ESC European Society of Cardiology

European Heart Journal - Case Reports (2018) **2**, 1–5
doi:10.1093/ehjcr/yty037

CASE REPORT

Diagnosis of a rare cardiac human herpesvirus-8 positive B-cell lymphoma manifestation: a case report of a transoesophageal echocardiography-guided trans-septal catheter biopsy

Christine M. Schneider[1], Alessandra Buiatti[1], Kristina Schwamborn[2], and Ralf J. Dirschinger[1]*

[1]Department of Cardiology, Klinikum rechts der Isar, Technical University Munich, Ismaningerstr. 22, 81675 Munich, Germany; and [2]Department of Pathology, Klinikum rechts der Isar, Technical University Munich, Trogerstr. 18, 81675 Munich, Germany

Received 6 November 2017; accepted 7 March 2018; online publish-ahead-of-print 9 April 2018

Introduction Human herpesvirus-8-associated B-cell lymphoma is a common disease entity in immunocompromised individuals, particularly in patients with chronic HIV-infection or AIDS. However, cardiac manifestations are extremely rare. Tissue for histopathology of left cardiac tumours is most commonly obtained by open surgery.

Case presentation In this report, we present a case of a solitary left atrial manifestation of an HHV8+ B-cell lymphoma in a 59-year-old patient presenting with B symptoms and a cardiac mass on echocardiography. Due to the high operative risk of the patient, a transcatheter/trans-septal biopsy was performed to establish the diagnosis.

Discussion In the era of routine trans-septal catheter interventions, this approach may represent a straight-forward, minimally invasive alternative for patients at high risk for surgery.

Keywords Case report • Trans-septal catheter biopsy • Transoesophageal echocardiography • Heart tumour • HHV-8+ • B-cell lymphoma • HIV

Learning points

- Only 0.5% of all non-Hodgkin lymphomas with extranodal disease have a primary cardiac localization. Among these, diffuse large B-cell lymphomas account for 80% of cardiac lymphomas with predominantly right atrial manifestation.
- Right-sided cardiac masses are easily accessible by a transvenous approach. To avoid systemic embolization, pathologic samples from left-sided cardiac tumours are more commonly obtained by open surgery.
- Transcatheter/trans-septal biopsy for left atrial tumours represents minimally invasive alternative for patients at high risk for surgery. The risk of embolization is not clear.

Introduction

Non-Hodgkin lymphomas (NHL) are frequent complications of long standing immunosuppression and HIV-infection. Particularly, human herpesvirus-8 (HHV-8) associated B-cell lymphomas most commonly arise in HIV-positive individuals, where patients typically present a nodal disease.[1] Less frequently, extranodal manifestations can occur and only 0.5% of all NHL extranodal lymphomas have a primary cardiac localization.[2,3] Among these, diffuse large B-cell lymphomas account for 80% of cardiac lymphomas with predominantly right atrial manifestation.[4–6]

* Corresponding author. Tel: +49 89 4140 9381, Fax: +49 89 4140 4900, Email: r.dirschinger@tum.de. This case report was reviewed by Francesco Lo Iudice and Hajnalka Vágó.

Timeline

Day	Events
1	49-year-old HIV+-patient presents with fever, night-sweats, and weight-loss of 9 kg within 5 months. Blood sampling: normochromic anaemia; blood cultures: negative. Positron emission tomography- computer tomography scan: generalized lymphadenopathy and splenomegaly.
2–4	Bone marrow biopsy & bronchoscopic biopsy: reactive lymphocytosis in the course of epstein barr virus infection (polymerase chain reaction positive), no malignancy. Transoesophageal echocardiography (TOE): left atrial mass (approximating 4 × 2 × 2 cm) attached to the atrial wall with diastolic protrusion into the left ventricle. Treatment initiation: oral anticoagulation with Rivaroxaban planned open resection of the tumour.
5–6	Cardiac surgery consultation considering patient at very high risk for surgery.
7	TOE-guided trans-septal catheter-based biopsy using a steerable introducer
9	Discharge of the patient.
10	Histopathological diagnosis of a human herpesvirus-8 positive B-cell lymphoma and initiation of an Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (R-CHOP) regimen.
6 months	Stable disease with R-CHOP regimen (50% dosage reduction). Left atrium (LA)-mass size stable.
8 months	Standard-dose R-CHOP regimen lead to partial remission with significant reduction of LA-mass dimensions and lymphadenopathy. New lesion on left hemithorax.
9 months	Patient died at home from unknown cause with no post-mortem exam performed.

Case presentation

A 59-year-old patient presented with fever, night-sweats, and a weight-loss of 9 kg within 5 months. The patient had a 30-year history of an HIV-infection with stable disease and HIV load below detection threshold under a raltegravir and emtricitabine/tenovofir treatment regimen.

Clinical examination revealed a generalized lymphadenopathy, the lungs were clear to auscultation, heart sounds notable for a normal S1, S2, no rubs, or murmurs heard. The abdomen was soft without tenderness. There was no evidence of peripheral oedema. Positron emission tomography- computer tomography (PET-CT) imaging workup revealed a generalized lymphadenopathy and splenomegaly. As no cardiac tumour was suspected at this time point, PET-CT was performed without suppression of myocardial glucose uptake.

Blood sampling showed normochromic anaemia and blood cultures obtained during spiking fever were negative. A subsequent bone marrow biopsy and bronchoscopic biopsy of peribronchial lymph nodes indicated reactive lymphocytosis in the course of epstein barr virus (EBV) infection (polymerase chain reaction positive) without evidence of malignancy.

Due to persistent symptoms and progressive dyspnoea, transthoracic echocardiography was performed. Hereby, a left atrial mass was detected. Transoesophageal echocardiography (TOE) demonstrated attachment of the mass (approximating 4 × 2 × 2 cm) to the atrial wall with diastolic protrusion into the left ventricle.

Because of the unknown embolic risk, oral anticoagulation with Rivaroxaban was initiated.

To determine the nature of the cardiac lesion, cardiac magnetic resonance imaging (CMRI) was performed. Hereby, a solitary left atrial tumour with exophytic protrusion into the atrial lumen was seen, exhibiting a homogenous isointense signal in T1- and T2-weighted and post-contrast sequences, making the diagnosis of thrombus, myxoma, or fibroelastoma unlikely (*Figure 1*).

Given the size and unknown origin of the intra-cardiac mass, operative resection of the tumour was aimed for, but the patient was considered inoperable due to his increasingly poor condition. In order to obtain histopathological diagnosis to allow specific treatment, we decided to pursue a trans-septal catheter-based biopsy.

The procedure was guided by TOE using a steerable introducer (Agilis^{TM} NXT, St. Jude Medical). After trans-septal puncture in the central fossa ovalis, multiple biopsies of the atrial mass were taken (*Figure 2A–C*, Supplementary material online, *Video S1*) without complication. The patient was discharged 2 days after the procedure.

Upon histopathological workup of the obtained samples, the diagnosis of an HHV-8 positive, diffuse large B-cell lymphoma was made (*Figure 2D*), and Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (R-CHOP) treatment regimen was initiated. This treatment resulted in a halt of tumour growth by echocardiography and eventually a size reduction that was confirmed on follow-up PET-CT scan 8 months after discharge (*Figure 3*), suggesting a partial remission. Unfortunately, the PET scan revealed a new thoracic lesion (*Figure 3*, arrow).

The patient—now in an increasingly poor condition—decided to avoid further radiation or chemotherapy treatment, chose a best supportive care regimen, and consequently no histopathological diagnosis of the new thoracic lesion was established. Nine months after discharge, the patient died at home from unknown cause with no post-mortem exam performed.

Discussion

Non-Hodgkin lymphomas are frequent complications of long standing HIV-infection or immunosuppression. Particularly, B-cell lymphomas containing genomic material from HHV-8 have been associated with chronic HIV-infection. Most commonly,

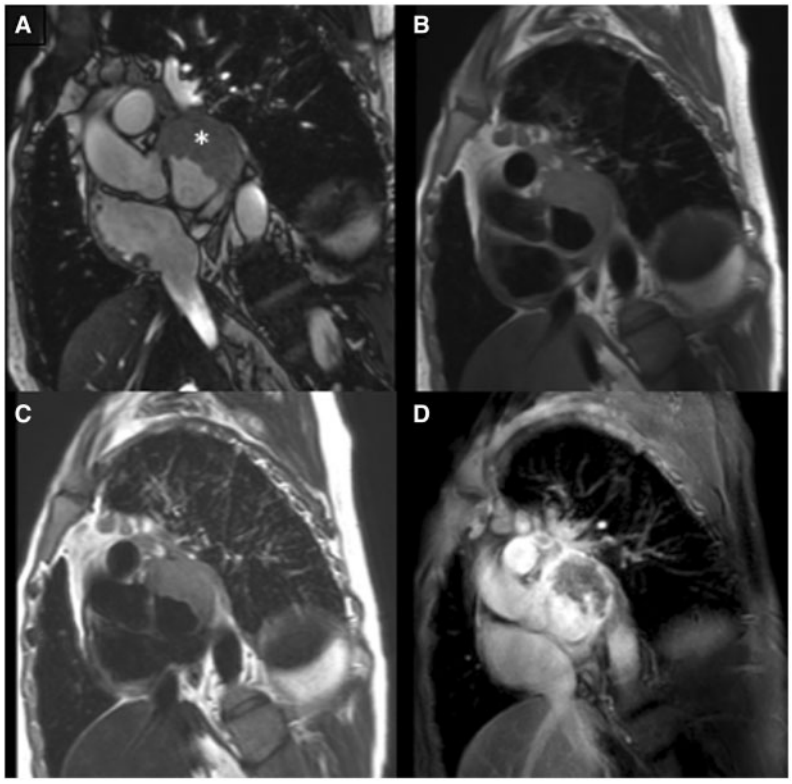

Figure 1 Cardiac magnetic resonance imaging demonstrating solitary left atrial tumour (asterisk) with exophytic protrusion into atrial lumen, shown on cine-sequence (*A*). Homogenous isointense signal in T1- (*B*) and T2-weighted sequence (*C*). (*D*) Five minutes after gadolinium administration no evidence of considerable contrast-enhancement of atrial mass. No increased perfusion compared with myocardium.

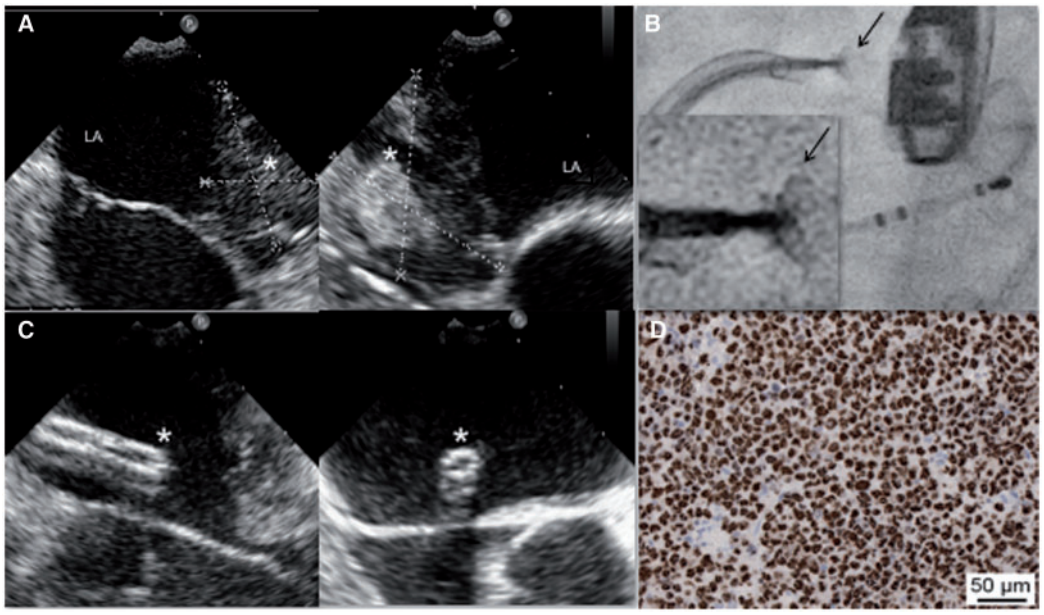

Figure 2 (*A*) Transoesophageal echocardiography demonstrating a left atrial mass (4 × 2 × 2 cm), indicated by asterisk, with attachment to the atrial wall and diastolic protrusion into the left ventricle. (*B*) Fluoroscopic image of transoesophageal echocardiography-guided trans-septal catheter-based biopsy using a steerable introducer. Arrows indicate biopsy forceps, insert depicts magnification of biopsy forceps. (*C*) Biopsy taking after trans-septal puncture in the fossa ovalis. Asterisk indicates the steerable introducer. (*D*) Immunohistochemistry for human herpesvirus-8 showing characteristic nuclear positivity of tumour cells.

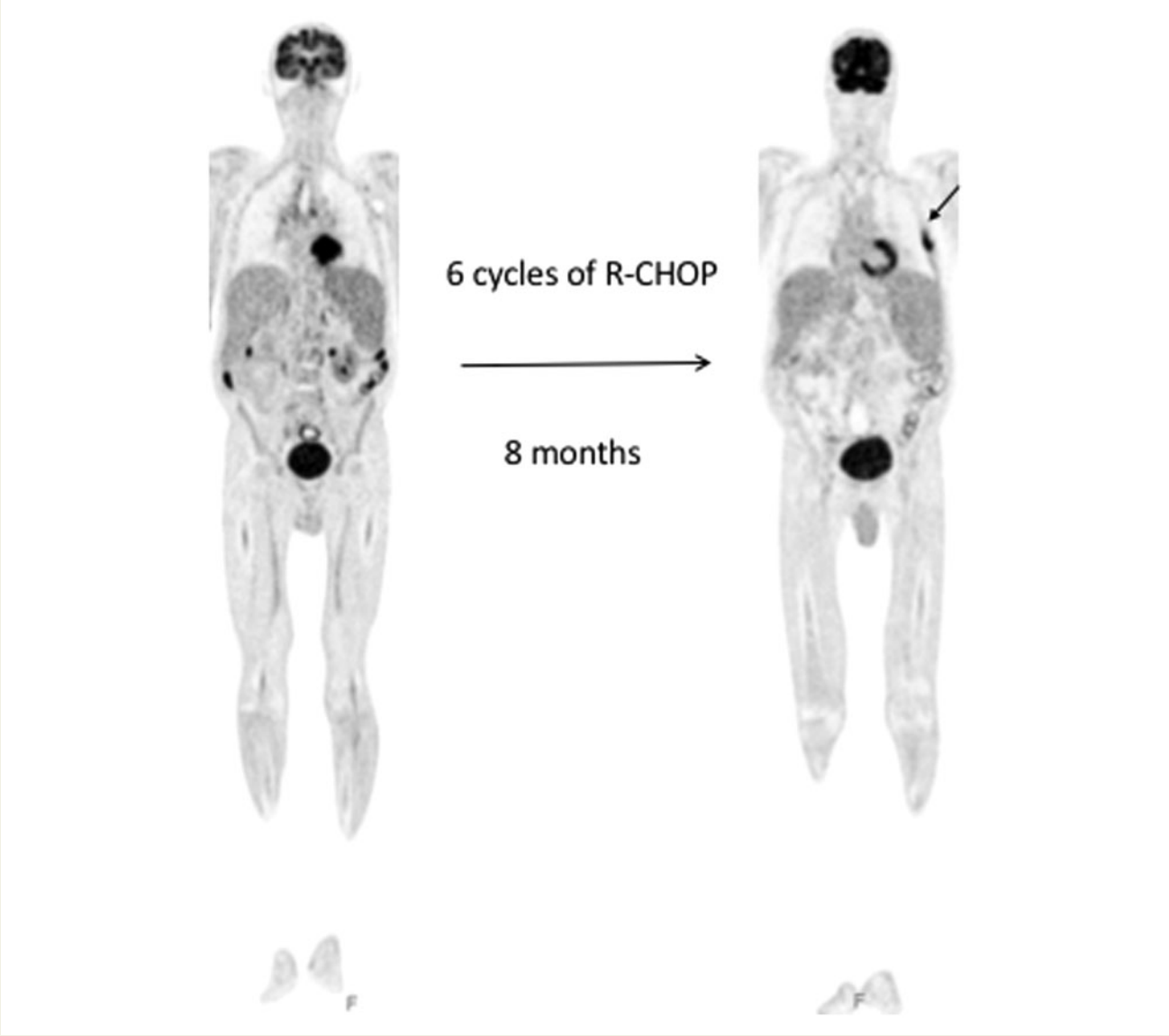

Figure 3 Positron emission tomography computed tomography scan with intensive tracer uptake of mediastinal lymph nodes and left atrial mass. After six cycles of R-CHOP treatment (three cycles with 50% dosage reduction) significant reduction of left atrial lymphoma dimension. New lesion in left hemithorax (indicated by the arrow). The second scan was performed after an 18-h fasting period. However, residual myocardial FDG uptake is seen, impeding the evaluation of the atrial mass.

Non-Hodgkin lymphoma patients present a nodal disease, typically restricted to body cavity-based lymphomas, e.g. primary effusion lymphomas. Less frequently, extranodal manifestations can occur.[2] Only 0.5% of all NHL extranodal lymphomas have a primary cardiac localization.[3] Among these, diffuse large B-cell lymphomas account for 80% of cardiac lymphomas[4] with predominantly right atrial manifestation.[5,6] To our knowledge, the case presented here is the first report of a primary HHV8+ B-cell lymphoma of the left atrium.

Improved imaging methods, particularly CMRI and cardiac 18-Fluorodeoxyglucose (^{18}F-FDG) PET imaging under suppression of myocardial glucose uptake, have improved diagnosis of cardiac masses.[7–9] Nevertheless, histopathology is still required in many cases to initiate appropriate treatment.

While right sided cardiac masses are easily accessible by a transvenous approach, very few trans-septal biopsies of left atrial tumours have been reported.[10,11] To avoid systemic embolization, pathological samples from left-sided cardiac tumours are more commonly obtained by open surgery. As trans-septal puncture has become a standard in routine procedures to treat arrhythmias or structural heart disease, techniques and material for this access route have improved in the past decade. Due to this development, the transcatheter/trans-septal approach for left atrial biopsy could represent a straight-forward and minimally invasive alternative for patients at high risk for a surgical procedure. Although systematic evidence will be needed to evaluate and quantify the risk of embolization with this diagnostic approach, trans-septal atrial biopsy may serve as a novel diagnostic tool in selected patients.

Supplementary material

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

Acknowledgements

We would like to thank Dr Christoph Spinner for guiding the diagnostic workup and referral of the patient to our department.

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.

References

1. Cesarman E, Chang Y, Moore PS, Said JW, Knowles DM. Kaposi's Sarcoma–associated herpesvirus-like DNA sequences in AIDS-related body-cavity–based lymphomas. *N Engl J Med* 1995;**332**:1186–1191.
2. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. *Blood* 2011;**117**:5019–5032.
3. Miguel CE, Bestetti RB. Primary cardiac lymphoma. *Int J Cardiol* 2011;**149**:358–363.
4. Giunta R, Cravero RG, Granata G, Sellitto A, Romano C, De Fanis U, Foccillo G, De Capite C, Santini M, Rossiello L, Rossiello R, Lucivero G. Primary cardiac T-cell lymphoma. *Ann Hematol* 2004;**83**:450–454.
5. Ikeda H, Nakamura S, Nishimaki H, Masuda K, Takeo T, Kasai K, Ohashi T, Sakamoto N, Wakida Y, Itoh G. Primary lymphoma of the heart: case report and literature review. *Pathol Int* 2004;**54**:187–195.
6. Carras S, Berger F, Chalabreysse L, Callet-Bauchut E, Cordier J-F, Salles G *et al*. Primary cardiac lymphoma: diagnosis, treatment and outcome in a modern series. *Hematol Oncol* 2017;**35**:510–519.
7. Kübler D, Gräfe M, Schnackenburg B, Knosalla C, Wassilew K, Hassel J-H, Ivanitzkaja E, Messroghli D, Fleck E, Kelle S. T1 and T2 mapping for tissue characterization of cardiac myxoma. *Int J Cardiol* 2013;**169**:e17–e20.
8. Scholtens AM, Verberne HJ, Budde RPJ, Lam MGEH. Additional heparin preadministration improves cardiac glucose metabolism suppression over low-carbohydrate diet alone in 18F-FDG PET imaging. *J Nucl Med* 2016;**57**:568–573.
9. Rischpler C, Dirschinger RJ, Nekolla SG, Kossmann H, Nicolosi S, Hanus F, van Marwick S, Kunze KP, Meinicke A, Götze K, Kastrati A, Langwieser N, Ibrahim T, Nahrendorf M, Schwaiger M, Laugwitz KL. Prospective evaluation of 18F-fluorodeoxyglucose uptake in postischemic myocardium by simultaneous positron emission tomography/magnetic resonance imaging as a prognostic marker of functional outcome. *Circ Cardiovasc Imaging* 2016;**9**:e004316.
10. Wong CW, Ruygrok P, Sutton T, Ding P, van Vliet C, Occleshaw C, Smith W. Transseptal fine needle aspiration of a large left atrial tumour. *Heart Lung Circ* 2010;**19**:438–439.
11. Satya K, Kalife G, Navarijo J, Rasekh A, Wilson JM. Transseptal biopsy of a left atrial mass with 3-dimensional transesophageal echocardiographic guidance. *Texas Heart Inst J* 2012;**39**:707–710.