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CASE REPORT
Cardiovascular imaging

Cardiac involvement in a female patient with Beçhet's disease: newer diagnostic and therapeutic approaches—a case report

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Background Behçet's disease (BD) is a multisystemic chronic inflammatory disorder. Cardiac manifestations in BD are extremely rare. There have been no reports of cardiac involvement of BD and especially endomyocardial fibrosis in the left ventricle (LV).

Case summary A 50-year-old woman presented at the emergency department experiencing palpitations and fatigue, accompanied by elevated levels of B-type natriuretic peptide. Her medical history included mucocutaneous involvement of BD. Vital signs were within normal ranges, and electrocardiography showed a normal sinus rhythm. Physical examination did not reveal any pathological findings. The 24 h ambulatory electrocardiogram monitoring indicated sinus rhythm with premature ventricular contractions. Transthoracic echocardiography demonstrated a reduced LV ejection fraction. Further investigation with cardiac magnetic resonance imaging reported diffused areas of subendocardial enhancement, indicative of fibrosis likely due to vasculitis probably associated with BD. The patient was administered tartrate metoprolol, eplerenone, and dapagliflozin in addition to the ongoing medical treatment for BD, which included methylprednisolone, colchicine, and apremilast. This treatment approach resulted in an improvement in the patient's clinical condition.

Discussion This case highlights that diffuse subendocardial fibrosis of the LV may be associated with the underlying BD.

Keywords Behçet's disease • Cardiac manifestations • Endomyocardial fibrosis • Case report

ESC curriculum 2.2 Echocardiography • 2.3 Cardiac magnetic resonance

Learning points

- To comprehend the cardiac complications, such as endomyocardial fibrosis, associated with Behcet's disease
- To describe the presence of subendocardial diffused fragmented myocardial fibrosis as a potential pattern of vasculitis on CMR

Introduction

Behçet's disease (BD) is a multisystemic chronic inflammatory disorder that affects vessels of all sizes. Cardiac involvement is among the life-threatening manifestations of BD leading to endomyocardial fibrosis, intravenous or intracardiac thrombus, endocarditis, myocarditis, pericarditis, coronary arteritis, myocardial infarction, aortic stenosis, mitral valve prolapse, periaortic pseudoaneurysm, pulmonary artery aneurysm, conduction system disturbances, and supraventricular or ventricular arrhythmias.[1] Even if cardiac involvement is rare in BD (up to 6%), the initial subclinical course of the disease and the possible malignant complications should alert physicians

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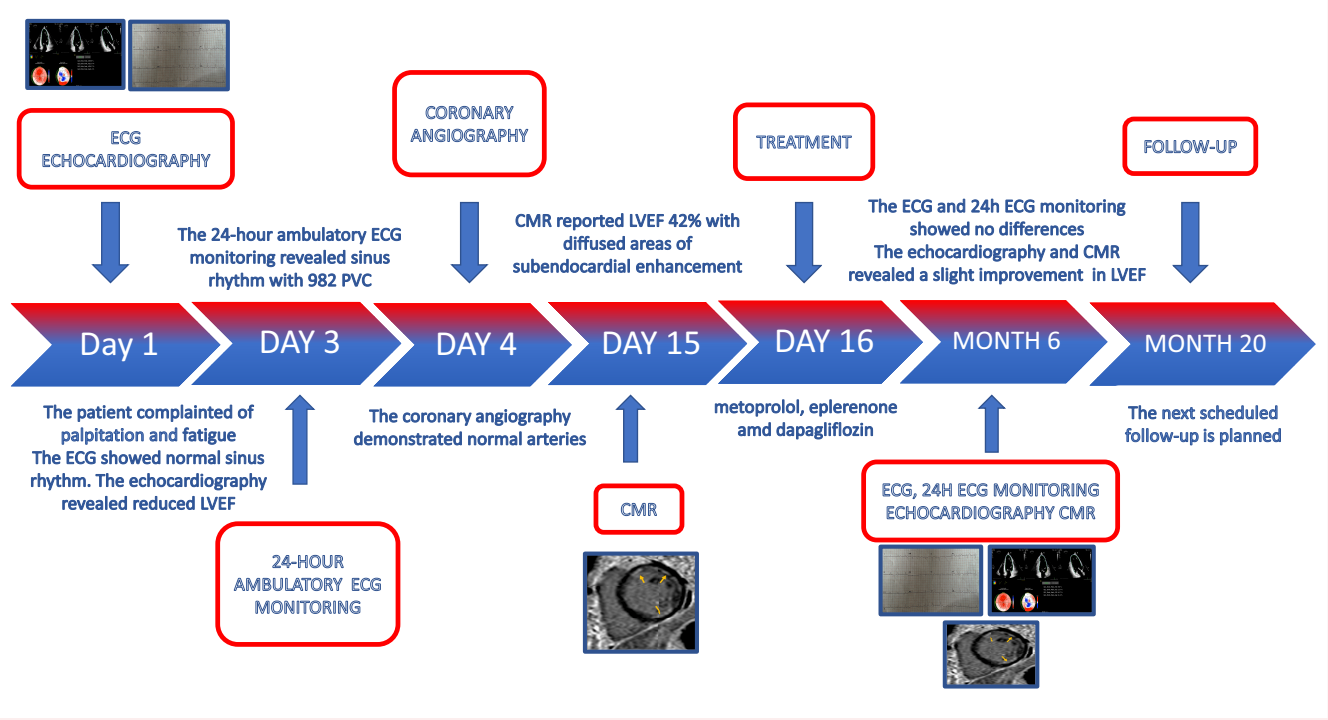
involved in the care of BD patients.[2] We present a 50-year-old woman with cardiac BD and left ventricular endomyocardial fibrosis.

Summary figure



History of presentation

A 50-year-old Greek woman with no cardiovascular risk factors was admitted to our hospital in August 2021 with palpitations and fatigue. Blood pressure measurements and heart rate were in normal range (110/75 mmHg, 70 b.p.m.). The clinical examination, laboratory tests (hs troponin I 3 ng/L, normal range < 14 ng/L), and chest radiography (X-ray) did not reveal any abnormal findings, apart from an elevation at B-type natriuretic peptide values (400 pg/mL, normal range < 100 pg/mL). Electrocardiography (ECG) showed normal sinus rhythm with poor progression of QRS in V1–V3 and normal QRS duration 80 ms.

The patient had no other past medical history aside from BD with mucocutaneous involvement, including oral and genital aphthosis, 16 years ago. The diagnosis was based on the International Criteria for Behçet's Disease, with the patient accumulating 5 points: 2 points for oral aphthosis, 2 points for genital aphthosis, and 1 point for a positive pathergy test. The patient has since received medical treatment (colchicine 0.5 mg once per day, methylprednisolone 2 mg once per day, and apremilast 30 mg twice per day).

Other immune-mediated inflammatory diseases that may present with recurrent aphthosis and heart involvement, e.g. systemic lupus erythematosus, ANCA-associated vasculitides, and inflammatory bowel diseases, were excluded after appropriately extensive workup, and HLA-B51 was negative.

Transthoracic echocardiography revealed a mildly enlarged left ventricle with slightly increased dimensions (left ventricular end-diastolic dimension: 52 mm, left ventricular end-systolic dimension: 37 mm, left ventricular end-diastolic volume: 96 mL, left ventricular end-systolic volume: 60 mL), normal wall thickness (7 mm), and reduced left ventricular ejection fraction (LVEF) ~35%–40% with diffuse hypokinesis more prominent at the basal segments of septal and posterolateral wall, with no signs of congestion, significant valvulopathy, or thrombus (see Supplementary material online, *Video S1*). Similarly, global longitudinal strain (GLS) was significantly reduced (GLS −11%) with segmental abnormalities particularly in septal and inferior myocardial wall (see Supplementary material online, *Video S1*; *Figure 1*). Concerning the arrhythmogenic risk, the 24 h ambulatory ECG monitoring revealed sinus rhythm with 982 monomorphic premature ventricular contractions (PVCs), two PVC couplets, and 585 supraventricular premature beats. The coronary angiography demonstrated normal arteries. Consequently, cardiac magnetic resonance (CMR) imaging showed a reduced LVEF with areas of subendocardial late gadolinium enhancement (LGE) (~24% LGE/LV mass) at the basal and medial segments of the anterior, anteroseptal, lateral and inferior walls, and at mid wall of basal inferoseptal wall of the left ventricle. Moreover, there was increased native T1 value (1131 ms, normal range 950–1050 ms) and raised extracellular volume fraction (ECV) at 34% (normal range 25 ± 4%) while the T2 value remained within the normal range (<59 ms) (*Figure 2*).

It was decided to optimize the maximum tolerated medical treatment to metoprolol tartrate 25 mg twice per day, eplerenone 25 mg once per day, dapagliflozin 10 mg once per day additionally with the medical treatment for BD (methylprednisolone 2 mg once per day, colchicine 0.5 mg once per day, and apremilast 30 mg twice per day). The

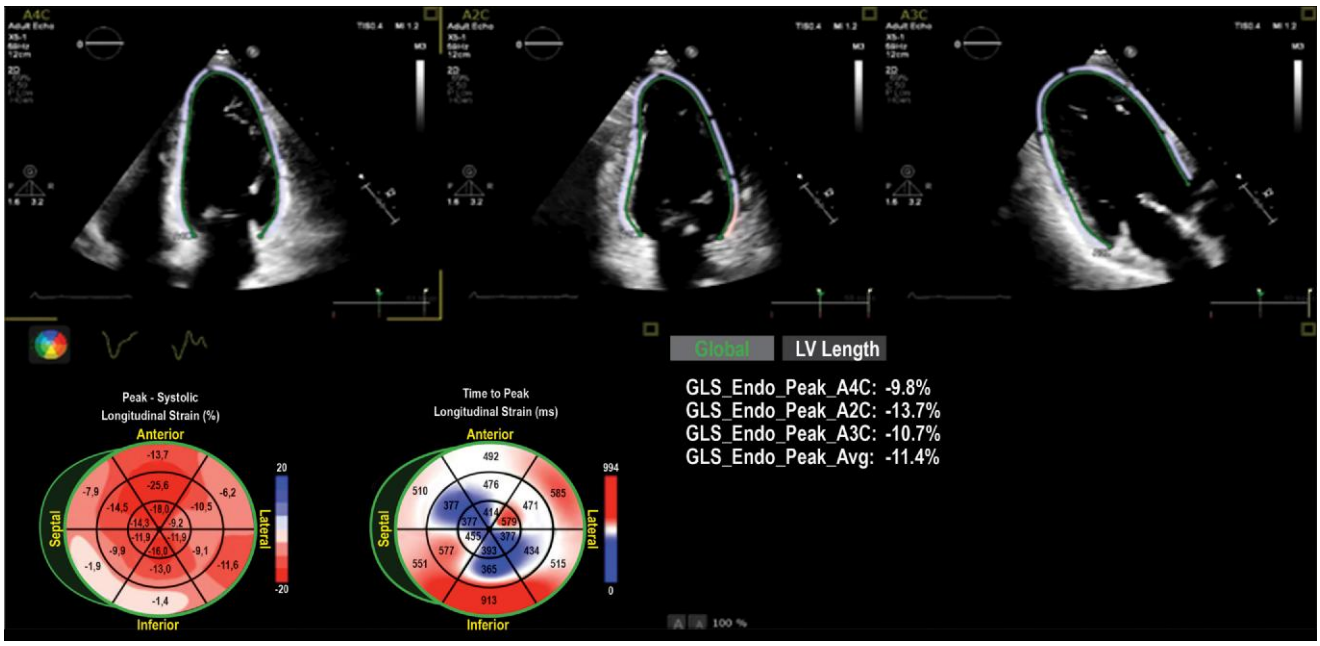


Figure 1 Transthoracic echocardiography. Global longitudinal strain assessment using speckle-tracking echocardiography showed a reduced average global longitudinal strain of −11%. The top row displayed regional strain maps in the apical four-chamber (A4C), apical two-chamber (A2C), and apical three-chamber (A3C) views. The left bullseye illustrated the regional longitudinal strain for each segment in the 18-segment model of the left ventricle. This figure was edited by professor Constantina Aggeli.

administration of ACEi/ARB/ARNi was ceased due to the occurrence of hypotension.

At the 6-month follow-up, the patient referred a mild improvement in symptoms. The ECG showed normal sinus rhythm, and the 24 h ambulatory ECG monitoring indicated a similar burden of ventricular ectopy. Transthoracic echocardiography revealed a slight improvement in LVEF (~45%) and in GLS (−14%) (see Supplementary material online, *Video S2*; *Figure 3*). Similarly, CMR showed a slight improvement in LVEF (50%) and a decrease in native T1 value (1082 ms) and in ECV (32%), with no significant changes in LGE (*Figure 4*). The patient continued with the same medical treatment as she had amelioration of symptoms and clinical improvement. It was decided to schedule follow-ups every 6 months, including 24 h ambulatory ECG monitoring and transthoracic echocardiography, depending on clinical status of the patient.

Discussion

The presence of fibrosis in left ventricle of the patient, without any documented history of myocarditis or a hereditary history of any type of cardiomyopathy, suggests a potential association with BD. The possible combination of BD with endomyocardial fibrosis appears to be extremely rare; since the first reported case in 1977 at necropsy, only 15 others have been described.[3] Apart from that, this case is also unique as it involves the left ventricle whereas the cardiovascular complications of BD mainly implicate the right ventricle and tricuspid valve.[4] Moreover, our patient has clinical interest due to the concomitant arrhythmic manifestation of ventricular ectopy.

The pathophysiologic mechanism of cardiac manifestations in BD is explained as a consequence of vasculitis, involving the endocardium, myocardium or both, and may be complicated by intraventricular thrombus.[5] While arteriole and artery involvement due to vasculitis, characterized by narrowing of lumen through fibroelastic proliferation and focal fibrinoid deposition, is well established in patients with BD, the association between arteritis and endomyocardial fibrosis is not fully understood.[5,6]

In most cases of BD, the patients are asymptomatic, and endomyocardial fibrosis is incidentally discovered through routine echocardiography and mainly affecting the right ventricle. Heart failure is the main clinical presentation of endomyocardial fibrosis, and the symptoms are related to the extent and location of the lesions.

In our case, the observed clinical and echocardiographic improvement may be attributed to remodelling of left ventricle as a result of heart failure treatment, although there is a lack of evidence on the use of standard HFrEF guideline-directed medical therapy in patients with BD.

Cardiac magnetic resonance is the gold standard diagnostic technique for myocardial tissue characterization and quantification of fibrosis through LGE. Moreover, CMR estimates extracellular volume and assesses the systolic/diastolic function of both ventricles. These data are correlated with myocardial function and arrhythmogenic risk. In our patient, CMR findings suggest the presence of fibrosis without coronary vessel distribution and are consistent with lesions from vasculitis (*Figures 3 and 4*). Since the patient had not history of myocarditis or hereditary cardiomyopathy, the CMR results may be associated with the underlying BD. Additionally, our patient did not meet the criteria for undergoing an endomyocardial biopsy, as there was no suspicion of fulminant/acute myocarditis accompanied by acute heart failure and/or arrythmias.[7] Positron emmision tomography/computed tomography (PET/CT) imaging did not provide significant results from the rheumatology perspective, as there was no clinical evidence of disease activity. While this imaging could be valuable for documenting systemic inflammation, it was not considered in our case due to its drawbacks, including high cost, radiation exposure, and limited tissue characterization capabilities, rendering it unsuitable for assessing fibrotic lesions often associated with connective tissue diseases.[8]

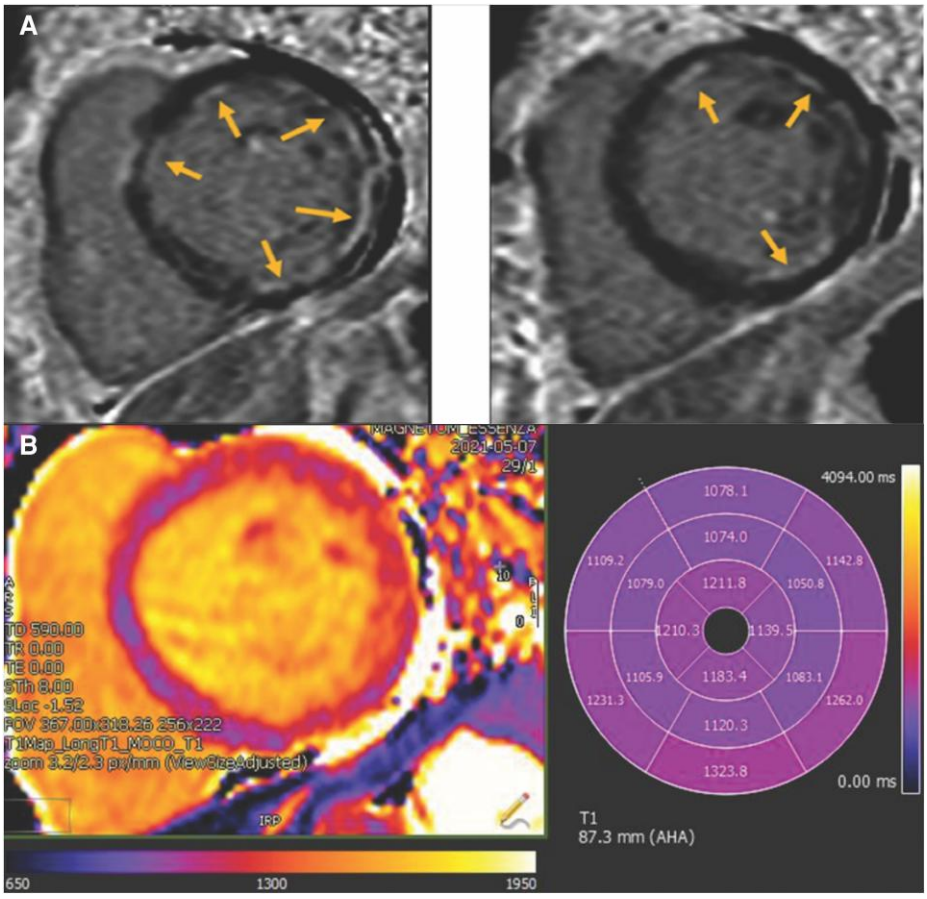


Figure 2 Cardiac magnetic resonance. (*A*) Delayed-enhancement cardiac magnetic resonance of short-axis view revealed subendocardial hyperenhancement of the left ventricle, suggesting fibrosis. (*B*) Native T1 mapping showed an elevated native myocardial T1 value. This figure was edited by Dr Alexios Antonopoulos.

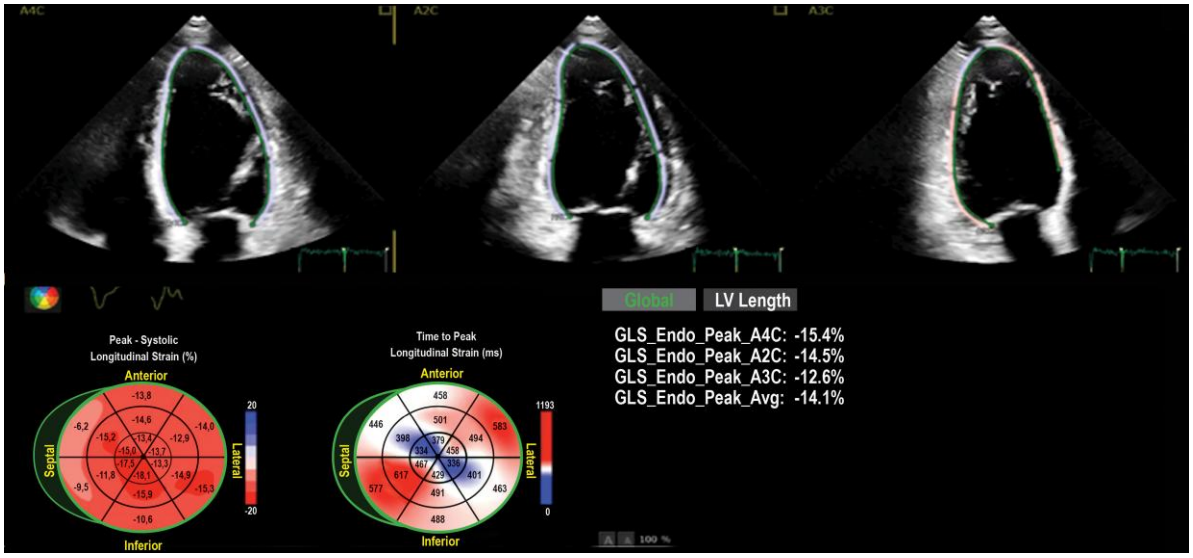


Figure 3 Transthoracic echocardiography. Follow-up transthoracic echocardiography showed a slight improvement in the average of global longitudinal strain of −14%. This figure was edited by professor Constantina Aggeli.

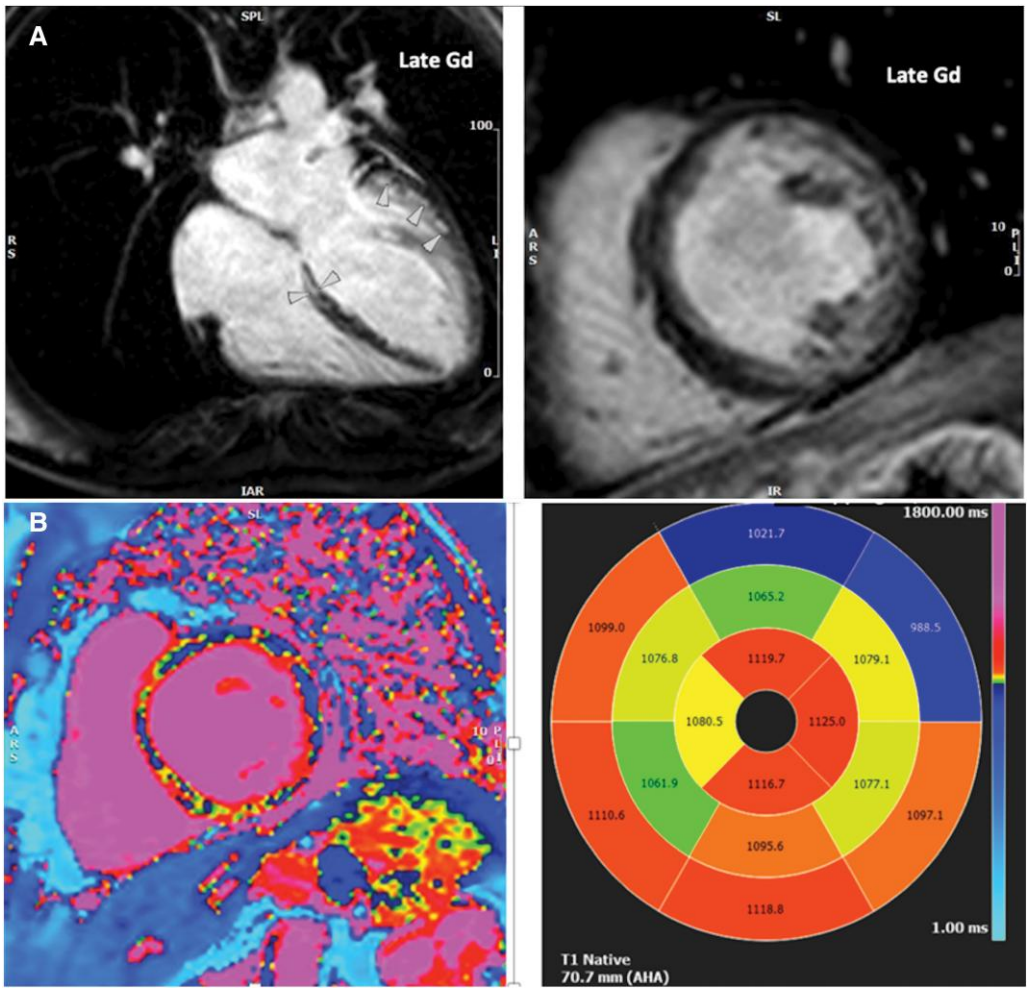


Figure 4 Cardiac magnetic resonance. (*A*) Follow-up delayed-enhancement cardiac magnetic resonance in the apical four-chamber and short-axis view showed no significant changes in subendocardial hyperenhancement (fibrosis) of the left ventricle. (*B*) Native T1 mapping revealed elevated extracellular volume fraction and increased myocardial T1 values. This figure was edited by Dr Alexios Antonopoulos.

It has been considered that autoimmune rheumatic diseases involve several mechanisms including re-entry due to myocardial scar, autoimmune myocardial inflammation through arrhythmogenic autoantibodies and inflammatory channelopathies, and increased wall stress due to depressed myocardial function.[9] Therefore, in addition to beta-blockers and aldosterone antagonists, anti-inflammatory treatment may play an important role in the management of heart failure and the suppression of ventricular ectopy in these patients.

Conclusions

While cardiac involvement in BD is rare, physicians' awareness is crucial for diagnosing this challenging condition with potential malignant complications. Imaging techniques, such as advanced echocardiography and CMR, play a key role in diagnosis and probably in follow-up. Treatment strategies should include heart failure medications, as well as anti-inflammatory and immunosuppressive agents. Further research is necessary to fully comprehend the pathophysiological mechanisms, enabling the development of targeted therapies for patients with cardiac BD.

Lead author biography

Dr Maria Kouremeti is a resident in 1st Cardiology Department Athens Medical School at Hippokration General Hospital. She is a PhD candidate in hypertension.

Supplementary material

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

Consent: Consent for publication was obtained from the patient, in accordance with the COPE best practice guidelines.

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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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