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GRAND ROUND
Cardiac imaging

Behçet's disease: a case report about a rare cause of intra-cardiac mass

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Background Intra-cardiac masses are always a challenging diagnosis, especially when it involves the right side of the heart. There are multiples aetiologies that can be responsible for these masses, namely thrombosis, neoplasm, or vegetations. Occasionally, these may be related to an autoimmune process not yet diagnosed. We present a case of a 17-year-old patient with an exuberant right ventricular mass due to a not yet diagnosed Behçet's disease. The best approach and treatment for these patients remains uncertain.

Case summary The authors present a case of a 17-year-old patient with a right ventricular mass who presented as an initial manifestation of Behçet's disease. It was firstly assumed as a thrombotic mass and medicated with anticoagulation, with no resolution. After performing a cardiac magnetic resonance, the case was discussed in a multidisciplinary team, including cardiology, paediatrics, and rheumatology, and the diagnosis of Behçet's disease with cardiac complication was established. The patient started immunosuppressive therapy with clinical and echocardiographic response.

Discussion Behçet's disease is a multi-systemic autoimmune vasculitis that usually manifests by recurrent oral and genital ulcers as well as ocular symptoms. Cardiac manifestations are rare but important aspects of the course of the disease, especially in what concerns morbidity burden. The treatment of these cardiovascular complications is generally empirical and involves the treatment of the underlying disease.

Keywords Case report • Behçet's disease • Autoimmune disease • Right ventricle mass • Acute pulmonary embolism

Learning points:

- Behçet's disease (BD) is multi-systemic autoimmune vasculitis that usually affects young males.
- The international criteria for BD include oral and genital aphtosis, ocular and skin lesions, central nervous system involvement, vascular manifestations, and pathergy test.
- Diagnosis of intra-cardiac masses is always challenging, being mandatory to differentiate between thrombus, neoplasm, or vegetation.
- In rare cases, BD may present cardiac manifestations, being right ventricle thrombus the most frequent complication among Mediterranean young adults.
- Treatment of these patients is not well defined, but it may include colchicine, corticosteroids, cyclophosphamide, warfarin, low molecular-weight heparin, or even thrombolytic therapy.

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Primary specialties involved other than cardiology

pediatrics, rheumatology, cardiac surgery, cardiac imaging, internal medicine

Introduction

Behçet's disease (BD) is a multisystem inflammatory disorder of unknown aetiology, affecting predominantly young adult males, whose geographic incidence matches the silk rout: Mediterranean, Middle East, and Asia.[1]

The most recognized clinical manifestations include recurrent oral aphthosis, genital ulcers, and uveitis.[2,3] Being a vasculitis, it can virtually affect any organ: skin, joints, gastrointestinal tract, genitourinary tract, central nervous system, cardiovascular system, and lungs.[1]

The disease presents itself with recurrent attacks affecting different organs at a time, followed by complete remissions.[3] Each acute episode is frequently accompanied by elevation of erythrocyte sedimentation rate, C-reactive protein (CRP), leucocyte, and platelet counts.[3]

The diagnosis is based on clinical scores. The most used criteria sets are the International Study Group Criteria published in 1990[4] and the revised International Criteria for Behçet's Disease (ICBD), updated in 2014.[1]

Cardiac involvement by the disease has different manifestations, according to the geographical origin. Among the Mediterranean patients, right chamber thrombus (mainly right ventricle thrombus) is a frequent manifestation, commonly presenting with haemoptysis, fever, and elevation of inflammatory parameters.[3] However, cardiac thrombus can occur before BD diagnosis, making it a challenging condition. The clinical case presented highlights the importance of early recognition of BD, as well as raising awareness of the integration of this disease in the differential diagnosis of intra-cardiac masses in young adults.

Timeline

Two months before	Started intermittent fever, right anterior chest pain, odynophagia, and weight loss. Medicated with antibiotics with no resolution.
One month before	Maintenance of long-standing fever and oral aphthosis. Referred to the Rheumatology clinic with a clinical suspicion of systemic inflammatory disease.
Three weeks before	A diagnostic work up was started by the Rheumatologist. Initiated 1 mg/day of colchicine. Suspension after 2 weeks due to diarrhoea.
Day 1	Came to emergency department with fever, acute sudden chest pain and haemoptysis. Angio-cardiac tomography showed pulmonary embolism and identified a mass filling the right ventricular (RV) cavity. Transthoracic echocardiogram (TTE) confirmed the presence of a large mass inside RV. Started anticoagulation therapy.
Days 2 and 3	Cardiac magnetic resonance was performed and confirmed a RV mass occupying the apical RV, constituted by thrombus and/or a non-vascularized mass of unknown origin. Refused for cardiac surgery.
Days 4–20	Treatment with non-fractionated heparin with no resolution. Started immunosuppressive therapy along with warfarin.
Days 20–36	Good tolerance to immunosuppressive therapy with clinical improvement. Discharged to rheumatology and cardiology clinics.
6 months later	TTE confirmed a reduction of the RV mass. Remains on cyclophosphamide and steroid-based therapy

Continued

Clinical case

We present the case of a 17-year-old Portuguese student, coming from a low socioeconomic status family and born from an HIV-positive mother, with no known toxic consumptions and no relevant previous history. During childhood, he was diagnosed with cognitive intellectual disability and attention deficit treated with risperidone and followed-up in the child psychiatry clinic. He had lived in the UK during the previous 2 years, and he had not travelled elsewhere. There were no other known infectious diseases among the family and no relevant recreational contacts.

He started complaining of intermittent fever (tympanic temperatures of 41–42°C) associated with right anterior chest pain, odynophagia, and dysphagia for solids with consequent weight loss (16% of his body weight). At first, he was presumptively diagnosed with a low respiratory infection and medicated with clarithromycin by his general practitioner. Just after the end of the antibiotic therapy, he had a recurrence of symptoms and '*de novo*' oral aphthosis, which led him to a new course of antibiotics.

Two months later, due to the maintenance of long-standing fever, oral aphthosis, and the development of a single genital ulcer, the patient came to the paediatric emergency department (PED). The physical examination highlighted the presence of poor general condition as well as the presence of painful oral and genital ulcers. Among the exams performed, the blood analysis showed thrombocytopenia (platelets 84 000/μL) and elevated inflammatory parameters: CRP 18 mg/dL (normal range < 0.3 mg/dL) and sedimentation rate 69 mm (normal range for age <16 mm/h). Serologic blood analyses ruled out sexually transmitted disease (HIV, HBV, HCV, and syphilis).

The remaining exams including chest X-ray were unremarkable. He was discharged under paracetamol-based therapy and referred to the Rheumatology clinic with a clinical suspicion of systemic inflammatory disease. At the rheumatology appointment, the diagnosis of BD was considered, and colchicine 1 mg/day was introduced, with clinical improvement. However, 2 weeks later, the patient decided to suspend the treatment due to complaints of diarrhoea.

One week after the suspension, he returned to the PED complaining of fever, acute sudden chest pain leading to several episodes of severe haemoptysis. He was slightly breathlessness although with SpO2 96% on room air, in sinus tachycardia (106 b.p.m.), and

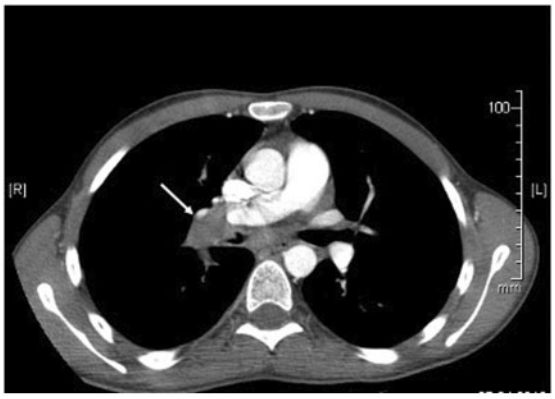

Figure 1 Thoracic angio-computed tomography showing occlusion of the middle and lower lobar branches of the right pulmonary artery.

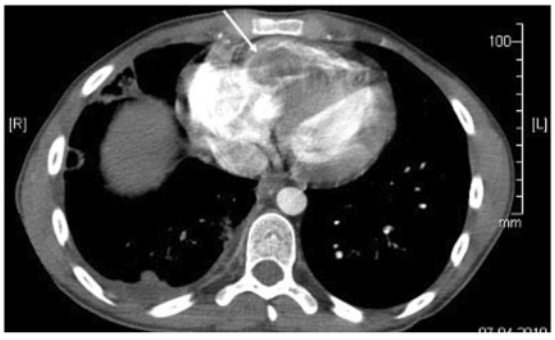

Figure 2 Thoracic angio-computed tomography showing a large mass inside the right ventricular.

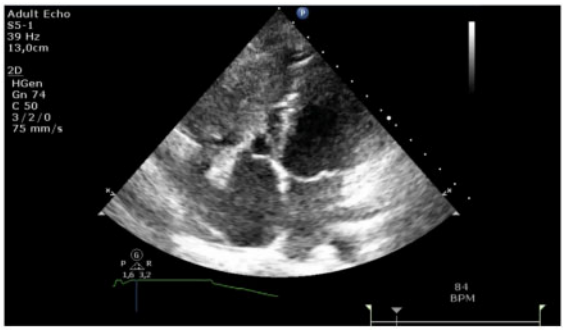

Figure 3 Transthoracic echocardiogram apical four-chamber view showing a large mass in the right ventricular with a hypermobile component prolapsing across the tricuspid valve.

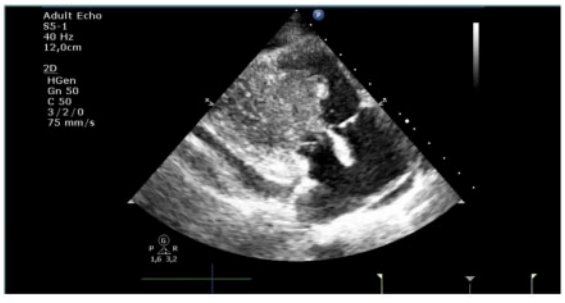

Figure 4 Transthoracic echocardiogram modified long-axis view showing large mass occupying almost the totality of the RV with a hypermobile component across the tricuspid valve.

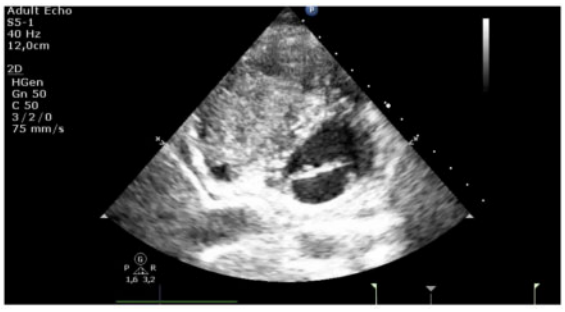

Figure 5 Transthoracic echocardiogram short-axis view showing a large mass inside the RV.

haemodynamically stable with normal cardiopulmonary auscultation. The blood analysis showed again thrombocytopenia (platelet count 70 000/μL), leucocytosis (leucocyte count 19 000/μL with 61% of neutrophil count), and elevated CRP (18 mg/dL). The chest X-ray revealed a heterogeneous hypodense sign on the right lung base.

He underwent an urgent angio-thoracic-cardiac tomography (CT), which showed occlusion of the mid and inferior lobar branches of the right pulmonary artery (PA) and identified a mass filling the right ventricular cavity (*Figures 1* and *2*).

He was promptly evaluated by the cardiologist in charge. The transthoracic echocardiogram confirmed a large mass (50 mm × 53 mm in maximum diameter) filling almost half of the right ventricle (RV) cavity, with a highly mobile component prolapsing across the tricuspid valve. There were no RV segmental contractile abnormalities, neither indirect signs of acute pulmonary hypertension but a mild circumferential pericardial effusion surrounding the RV. Left ventricle ejection fraction was preserved (*Figures 3*, *4*, and *5*).

In the setting of an acute thromboembolism caused by the embolization of a large RV mass whose aetiology was unknown, we decided to proceed to a cardiac magnetic resonance (CMR) for tissue characterization. It revealed an isointense RV mass (30 mm × 35 mm × 52 mm) with the cardiac muscle in T1 and T2 weighted sequences, with no loss of signal in T1-weighted fat saturation images. The early and late gadolinium enhancement images also showed an hypointense signal. This mas occupied the apical RV with a mobile component reaching the right atrial, whose out-surface was mainly constituted by thrombus and the inward filled with thrombus and/or a non-vascularized mass of unknown origin (*Figures 6* and *7*).

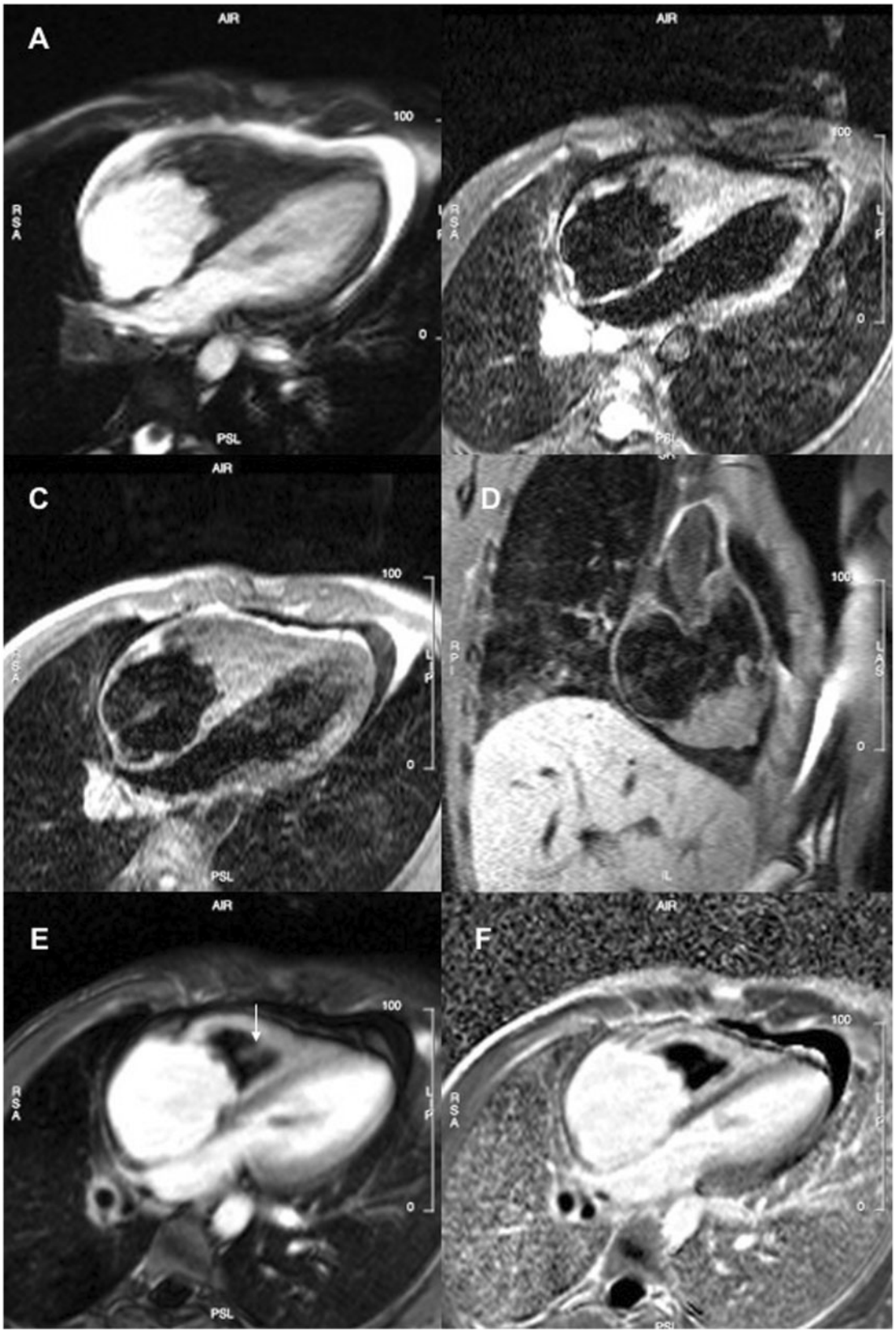

Figure 6 Cardiac magnetic resonance revealed a mass isointense with the cardiac muscle in T1 and T2 weighted sequences (*A–C*), with no loss of signal in T1-weighted fat saturation images (*D*). The early and late gadolinium enhancement images also showed an hypointense signal (*E,F*). All these findings were compatible with the presence of thrombus.

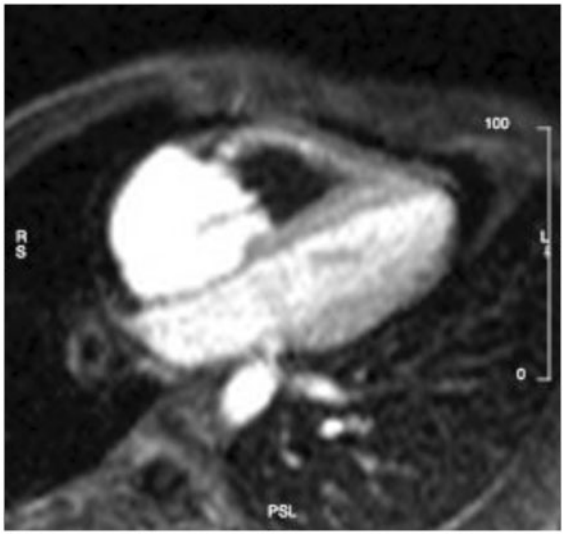

Figure 7 First pass perfusion cardiac magnetic resonance images showing an hypointense signal compatible with the presence of thrombus.

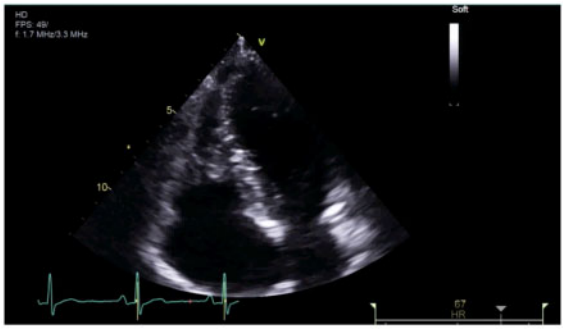

Figure 8 Transthoracic echocardiogram apical four-chamber view 6 months later showed a decrease in right ventricular mass dimensions.

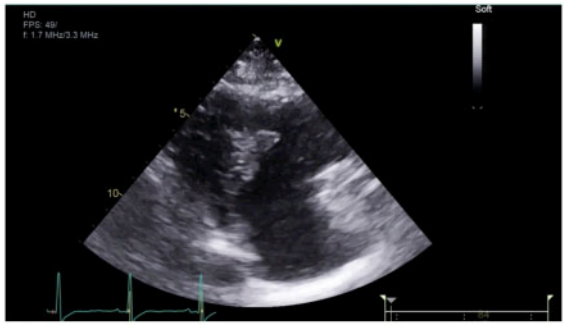

Figure 9 Transthoracic echocardiogram modified long-axis view 6 months later showing a decreasing in right ventricular mass dimensions with resolution of the mobile component.

The patient was discussed in a multidisciplinary team, including physicians from the cardiology, paediatric, rheumatology, internal medicine, and cardiac surgery departments. Surgical removal of the RV mass/thrombus was discussed; however, it was considered an aggressive approach for an inflammatory mass with a high thrombotic component.

He was then managed on IV anticoagulation (non-fractionated heparin with a target activated partial thromboplastin time of 50–70 s), and amoxicillin-based therapy, taking into account consequent peripheral pulmonary infarction.

Despite weeks of treatment, there was no RV mass regression. The diagnosis of BD manifested with an acute cardiac complication was made. Therefore, after being ruled out ongoing infection and latent tuberculosis, he started immunosuppressive therapy (corticosteroids 1 mg/kg/day and cyclophosphamide 750 mg/m^2 pulses every month) along with oral anticoagulation (warfarin) with a target international normalized ratio of 2–3.

After 6 months, he presented a slight decrease in the RV mass burden by TTE (*Figures 8* and *9*).

He remained on warfarin, cyclophosphamide, and steroid-based therapy for 1 year and repeated CMR, which revealed complete resolution of the RV mass, maintaining only RV hypertrabeculation (*Figure 10*).

Discussion

Behçet's disease (BD) is a multisystem autoimmune vasculitis that usually manifests itself by recurrent oral and genital ulcers and ocular symptoms, as well as by other abnormalities, namely musculoskeletal, neurological, pulmonary, gastrointestinal, and cardiac.[5]

Its diagnosis relies on clinical-based scores, being the ICBD one of the most used in clinical practice (Table 1).[1]

Common to many other rheumatic diseases, there is no characteristic laboratory test to make the diagnosis, but the recurrent attacks are commonly accompanied by unspecific raise in the inflammatory parameters, particularly leucocyte count and CRP.[3]

In the clinical case presented, the patient manifested recurrent mucocutaneous lesions, namely, oral aphthosis and genital ulcers, which are the clinical hallmark of this disease. Therefore, looking retrospectively he had had, by that time enough criteria for a definite BD diagnosis (≥4 points according to the ICBD score),[1] which was postponed some months when he finally was evaluated for the Rheumatology team.

However, the clinical presentation with chest pain and haemoptysis, as well as the presence of a large right ventricle mass, led to a delay in the final diagnosis.

In fact, among the causes of intracardiac mass/thrombus currently seen in the clinical practice, this is an exceptional cause.

The aetiological diagnosis of a cardiac mass is always challenging, especially when it involves the right side of the heart. In these cases, it is mandatory to differentiate between thrombi, neoplasm, or vegetations.[6] When the former occurs, they usually result in the mobilization of venous thrombi into the heart.[7] Transthoracic

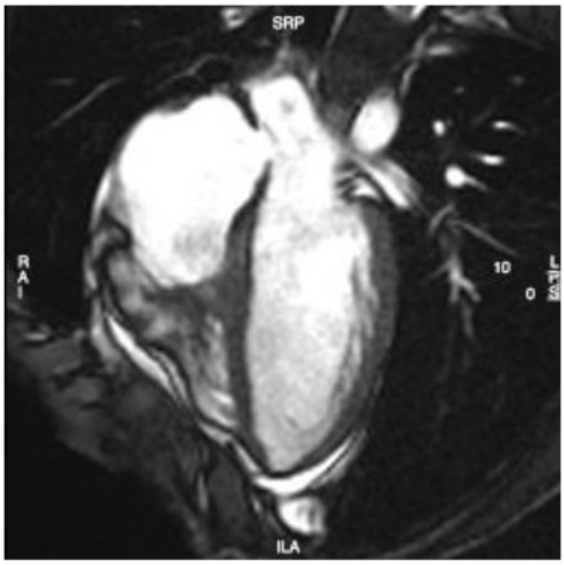

Figure 10 Four-chamber view on cardiac magnetic resonance performed after 1 year of therapy showing resolution of the right ventricular mass.

echocardiography remains an important tool in the initial approach of right cardiac masses; however, the information provided is often insufficient.[7] The performance of cardiac magnetic resonance imaging (MRI) or CT may be decisive in the differential diagnosis due to their higher sensitivity and specificity.[7]

In our patient, the performance of cardiac MRI was essential for the final diagnosis, once it revealed the presence of an inflammatory mass with a high thrombotic component, in a patient with a suspicion of BD.

In fact, among Mediterranean young patients, this is one of the most recognized cardiac presentations of this disease,[8–10] and in some cases, it can precede BD diagnosis.[10] The exact pathological mechanism of thrombus formation in these patients is still unknown. In most cases, it is an inflammatory/autoimmune process, but it could also be fibrosis or even normal myocardium.[11]

In BD, RV is the most common chamber affected by thrombotic masses, followed by the right atria and systemic venous vessels.[10] Multi-chamber thrombi were found in 16% of patients with BD-associated cardiac masses.[11]

Besides thrombi, many other cardiac complications can develop in the setting of a BD, such as pericarditis, cardiomyopathy, myocarditis, endocarditis, valvular dysfunction, conduction abnormalities, coronary artery disease, pseudoaneurysm, or rupture of the sinus of Valsalva.[11]

There are no current guidelines neither randomized controlled trials concerning the treatment of BD-related cardiac involvement. Therefore, we only have access to data coming from published clinical cases and based on the experience of high-volume centres.

Several therapies have been reported and it may include colchicine, corticosteroids, cyclophosphamide, warfarin, low molecular-weight heparin, or even thrombolytic therapy.[10]

In our case, the conservative therapeutic management including an IV anticoagulant was firstly unsuccessful. A regression was achieved after adding immunosuppressive therapy including cytotoxic and immunomodulators.[3] In fact, there are some cases reported in the literature, in which anticoagulation alone has failed to promote regression or resolution of these masses, being only possible after the introduction of immunosuppressive therapy.[10,12] In the present case, the failure of anticoagulation therapy alone may possibly be explained by the presence of the inflammatory component of the mass.

In addition, as shown by other cases, cardiac surgery is discouraged due to high recurrence rates and embolization.[13]

Acute cardiac-related BD presentations carry a worse prognosis. The majority of fatal BD cases with intracardiac thrombus in the literature describe haemoptysis as a cause of death. Therefore, anticoagulation in acute BD should be carefully managed, particularly during the initial phase.[13]

This case presented an increased complexity in terms of diagnostic management because the primary rheumatologic diagnosis was uncertain by the time of the cardiac complication. The multidisciplinary approach, including the clinical discussion among clinical cardiology, cardiac imaging, cardiac surgery, rheumatology, paediatrics, and internal medicine was crucial to recognize the final diagnosis and its complications and to select the successful treatment.

Table 1 International criteria for Behçet's disease point score system. Behçet's diagnosis is considered if the patient presents ≥ 4 points

International criteria for Behçet's disease	Points
Genital ulcers	2
Oral aphthosis	2
Ocular lesions	2
Vascular manifestations	1
Skin lesions	1
Neurological manifestations	1
Positive pathergy test (optional)	1

Lead author biography

Alexandra Briosa is 28 years old. She is a 3rd year cardiology resident in Hospital Garcia de Orta, Almada, Portugal.

Supplementary material

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

Slide sets: A fully edited slide set detailing these cases 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 images and associated text has been obtained from the patient in line with COPE guidance.

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