
CASE REPORT

Positron-emission Tomography–Computed Tomography for Detection of Primary Pericardial Lymphoma

JCY Lee¹, KH Tsang¹, W Cheuk², MK Chan¹

¹Department of Radiology and Imaging, and ²Department of Pathology, Queen Elizabeth Hospital, Jordan, Hong Kong

ABSTRACT

Primary pericardial lymphoma is rare in immunocompetent patients. Its symptoms are non-specific and may lead to a delayed diagnosis. Early detection and characterisation by computed tomography and positron-emission tomography–computed tomography, and prompt intervention can result in a favourable prognosis. We report a case of primary pericardial lymphoma in an immunocompetent man who underwent chemotherapy and achieved complete resolution. Clinical, radiological, and pathological manifestations, and differential diagnoses are described.

Key Words: Fluorodeoxyglucose F18; Lymphoma; Pericardium; Positron emission tomography computed tomography

中文摘要

PET/CT檢出原發性心包淋巴瘤

李俊賢、曾劍鴻、卓華、陳文光

原發性心包淋巴瘤在具有正常免疫能力的人中很少見。其症狀非特異性，故可能導致延遲診斷。通過CT和PET/CT及早檢測和確定其表徵，以及及時的干預可達致較好的預後。本文報告一名免疫功能正常男子患有原發性心包淋巴瘤，並在接受化療後完全緩解。本文描述其臨床、放射學和病理學表現和鑑別診斷。

INTRODUCTION

The prevalence of primary pericardial neoplasms is 0.001% to 0.007%.¹ Among these neoplasms, mesothelioma is the most common, followed by sarcoma and lymphoma. Symptoms and severity depend on the tumour location and its relationship with adjacent

structures such as the myocardium and great vessels. We report a case of primary pericardial lymphoma in an immunocompetent man who underwent chemotherapy and achieved complete resolution. Clinical, radiological, and pathological manifestations, and differential diagnoses are described.

Correspondence: Dr JCY Lee, Department of Radiology and Imaging, Queen Elizabeth Hospital, Jordan, Kowloon, Hong Kong.
Email: jonanleecy@gmail.com

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CASE REPORT

In April 2015, a 60-year-old man presented to the Queen Elizabeth Hospital, Hong Kong, with a 6-week history of gradually progressive exertional dyspnoea. He did not smoke or drink alcohol. He had no chest pain, dizziness, or palpitations. His exercise tolerance had reduced to climbing two flights of stairs. Electrocardiographic findings were unremarkable apart from atrial fibrillation. Blood tests showed a normal haemoglobin level and white blood cell count. Autoimmune markers (rheumatoid factor, antinuclear antibody, and antineutrophil cytoplasmic antibody), inflammatory markers (erythrocyte sedimentation rate and C-reactive protein), and tumour markers (alpha-fetoprotein and beta-human chorionic gonadotropin) all tested negative.

Chest radiography showed an enlarged cardiac silhouette with prominent pulmonary vascularity (Figure 1). Transthoracic echocardiography revealed a mildly impaired left ventricular ejection fraction (50%-55%), severe pulmonary hypertension, a thin rim of pericardial effusion at the basal posterior wall without any tamponade effect, but no evidence of intracardiac shunting, pericardial wall thickening, or mass lesion (Figure 2).

Chronic pulmonary embolism was suspected. Computed tomography (CT) pulmonary angiography with intravenous contrast injection showed a rim of infiltrative low-attenuation soft tissue in the pericardium enveloping the heart, mainly over the right and left

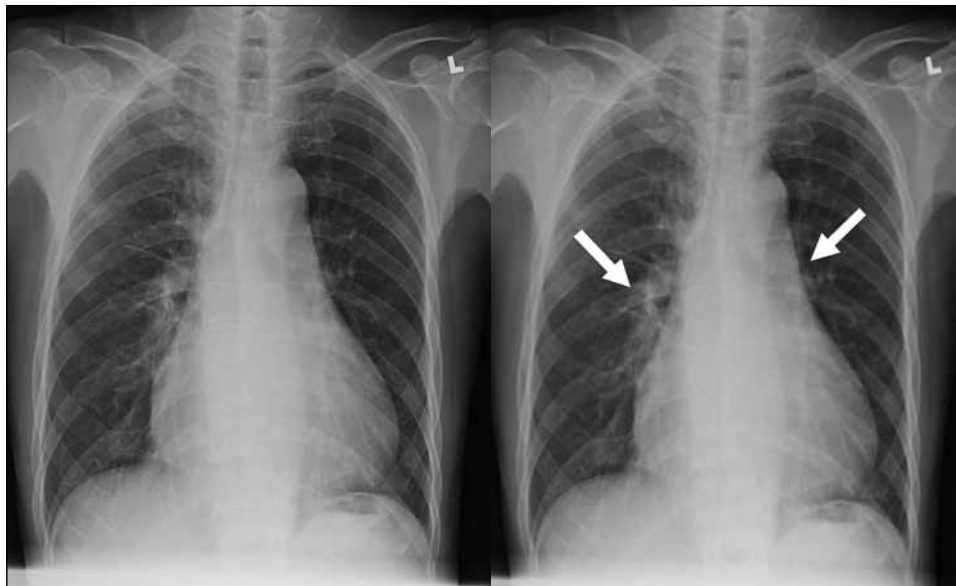


Figure 1. Chest radiograph showing an enlarged cardiac silhouette with prominent pulmonary vascularity (arrows). There is no pruning of peripheral vessels, hilum convergence sign due to a dilated pulmonary artery, globular enlargement of cardiac shadow (pericardial effusion), or pleural effusion.

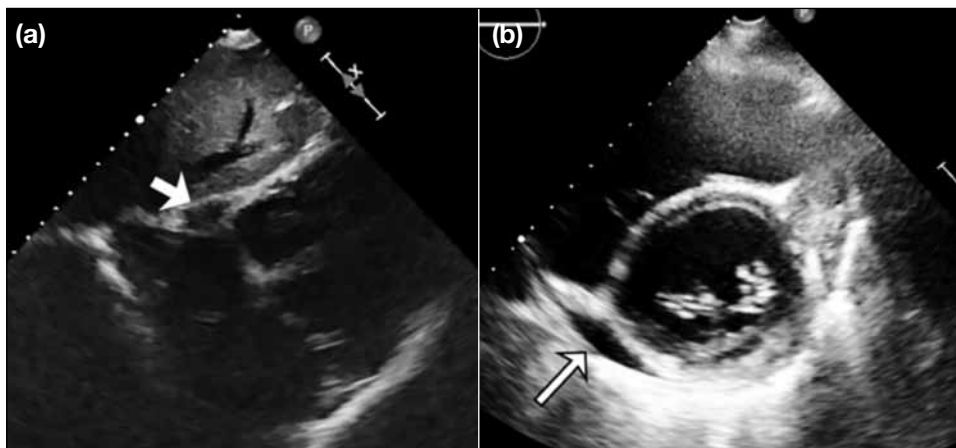


Figure 2. Transthoracic echocardiogram in the (a) subcostal view and (b) parasternal short-axis view showing only a thin rim of pericardial effusion at the basal posterior wall (arrows). (Images courtesy of Dr CK Kwok, Cardiology Division, Department of Medicine, Queen Elizabeth Hospital).

atria (Figure 3). These soft-tissue lesions showed mild contrast enhancement. There was loss of the epicardial fat plane (suggestive of epicardial involvement) and involvement of the aortic root and interatrial septum, but no calcification. There were no filling defects in the pulmonary arteries, which was suggestive of pulmonary embolism. Malignancy was thus suspected.

The patient was given a carbohydrate-restricted diet to suppress physiological myocardial glucose uptake. Examination by ^{18}F -fluoro-2-deoxy-D-glucose (^{18}F -FDG) positron-emission tomography (PET) combined with CT revealed diffuse hypermetabolic infiltrative pericardial soft-tissue thickening and a lobulated hypermetabolic soft-tissue lesion at the right hilum. Both encased the aortic arch, pulmonary trunk, and aortic root, and reached the roof of the aortic arch (Figure 4). The increased pericardial FDG activity was most prominent near the bilateral atria, followed by the thickened interatrial septum. There were no hypermetabolic masses in the lungs or pleurae.

A provisional diagnosis of pericardial malignancy, possibly lymphoma, was made. The patient was referred to a cardiothoracic surgeon and underwent video-assisted thoracoscopic surgery. Intra-operative findings showed that the anterior mediastinal fat over the aortic arch had been replaced by hard tumour tissue, and the left phrenic nerve had also been infiltrated by the tumour. There was no pleural effusion or deposits. The tumour tissue was biopsied. Microscopic examination revealed diffuse infiltration of neoplastic lymphoid cells comprising scattered large cells with irregular,

convoluted clefted nuclei (Figure 5). The cells were shown to express CD20, Pax5, CD23, and possibly CD10, and showed a high proliferation index of approximately 65% by anti-Ki-67 antibody staining. These features were consistent with primary mediastinal large B-cell lymphoma (Figure 6).

The patient was treated with steroid therapy and chemotherapy (eight cycles of rituximab, cyclophosphamide, etoposide, vincristine, and prednisone). During the mid-treatment cycle, ^{18}F -FDG PET/CT showed a reduction in tumour size and FDG uptake in the mediastinal and pericardial soft tissues. At the 4-month follow-up visit after completion of chemotherapy, ^{18}F -FDG PET/CT showed complete resolution of FDG uptake along the pericardium (Figure 7).

DISCUSSION

Pericardial involvement of mediastinal large B-cell lymphoma is usually caused by metastasis from the mediastinum in patients with extensive systemic disease. Pericardial malignancy secondary to direct invasion or metastasis is 100 to 1000 times more prevalent than primary pericardial malignancy.² In our patient, the main bulk of the tumour occurred at the pericardium, with limited extracardiac dissemination, suggesting the pericardium to be the primary site of involvement.

Most primary cardiac lymphomas are diffuse large B-cell lymphomas and usually manifest in the fifth decade of life.³ The right atrium is the most common site of involvement, followed by the pericardium and



Figure 3. (a) Axial contrast-enhanced computed tomogram of the thorax showing a rim of infiltrative low-attenuation soft tissue in the pericardium enveloping the heart, mainly over the atrial region (arrows), and (b) involvement of the interatrial septum (white arrow) and aortic root (black arrow). (c) Coronal reformatted computed tomogram showing pericardial soft-tissue encasement extending to the aortic arch (arrow) and absence of discrete mediastinal lymphadenopathy.

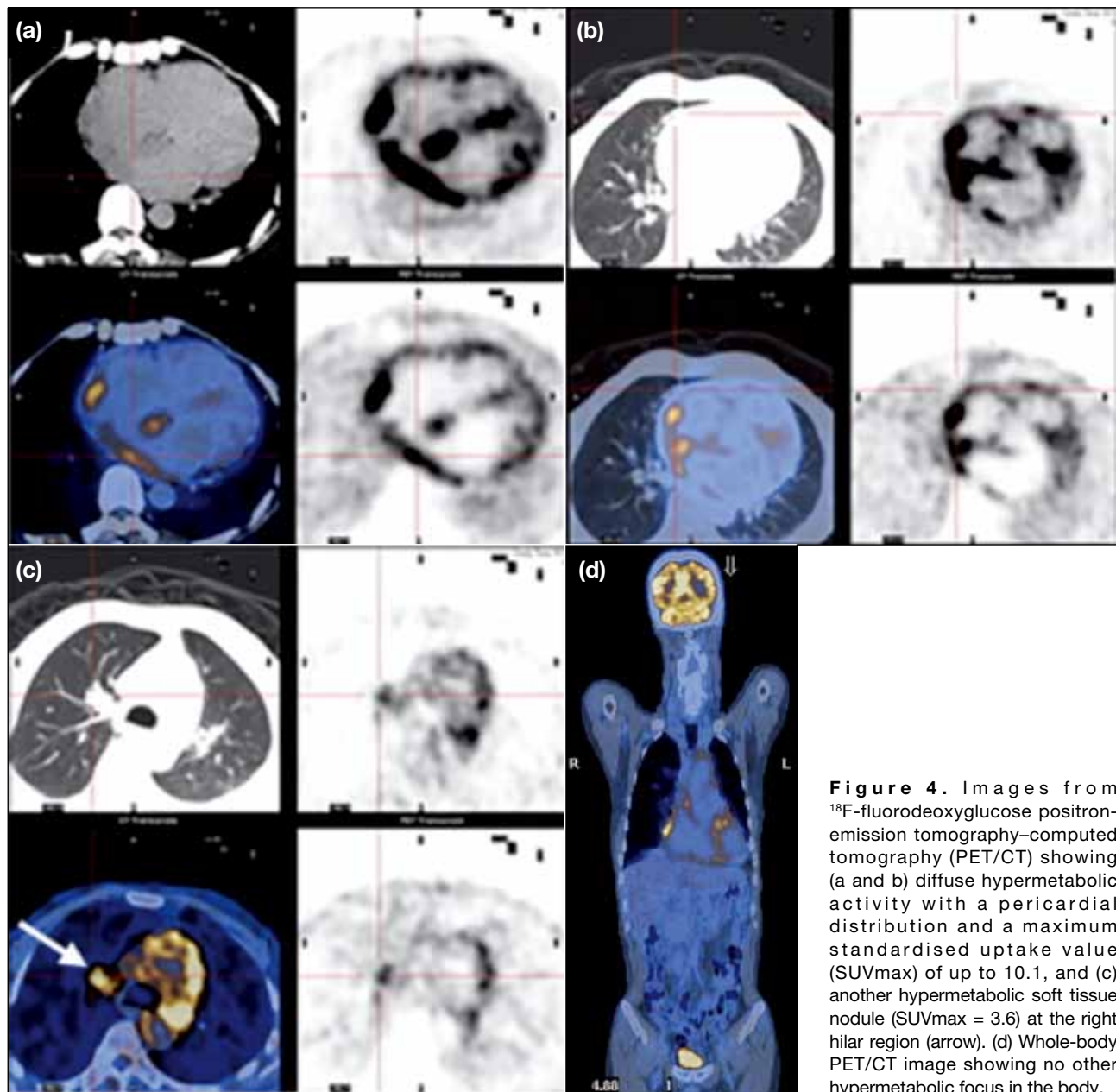


Figure 4. Images from ^{18}F -fluorodeoxyglucose positron-emission tomography-computed tomography (PET/CT) showing (a and b) diffuse hypermetabolic activity with a pericardial distribution and a maximum standardised uptake value (SUVmax) of up to 10.1, and (c) another hypermetabolic soft tissue nodule (SUVmax = 3.6) at the right hilar region (arrow). (d) Whole-body PET/CT image showing no other hypermetabolic focus in the body.

right ventricle.⁴ Usual features include infiltration of atrial walls with extension along the epicardial surface⁵ and interatrial septal involvement.⁶ In our patient, there was also thickening of the interatrial septum and a corresponding increase in FDG uptake during ^{18}F -FDG PET/CT.

The patient in our case was deemed immunocompetent. Primary cardiac lymphoma is rare in immunocompetent patients. It usually occurs in immunocompromised patients, in whom the pericardium is the sole or

predominant site of involvement. Primary pericardial lymphoma should be differentiated from primary effusion lymphoma in patients with acquired immunodeficiency syndrome (AIDS), who usually present with a large pericardial effusion. Primary effusion lymphoma is associated with human herpesvirus 8 infection and accounts for 4% of AIDS-related lymphomas.⁷

Clinical symptoms of pericardial tumour are usually non-specific, such as fatigue, exertional dyspnoea,

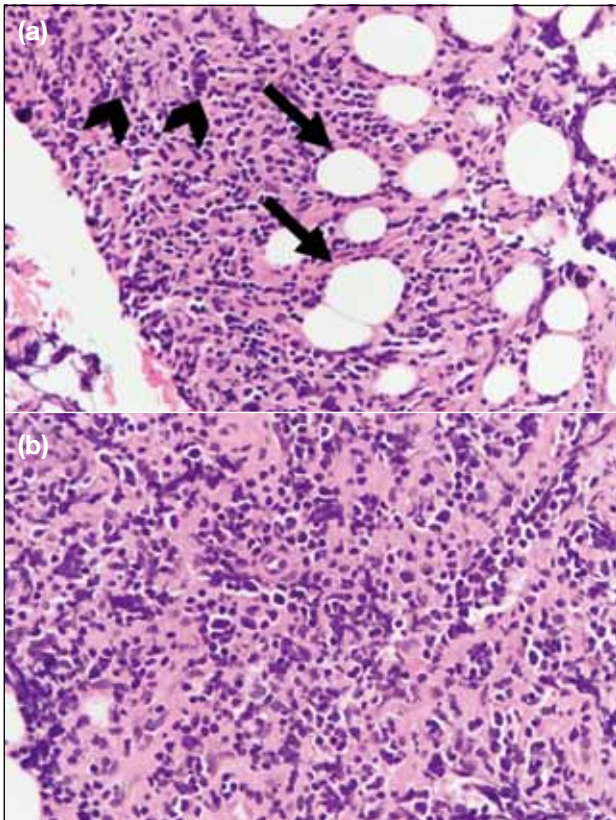


Figure 5. (a) Infiltration of pericardial adipose tissue (arrows) by diffuse sheets of lymphoid cells (arrowheads) in a permeative pattern. (b) Marked nuclear irregularity in neoplastic lymphoid cells (H&E; original magnification for both, x 200).

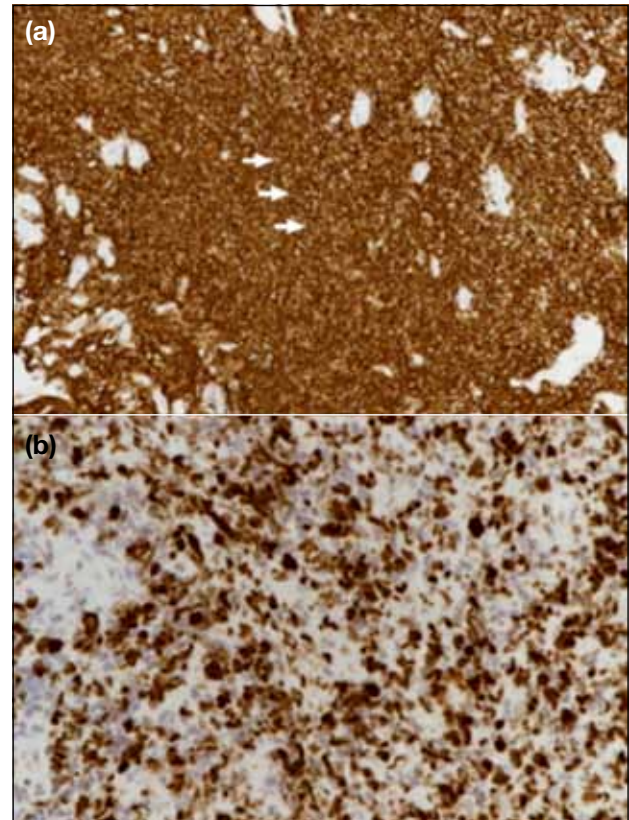


Figure 6. Immunohistochemical staining of (a) B-cell marker CD20 showing dense sheets of positive cells (arrows), and (b) Ki-67 showing a high proliferation index of approximately 65% (original magnification for both, x 200).

chest pain, and lower-limb swelling. Pericardial tumour can be an incidental finding for an unrelated illness.⁸ Symptoms may be caused by pericardial effusion, constrictive pericarditis, or mass effect on the adjacent mediastinal structures and great vessels. Patients may present with pulmonary hypertension and right heart failure, and occasionally with cardiac tamponade and low-output cardiac failure, which all require prompt life-saving treatment.⁶

Electrocardiography findings are variable and may show right bundle branch block or atrioventricular conduction abnormalities. Transthoracic echocardiography has a limited role in the assessment of pericardial disease, owing to its restricted acoustic window for pericardial assessment.⁹ Pericardial thickening or masses may be masked, and only 55% of cardiac masses may be detected.⁵ Therefore, in suspected cases, CT, PET/CT, or magnetic resonance imaging should be performed despite normal echocardiographic findings.¹⁰

Computed tomography can detect, characterise, and assess the extent of pericardial lesions. It provides a larger field of view than transthoracic echocardiography. Its excellent spatial resolution enables localisation of pericardial lesions. Furthermore, CT images are easily reproducible.

Examination by ¹⁸F-FDG PET/CT is useful in assessing metabolic activity, nodal involvement, and distal metastasis, and in monitoring treatment response. However, restriction of the patient's carbohydrate intake is important to limit myocardial glucose utilisation. During fasting, the myocardium utilises free fatty acids predominantly to fulfil its metabolic requirement.¹¹ After a carbohydrate-rich meal, the myocardium turns to glucose as its energy source. Glucose metabolism results in an abnormally high myocardial FDG uptake and affects the diagnostic capability in and around the heart.¹² Despite adequate fasting to limit myocardial glucose substrate use, cardiac FDG uptake still occurs

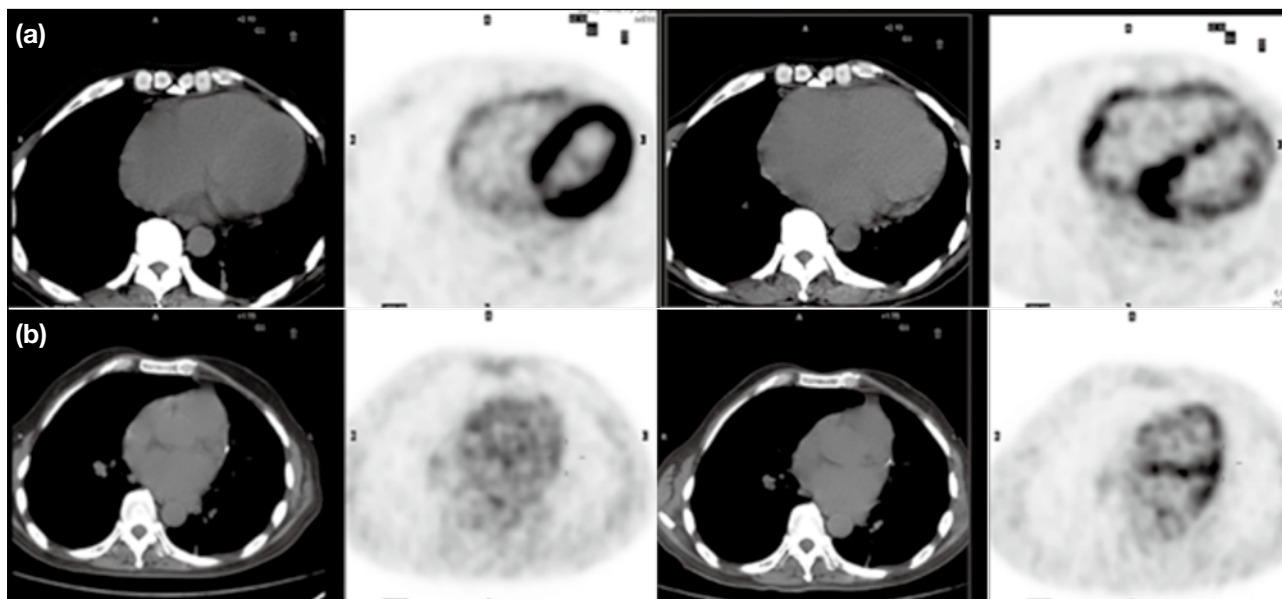


Figure 7. Images from ^{18}F -fluorodeoxyglucose (FDG) positron-emission tomography–computed tomography (a) at the mid-treatment cycle, showing normal myocardial uptake and a reduction in pericardial soft-tissue thickness and maximum standardised uptake value (SUVmax = 5.0), and (b) on completion of treatment, showing complete resolution of abnormal FDG uptake.

and is often diffuse and intense. Regional FDG uptake in the lateral left ventricular wall is well recognised as a physiological variant and may confound interpretation. A low-carbohydrate meal and prolonged fasting (>12 hours) further reduces myocardial FDG metabolism.^{13,14} Pericardial FDG uptake is always a pathological finding, although the FDG uptake alone cannot reliably differentiate benign inflammation from malignancy.

Magnetic resonance imaging is particularly useful in assessing myocardial invasion and cardiac function.⁹ It can characterise pericardial masses by its signal characteristics without the use of ionising radiation.

The differential diagnosis of primary mediastinal large B-cell lymphoma includes primary pericardial mesothelioma or sarcoma. All have similar imaging findings of pericardial thickening and soft-tissue masses encasing the heart, with heterogeneous enhancement and avid FDG uptake on ^{18}F -FDG PET/CT. In most cases, surgical biopsy and histopathological analysis are required for a definitive diagnosis.

The clinical outcome of primary cardiac tumours varies. Early diagnosis and treatment (surgery and / or chemotherapy) may improve the prognosis.¹⁵

Prompt detection and characterisation can be done by echocardiography, CT, and PET/CT. Although the prognosis for primary or secondary lymphomatous involvement of the heart is usually poor, the patient in our case was treated early and complete remission was achieved.

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