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CASE REPORT
Cardiovascular imaging

Massive myocardial infiltration by primary anaplastic T-cell lymphoma: a case report

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Background Myocardial infiltration by primary cardiac neoplasm is a rare entity, providing diagnostic and therapeutic challenges. The pathological spectrum includes more frequently benign forms. Refractory heart failure, pericardial effusion, and arrhythmias due to infiltrative mass are the most common clinical manifestations.

Case summary We describe the case of a 35-year-old man complaining of shortness of breath and weight loss in the last 2 months. A previous acute myeloid leukaemia treated with allogenic bone marrow transplant was reported. Transthoracic echocardiography revealed an apical thrombus in the left ventricle, with inferior and septal hypokinesia conditioning a mildly reduced ejection fraction, circumferential pericardial effusion, and abnormal right ventricular thickening. Cardiac magnetic resonance confirmed diffuse thickening of the right ventricular free wall due to myocardial infiltration. Positron emission tomography showed the presence of neoplastic tissue with increased metabolic activity. A pericardiectomy was performed showing a widespread cardiac neoplastic infiltration. Histopathological analysis done on right ventricular pathological samples obtained during cardiac surgery revealed the presence of a rare and aggressive cardiac anaplastic T-cell non-Hodgkin lymphoma. Few days after the operation, the patient developed refractory cardiogenic shock and unluckily died before initiating an adequate antineoplastic therapy.

Discussion Primary cardiac lymphoma is not frequent, and the lack of specific symptoms makes the diagnosis extremely challenging and often limited to autopsy findings. Our case highlights the importance of an appropriate diagnostic algorithm, requiring non-invasive multimodality assessment imaging and then invasive cardiac biopsy. This approach may allow an early diagnosis and an adequate therapy for this otherwise fatal pathology.

Keywords Myocardial infiltration • Primary cardiac lymphoma • Cardiac magnetic resonance • Echocardiography • Non-Hodgkin lymphoma • Case report

ESC Curriculum 6.8 Cardiac tumours • 2.1 Imaging modalities • 2.4 Cardiac computed tomography • 2.3 Cardiac magnetic resonance • 2.2 Echocardiography

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Learning points

- Primary cardiac lymphomas are rapidly growing tumours that involve predominantly the right side of the heart.
- Extranodal lymphomas are increasingly seen with acquired immunodeficiencies such as HIV infection or after bone marrow and solid organ transplantation.
- Exceptional diagnostic and therapeutic challenges were provided due to the rarity of this tumour.
- Multimodality imaging is essential to determine the characteristics of a cardiac neoplasm.
- Non-specific signs and symptoms, late diagnosis, and rapid evolution of cardiac involvement are the major factors affecting the outcome.
- Overall prognosis is poor, and treatment options are limited.

Introduction

Primary cardiac neoplasm is a rare entity. The pathological spectrum includes more frequently benign forms, with cardiac myxoma being the most prevalent one. Regarding malignant tumours, primary cardiac lymphoma (PCL) accounts for <2% of cardiac neoplasms.[1] Primary cardiac lymphoma is a subtype of non-Hodgkin B cell lymphoma. Given the lack of specific symptoms, the diagnosis of PCL may be challenging. Refractory heart failure, pericardial effusion, and arrhythmias due to infiltrative mass are the most common clinical features.[2] A multimodality imaging, with echocardiography, computed tomography (CT), and cardiac magnetic resonance imaging (MRI), is crucial to determine the characteristics of a cardiac tumour and can guide towards the diagnosis of PCL. This report presents an interesting case of a rare and aggressive anaplastic T-cell non-Hodgkin lymphoma involving mainly the right side of the heart.

Timeline

Two years prior to admission	An acute myeloid leukaemia treated with allogenic bone marrow transplant was reported.
Six months prior to admission	Leukaemia relapse treated with chemotherapy and in pathological complete remission at hospital admission.
Day 1	Hospital admission for shortness of breath and weight loss.
Day 2	An abnormal right ventricular thickening was revealed by echocardiography.
Day 6	Myocardial infiltration of the right ventricular free wall was suspected by cardiac magnetic resonance imaging.
Day 8	At chest computed tomography scan, the right coronary artery appeared to be incorporated by the pathological tissue.
Day 10	Cardiac positron emission tomography showed the presence of neoplastic tissue with increased metabolic activity.
Day 11	A percutaneous endomyocardial biopsy obtained during cardiac catheterization was inconclusive.
Day 13	The patient's haemodynamic status rapidly worsened.
Day 15	A pericardiectomy was performed, taking in pathological samples for histopathological analysis.
Day 26	Histopathological analysis on right ventricular pathological samples taken during surgery revealed tissue involvement by a cardiac anaplastic large T-cell non-Hodgkin lymphoma.
Day 27	The patient developed a refractory cardiogenic shock and died before initiating an adequate antineoplastic therapy.

Continued

Case presentation

A 35-year-old man without cardiovascular risk factors presented in the Emergency Department complaining of shortness of breath and weight loss in the last 2 months. A previous history of acute myeloid leukaemia treated with allogenic bone marrow transplant and subsequent relapse treated with chemotherapy was reported. Pathological complete remission with azacitidine and venetoclax was described, and disease-free survival was reported at the latest follow-up 4 months before. Upon admission, body temperature was 37.1°C, heart rate was 87 beats per minute, saturation on room air oxygen was 98%, and blood pressure was 130/80 mmHg. Physical examination showed normal heart sounds, without murmur, and bilateral lower extremities pitting oedema. Q-waves in inferior leads, diffuse T-waves inversion, and low QRS voltage were present at electrocardiography (*Figure 1*). Blood tests revealed leucocytopenia (2900/μL, with normal value 4500–11 000/μL), normal renal, and liver function. Blast cells were not detected on peripheral blood smear. Transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE) demonstrated inferior and septal hypokinesia conditioning a mildly reduced left ventricular ejection fraction (45%), circumferential pericardial effusion without cardiac tamponade, and abnormal right ventricular thickening (*Figure 2*, in-line video, and see Supplementary material online, *Video S1*). Furthermore, an apical thrombus in the left ventricle was present (*Figure 3*, in-line video, and see Supplementary material online, *Video S2*). Echocardiographic parameters of longitudinal function of the right ventricle were normal. The patient was admitted to the coronary care unit, and anticoagulation therapy with low-molecular-weight heparin was started, with evidence of thrombus resolution in approximately 10 days. Cardiac MRI confirmed a diffuse thickening of the right ventricular free wall (maximum diameter 30 mm). The tissue was isointense on T1-weighed images, without late gadolinium enhancement (LGE), suggestive for myocardial infiltration primarily of the right ventricle, extending to the right atrium and left ventricle. A subendocardial LGE of left ventricular inferior wall was also observed, with ischemic distribution (*Figure 4*, in-line video, and see Supplementary material online, *Video S3*). An elevation of high-sensitivity troponin I values was documented, and coronary angiography was performed indicating no atherosclerotic coronary artery disease. However, at chest CT scan, the right coronary artery appeared to be incorporated by the pathological tissue (see Supplementary material online, *Video S4*). Positron emission tomography showed the presence of neoplastic tissue with

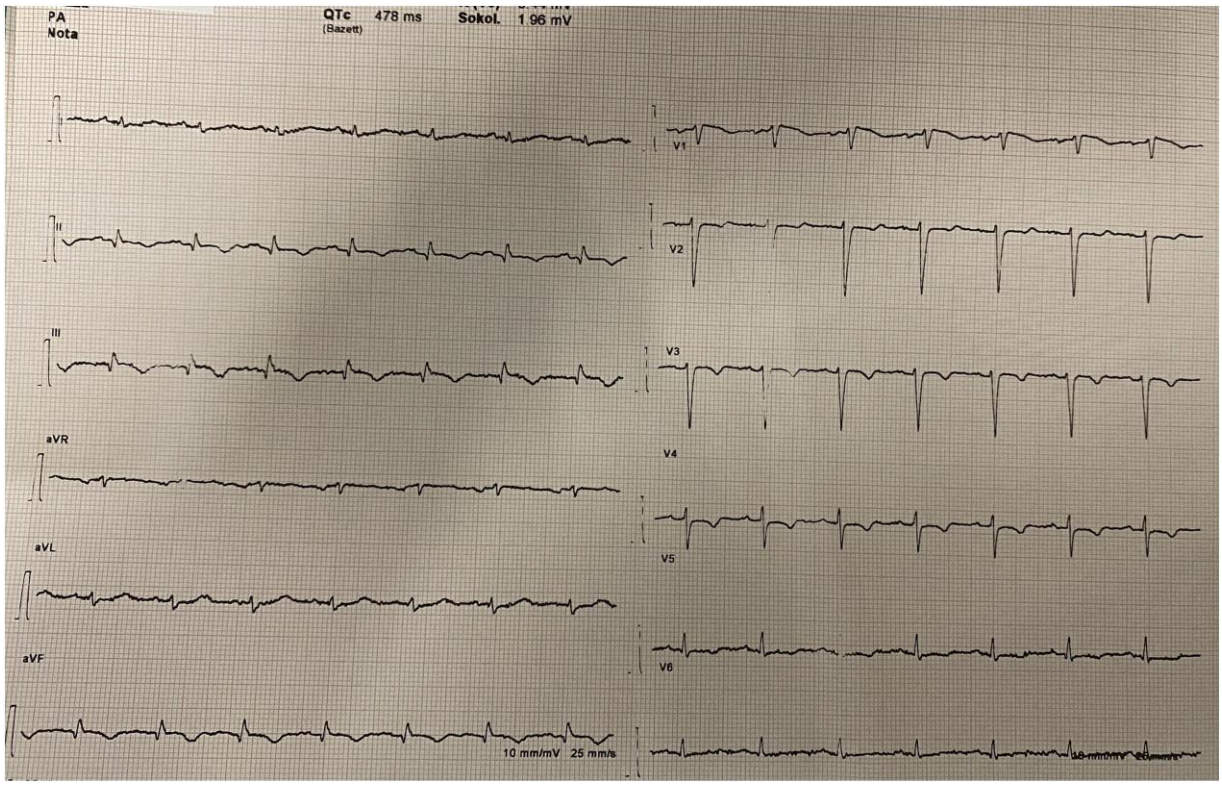

Figure 1 Q-waves in inferior leads, diffuse T-waves inversion, and low QRS voltage were revealed by 12-lead electrocardiography.

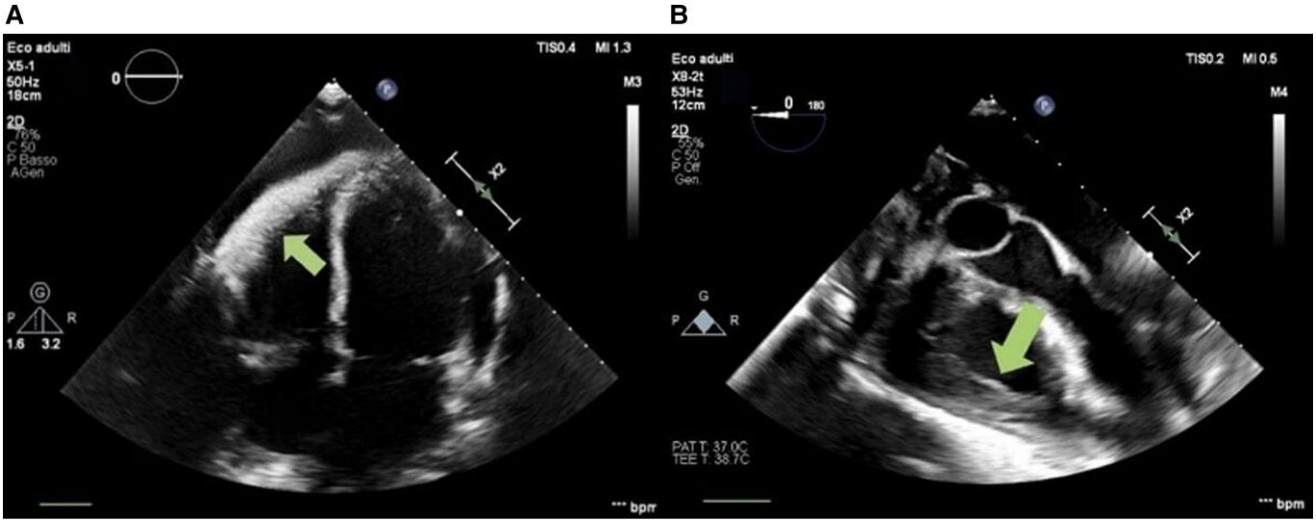

Figure 2 Transthoracic at apical four-chamber view (*A*) and transoesophageal at mid-oesophageal four-chamber view 0-degrees (*B*) echocardiogram showed abnormal right ventricular thickening (arrows).

increased metabolic activity within the heart, in ascending aorta and aortic arch (*Figure 5*). No neoplastic localization was found at bone marrow biopsy. During hospitalization, patient's haemodynamic status rapidly worsened in few days. A sustained ventricular tachycardia occurred and was successfully treated with intravenous amiodarone and metoprolol. Subsequent TTE and TOE revealed severe impairment of the right ventricular function and dilatation of the inferior vena cava (see Supplementary material online, *Video S5*). Since percutaneous

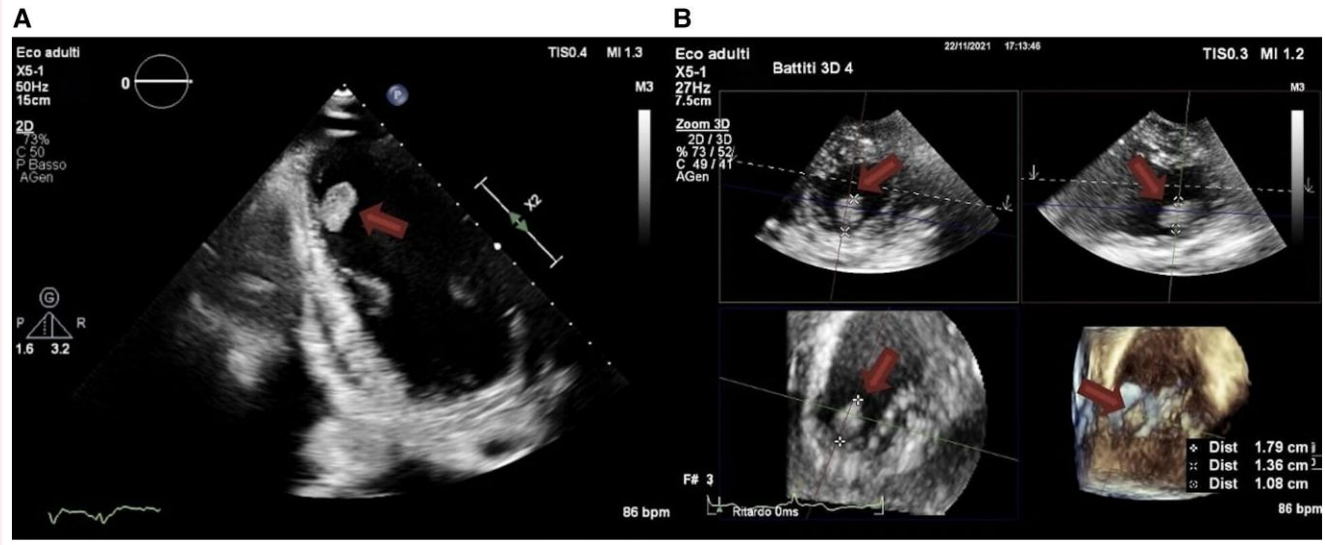

Figure 3 Transthoracic two-dimensional (*A*) and three-dimensional (*B*) echocardiography showed an apical thrombus in the left ventricle (arrows).

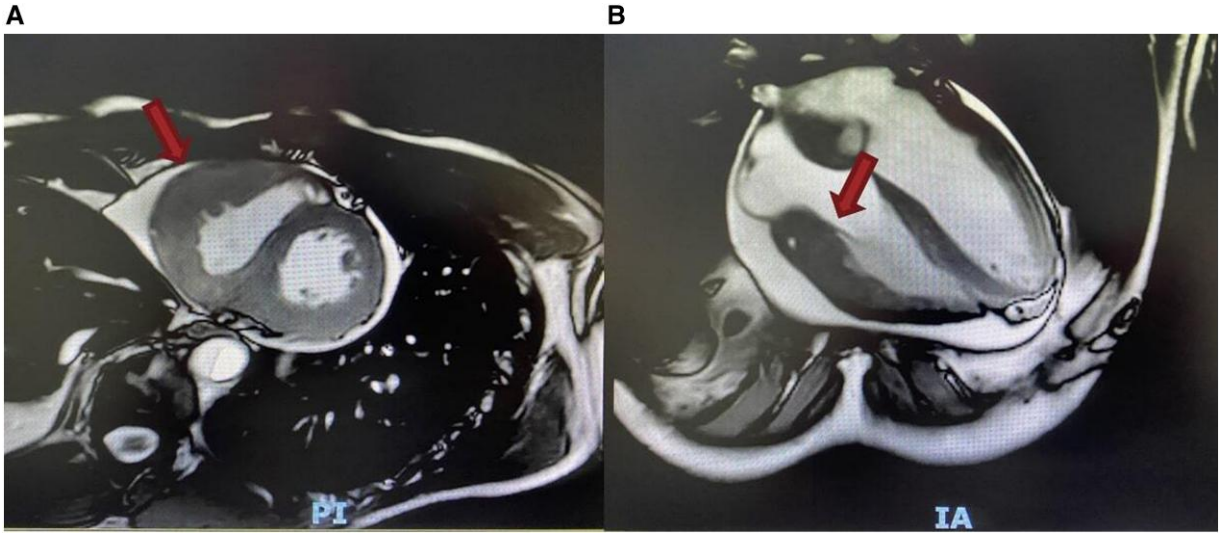

Figure 4 Cardiac magnetic resonance imaging confirmed thickening of the right ventricular free wall due to myocardial infiltration (arrows) in short-axis view (*A*) and four-chamber view (*B*).

endomyocardial biopsy obtained during cardiac catheterization was inconclusive, a surgical pericardiectomy was performed via median sternotomy; it showed widespread cardiac neoplastic infiltration. Histopathological analysis on right ventricular pathological samples taken during surgery demonstrated tissue involvement by a rare and aggressive cardiac anaplastic large T-cell non-Hodgkin lymphoma (BCL2+, CD4+, CD30+, ALK−, and Ki-67 90%). The atypical lymphoid cells were large-sized with abundant cytoplasm, growing in a cohesive pattern (see Supplementary material online, *Figure S6*). Few days after surgery, the patient developed refractory cardiogenic shock treated with dobutamine and norepinephrine. He unluckily passed away in 1 day, before initiating an adequate antineoplastic therapy.

Discussion

Cardiac masses arising from the heart are potentially lethal, and almost 75% of them are benign. Metastatic deposits represent the lion's share of cardiac malignancies, whereas the most common primary malignant tumours are lymphomas and sarcomas.[3] Approximately 80% of cases of primary cardiac lymphoma in immunocompetent hosts are represented by diffuse B-cell lymphoma, whereas in patients with immunodeficiency states, such as those with HIV infection or after bone marrow and solid organ transplantation, small non-cleaved or immunoblastic lymphomas are more frequent.[4] Cardiac lymphomas generally

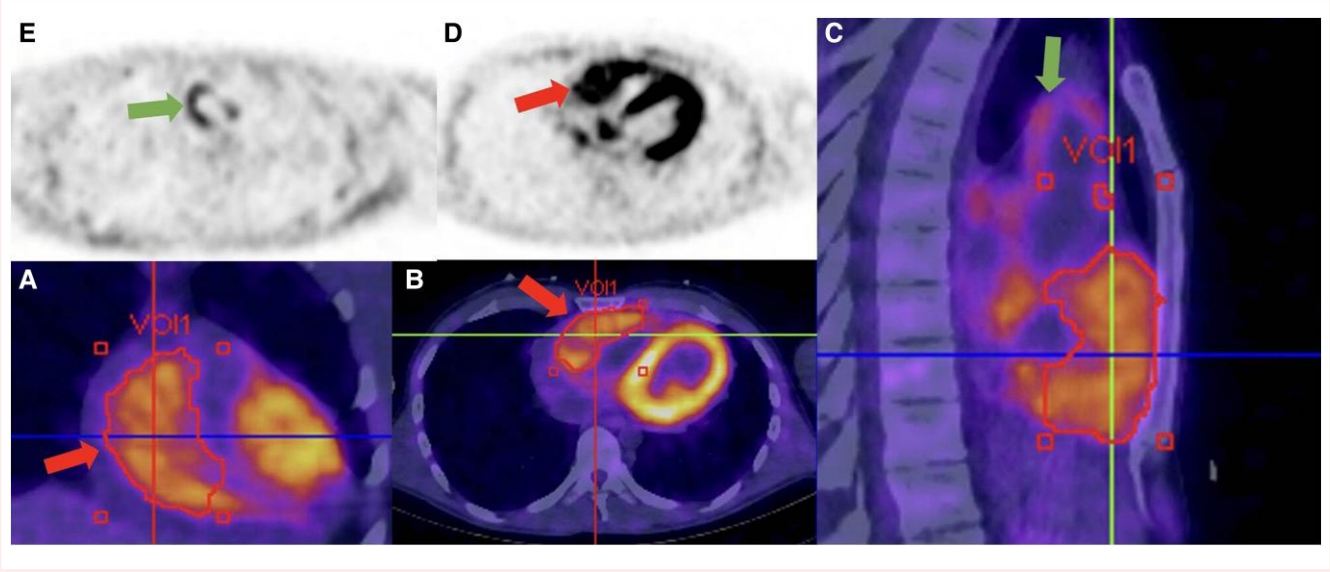

Figure 5 Cardiac positron emission tomography showed a neoplastic tissue with increased metabolic activity (*A*, *B* and *D*, arrows). Similar characteristics were also evident in ascending aorta and aortic arch (*C* and *E*, arrows).

involve the right side of the heart, but may also involve valves, ascending aorta or pulmonary artery, often presenting as a nodular or polypoid mass with variable myocardial infiltration.[5] Indicators of malignancy are pericardial effusion, sometimes complicated with cardiac tamponade, irregular lesion borders of the mass, and lymphomatous myocardial infiltration. Although rare, cardiac conduction disturbances may be the first manifestation of cardiac lymphoma or of its treatment failure.[6] T-cell lymphomas are more likely to spread widely, with pericardial effusion being more closely linked to the expansion of the disease.[7] Ventricular thrombosis is generally due to malignancy-related hypercoagulability. The common presentation is a mass in one or multiple chambers of the heart, whereas an isolated lymphomatous infiltration of the myocardium is more rarely observed.[8] As reported in the latest European Society of Cardiology (ESC) guidelines on cardio-oncology,[9] a multimodality imaging is important to assess the characteristics of a cardiac tumour. Echocardiography usually represents the first imaging step, while cardiac CT scan and MRI offer further tissue characterization and anatomical information. Unlike other malignant tumours, such as sarcomas, lymphomas generally lack regions of central necrosis and haemorrhage. As a result, at cardiac MRI sequences, lymphomas are typically homogeneous and isointense on T1- and T2-weighted images. Similarly, unlike other malignant tumours, there is generally minimal contrast agent uptake.[10] Of note, nuclear imaging is useful for the therapeutic management and to evaluate the response to chemotherapy.[11] Biopsy and histopathological evaluation are required to confirm the diagnosis if a primary tumour is suspected, and/or diagnosis is uncertain at imaging.[9–12] In our case, percutaneous endomyocardial biopsy was inconclusive, then a surgical pericardiectomy was performed and provided samples for histopathological analysis. In selected cases, cytological examination of pericardial fluid may help to reach a diagnosis by detection monoclonal lymphocytes at flow cytometry analysis. In our patient, the diagnosis of PCL was based on REAL (Revised European American Lymphoma) classification.[13] The most frequent differential diagnosis facing a cardiac mass includes intracardiac thrombus, which usually arises in the left ventricle in the setting of hypokinetic-dilated cardiomyopathy, and a benign mesenchymal tumour, mostly myxoma, attached to the endocardial surface by a stalk and possibly associated with emboli-related symptoms.[14] With regard to treatment, chemotherapy has shown to have the greatest effect on survival in patients with lymphoma,[1] while surgical removal of the mass is generally not indicated. However, because of the rarity of the disease, robust data are lacking. Overall, prognosis is poor, with a median survival <1 year after the diagnosis.

In conclusion, this case highlights the importance of an appropriate diagnostic algorithm, requiring a non-invasive, multimodality assessment imaging and then invasive cardiac biopsy.[9] This approach may allow an early diagnosis and an adequate therapy of this otherwise fatal pathology. Non-specific signs and symptoms, late diagnosis, and rapid evolution of cardiac involvement are the major factors affecting outcome.

Lead author biography

Luca Cumitini was born in Turin, Italy, in 1993. He graduated as a medical doctor in School of Medicine of Turin University in 2019. He is currently a cardiology resident in the Department of Thoracic and Cardiovascular Diseases of University of Eastern Piedmont, Novara, Italy. He has a special interest for heart failure and intensive cardiac care.

Supplementary material

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

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors 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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Data availability

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

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