ESC European Society of Cardiology

European Heart Journal - Case Reports (2023) **7**, 1–6
https://doi.org/10.1093/ehjcr/ytad463

CASE REPORT
Electrophysiology

Brugada phenocopy with altered ST-segment elevation in pericardial diffuse large B-cell lymphoma and effusive–constrictive pericarditis: a case report

Yohei Ishibashi [1,2]*, Shanshan Zhang[1], Shuntaro Tamura[1], and Hideki Ishii[1]

[1]Department of Cardiovascular Medicine, Gunma University Graduate School of Medicine, 3-39-15, Showa Maebashi, Gunma 371-8511, Japan; and [2]Department of Cardiology, National Hospital Organization Takasaki General Medical Center, 36, Takamatsu Takasaki, Gunma 370-0829, Japan

Received 18 April 2023; revised 26 August 2023; accepted 11 September 2023; online publish-ahead-of-print 17 October 2023

Background Cardiac lymphoma is a rare disease. Effusive–constrictive pericarditis can be a characteristic of pericardial involvement in patients with this disease. Conversely, a phenotype with electrocardiogram changes similar to those of Brugada syndrome is called Brugada phenocopy, and these changes improve after treatment.

Case summary A 71-year-old man was transported to our hospital with chest pain, hypotension, and ST-segment elevation in V1 and V2 leads during maintenance dialysis for renal failure. After arrival at the hospital, his ST-segment elevation disappeared, and emergency coronary angiography scan revealed no significant coronary artery stenoses or obstructions. His computed tomography and echocardiography scans revealed pericardial effusion and an intrapericardial mass. Further, his blood pressure dropped and ST-segment elevation recurred during dialysis after 7 days. Thus, pericardiocentesis was performed, but haemodynamic improvement was insufficient, and right catheterization findings suggested effusive–constrictive pericarditis. Meanwhile, flow cytometry of the pericardial fluid suggested the diagnosis of B-cell lymphoma; however, radical chemoradiotherapy was impossible because of cardiogenic shock. The patient died on Day 17. Further, autopsy revealed diffuse large B-cell lymphoma with pericardial and myocardial infiltration.

Discussion Cardiac lymphoma is rare but can be associated with effusive–constrictive pericarditis, which may be difficult to manage even with pericardial drainage. In such cases, radical treatment, including chemotherapy, should be promptly considered, if possible. Our patient presented with Brugada-type electrocardiogram but no syncope or family history, suggesting Brugada phenocopy and not true Brugada syndrome due to cardiac lymphoma. Notably, temporary improvement in ST-segment elevation was observed despite the absence of treatment.

Keywords Brugada-type electrocardiogram • Cardiac tumour • Cardio-oncology • Dip and plateau • Pericardial effusion • Pericardiocentesis • Case report

ESC curriculum 6.6 Pericardial disease • 6.8 Cardiac tumours

Learning points

- This report aimed to suspect and diagnose rare but sometimes treatable cardiac lymphoma.
- The report identified the possibility of effusive–constrictive pericarditis, which is difficult to manage haemodynamically even with pericardial drainage.
- Further research is warranted to better understand Brugada phenocopy.

* Corresponding author. Tel: +81 27 220 8153, Fax: +81 27 220 8159, Email: yishibashi.oct13@gmail.com
Handling Editor: Fabian Barbieri
Peer-reviewers: Ryaan El-Andari
Compliance Editor: Oliver Brown

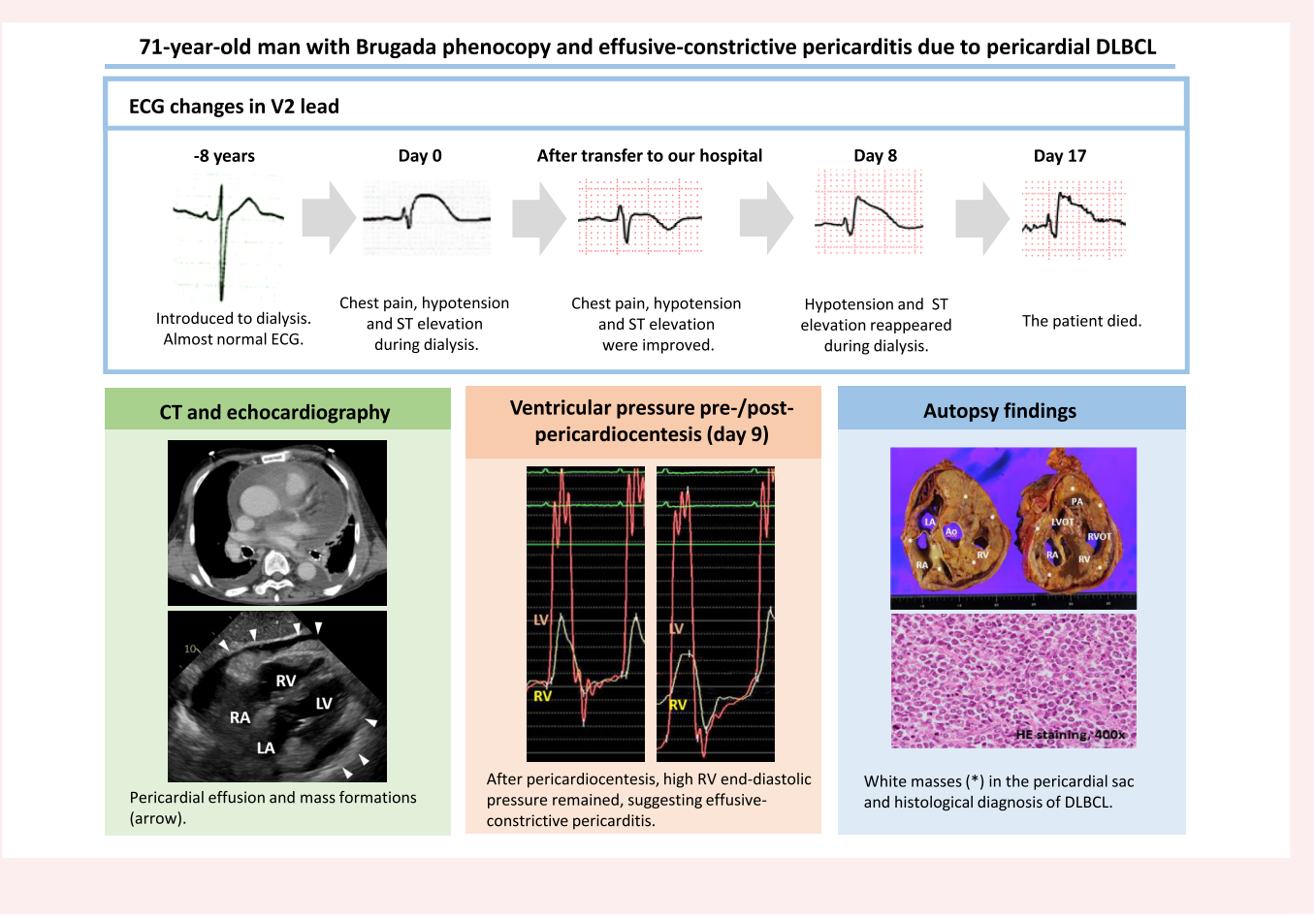
Introduction

Cardiac malignant lymphoma is a rare disease,[1] with diffuse large B-cell lymphoma (DLBCL) being the most common finding.[2] In patients with this disease, pericardial lesions may present with restrictive disorders owing to pericardial effusion and thickening and may be associated with effusive–constrictive pericarditis, in which pericardial drainage does not improve restrictive disorders.[3]

Notably, Brugada syndrome is a genetic disorder characterized by sudden cardiac death.[4] However, many cases of coved-type ST-segment elevation similar to Brugada syndrome occur because of electrolyte abnormalities, mechanical heart compression, myocardial ischaemia, and pericardial disease. In these cases, electrocardiographic changes disappear after resolving the underlying cause. Moreover, it has been proposed that cases presenting with Brugada-type electrocardiogram (ECG) due to such causes should be diagnosed as Brugada phenocopy even though they are not true cases of Brugada syndrome.[5]

Herein, we report a case of pericardial DLBCL with effusive–constrictive pericarditis and Brugada phenocopy.

Summary figure



Case presentation

A 71-year-old man experienced chest pain and reduced blood pressure during maintenance dialysis. His ECG revealed coved-type ST-segment elevation in V1 and V2 leads (*Figure 1B*) and was transported to our hospital.

The patient underwent maintenance dialysis for chronic renal failure for 8 years. He had a history of diabetic nephropathy, hypertension, hyperuricaemia, and secondary hyperparathyroidism but no history of cardiac disease or syncope and no family history of cardiac disease or sudden death. Three months ago, his ECG revealed no significant ST-segment changes (*Figure 1A*).

He had received many drug prescriptions from the previous hospital, including furosemide, polystyrene sulfonate, lanthanum carbonate, bixalomer, cinacalcet, and ferrous fumarate for renal failure, secondary hyperparathyroidism, and anaemia and allopurinol for hyperuricaemia. Moreover, beraprost and clopidogrel were probably prescribed for peripheral circulatory impairment. Furthermore, many symptomatic drugs such as ambroxol, omeprazole, rebamipide, tramadol, nalfurafine, vitamins, and bowel regulators were prescribed.

When he was transported to our hospital, his vital signs were normal, but pitting oedema was noted in both lower extremities. However, clinical signs such as Kussmaul's sign were not assessed. His blood test results revealed mildly elevated Troponin I and brain natriuretic peptide levels [0.83 ng/mL (cutoff, < 0.1 ng/mL) and 600 pg/mL (cutoff, < 18 pg/mL), respectively]. His potassium level was 3.6 mEq/L, and all other electrolyte levels were within the normal limit. Notably, the level of the soluble Interleukin 2 receptor was markedly elevated (17 000 U/mL). Electrocardiogram obtained after the patient's arrival at the hospital revealed an improved ST-segment elevation (*Figure 1C*). Moreover, emergent coronary angiography was performed to rule out acute coronary syndrome, and it revealed no significant stenosis or obstruction. Contrast-enhanced computed tomography and transthoracic echocardiography scans revealed circumferential pericardial effusion of 2–3 cm, pericardial thickening, formation of a mass adhering to the atria and ventricles

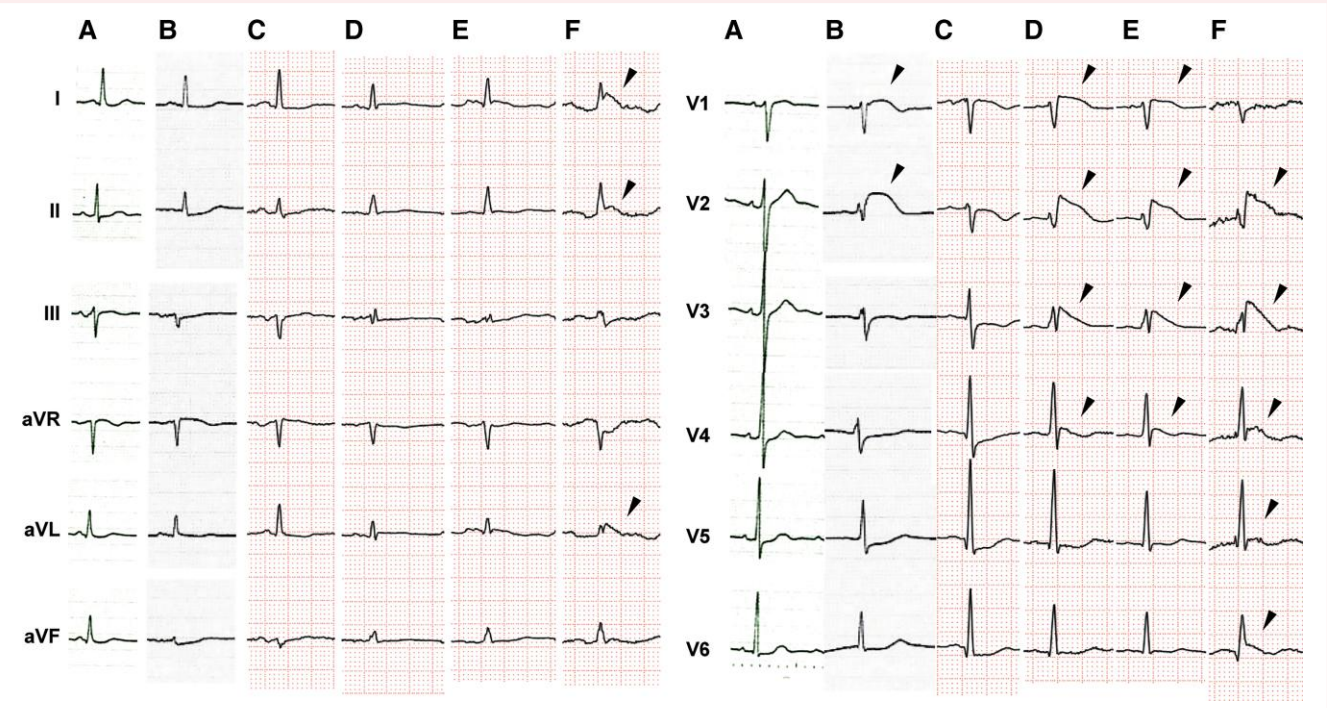


Figure 1 Changes in 12-lead electrocardiogram. Electrocardiograms obtained 3 months earlier (*A*), at the time of chest pain during dialysis (*B*), after patient transfer (*C*), on Day 8 when the patient's blood pressure dropped again (*D*), on Day 10 during pericardial drainage (*E*), and on Day 13 (*F*). ST-segment elevation (arrows) varied. aVF, augmented vector foot; aVL, augmented vector left; aVR, augmented vector right.

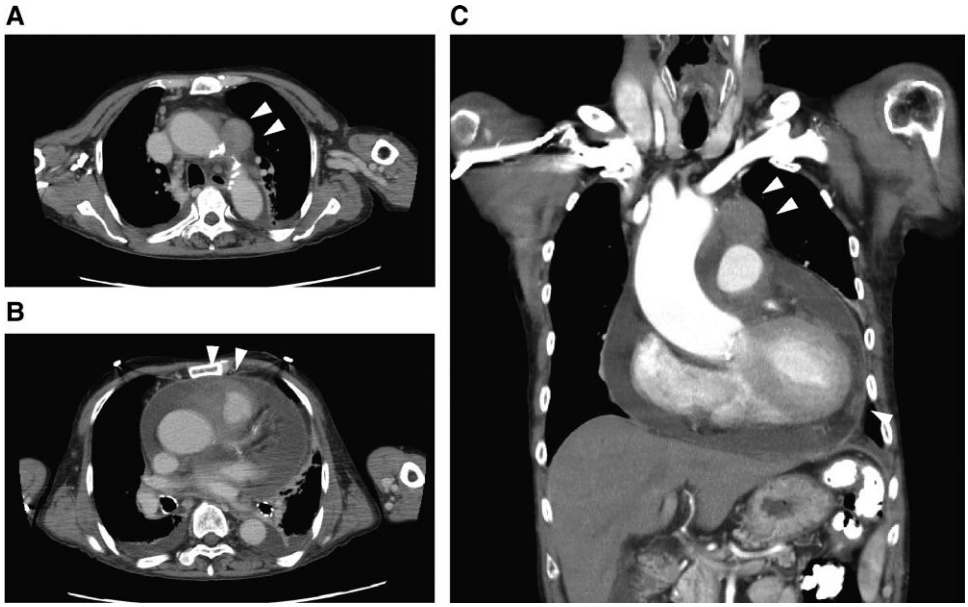


Figure 2 Contrast-enhanced computed tomography. The transverse (*A*, *B*) and coronal (*C*) sections. A large amount of pericardial effusion and thickening as well as a mass (arrow) were observed.

of the visceral epicardium and mild collapse of the right atrium (*Figures 2* and *3*).

The patient exhibited no chest symptoms for a while after admission, and his vital signs and general condition were stable. Therefore, he was scheduled to undergo thorough examinations such as positron emission tomography (PET), and pericardiocentesis was considered as a standby procedure after these examinations. However, 8 days after admission, before performing the scheduled PET, his blood pressure

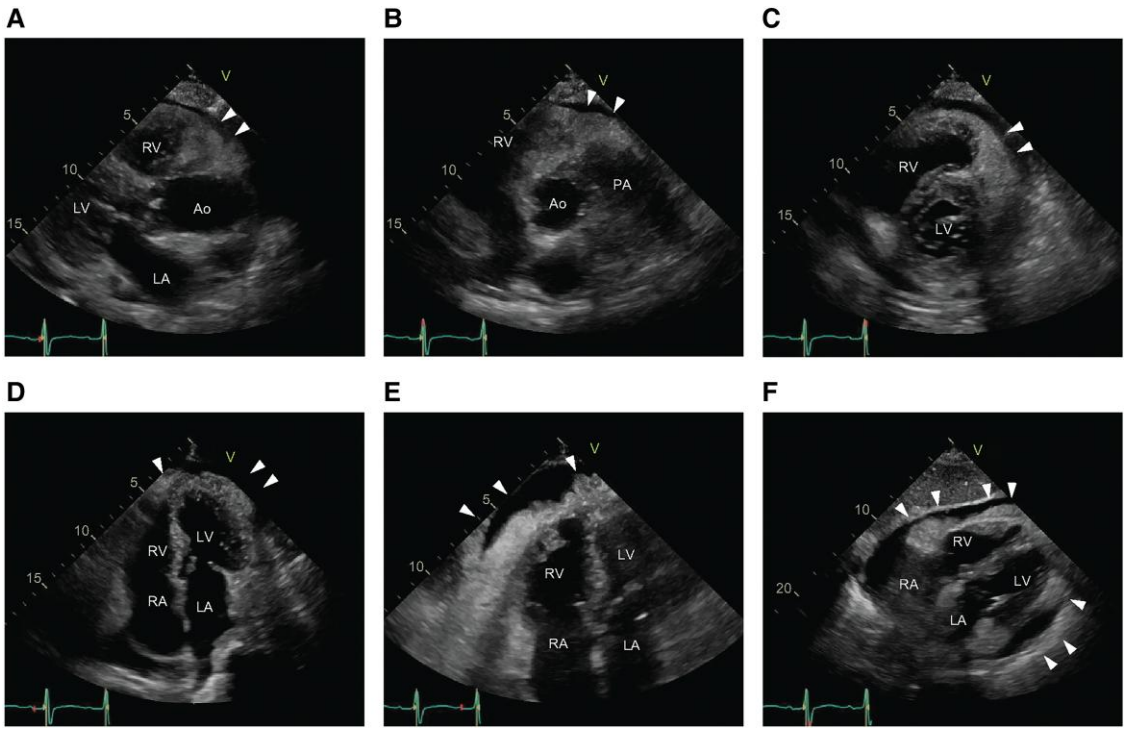


Figure 3 Transthoracic echocardiography. Parasternal long axis (*A*), short axis (*B*, *C*), apical four-chamber (*D*, *E*), and orbital (*F*) views. Pericardial effusion and thickening and mass formation (arrow) were observed. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

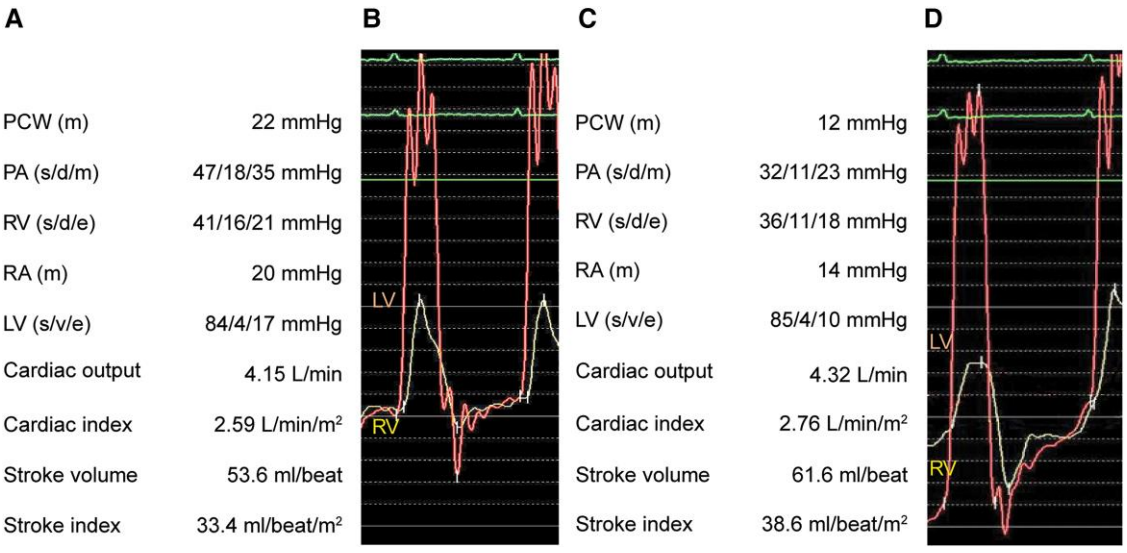


Figure 4 Cardiac catheterization before and after pericardiocentesis. Pulmonary capillary wedge pressure, pulmonary artery, and right atrium pressure were high before pericardiocentesis (*A*). Both waveforms of high left ventricle and right ventricle end-diastolic pressures revealed dip and plateau patterns (*B*). Pulmonary capillary wedge pressure and pulmonary artery pressure improved after pericardiocentesis, but right atrium pressure remained high (*C*). Right ventricle end-diastolic pressure also remained high, with dip and plateau patterns (*D*). PCW, pulmonary capillary wedge pressure; PA, pulmonary artery; RA, right atrium; RV, right ventricle; LV, left ventricle; s, systole; d, diastole; m, mean; e, end-diastole.

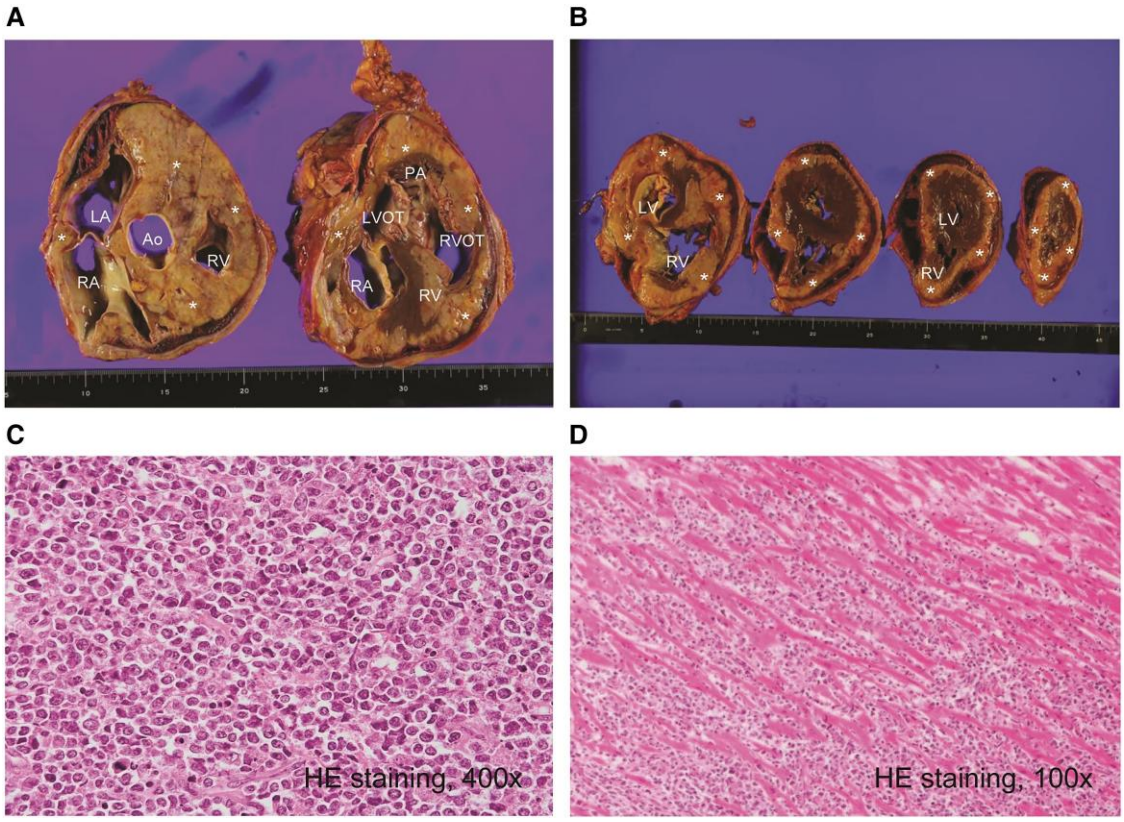


Figure 5 Autopsy findings. A white mass (*) occupied the pericardial sac and further infiltrated the ventricular wall from the epicardial side in the split plane of the short axis of the heart (*A*, *B*). Haematoxylin–eosin staining of the mass (*C*) and left ventricular myocardium (*D*) revealed diffuse proliferation of atypical lymphocytes. Ao, aorta; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract.

dropped, and ST-segment elevation reappeared during dialysis (*Figure 1D*). Moreover, his haemodynamic status did not improve despite the discontinuation of dialysis, and on Day 9, pericardiocentesis and drainage were performed. Further, 450 mL of exudative pericardial fluid was drained. Subsequently, pulmonary congestion and hypertension improved, but right atrial pressure remained high, and dip and plateau findings of right ventricular pressure remained (*Figure 4D*). Therefore, the patient was diagnosed with effusive–constrictive pericarditis. Moreover, pericardial fluid cytology and flow cytometry suggested B-cell lymphoma.

The circulation did not improve; thus, continuous haemodiafiltration was performed, and high doses of noradrenaline and dopamine were administered. However, the coved-type ST-segment elevation remained (*Figure 1F*) and subsequently worsened (*Figure 1E*). Chemotherapy for lymphoma was impossible owing to unstable circulation, and the patient died on Day 17.

Autopsy revealed a markedly enlarged heart with white masses in the pericardial sac, pericardium, and epicardial side myocardium. Histological findings indicated diffuse proliferation of atypical lymphocytes, with prominent nuclear fission images. Immunostaining revealed the following: CD20 (+), CD3 (−), CD10 (−), BCL-6 (+), MUM-1 (+), CD5 (−), and EBER (−). Based on these findings, a diagnosis of non-germinal centre B-type DLBCL was made. Additionally, infiltration and metastasis were observed in the hilar region, right lung, adrenal glands, mesentery, and pancreas (*Figure 5*).

Discussion

Primary cardiac tumours are reported in 0.02% of cases. In particular, primary cardiac lymphoma accounts for 1–2% of these cases.[1] Notably, more than half of cardiac lymphomas are identified as DLBCL.[2] These lymphomas present with various pathologies, including heart failure, arrhythmias, and myocardial ischaemia. Moreover, they have been reported with constrictive pericarditis.[1,6]

Constrictive pericarditis with haemodynamically significant pericardial fluid is known as effusive–constrictive pericarditis. It can be diagnosed by the absence of a decrease in right atrial pressure of >10 mmHg or 50% after pericardiocentesis, as noted in the present case.[3] In the literature, only a few cases of effusive–constrictive pericarditis with cardiac lymphoma have been reported,[7] but haemodynamics should be carefully monitored even after pericardiocentesis because half of the patients with cardiac lymphoma have pericardial effusions.[2]

Brugada syndrome is a genetic disorder associated with a risk of ventricular fibrillation and sudden cardiac death despite the presence of a normal heart. Its diagnosis is based on coved-type ST-segment elevation on right-sided chest leads.[4] Our patient had no history of syncope or family history. Moreover, fever and ventricular arrhythmias were not identified during the clinical course. Based on these findings, Brugada syndrome, including fever-induced Brugada syndrome,[8] should be ruled out.

Conversely, the absence of true Brugada syndrome despite Brugada-type ECG has been defined as Brugada phenocopy.[5] Many

cases of Brugada phenocopy have been reported and classified into six categories: metabolic conditions, mechanical compression, ischaemia, myocardial and pericardial disease, ECG modulation, and miscellaneous.[9] We considered that our patient had Brugada phenocopy due to mechanical compression or myocardial and pericardial disease based on his autopsy findings. A possible mechanism for the presentation of Brugada-type ECG could be the formation of a potential gradient between the epicardial and endocardial sides of the myocardium due to myocardial compression by the pericardial tumour and infiltration of the tumour into the myocardium from the epicardial side. Notably, Brugada phenocopy due to lymphoma has been reported in cases of compression due to mediastinal tumours[10,11] and in a few cases due to cardiac lymphoma.[12,13]

Brugada-type ECG resolves along with Brugada phenocopy.[5] However, in the present case, Brugada-type ECG disappeared on the same day and reappeared after 7 days despite the absence of treatment. Notably, the lymphoma itself was unlikely to rapidly shrink or expand, and the patient was not febrile. His electrolytes were normal, with no other metabolic abnormalities. Moreover, his troponin levels did not increase suddenly, which is suggestive of coronary spasm. This change could not be explained but may be related to electrolytes, haemodynamic changes, and micro-circulatory impairment during dialysis.[14,15]

In summary, our patient presented with pericardial DLBCL and effusive–constrictive pericarditis. Attention should be paid to haemodynamics after pericardiocentesis in cases of cardiac lymphoma with pericardial fluid. This case was considered to be Brugada phenocopy due to pericardial DLBCL with variable ST-segment changes during the course. However, further research is required to better understand Brugada phenocopy.

Lead author biography

The author focuses on cardiovascular diseases at Gunma University and its affiliated hospitals and is engaged in cardiovascular care in the community. He specializes in ischaemic heart disease and cardiac nuclear medicine and regularly performs medical treatment and research.

Acknowledgements

The authors thank Dr Takaaki Sano, Division of Diagnostic Pathology, Gunma University Graduate School of Medicine, for providing detailed information about the autopsy findings of this case. The authors also thank Enago (www.enago.jp) for the English language review.

Consent: The authors confirm that written consent for the submission and publication of this case report, including the images and associated text, was obtained from the patient's family in accordance with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data underlying this manuscript is available in the article and in its online supplementary material.

References

1. Miguel CE, Bestetti RB. Primary cardiac lymphoma. *Int J Cardiol* 2011;**149**:358–363.
2. Chen H, Qian S, Shi P, Liu L, Yang F. A presentation, treatment, and survival analysis of primary cardiac lymphoma cases reported from 2009 to 2019. *Int J Hematol* 2020;**112**:65–73.
3. Baranchuk A, Nguyen T, Ryu MH, Femenía F, Zareba W, Wilde AAM, *et al.* Brugada phenocopy: new terminology and proposed classification. *Ann Noninvasive Electrocardiol* 2012;**17**:299–314.
4. Noma T, Mizushige K, Kohno M. Constrictive pericarditis caused by infiltration of non-Hodgkin's lymphoma. *Heart* 2002;**88**:148.
5. Miranda WR, Oh JK. Effusive–constrictive pericarditis. *Cardiol Clin* 2017;**35**:551–558.
6. Anaya-Cisneros M, Tong MS, Calvo AR. Effusive–constrictive pericarditis secondary to primary pericardial lymphoma: a case report. *World J Oncol* 2012;**3**:87–90.
7. Brugada J, Campuzano O, Arbelo E, Sarquella-Brugada G, Brugada R. Present status of Brugada syndrome: JACC state-of-the-art review. *J Am Coll Cardiol* 2018;**72**:1046–1059.
8. Adler A, Topaz G, Heller K, Zeltser D, Ohayon T, Rozovski U, *et al.* Fever-induced Brugada pattern: how common is it and what does it mean? *Heart Rhythm* 2013;**10**:1375–1382.
9. Anselm DD, Baranchuk A. Brugada phenocopy: redefinition and updated classification. *Am J Cardiol* 2013;**111**:453.
10. Tarín N, Farré J, Rubio JM, Tuñón J, Castro-Dorticós J. Brugada-like electrocardiographic pattern in a patient with a mediastinal tumor. *Pacing Clin Electrophysiol* 1999;**22**:1264–1266.
11. Pérez-Riera AR, Barbosa Barros R, Daminello-Raimundo R, Resende Barbosa MPC, de Abreu LC. Brugada phenocopy caused by a compressive mediastinal tumor. *Ann Noninvasive Electrocardiol* 2018;**23**:e12509.
12. Sato N. Brugada-like ECG associated with primary cardiac lymphoma. *J Clin Exp Cardiol* 2011;**2**:2.
13. Guimarães JP, Trigo J, Fonçalves F, Moreira JI. ST-segment elevation in a patient with cardiac lymphoma. *Neth Heart J* 2020;**28**:496–497.
14. Schüttler D, Schönermarck U, Wenner F, Toepfer M, Rizas KD, Bauer A, *et al.* Large potassium shifts during dialysis enhance cardiac repolarization instability. *J Nephrol* 2021;**34**:1301–1305.
15. McIntyre CW, Burton JO, Selby NM, Leccisotti L, Korsheed S, Baker CSR, *et al.* Hemodialysis-induced cardiac dysfunction is associated with an acute reduction in global and segmental myocardial blood flow. *Clin J Am Soc Nephrol* 2008;**3**:19–26.