/L). Electrocardiogram showed atrial fibrillation with high ventricular response,

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* Corresponding author at: Department of Cardiovascular Surgery, Università Campus Bio-Medico di Roma, via Álvaro del Portillo 21, 00128 Rome, Italy.
E-mail address: a.nenna@unicampus.it (A. Nenna).

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incomplete left bundle branch block, and Q wave alterations. Physical examination showed irregular pulse with distant heart sounds. Echocardiography demonstrated a 12-mm pericardial effusion with slight compression on right chambers, with slightly reduced ejection fraction (45%). Previous medical history was unremarkable, except for well-controlled mild hypertension and smoking habit. Hemoglobin was 12.1 g/dL with no abnormalities in white blood cells count and platelet count. Subcutaneous enoxaparin (100 UI/kg b.i.d.) was started and 5 mg metoprolol were administered to slow ventricular response. Considering the clinical presentation and instrumental findings, the patient was referred for a computed tomography (CT) scan of the heart with angiographic reconstructions.

Heart CT scan showed no signs of coronary heart disease. However, pericardium was thickened with minimal infiltration of right atrium and greater infiltration of the right ventricle from the right atrioventricular region until the ascending aorta (10 cm × 4 cm × 12 cm), and determining compression of the right ventricle. With a primary diagnosis of pericardial tumor, a whole-body CT scan was performed and no other site of disease was found. Magnetic resonance imaging (MRI) of the heart confirmed a huge soft tissue mass (12 cm × 4.4 cm × 1.2 cm) infiltrating the myocardium in the right chambers. The mass was extending around the anterior surface of the ascending aorta (Fig. 1). The exact histological diagnosis was considered mandatory and therefore an open biopsy was planned.

A 3 cm sub-xiphoidal incision was performed under deep sedation with spontaneous ventilation to perform a pericardial biopsy. After accurate lysis of adherences, a 5 cm × 3 cm portion of pericardium was removed from above the right ventricle, thus ameliorating the extrinsic compression on the chamber. Overall duration of the surgical procedure was about 15 min, with no complications. After surgery, a chest tube was placed in the pericardium and was removed two days after procedure. Postoperative course was uneventful, and the patient was discharged on the 3rd postoperative day in good clinical condition, asymptomatic, with no transfusional requirements.

Histological examination demonstrated the presence of fibro-adipose tissue infiltrated by a population of loosely attached cells with big nuclei, prominent nucleoli, and numerous mitoses (Fig. 2A). Immunohistochemistry showed in these cells expression of CD20 (Fig. 2B), CD79a (Fig. 2C), Ki67 expression was 95% (Fig. 2D); MUM1 (Fig. 1E) and Bcl-6 (Fig. 2F) were also expressed. Moreover, CD5 and Bcl-2 were also positive, while CD10, CD3, CD30, CD138, and HHV-8 were negative. The result of Epstein–Barr encoding region in situ hybridization analysis was negative. Fluorescent in situ hybridization analysis revealed MYC and BCL6 gene rearrangement (Fig. 2G), and no rearrangement for BCL-2.

The case was diagnosed as having diffuse large B cell non-Hodgkin lymphoma, NOS [4], activated B cell (ABC) type according to Hans' classification, MYC/BCL6 double hit [5]. The patient received 6 cycles of immuno-chemotherapy (rituximab plus cyclophosphamide, vincristine, and methylprednisolone), with no complications, obtaining a complete remission diagnosed by CT scan and an improvement in ejection fraction (60%). After 8 months, the patient had a sudden loss of consciousness and cerebral CT scan revealed a devastating central nervous system relapse, with cerebral edema and median shift; after palliative treatments, the patient died after a few days.

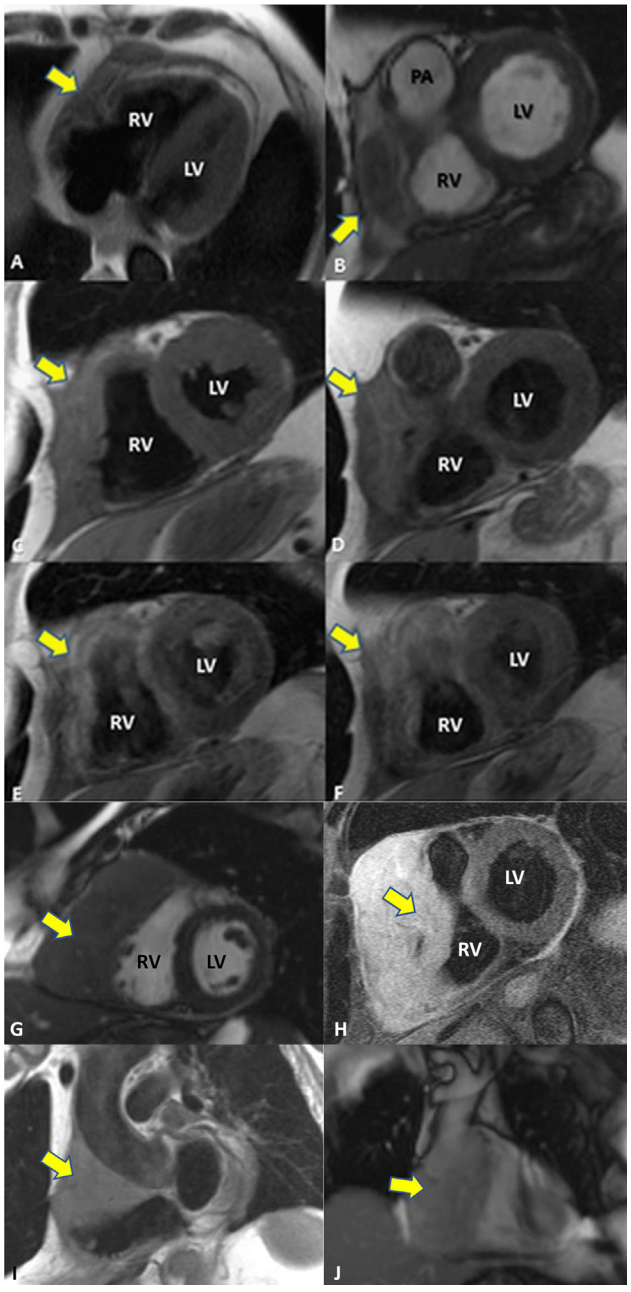

Fig. 1. Magnetic resonance imaging of the pericardial lymphoma. (A) T2-weighted 4 chambers image demonstrates right atrio-ventricular pericardial thickening (arrow). (B) Steady state short-axis image confirms thickening of the right pericardium extending from the level of the pulmonary artery to the diaphragmatic surface of the right ventricle. (C, D) T1-weighted short-axis images delineate the extension of the pericardial mass to the right ventricular myocardium. Panel C is more apical than Panel D. (E, F) Post-contrast T1-weighted short-axis images show homogeneous enhancement of both pericardial layers and right ventricular wall. Panel E is more apical than Panel F. (G, H) T1-weighted (G) and T2-weighted (H) sagittal plane images show the compression on the right ventricle. Panel G is more apical than Panel H. (I, J) coronary plane images indicating the anatomical relationships between the tumor and the great vessels. Panel J is more external than Panel I.
RV, right ventricle; LV, left ventricle; PA, pulmonary artery.

Discussion

Pharmacologic treatment of primary cardiac lymphomas results in a complete remission in more than 60% of patients, while surgical eradication of the tumor is associated with poorer prognosis [6,7]. However, early surgery should be considered if the tumor impairs hemodynamics, as described in this case. A sub-xiphoidal approach can be easily performed without general anesthesia and allows the removal of an adequate portion of the

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