

CASE REPORTS

Echocardiographic assessment of a cardiac lymphoma: beyond two-dimensional imaging

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Lymphoma is usually recognized as the third most frequent metastatic malignancy involving the heart. In recent years, the incidence of cardiac lymphoma has increased, mainly because of HIV-infected patients. We present a case of secondary cardiac lymphoma in an HIV patient presenting with heart failure. Transthoracic echocardiography showed increased left ventricular (LV) wall thickness and an extensive mass in the right cavities with involvement of the tricuspid annulus (*Figure 1*). Doppler tissue imaging (DTI) showed reduced systolic and diastolic velocities at mitral and tricuspid annulus, compatible with systolic and diastolic myocardial dysfunction, likely owing to infiltration. After 2 weeks of chemotherapy, repeated exam showed significant reduction of the tumour mass and of the LV wall thickness, as well as normalized systolic and diastolic velocities at mitral and tricuspid annulus, as assessed by DTI. Use of transthoracic echocardiography, mostly two-dimensional imaging, has been described for several years for the diagnosis of cardiac involvement as well as for the assessment of tumour regression in response to chemotherapy. The present case report highlights the potential utility of other echocardiographic modalities, particularly DTI, for the assessment of cardiac lymphoma but also for monitoring the tumour response to adequate therapy.

Introduction

When considering malignant tumours affecting the heart, secondary malignancies are far more frequent than primary tumours. Lymphoma is usually recognized as the third most frequent metastatic malignancy involving the heart, when considering absolute numbers (following lung and breast carcinomas), being the second most frequent, when considering relative incidence of metastasis (following melanoma).¹ Cardiac involvement by malignant lymphoma is more common than usually assumed, with autopsy series documenting cardiac involvement in nearly 20–25% of non-Hodgkin lymphomas (NHL).^{2–4} Moreover, the incidence of cardiac lymphomas has increased in recent years, mainly because of HIV infection.^{5,6}

Assessment of a cardiac lymphoma is usually based on two-dimensional imaging evaluation. However, other echocardiographic modalities, such as Doppler tissue imaging (DTI), can offer additional information about potentially infiltrative malignancies such as lymphoma.

We present a case of secondary cardiac lymphoma in an HIV-infected patient.

Case report

A 68-year-old man was admitted with fatigue, shortness of breath, and peripheral oedema with 1 week of evolution. He also presented a 3-month history of postprandial fullness and 40-kg weight loss in approximately 7 weeks. He was known to be HIV-positive since 2002. In 2006 he was started on antiretroviral therapy because of his low CD4-positive lymphocyte count (112 CD4-positive lymphocytes per microlitre) and a high viral load (176 copies/ μ L). He was also a diabetic (type 2) and had ulcerative colitis.

On physical examination, he presented muscle wasting, with bilateral malleolar oedema and absence of breath sounds in the lower half of the right hemithorax. His electrocardiogram showed sinus tachycardia with right axis deviation, Sokolow-Lyon criteria for left ventricular (LV) hypertrophy and T wave inversion in inferior leads. The chest X-ray revealed pleural effusion on the right side. Cytopathological examination of the fluid revealed 84% of

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nucleated cells to be atypical lymphoid cells, and immunophenotypic characteristics suggested large B-cell NHL.

Transthoracic echocardiography showed increased LV wall thickness and an extensive mass in the right cavities with involvement of the tricuspid annulus (Figure 1A and B; see Supplementary data online, Videos 1 and 2). LV systolic function was assessed using the ejection fraction (EF) calculation by the modified Simpson's rule approach (EF = 50%) and peak mitral annular systolic velocity (S') determination ($S' = 4.87$ cm/s) in the lateral area (Figure 2B). Integrating both results, the patient had preserved EF but impaired LV longitudinal systolic function as assessed by DTI. DTI also demonstrated severe right ventricular (RV) function impairment with a peak tricuspid annular systolic velocity (St) of 4.28 cm/s (Figure 2C). Inferior vena cava (IVC) appeared dilated, with a respiratory variability of <50%; minor tricuspid regurgitation allowed the estimation of pulmonary systolic artery pressure (PSAP) in 50–55 mmHg. DTI revealed an E/E' ratio of 12, which was in accordance with moderate diastolic dysfunction as assessed by pulse-wave Doppler of the transmitral flow [pseudo-normal pattern (Figure 2A)], pulmonary vein flow (systolic wave velocity inferior to

diastolic wave velocity), and mitral annulus DTI (reduced annular velocities).

Transoesophageal echocardiography confirmed the presence of an extensive mass involving the right cavities and the pericardium, with minimal pericardial effusion (Figure 3A). A little mass was visualized in the right atrial appendage (Figure 3B). Attending to its localization, different echogenicity and mobility, it was considered consistent with a thrombus. This finding, in addition to the clinical picture, right-axis deviation on ECG, and transthoracic information (namely RV dysfunction and pulmonary hypertension), raised the hypothesis of concomitant pulmonary embolism. In addition, pulmonary embolism could have been, at least partially, responsible for the reduction in DTI velocities of the tricuspid annulus. A computed tomography (CT) scan was promptly performed and discarded the presence of pulmonary embolism. Cerebral, thoracic, and abdominal CT scan confirmed that no other organ was found to be involved by the lymphoma.

The patient was started on a chemotherapeutic regimen with cyclophosphamide, vincristine, adriamycin, and prednisolone associated to rituximab, a monoclonal antibody

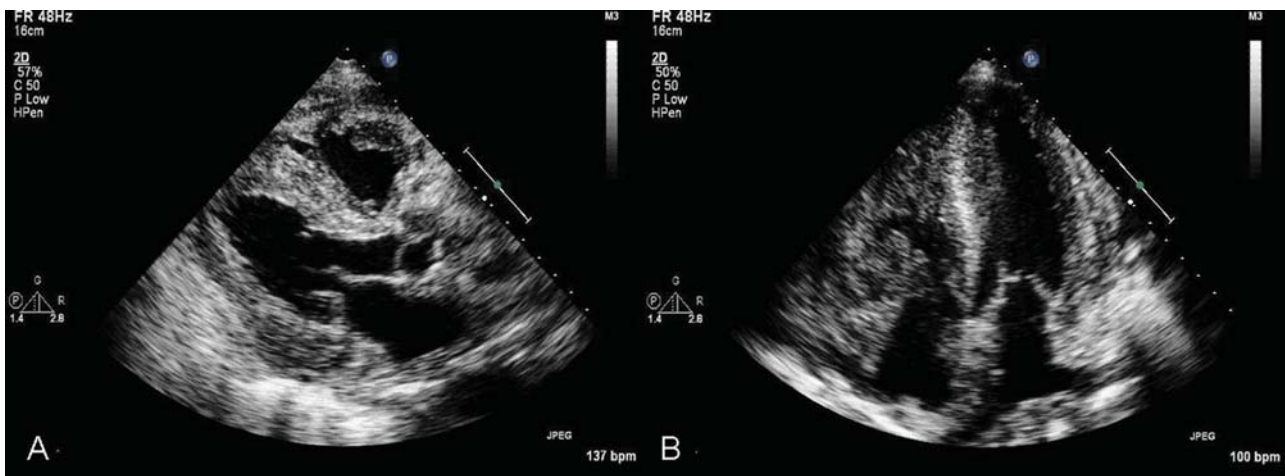


Figure 1 First transthoracic echocardiogram; two-dimensional imaging of parasternal view (A) and apical four-chamber view (B) showing increased left ventricular wall thickness and an extensive mass in the right cavities with involvement of the tricuspid annulus.

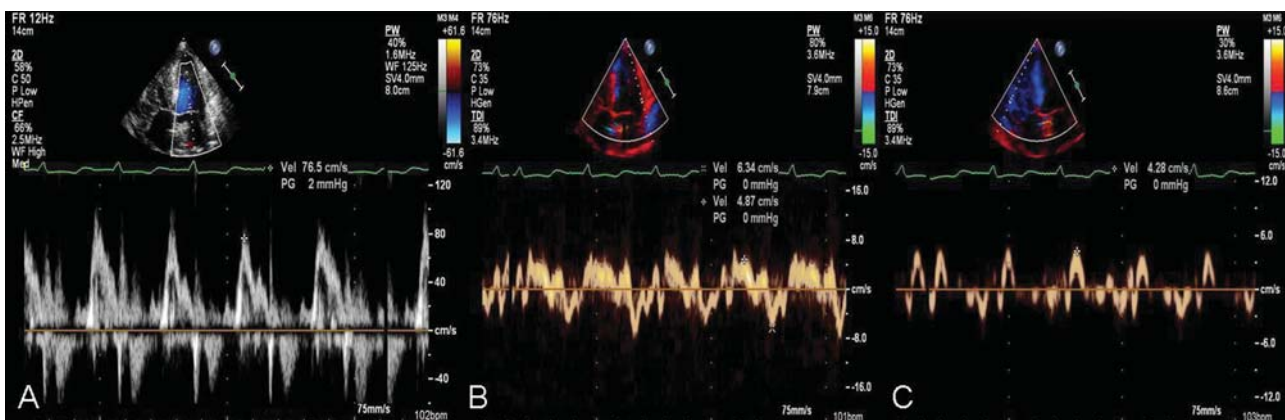


Figure 2 First transthoracic echocardiogram; pulse-wave Doppler of the transmitral flow (A) showing a pseudo-normal pattern; DTI at the mitral annulus with reduced peak mitral annular systolic and diastolic velocities (S' and E') in the lateral area (B), as well as reduced peak tricuspid annular systolic velocity (St) (C).



Figure 3 Transoesophageal echocardiography showing an extensive mass in the right cavities (A) and most likely a thrombus in the right atrial appendage (B).



Figure 4 Transthoracic echocardiogram after 15 days of chemotherapy; two-dimensional imaging of parasternal view (A) and apical four-chambers view (B) showing significant reduction of the tumour mass and also of the left ventricular wall thickness.

against the protein CD 20. Oral anticoagulation was also initiated, given the possible thrombus in the right atrial appendage. Additional medical treatment consisted of diuretics (furosemide and spironolactone), an angiotensin-converting enzyme inhibitor, and oral anti-diabetic agents.

His clinical condition improved significantly 2 weeks later. The new echocardiogram showed significant reduction of the tumour mass and of the LV wall thickness (Figure 4A and B; see Supplementary data online, Video 3). LVEF was normal (EF = 58%) and DTI revealed normalized mitral annulus velocity with $S' = 8$ cm/s (in the lateral area of the mitral annulus) (Figure 5B). A significant improvement of right ventricular systolic function was also evidenced by DTI with $St = 11.9$ cm/s (Figure 5C). In addition to the important reduction in LV wall thickness, the echocardiographic exam revealed improvement in diastolic function, with transmitral flow showing relaxation anomaly and an E/E' ratio of 4 (Figure 5A and B). A decrease in PSAP (40 mmHg) was observed as well as a non-dilated IVC with normalized respiratory variability. These findings favoured the hypothesis of an extensive infiltration of the left and right ventricles by lymphoma cells with consequent impairment of LV and right ventricular contractility and relaxation. Based on the

clinical and echocardiographic evolution of the patient, the same chemotherapeutic regimen was maintained.

The patient's treatment was completed after 4 months of chemotherapy and he underwent another transthoracic echocardiogram. No mass was visualized and the remaining exam was unchanged when compared with the previous one. On his last visit (8 months later), he was doing well and there was no evidence of recurrence.

Discussion

As referred previously, the incidence of cardiac lymphomas has considerably increased, mainly in HIV-infected patients.^{5,6} It is the second most frequent malignancy in HIV-infected patients, after Kaposi's sarcoma.^{7,8} The incidence of NHL among HIV-positive patients has been reported to be 2.9%, a nearly 60 times higher incidence when compared with general population.^{9,10}

The clinical presentation of cardiac lymphoma can be varied: heart failure, pericardial effusion, arrhythmias, or on the opposite, no cardiac manifestations.⁵ The possibility of cardiac involvement in patients with lymphoma should always be considered, particularly in the presence of HIV

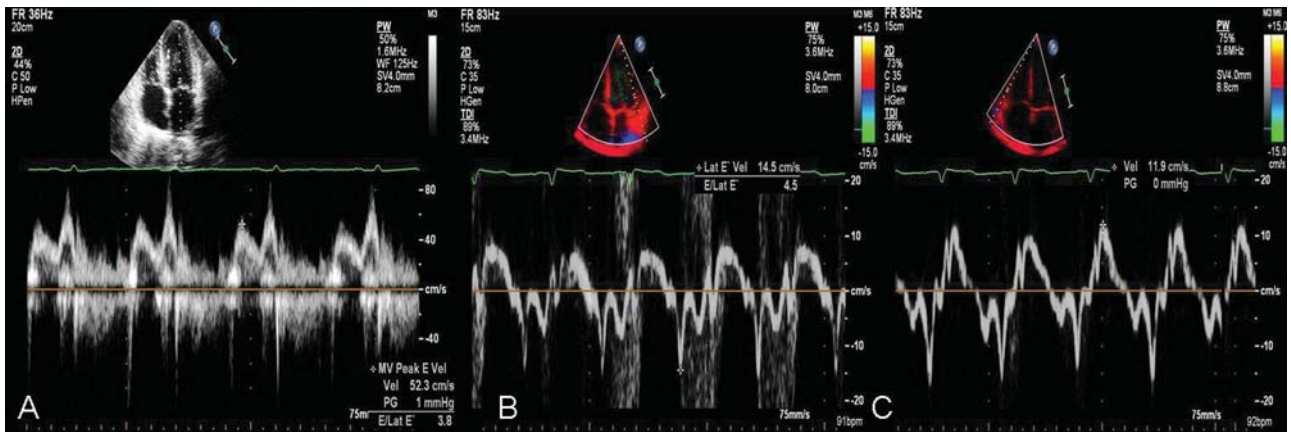


Figure 5 Transthoracic echocardiography after 15 days of chemotherapy; pulse-wave Doppler of the transmitral flow (A) showing relaxation anomaly; DTI at the mitral annulus with normalized peak mitral annular systolic and diastolic velocities (S' and E') in the lateral area (B), as well as normalized peak tricuspid annular systolic velocity (St) (C).

infection.⁹ Cardiac lymphoma most commonly presents as a nodular or polypoid mass with variable myocardial infiltration.⁸

When assessing a cardiac lymphoma, two-dimensional imaging allows the accurate evaluation and quantification of masses and ventricular wall thickening. In addition, Doppler study, particularly DTI, appears to be useful in assessing myocardial impairment owing to infiltration. Klein *et al.*^{11,12} demonstrated the correlation between Doppler-filling patterns and the degree of amyloid infiltration as measured by LV wall thickness, when evaluating cardiac amyloidosis. The existence of such correlation could be hypothesized for the infiltrative component of cardiac lymphoma. However, it should be noted that the ability of Doppler study, namely E/E' , to predict LV-filling pressures in cardiac lymphoma remains to be established. DTI was also very useful to quantify RV systolic dysfunction in our patient since other methods, such as tricuspid annular plane systolic excursion (TAPSE), were unavailable because of marked anatomical deformation of the tricuspid annulus.¹³

Besides allowing a better visualization of the cardiac mass and its relationship with cardiac structures, transoesophageal echocardiography allowed the distinction of a probable thrombus, from the neoplasm, in the right atrial appendage.

Prognosis of HIV-associated cardiac NHL is generally poor. Although clinical improvement and significant tumour regression has been described with combination chemotherapy, early post-chemotherapy death may occur in consequence of massive pulmonary emboli, refractory heart failure, and cardiac arrhythmias.^{7,14}

In conclusion, this case highlights not only the utility of echocardiography imaging, but also the potential utility of its various modalities and techniques, such as two-dimensional imaging, DTI, and transoesophageal echocardiography among others, to assess cardiac involvement by lymphoma. Echocardiography imaging is also helpful to monitor the response to the chemotherapeutic regimen instituted, and to define possible adjuvant therapies, such as anticoagulation in the presence of concomitant thrombus.

Supplementary data

Supplementary data are available at *European Journal of Echocardiography* online.

Conflict of interest: none declared.

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