

Case Report

Recurrence of Testicular Large B-Cell Non-Hodgkin's Lymphoma Presenting as Right Atrium Mass: A Case Report

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Abstract

Among malignant tumors of the heart, primary malignant lymphomas are uncommon and when they occur they usually are Non-Hodgkin's B-cell Lymphomas (NHL). Secondary cardiac involvement from NHL is often late diagnosed and associated to poor prognosis.

We report an unusual a case of secondary cardiac involvement from primary testicle large B-cell lymphoma in a 71-year-old male. The patient was initially referred to our PET Unit for first line therapy response evaluation that showed complete metabolic response. During follow-up, 22 months after primary tumour diagnosis, the patient experienced onset of dyspnoea and superior vena cava syndrome. A CT study identified a mass of uncertain nature (either a clot or a tumour) in the right atrium, extended to the superior cava vein. The lesion was then studied with MRI and cardiac echocardiography, but conventional imaging was not able to clearly distinguish whether it was a clot or a tumour. 18F-FDG PET/CT (PET/CT) study demonstrated an intense uptake in the right atrium suggestive of tumour, which was subsequently confirmed by endocardiac biopsy as lymphoma relapse. The patient was therefore treated with eight cycles of chemotherapy. Cardiac US and PET/CT then showed complete response to therapy.

This case demonstrates the added value of PET/CT compared to conventional imaging: it allowed an accurate extension of the metabolic activity of the cardiac lesion and oriented the diagnosis towards tumour. Proper patient preparation (fasting and carbohydrates-free diet) aimed at reducing myocardial physiological FDG uptake for a better study of the heart is recommended. In future a wide use of PET/CT in this kind of patients could be useful in addition to conventional imaging in order to reach early diagnosis and set proper patient management and treatment.

Keywords: Cardiac mass; Non-Hodgkin lymphoma; PET/CT; 18F-FDG

Introduction

The role of 18F-FDG PET/CT (PET/CT) in the assessment of patients with lymphoma is well established and this technique is used as a routine study for staging (baseline study), evaluation of response to treatment and residual disease and identification of possible disease relapse. Although being rare it is important to diagnose cardiac lymphoma localizations and PET/CT can play an important role in that respect. Conventional imaging, like CT or MRI, allows the depiction of extension and anatomical details of a potentially tumoral cardiac mass, but cannot show the grade of

metabolic activity of the lesion as PET/CT is able to do.

However physiological FDG uptake in myocardial tissue can interfere with the study of this region, being usually highly variable and unpredictable. In order to minimize this phenomenon the patient has to undergo a preparation consisting of a carbohydrate-free diet the day before examination and of fasting for at least six hours before the scan.

Case Report

In January 2009, a 71-year-old man was diagnosed with a testicle large B-cell lymphoma (NHL) and he was subsequently operated (right orchectomy) and treated with eight cycles of R-CHOP first-line chemotherapy (February-July 2009). Treatment

evaluation was performed by the mean of CT and PET/CT imaging after six cycles of therapy (mid-treatment scan) and a complete early response was proved.

Patient's follow up was then in charge of the Haematology Unit. In December 2010, 22 months after diagnosis, the patient suddenly started suffering from dyspnoea with minimal exertion, superior vena cava syndrome and collar of Stokes: he was admitted to the Emergency Room and afterwards, to the Haematology Unit for an adequate treatment. A CT scan showed a 60 x 44 mm mass in the right atrium, with a longitudinal diameter of 80 mm and irregular shape, partially involving superior vena cava, right jugular vein and left brachiocephalic vein up to the left jugular vein; a concurrent thickening of the left atrial wall was also demonstrated. The mass did not show a significant density enhancement after contrast agent administration (Figure 1).



Figure 1: December 2010 - CT scan demonstrating an irregular shaped mass in the right atrium (60 x 44 mm, with a longitudinal diameter of 80 mm), partially involving superior vena cava, right jugular vein and left brachiocephalic vein up to the left jugular vein: the finding did not show significant hyperintensity after contrast enhanced agent. A concurrent thickening of the left atrial wall was also displayed.

Radiologist suggested a further study with MRI in order to clarify the nature of that mass: BB T1, T2 and FAT-SAT sequences were performed. The right atrial mass, partially involving superior vena cava and upper veins, was confirmed. The mass showed only mild contrast agent uptake. Therefore, the study was not considered fully conclusive concerning the differential diagnosis between clot and lymphoma lesion. (Figure 2,3).

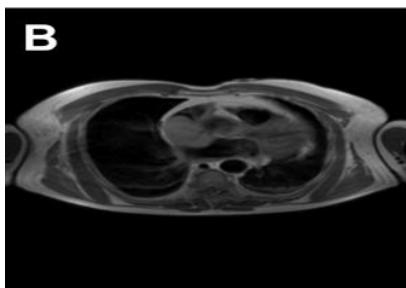


Figure 2: January 2011 - An MRI scan was suggested in order to clarify the nature of the finding demonstrated by CT. The BB T1 sequences above confirmed the right atrial mass, partially involving superior vena cava.

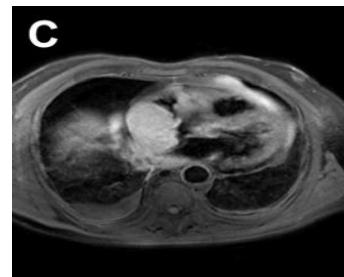


Figure 3: January 2011 - Contrast enhanced MRI images after gadolinium administration: BB T1 sequences showed mild delayed enhancement in the right atrial mass.

Subsequent echocardiography similarly just confirmed the already known mass. It was then decided to perform a PET/CT scan (January 2011), as suggested by radiologist; the study revealed an intense FDG uptake involving the whole right atrium with an SUV max equal to 9.4, indicating a tumour lesion rather than a clot, but no metabolic activity was observed in the upper veins, and no evidence of pathologic distant hypermetabolic localizations was found (Figure 4).

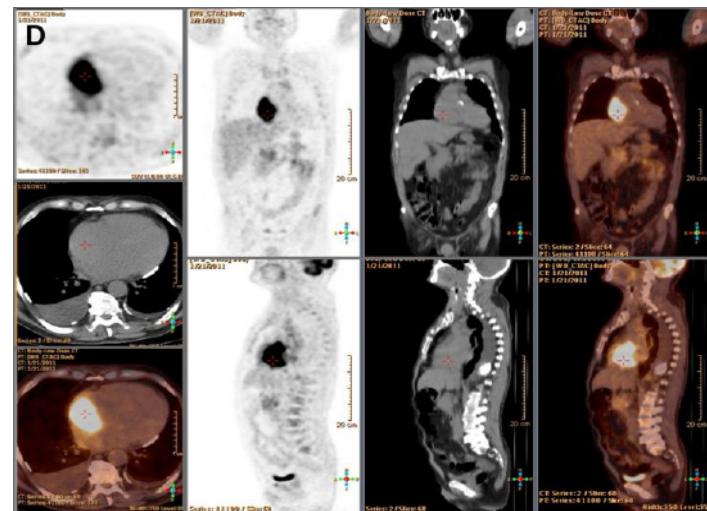


Figure 4: January 21st 2011 - ¹⁸F-FDG-PET/CT scan showing an intense uptake in the right atrium (SUV max 9.4) indicating a tumour lesion rather than a clot. No metabolic activity was observed in the upper veins where CT showed lesional involvement. The highly metabolic right atrial mass was later histologically defined as lymphoma relapse. Therefore the patient was addressed to chemotherapy.

An endocardial biopsy confirmed the clinical suspicion of large B-cell non-Hodgkin lymphoma. The Patient was therefore treated with 8 cycles of chemotherapy (R-COMP), thrombotic prophylaxis, steroids, diuretic, antibiotic therapy and neutrophil growth factors for neutropenia prophylaxis. The patient had a fast resolution of previously reported symptoms (such as dyspnoea, collar of Stokes, pleural effusion). During therapy an episode of

urinary infection by *KlebsiellaPneumoniae*, treated with antibiotic, and an episode of atrial fibrillation with spontaneous resolution occurred. The chemotherapy was welltolerated, and a PET/CT scan after the seventh cycle of R-COMP (June 2011) showed a complete metabolic disease remission (SUVmax of 1.9 versus previous valueof 9.4)(Figure 5). USexamination after treatment completionshowed a thickening of the right atrial wallin absence of the previously detectedmass.

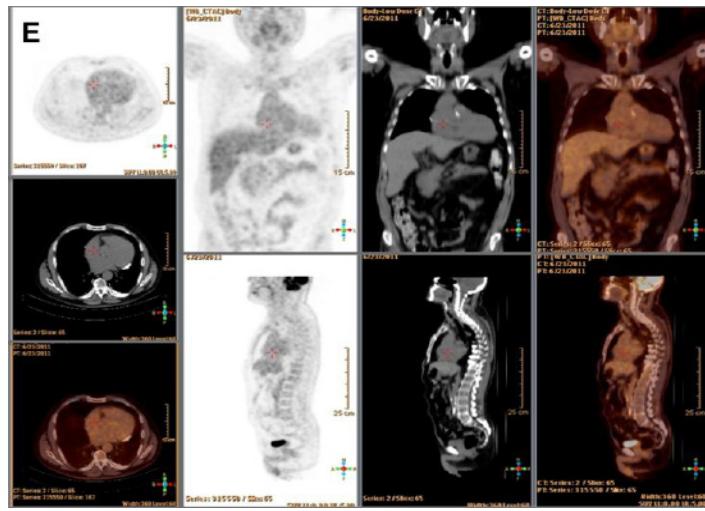


Figure 5: June 2011-18F-FDG PET/CT scan after 7 of 8 courses of chemotherapy (R-COMP) demonstrated radiotracer uptake normalization in the right atrium (SUV max of 1.9 versus pre-treatment value of 9.4): the right atrial lymphoma relapse showed a complete metabolic response to treatment.

Discussion

Cardiac masses that arise in the heart are potentially lethal, either benign or malignant. Almost 75% of primary cardiac masses are benign, but, when malignant, they are mainly sarcomas or lymphomas [1].Secondary cardiac involvement is far more common than primary cardiac tumoursand it has been documented in 8.7-27.2% of clinical cases of lymphoma[2]. The majority of intracavitarytumoursdevelop on the right side of the heart, a finding thatremains unclear [3]in fact, no tendency in the site of cardiac tumours formation has also been reported, especially for primary cardiac involvement [4].

The onset of a secondary cardiac mass typicallyoccurs a few years after primary NHL diagnosis,with a median of 20 months after diagnosis [5,6]:our case meets literature findings having been detected 22months after diagnosis. Cardiac involvement by lymphoma in autopsy has been described in 16% of patients with Hodgkin disease and 18% of patients with NHL[5].Even ifsometimes the myocardial involvement is important, clinical signs and symptoms of cardiac dysfunction (such as chest pain, dyspnoea,

arrhythmia and oedema) may remain undetectable, with cardiac involvement being found only after patient's death.Patientsaffected by malignant lymphoma associated with cardiac lesions are at high risk of sudden death, even if they are at an early stage based on clinical findings. Their prognosis is poor and most of these patients die before the starting of therapy [5-8]. This poor outcome may be, in most cases, due to a delayed diagnosis and treatment. Available literature suggests systemic chemotherapy is the only effective therapy, with,however,a theoretical risk of cardiac wall perforationas drawback [9,10].

In a recentretrospective analysis of 94 cases of NHL with biopsy-proven cardiac involvement publishedin PubMed between 1990 and 2015,Gordon MJ et al. [11] found that chemotherapy treatment was associated with a significant prolongation in median survival (18 vs. 1 month, HR 0.16, 95% CI, 0.47–0.54, P = 0.0003), and patients diagnosed in the chemo-immunotherapy era demonstrated a trend toward better outcomes as well as those who survived more than 1 month after diagnosis. Those findings have strong implications indicating that patients with cardiac involvement by NHL may be salvaged with modern regimens. In our case, eight cycles of R-COMP led to a complete remission without significant complications.Moreover they highlight the importance of early diagnosis and prompt treatment for those patients. Clinicians should be aware of the potential for cardiac involvement in patients with NHL, including indolent subtypes[11].Furthermore, primary testicular lymphoma (that in the vast majority of cases is histologically diffuse large B-cell Lymphoma)hasmarkedextranodal tropism, andshows a tendency to disseminate systematically to severalextranodalsites;in fact, relapsesoftenoccurat multiple extranodalsitesincluding the centralnervoussystem, skin, contralateraltestis, lung, pleura, soft tissues,adrenal glands, liver and bone marrow[12-14].

Conventional diagnostic techniques show limitations in the early diagnosis and characterization of cardiac involvement from malignant lymphoma. In our case, MRI, cardiac US and PET/CT-provided more specific findings than CT. Echocardiography is the first non-invasive way to examine the four chambers of the heart and pericardium and assessphysio-ptologic and hemodynamic effects of a cardiac mass, but the transthoracic approach is burdened with a restricted acoustic window.Trans-EsophagealEchocardiography (TEE) provides a larger imaging field with higher sensitivity compared to the transthoracic approach [15,16].

CTshows morphology, location and extension of cardiac masses with a larger field of view, while MRI signal intensity with contrast enhancement results in better-quality images as far as tumoral anatomy andmyocardial and pericardial infiltration,blood flow and cardiac function are concerned[17,18]. PET/CT imaging has been reported to reveal previously unsuspected cardiac involvement, to characterizethe extension and the metabolic activity

of the cardiac mass in order to help determine whether it is benign or malignant, and subsequently to assess the response to therapy [19-21]. In our case it was possible to suspect lymphoma, better characterize tumour activity and assess its complete response to chemotherapy before echocardiography. Moreover, due to lymphoma history, on the basis of CT findings, PET/CT could clinically have been considered before MRI for mass characterization and restaging. Various tumours presenting in the heart, including angiosarcoma, may show similar features on different imaging modalities, including FDG uptake, even though a lower radiotracer avidity may suggest such histotype; in that respect, biopsy remains crucial in order to reach a correct histologic diagnosis and chose the appropriate treatment [22]: e.g. chemotherapy for lymphoma and surgery for angiosarcoma.

Being a whole body imaging modality, PET/CT is also useful for the detection of distant disease localizations, which may be missed on conventional imaging modalities [22]. It is recommended to adopt a proper preparation in order to reduce myocardial FDG uptake and obtain a favourable tumour to background contrast: patient has to fast for at least six hours before the scan and have a carbohydrate-free diet (fatty meals) the day before examination (starting at least 18 hours prior to examination) [23,24].

The case we are reporting highlights how lymphoma can present in atrium, and, besides, how PET/CT can early detect and better characterize lesions in the heart compared to conventional imaging. In fact it was initially thought that the atrial mass was a clot: US, CT and MRI were not able to fully clarify its nature, whereas PET/CT enabled to suspect a lymphoma relapse later confirmed by biopsy. It is important to early diagnose cardiac involvement, which is a clinically underestimated occurrence that determines a poor prognosis: PET/CT turned out to be especially valuable in this case. These findings strengthen the important role of PET/CT in cardiac lymphoma reported in literature in other case reports. It could be useful to use it widely in future in this kind of patients to improve conventional imaging performance, adding the metabolic evaluation of lesions, in order to reach a timely diagnosis and set a tailored therapy and a proper patient management.

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