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CASE REPORT

An unprecedented case report of primary cardiac lymphoma exclusive to left ventricle: a diagnostic and therapeutic challenge

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Introduction Primary cardiac lymphoma accounts for <2% of all primary cardiac tumours. It is uncommon in immunocompetent patients, often fatal and diagnosed at autopsy. Tumour usually involves the right heart chambers and pericardium. With advances in imaging, early diagnosis is possible and treatment including chemotherapy and surgery affords good prognosis.

Case presentation We present a 50-year-old woman with abdominal pain and fevers for 5 days. Computed tomography of the abdomen showed splenic and renal infarcts but no mass or vegetation was noted on echocardiography. Thoracic computed tomography divulged a large left ventricular filling defect. Cardiac magnetic resonance imaging delineated a 3.5 × 4.5 cm anterobasal mass with frond-like projections and endocardial invasion without extracardiac involvement suggestive of a low-vascularity tumour. Echo-guided endomyocardial biopsy and minithoracotomy with needle biopsy were inconclusive. A sarcoid-protocol cardiac positron emission tomography-fluorodeoxyglucose scan showed focally elevated uptake in the basal anteroseptum without extracardiac uptake, supporting a malignant entity. This prompted open heart mass resection. Pathology revealed diffuse large B-cell lymphoma.

Discussion Our case is a unique report of cardiac lymphoma isolated to the left ventricle. Location of the tumour and lack of specific imaging characteristics made it a diagnostic challenge. It underscores the importance of including lymphoma in the differential for intracardiac masses as it is responsive to chemotherapy. Additionally, it emphasizes the complementary role of imaging modalities and multidisciplinary team approach in diagnosis. Early diagnosis and therapy is the key to establishing successful outcomes.

Keywords Primary cardiac lymphoma • PET-FDG • Cardiac MRI • Cardiac tumour • Case report

Learning points

- This case is a rare presentation of lymphoma exclusive to the left ventricle.
- It underscores the importance of keeping a broad differential, multimodality radiological approach for diagnostic work-up and multidisciplinary clinical approach.
- It illustrates an example of performing high-risk surgical resection for diagnostic and therapeutic purpose in a chemotherapy-responsive tumour. The success is accentuated by the patient's continued excellent outcome.

Introduction

Primary cardiac lymphoma (PCL) is a non-Hodgkin's lymphoma that involves the heart and/or pericardium.[1] It is rare, accounting for 2% of primary cardiac tumours[1,2] and often presents with non-specific clinical and imaging features, posing a diagnostic challenge. The tumour is less common in immunocompetent patients and usually involves the right heart chambers and pericardium.[3] Primary cardiac lymphoma should be distinguished from secondary neoplasms and from other primary cardiac tumours including myxoma (most common benign tumour) and angiosarcoma (most common malignant tumour). Cytology is paramount for definitive diagnosis. It is often

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fatal and diagnosed at autopsy. Early diagnosis and therapy is key to establishing good clinical outcomes.

Timeline

Date	Events
21/08/2016	Index presentation with abdominal pain; computed tomography of abdomen and pelvis showed splenic and bilateral renal infarcts; computed tomography with angiography (CTA) of the chest showed a filling defect in the left ventricle
25/08/2016	Cardiac magnetic resonance imaging showed left ventricular (LV) mass
31/08/2016	Transoesophageal echocardiogram guided endomyocardial biopsy
02/09/2016	Biopsy yield showed an indefinite diagnosis
07/09/2016	True cut needle biopsy of LV mass via left anterior thoracotomy performed. Procedure was complicated by ventricular tachycardia and complete heart block requiring temporary pacemaker with subsequent resolution
08/09/2016	Biopsy yield showed normal myocardium with no tumour cells
12/09/2016	Cardiac viability positron emission tomography scan showed high standardized uptake value uptake of tumour pointing towards malignant tumour; patient discharged on lovenox with plan for coronary CTA for pre-op planning
28/09/2016	Admitted for pericardial tamponade requiring pericardial window drain
30/09/2016	Open thoracotomy performed, with resection of mass via left atrial approach, repair of mitral valve with anterior leaflet primary reconstruction and edge-to-edge repair, A3-P3
03/10/2016	Patient discharged
14/10/2016	Patient re-admitted with sepsis resulting from mediastinitis due to a wound abscess and infection with methicillin-resistant Staphylococcus aureus (MRSA). Incision and drainage performed with wound-vac placement. Patient completed 6-week course of vancomycin
22/10/2016	Cycle # 1 of 6 of chemotherapy (refer to text for details)
14/02/2016	Cycle # 6 of 6 of chemotherapy
27/03/2017	Cardiac magnetic resonance imaging performed: previously seen mass no longer present. Systolic and diastolic function noted to be within normal range

Case description

A 50-year-old Caucasian woman with no significant medical history presented to our hospital with abdominal pain, nausea, vomiting, and a low-grade fever for 5 days. Her exam was remarkable for periumbilical tenderness to deep palpation. Her cardiovascular exam was normal, with clear S1 and S2, regular rate, no murmurs, gallops, or rubs. Laboratory studies revealed moderately elevated lactate dehydrogenase at 301 units/L (110–216) and elevated non-specific inflammatory markers—erythrocyte sedimentation rate at 76 mm/h (0–20) and c-reactive protein at 16.5 mg/dL (<0.8). Electrolytes, cardiac biomarkers, complete blood count, and electrocardiogram were normal. A non-contrast abdominal computed tomography (CT) showed wedge-shaped bilateral renal and splenic infarcts and colonic wall thickening. Blood cultures were obtained, empiric antibiotics begun, and intravenous heparin initiated for suspected emboli. Vasculitic, thrombophilic and infectious work-up were ordered (later returned negative). Transthoracic echocardiogram (technically difficult due to body habitus) showed an ejection fraction of 65%, but no vegetation, thrombus, mass or intra-cardiac shunt. A CT chest and abdomen with contrast was performed to confirm splenic and renal infarcts, to assess for other areas of systemic embolization, and to assess for vasculitic changes in the great vessels.

The CT did not show vasculitis but revealed a filling defect in the left ventricle measuring 3.5 cm × 4.5 cm, concerning for thrombus (*Figure 1*). Cardiac magnetic resonance imaging (MRI) was performed for further tissue characterization and showed a poorly defined mass invading the anterior wall and septum with projections into the left ventricle (*Figure 2A–E*). Late gadolinium enhancement imaging with long inversion time revealed a mass homogeneous with the myocardium, suggesting that this was not a thrombus. The mass was slightly hyperintense on T1 and T2 weighted sequences (*Figure 2C* and *D*). Rest perfusion revealed mild appearance of vascularity (*Figure 2E*). Tissue characteristics by MRI suggested malignancy, but tissue biopsy was recommended for confirmation.

Guided by transoesophageal echocardiogram (TOE), left ventricular (LV) endomyocardial biopsy was attempted but was inconclusive as the procedure was aborted prematurely due to ventricular arrhythmias. Noted on TOE was a large and complex mass invading the anteroseptum (*Figure 3A–E*), with attached smaller mobile echodensities causing intermittent obstruction of the left ventricular outflow tract (*Figure 3C–E*). Cardiac positron emission tomography (PET) imaging was performed with 18F-fluorodeoxyglucose (FDG) to determine if the mass was indeed malignant. This was performed after a high-fat diet for 24 h and injection of heparin to suppress baseline myocardial glucose uptake. The PET imaging showed a focal area of increased FDG uptake in the basal anteroseptum of the left ventricle with a maximum standardized uptake value of 10.7, consistent with a malignant rather than benign mass (*Figure 4*). A second biopsy attempted by left anterior mini-thoracotomy and needle biopsy failed to obtain adequate specimens primarily due to location of the mass on the septum. The patient was subsequently discharged in stable condition with outpatient appointments with the cardiac surgeon. However, she

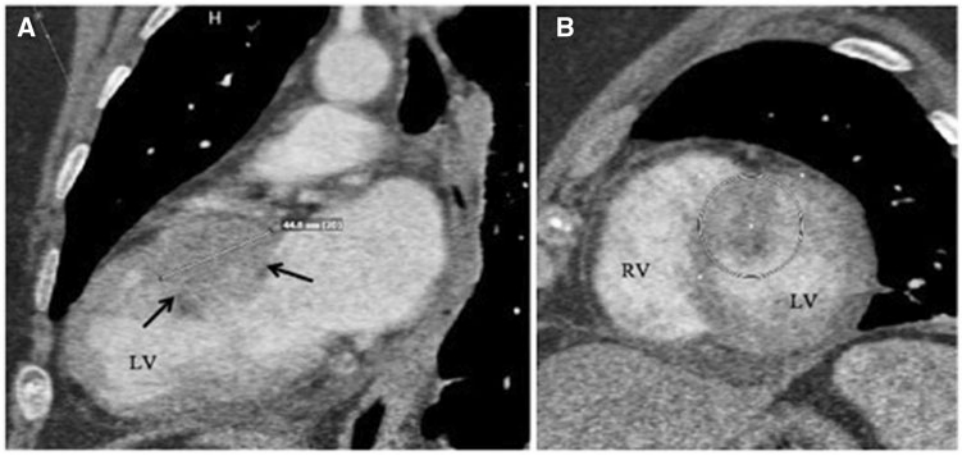

Figure 1 Computed tomography angiogram of Thorax. (*A*) Sagittal reconstruction. Arrows trace inferior outline of the anterobasal hypointense filling defect in the left ventricle, with radiographic measurement pictured (approximately 4.5 cm in longitudinal diameter); (*B*) Axial slice, short-axis view. Circle outlines the filling defect noted anteriorly in the left ventricle. LV, left ventricle; RV, right ventricle.

returned a week later with pericardial effusion and tamponade physiology. Prior echocardiograms had not shown effusion. Therefore, a slowly expanding iatrogenic effusion post-biopsy was suspected to be the aetiology. A subxyphoid pericardial window was created with subsequent resolution of tamponade.

Owing to inconclusive biopsies, given the malignant appearance, and out of concern for further systemic emboli, complete resection was performed in a high risk open-heart surgery that included mitral valve repair. Pathology yielded diffuse large B-cell lymphoma (DLBCL) (*Figure 5*). She completed six cycles of chemotherapy with R-EPOCH (rituximab + etoposide + prednisolone + Oncovin/vincristine + cyclophosphamide + hydroxydaunorubicin). A PET scan before the third cycle showed no FDG-avid lesions. Repeat cardiac MRI 6 months post-resection and chemotherapy showed no residual mass (*Figure 2F*). At the time of this manuscript (more than a year from presentation), she is alive and has normal functional capacity.

Discussion

Isolated LV involvement of DLBCL is exceedingly rare. The unusual location of the tumour, lack of specific imaging characteristics, and clinical presentation with embolic phenomena made it a diagnostic challenge. The MRI suggested a malignant tumour, which was confirmed with high-intensity FDG uptake on PET imaging. Additionally, the PET scan showed no evidence of extracardiac disease. These findings confirmed the need for open biopsy and resection for diagnostic and therapeutic purposes. Prior studies recommend percutaneous endomyocardial biopsy for diagnosis because the tumour is commonly located in the right-sided chambers, and because surgical resection is not needed in this chemo-sensitive tumour.[3,4] The left ventricular location of tumour in our patient required surgery for biopsy.

Petrich *et al.*[3] report constitutional symptoms, heart failure, and pericardial effusion as the most common presenting symptoms and signs of PCL. Our patient interestingly presented with constitutional symptoms and systemic embolic phenomena. To our knowledge, this is the first report of a PCL presenting in this fashion, although there is a case report of mixed cardiac myxoma and lymphoma presenting with peripheral emboli.[5] Unlike PCL, cardiac metastasis from extracardiac lymphoma is more common, and they largely occur in immunocompromised patients such as in HIV patients. Pericardial invasion and associated pericardial effusion is often present.[6] Our patient was immunocompetent, was HIV negative, and did not have pericardial involvement or effusion (effusion and tamponade noted under case description was iatrogenic post-biopsy).

Unlike other malignancies such as sarcomas, lymphomas are reported to lack areas of central necrosis and haemorrhage on MRI. Consequently, they are typically homogeneous and isointense on T1- and T2-weighted imaging with minimal contrast uptake at late gadolinium enhancement (LGE).[6] Characteristics of other tumours are outlined in *Table 1*. Our patient's MRI showed slightly hyperintense T1- and T2-weighted images with no uptake on LGE (*Figure 2*). The findings neither fit the pattern reported for lymphomas, sarcomas, or myxomas. Of note, prior reports are based on PCL affecting right-sided chambers while our report highlights imaging characteristics in LV PCL—which may not follow previously reported patterns. Hence, FDG-PET was performed for confirmation of malignancy before undertaking high-risk open surgical biopsy.

The case not only brings forth a rare clinical entity, but also underscores the challenges of tissue characterization of tumours even with multimodality imaging. Despite the lack of malignant findings on initial percutaneous biopsy, the decision to pursue high-risk open-heart resection was based on strong evidence of malignancy by FDG-PET imaging. The lack of extracardiac involvement made cardiac tissue diagnosis imperative and proved highly effective for treatment – especially because the tumour is highly sensitive to rituximab-based chemotherapy.[3,4]

Patient's perspective

Our case was an extraordinary learning experience from a medical and humanitarian perspective. The patient was initially disheartened

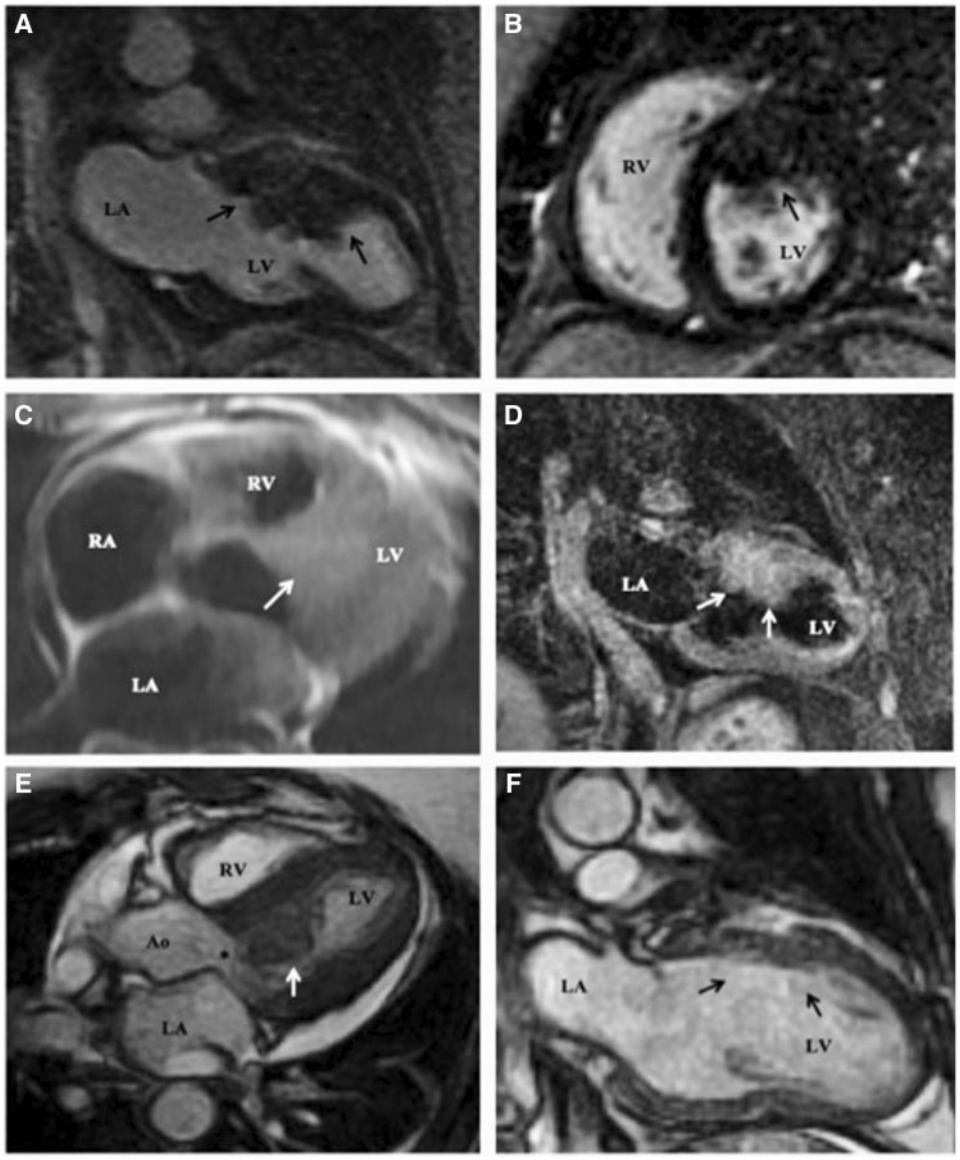

Figure 2 Cardiac magnetic resonance imaging. (*A*) Late gadolinium enhancement two-chamber view. Arrows point to mass protruding into the left ventricular cavity and invading the anterior wall; near no uptake of gadolinium noted; click on link to video file two-chamber steady state free precession cine; (*B*) late gadolinium enhancement short-axis. Arrow points to anterior/anteroseptal mass; no gadolinium uptake noted; (*C*) T1-weighted, black blood, double inversion, axial view. Arrow points to slightly hyperintense anteroseptal mass; (*D*) T2-weighted, triple inversion, two-chamber view. Arrows identify slightly hyperintense mass; (*E*) Steady state free precession three-chamber view. Arrow points to mass invading the anteroseptum and partially obstructing the left ventricular outflow tract represented by the asterisk; (*F*) late gadolinium enhancement two-chamber view from magnetic resonance imaging performed after resection and several cycles of chemotherapy. Arrows point to site of mass resection, now showing no residual mass. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

upon realizing that her seemingly benign presentation had turned into the dreadful possibility of a malignant cardiac tumour. The difficulties experienced by the medical team due to unsuccessful biopsies further tested her conviction. She showed exemplary courage and placed her faith in our specialists. With her determination, dedicated support from her family and integration of our care-teams, a successful outcome was facilitated. She was very satisfied with the outcome, and with the frequent communication and reassurance she received from her caretakers. She has remained compliant with follow-up visits and has completed her chemotherapy sessions. She is

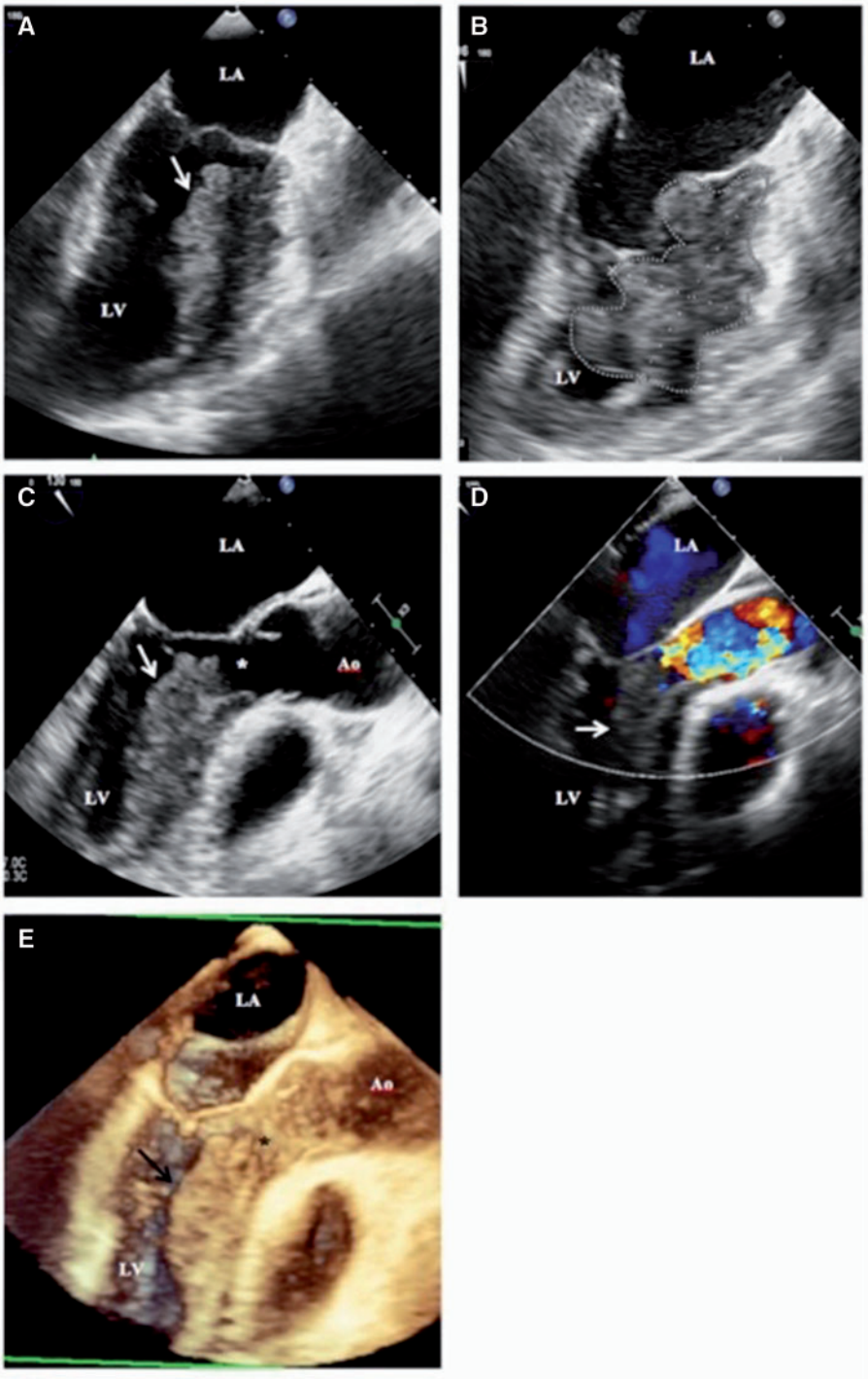

Figure 3 Transoesophageal echocardiogram. (*A*) Mid-oesophageal two-chamber view, ~90°. Arrow points to mass occupying the left ventricular cavity; (*B*) Mid-oesophageal two-chamber view, ~90°. Dotted tracing outlines the irregularly shaped mass invading the anterior wall of the myocardium. Mass was measured at 5.4 × 3.3 cm with calculated area of 12.2 cm^2; (*C*) Mid-oesophageal left ventricular outflow tract view, ~130°. Arrow points to mass encroaching into the left ventricular outflow tract (asterisk) during systole; (*D*) Colour Doppler, mid-oesophageal left ventricular outflow tract view, ~130°. Turbulent flow is noted in the left ventricular outflow tract suggesting some degree of obstruction by mass (arrow); (*E*) 3D rendering, mid-oesophageal left ventricular outflow tract view, ~130°. The mass (arrow) is shown partially obstructing the left ventricular outflow tract (asterisk) during systole. Ao, aorta; LA, left atrium; LV, left ventricle.

Table 1 Tumour characteristics on cardiac MRI[6]

Mass	T1-weighted image (relative to myocardium)	T2-weighted image (relative to myocardium)	Late gadolinium enhancement imaging
Thrombus	Low signal intensity (high if recent)	Low signal intensity (high if recent)	No uptake
Angiosarcoma	Heterogeneous	Heterogeneous	Heterogeneous
Rhabdomyosarcoma	Isointense (homogeneous)	Hyperintense	Homogeneous
Fibrosarcoma	Isointense (homogeneous)	Hyperintense	Heterogeneous
Myxoma (benign)	Isointense (homogeneous)	Hyperintense	Heterogeneous
Lymphoma	Isointense (homogeneous)	Isointense (homogeneous)	No/minimal uptake
Our patient's mass	Hyperintense	Hyperintense	Homogeneous

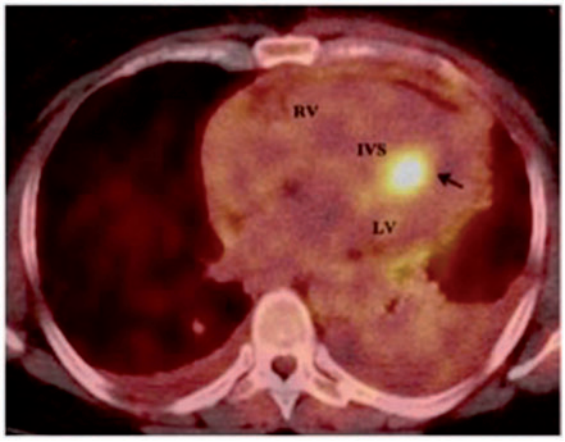

Figure 4 Positron emission tomography-18F-fluorodeoxyglucose image, axial slice showing four cardiac chambers. Arrow points to focal area of hyperintense uptake in the mid to basal ventricular septum. The maximum standardized uptake value of the mass measured 10.7, suggestive of a malignant entity. IVS, interventricular septum; LV, left ventricle; RV, right ventricle.

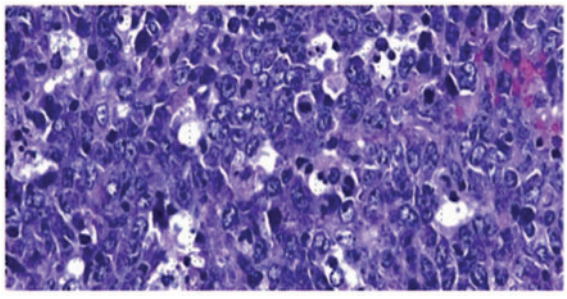

Figure 5 Histopathology of mass post-resection, haematoxylin and eosin stain, 40× magnification. To be noted is the background 'starry sky' appearance with tingible body macrophages. Cells have large vesicular nuclei with 2–3 chromocentres and show prominent mitotic activity. These findings are known to be specific for lymphoma.

doing well, and at last outpatient visit, was looking forward to attending her daughter's wedding.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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