Asymptomatic cardiac lymphoma in a hepatitis C virus-positive thalassemic patient

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Primary cardiac non-Hodgkin lymphomas are fast-growing intracavitary and/or intramyocardial nodular masses, while secondary lymphomas most commonly infiltrate the cardiac tissue. By any definition, cardiac non-Hodgkin lymphomas usually manifest through arrhythmias, refractory heart failure, pericardial effusion, and embolic stroke. We here describe a case of a cardiac non-Hodgkin lymphoma in which the following, previously undescribed features manifest simultaneously. It occurred in a polytransfused hepatitis C virus-positive splenectomized thalassemic patient; it rapidly grew, giving rise to an enormous right atrial mass and, this notwithstanding, it was completely asymptomatic. This cardiac lymphoma was discovered during staging for a CD20$^+$ large B-cell lymphoma of the tonsils. In particular, transesophageal echocardiography, showing that this prolapsing mass had a wide base on the atrial wall, led us to strongly suspect the lymphomatous origin of the mass itself. Notwithstanding anti-CD20 antibody therapy, urgent surgery was unavoidable and histology revealed that the mass consisted of lymphoma proliferation infiltrating even the right atrial wall and the pericardium. During the postoperative course the patient presented with a massive, fatal hemopericardium consequent to intravascular disseminated coagulation. This very unusual case, occurring in a hepatitis C virus-positive thalassemic patient, suggests that a case control study on the incidence of non-Hodgkin lymphoma in such patients may be interesting.

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The co-authors dedicate this report to Alessandro Ricchi, Antonio Carta and Gian Marco Pinna who, flying in the sky of Sardinia to save a life, passed away on February 24, 2004. They will not be forgotten.

Introduction

Cardiac non-Hodgkin lymphomas (NHLs) may be distinguished in primary NHLs which are confined to the heart and/or pericardium[1], and in cardiac NHLs secondary to a systemic NHL. The former are extremely rare especially in immunocompetent patients[2]; the latter occur in about 20% of patients with intrathoracic lymphoma[3].

In general, primary cardiac NHLs are fast-growing intracavitary and/or intramyocardial nodular masses while secondary NHLs most commonly infiltrate the cardiac tissue. By any definition, cardiac NHLs usually manifest through arrhythmias, refractory heart failure, pericardial effusion, and embolic stroke.

We here describe a case of cardiac NHL in which the following, previously undescribed features manifest simultaneously. It occurred in a polytransfused hepatitis C virus (HCV)-positive splenectomized thalassemic patient; it rapidly grew, giving rise to an enormous right atrial mass and, this notwithstanding, it was completely asymptomatic. This cardiac NHL which, at various imaging techniques, mimicked a mural thrombus or a primary cardiac NHL was discovered during staging for a large B-cell lymphoma of the tonsils.

Case report

The patient was a 35-year-old Sardinian woman with homozygous beta-thalassemia major, genotype $B^{\circ}_{39}/B^{\circ}_{39}$. She had been hypertransfused from the age of 17 months, regularly chelated by desferrioxamine and splenectomized at the age of 28 years. Unfortunately, she developed severe iron overload (serum ferritin value 8871 ng/ml) as well as an advanced HCV-related active liver cirrhosis (HCV-RNA 849 303 IU/ml,

aspartate and alanine aminotransferases 105 and 65 IU/l respectively) with massive hepatomegaly and portal hypertension.

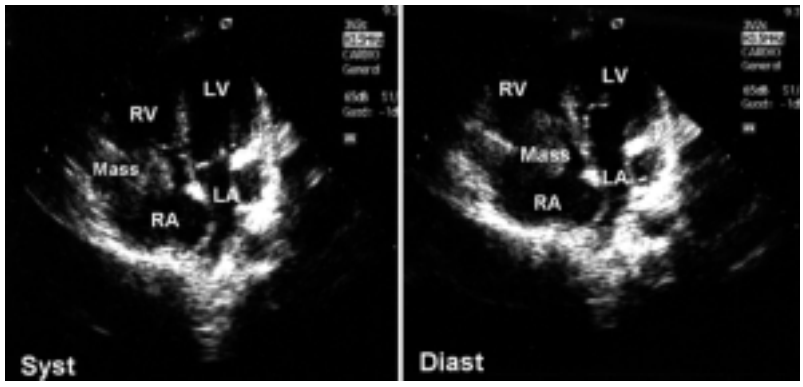
In May 2003, the patient presented with an isolated episode of paroxysmal atrial fibrillation/flutter, rapidly converted to sinus rhythm by beta-blockers. Echocardiography, performed on this occasion, did not show any cardiac alterations with the exception of the restrictive thalassemic cardiomyopathy findings.

In September 2003, because of a cervical lymphoadenopathy and an enlargement of the left palatine tonsil, a biopsy was performed and the diagnosis was "diffuse, large B-cell NHL, $CD20^+$ and $CD79a^+$". The patient was then referred to the Institute of Hematology for staging and therapy.

Whole body computed tomography scanning did not reveal any thoracic or abdominal lymph nodes but a hypodense thrombus-like mass was found in the right atrium. Transthoracic echocardiography revealed a 45 $\times$ 38 mm mass prolapsing into the ventricle during diastole and obstructing ventricular filling at end diastole. Transesophageal echocardiography (TEE) showed that this inhomogeneous and lobular mass had a wide implant base on the anterolateral wall of the atrium which appeared to be thickened and hypomobile (Figs. 1 and 2). Although ^{67}Ga scintigraphy was inconclusive, the TEE finding clearly pointed to a neoplastic origin of the mass.

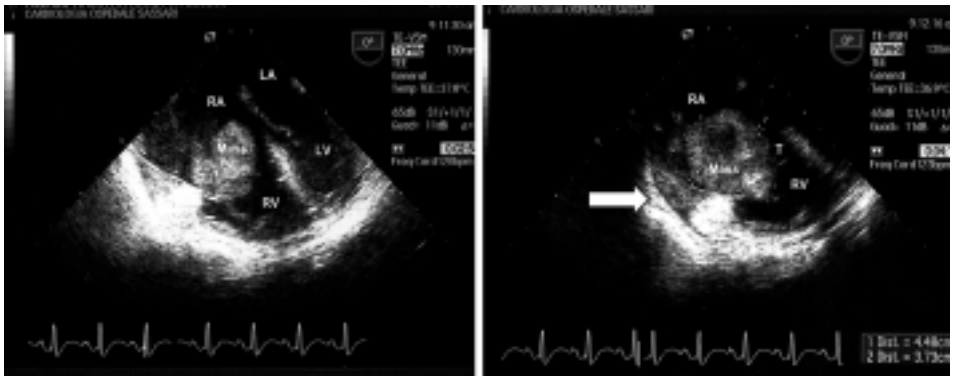
Intramyocardial biopsy was considered a high-risk procedure and was not performed. Notably, ECG showed a normal sinus rhythm of 98 b/min without other alterations and, on auscultation, there was a second/sixth systolic ejection murmur compatible with the status of chronic anemia. Taking into account the uncertainty regarding the origin of the atrial mass as well as the coexisting severe liver disease, we judged polychemotherapy hazardous and the patient was anticoagulated and treatment with anti-CD20 monoclonal antibodies started.

In October 2003, while the patient was on the third rituximab cycle, a cardiac magnetic resonance confirmed that the mass was increasingly obstructing ventricular filling but it did not add further information about its origin. Thus a surgical approach became ur-



A B

Figure 1. *Transesophageal echocardiogram showing a thick mass, occupying most of the right atrium (RA)* (A) *and prolapsing into the right ventricle (RV) during diastole* (B). *LA = left atrium; LV = left ventricle.*



A B

Figure 2. *Transesophageal echocardiogram showing the inhomogeneity of the voluminous neoplastic mass* (A) *and the remarkable thickening, due to neoplastic infiltration, of the anterolateral wall of the right atrium (RA) and of the tricuspid annulus (T)* (B, white arrow). *LA = left atrium; LV = left ventricle; RV = right ventricle.*

gent and it was performed at the Cardiac Surgery Division. The resection of the mass was performed on cardiopulmonary bypass with normothermia by a transatrial approach. On inspection, a grayish-wine colored, lobular mass was found. The mass had a gummy soft consistence and originated above the inferior vena cava outlet with a large base arising from the atrial wall. Histologic analysis confirmed that the mass consisted of NHL proliferation infiltrating even the right atrial wall and the pericardium. During the 48-hour postoperative course a massive, fatal hemopericardium with cardiac tamponade occurred. This complication did not respond to prompt reoperation and was determined by an intravascular disseminated coagulation with the following characteristics: platelet count from 140 000/mm^3 before surgery to ~1000/mm^3 after surgery; D-dimer 840 μg/mm^3 (normal values 0-200 μg/mm^3); fibrinogen 83 mg/dl (normal values 200-400 mg/dl); antithrombin III 50% (normal values 80-130%). *Post-mortem* examination was not possible.

Discussion

This very unusual case deserves some comments. First, the polypoid aspect of the lymphomatous atrial mass, prolapsing into the ventricle is quite similar to the case recently reported by Wilhite and Quigley[4]. In this paper, a primary anaplastic left atrial NHL, harboring a mural fibrin thrombus was described. However, that case had a tumor stalk while the present one is really a secondary CD30$^-$ NHL with a wide base infiltrating the atrial myocardium and with no fibrin deposits at histology. In this respect it has to be stressed that neither the magnetic resonance nor the ^{67}Ga scans allowed us to resolve the challenging differential diagnosis between atrial thrombus and tumor. In our experience, just as in that of others[5,6], TEE proved to be the most informative imaging technique.

Even the clinical and therapeutic aspects of this case deserve some comments. In a Medline search, we have been able to find only about 60 cardiac NHL cases published since the year 2000 (key words: cardiac, lymphoma). The presentation symptoms were available for 40 of them and all but one showed severe cardiac events, mainly heart failure and arrhythmias. Surprisingly, the present atrial NHL, despite its rapid growth (a few weeks) in a thalassemia-impaired myocardium, was totally silent.

Standard CHOP chemotherapy is the recommended cardiac NHL therapy[7]. The presence of both a thalassemic cardiomyopathy and severe liver damage, however, constituted a significant deterrent against the employment of anthracycline and antimetabolite drugs. Rituximab administration, successfully employed in one case of cardiac NHL[8], reduced the size of the tumor within the tonsils but it did not influence the progression of the cardiac mass. Therefore, surgical intervention, which in general seems to be discouraged[9,10], proved to be obligatory as well as urgent in this patient owing to the increasingly obstructed ventricular filling.

Finally, this enormous cardiac localization of a systemic high-grade NHL occurred in an HCV-positive thalassemic patient. This is the fifth case of cardiac NHL in thalassemia[11]. The HCV carrier state has even been recently associated with a higher NHL incidence in Italy[12] and thalassemia shows a well-documented high incidence of HCV infection. As both these immunodeficient conditions seem to facilitate lymphomagenesis[13,14], a case control study on the incidence of NHL in HCV-positive thalassemia patients might be interesting.

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