

A rare but serious manifestation of Behçet's disease: intracardiac thrombus in 22 patients

H. Emmungil¹, N.Ş. Yaşar Bilge², O. Küçükşahin³, L. Kiliç⁴, S. Okutucu⁵, S. Gücenmez¹, U. Kalyoncu⁴, T. Kaşifoğlu², M. Turgay³, K. Aksu¹

¹Department of Internal Medicine, Division of Rheumatology, Ege University, İzmir, Turkey; ²Division of Rheumatology, Department of Internal Medicine, Eskişehir Osmangazi University, Eskişehir, Turkey; ³Division of Rheumatology, Department of Internal Medicine, Ankara University, Ankara, Turkey; ⁴Division of Rheumatology, Department of Internal Medicine, ⁵Department of Cardiology, Hacettepe University, Ankara, Turkey.

Hakan Emmungil, MD
N. Sule Yaşar Bilge, MD
Orhan Küçükşahin, MD
Levent Kiliç, MD
Sercan Okutucu, MD
Sercan Gücenmez, MD
Umut Kalyoncu, MD
Timuçin Kaşifoğlu, MD
Murat Turgay, MD
Kenan Aksu, MD

Please address correspondence to:
Hakan Emmungil, MD,
Division of Rheumatology,
Department of Internal Medicine,
Ege University,
35100 İzmir, Turkey.
E-mail: emmungil@myynet.com

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ABSTRACT

Objective. Behçet's disease (BD) is a chronic, multisystemic disorder characterised by recurrent oral aphthous ulcers, genital ulcers and ocular inflammation. Vasculitis and thrombotic events are the most important causes of mortality. Vena cava thrombosis, pulmonary artery aneurysms, Budd-Chiari syndrome, peripheral artery aneurysms, dural sinus thrombosis and abdominal aorta aneurysms are the other less common vascular manifestations of BD. Cardiac involvement in BD is a rare and life-threatening complication. The aim of this study was to assess the clinical characteristics and outcome of patients with BD who have intracardiac thrombus.

Methods. The hospital files of BD patients followed by rheumatology clinics of four medical centres (Ankara University, Ege University, Hacettepe University and Eskişehir Osmangazi University Hospitals) were retrospectively evaluated. Data included patients' demographic and clinical features, laboratory findings and outcome. All patients fulfilled three or more of the International Study Group Criteria for BD.

Results. Twenty-two patients with intracardiac thrombus were evaluated. The mean age of patients with intracardiac thrombosis was 29.1 yrs (22-44) and there was a male predominance with a ratio of 20:2. Cardiac involvement was the first clinical manifestation of BD in 9 of the 22 patients. Initial symptoms of the patients were fever (n=18, 81%), dyspnea (n=9, 40%) chest pain (n=9, 40%) and haemoptysis (n=7, 31.8%). Sixteen patients (72%) had pulmonary arteritis and 10 (45%) patients had venous system lesions included deep vein, inferior vena cava and hepatic vein. Intra-cardiac thrombus were found only in the right cavities in 17 patients (77%), only in the left

cavities in 2 patients (9%), and in both left and right cavities of the heart in 3 patients (13.6%). Once the cardiac lesion was diagnosed as a complication of BD, high dose (1mg/kg/d) prednisone (n=22, 100%) plus cyclophosphamide (n=18, 81%) or azathioprine (n=3, 13.6%) and warfarin (n=8, 36.3% (after the elimination of pulmonary aneurysm) therapy for anticoagulation was initiated. Four patients (18%) had high dose prednisone plus cyclophosphamide plus interferon- α (IFN- α) combination treatment and two patients (n=2, 9%) had high dose prednisone plus cyclophosphamide or plus azathioprine combination treatment. After treatment, the intra-cardiac thrombus disappeared in 13 cases and the size of the thrombus reduced in 7 cases. One patient died because of recurrent intra-cardiac thrombus and massive pulmonary arteritis in the emergency department.

Conclusion. Intracardiac thrombus in BD is more common in young men. The right side of the heart is usually involved and cardiac involvement is often accompanied by pulmonary artery occlusion possibly due to pulmonary arteritis. Early and aggressive immunosuppressive and/or anticoagulation therapy are life-saving.

Introduction

Behçet's disease (BD) is a chronic, multi-systemic disorder characterised by recurrent oral aphthous ulcers, genital ulcers and ocular inflammation (1). BD can cause inflammation in almost every organ. Skin lesions, arthropathy, neurologic manifestations, cardiovascular and gastrointestinal system involvements are the other common clinical findings of the disease. Vasculitis and thrombotic events are the most important causes of morbidity and mortality (2). Vascular involvement usually manifests as deep vein thrombosis. Vena

Competing interests: none declared.

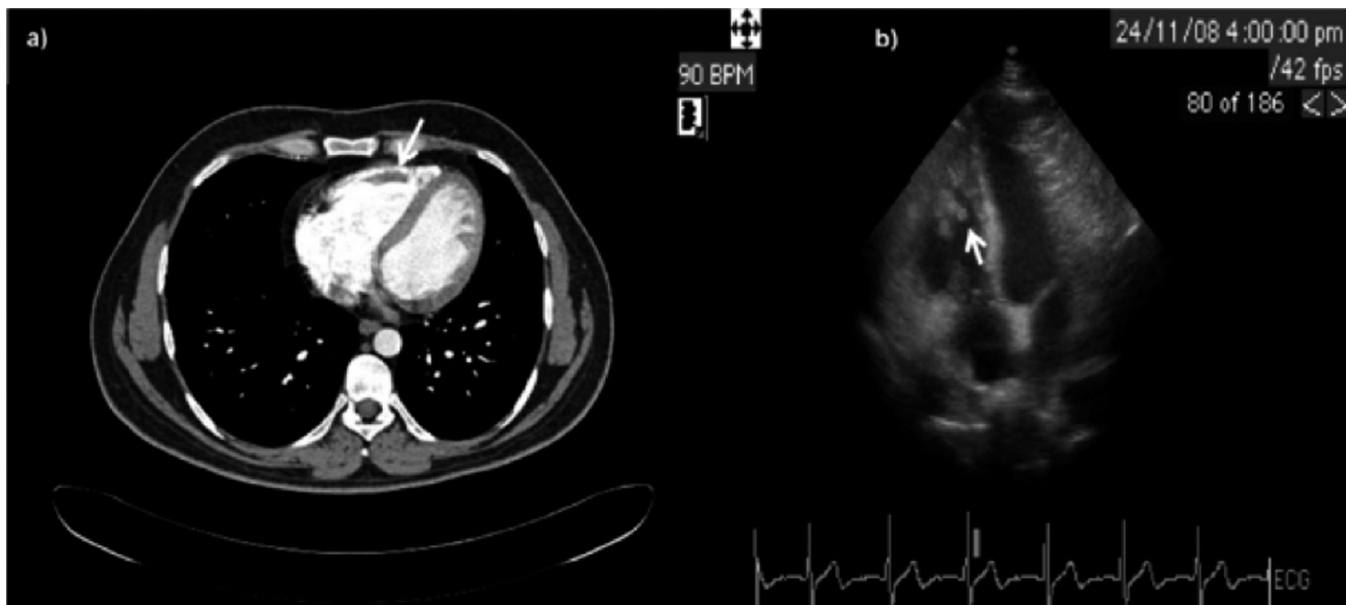


Fig. 1. (A) Computed tomography of the thorax revealed a 20 × 5 mm hypodense lesion in the right ventricular apex (shown with arrow). (B) Transthoracic echocardiography (TTE) revealed a 16 × 4 mm thrombus in the apex of the right ventricle (shown with arrow).

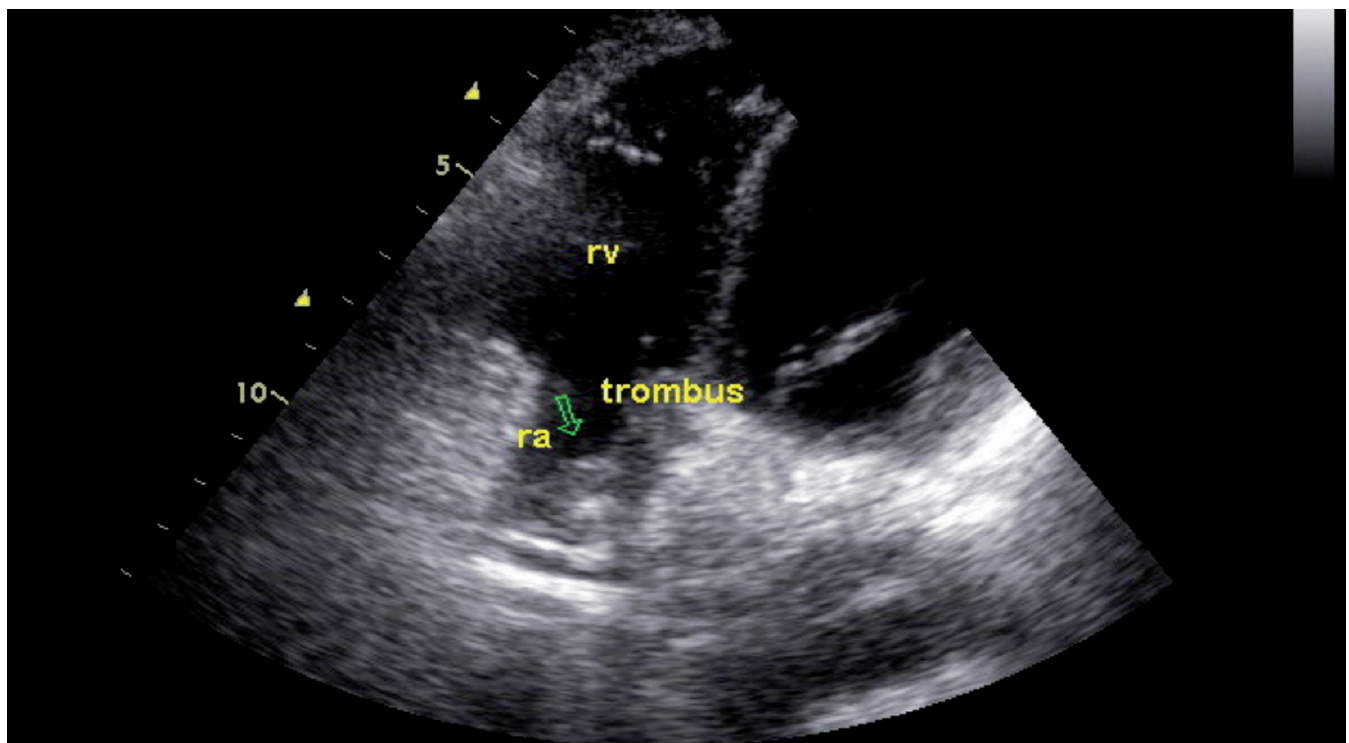


Fig. 2. Transthoracic echocardiography showed a mobile mass filling the half of the right atrium (4.5 × 3 cm in size) (arrow) extending the right ventricle (1.5 × 1.6 cm in size) and into the vena cava.

cava thrombosis, pulmonary artery aneurysms, Budd-Chiari syndrome, peripheral artery aneurysms, dural sinus thrombosis and abdominal aorta aneurysms are the other less common vascular manifestations of BD (3). Pulmonary arterial and cardiac involvements in BD are rare but life-threatening complications.

Cardiac involvement including pericarditis, myocarditis, endocarditis, intracardiac thrombus, coronary arteritis and aneurysms is reported in 1-6% of the BD patients (4). Patients with cardiac involvement have a poorer prognosis than those without (4). Intra-cardiac thrombus is rarely seen even among patients with cardiac involvement.

Herein, we report 22 BD patients with intra-cardiac thrombus.

Methods and patients

The hospital files of BD patients followed by rheumatology clinics of four medical centres (Ankara University, Ege University, Hacettepe University and Eskişehir Osmangazi University

Hospitals) were retrospectively evaluated. Data included patients' demographic and clinical features, laboratory findings and outcome. All patients fulfilled three or more International Study Group Criteria for Behçet's Disease (5). Descriptive statistics included the mean (standard deviation) or median (interquartile range) as appropriate for continuous variables, and frequency (percentage) for categorical variables. Univariate analysis included the chi-squared or Fisher exact test as appropriate to compare categorical variables. A p -value <0.05 was considered as significant. All tests were performed using version 15.0 of SPSS software for Windows (SPSS Inc., Chicago, IL).

Results

The hospital files of the 2216 BD patients were evaluated and 22 patients had intra-cardiac thrombus. BD patients with intra-cardiac thrombus included 20 males and 2 females, with a male predominance (90%). The mean age by the time of cardiac mass lesion was 29.1 ± 5.9 (ranging between 22 to 44 yrs). Clinical manifestations of these 22 BD patients included oral aphthous ulceration ($n=22$, 100%), genital ulceration ($n=18$, 81%), ocular involvement ($n=7$, 31%), skin lesions ($n=17$, 77%), arthritis ($n=3$, 13%), cerebral infarction ($n=2$, 9%) and positive pathergy test ($n=9$, 41%). Ten patients had venous vascular involvements ($n=10$, 45%) included deep vein (acute, subacute or chronic $n=9$, 40%), inferior vena cava ($n=3$, 13%) and hepatic vein ($n=2$, 9%). Seven patients (31.8%) had family history of BD. None of the patients had gastrointestinal involvement. HLA-B51 was found to be positive in ten of the twelve (50%) patients tested. The mean levels of erythrocyte sedimentation rate (ESR) was 61.7 mm/h (0–20), C-reactive protein (CRP) was 9.1 mg/dl (0–0.8), respectively, by the time of intra-cardiac thrombus.

Intra-cardiac thrombus was the presenting symptom of BD in 9 (40.9%) of the 22 patients. If thrombus was the presenting symptom it occurred 6 to 12 months prior to other symptoms. Intra-cardiac thrombus was appeared in first five year of the disease in 17 of the pa-

tients ($n=17$, 77%). Initial symptoms of the patients were fever ($n=18$, 81%), dyspnea ($n=9$, 40%) chest pain ($n=9$, 40%) and haemoptysis ($n=7$, 31.8%). Sixteen patients (72%) had pulmonary arteritis and 6 patients (27%) had major vessel involvements (inferior vena cava, hepatic vein and renal artery) simultaneously with cardiac thrombus. Five patients (22%) had arterial aneurysm (four pulmonary arterial and 1 abdominal aortic) detected at the same time with cardiac thrombus.

Laboratory tests for thrombophilia, including antiphospholipid antibodies (anti-cardiolipin antibody, anti- β_2 glycoprotein 1 antibody), genetic procoagulant factors (protein S, protein C, antithrombin III, activated protein C resistance, factor V Leiden mutation) were performed in 18 cases with intracardiac thrombus, and they were negative except methylene-tetra-hydro-folate reductase (MTHFR) gene mutations which was positive in 6 patients (two homozygote and four heterozygote). ANA (antinuclear antibody) and ANCA (anti-neutrophil cytoplasmic antibody) tests were performed in 19 of the patients and were found to be negative.

Transthoracic echocardiography was conducted in all patients (Fig. 1 and 2). Intra-cardiac thrombus were found only in the right cavity in 17 patients (77%), only in the left cavity in 2 patients (9%), and in both left and right cavities of the heart in 3 patients (13.6%). The thrombus were attached to the free wall or the septum, extending into inferior vena cava or tricuspid or pulmonary valves, and the size of the thrombus varied from 2 to 51 mm. Sixteen patients had pulmonary occlusion or pulmonary artery thrombus simultaneously with cardiac thrombus and pulmonary arterial aneurysm detected in four patients by the time of intra-cardiac thrombus.

Despite the limited number of patients, we carried out some analyses. When the duration of BD was divided into early disease and late disease, and compared with pulmonary vascular complications we could not find any relationship. However, in the late disease (disease duration more than 1 year) had a trend to have a relation with more non-pulmonary vascular complications, natu-

rally ($p=0.054$). There was no relationship between patients having a familial history of BD and who have not with respect to the demographics and clinical findings.

Once the cardiac lesion was diagnosed as a component of BD, high dose (1mg/kg/d) prednisone ($n=22$, 100%) plus cyclophosphamide (CYP) ($n=18$, 81%) or azathioprine (AZA) ($n=3$, 13.6%) and warfarin ($n=8$, 36.3% (after the elimination of pulmonary aneurysm) therapy for anticoagulation was initiated. Four patients (18%) had high dose prednisone plus cyclophosphamide plus interferon- α (IFN- α) combination treatment and two patients ($n=2$, 9%) had high dose prednisone plus CYP plus AZA combination treatment. IFN- α therapy was initiated by 9 million unit/3 times/week, than decreased to 3–4, 5 mu/3 times/week during one years. Intensive immunosuppressive therapy was applied during 6–12 months, mean duration was 9 months. After induction treatment with CYP or CYP and AZA, AZA was used for maintenance among these patients. After induction treatment with CYP and IFN- α , only IFN- α was used for maintenance. Prednisone has been administered as 1 g IV pulses in 3 consecutive days followed by 1 mg/kg/day po in all patients. It was tapered by 10 mg/mo after the first month and usually continued for at least 1–2 years 5–10 mg/d.

Only two patients underwent surgery because of intra-cardiac thrombus. Surgery was performed because of the haemodynamic instability in one patient during the 3-day hospitalisation period. After the surgery the patient was seen by rheumatologist and diagnosed as BD and treated only with AZA. After six months of treatment the follow-up was uneventful. Despite long-term oral anticoagulation and immunosuppressive treatment, right ventricle (RV) thrombus persisted in another patient. The patient underwent operation and a 20x20 mm mass originating 3 to 4 cm away from pulmonary valve was removed. Frozen section of the mass revealed a diagnosis of exudative fibrous mass consistent with organising thrombus. A cardiac magnetic resonance imaging and a transthoracic

echocardiogram failed to show any recurrence 2 years after the operation.

After treatment, the intra-cardiac thrombus disappeared in 13 cases and the size of the thrombus reduced in 7 cases. One patient died because of recurrent intra-cardiac thrombus and massive pulmonary arteritis in the emergency department. Pulmonary arterial aneurysm disappeared in two patients and near-complete decline in another two patients. After the intensive immunosuppressive therapy, abdominal arterial aneurysm was regressed by 70% in one patient.

The clinical features of BD patients with intra-cardiac thrombus are summarised in Table I.

Discussion

Herein, we report one of the largest series, 22 BD patients with intra-cardiac thrombus who fulfilled the International Study Group Criteria for BD. Highlights of the common clinical features of the 22 patients are mostly young men, fever, chest pain and dyspnea as the presenting symptoms, mostly right side cardiac involvement and frequently associated with pulmonary arterial and peripheral vascular involvement. Cardiac involvement was reported in 1–5% of BD patients in previous studies (6, 7) and in 16.5% of cases in a Japanese systematic necropsic study (8). Cardiomegaly, endocarditis, pericarditis and less commonly, myocardial infarction and myocarditis are reported as the clinical manifestations of cardiac involvement in BD patients (6). Intra-cardiac thrombus is a rare entity of cardiac manifestation in BD and appears as case reports in the literature. It has been noticed that cardiac thrombi of BD is frequently seen among young man and may be the first manifestation of BD. Similar to the published cases cardiac thrombi was the first clinical sign of BD in 9 of the 22 patients (40.9%) with a male predominance (90%) in our series. As thrombophelbitis and other major systemic involvements of BD such as ocular, pulmonary arterial and central nervous system, intracardiac thrombus is also associated with a male predominance (19).

Fever, dyspnea, chest pain and hemoptysis were the initial symptoms of pa-

tients and by virtue of fever, chest pain and cardiac mass; cardiac thrombi of BD may be misdiagnosed as infective endocarditis. Some echocardiographic findings, such as vegetation-like lesions and echo-free spaces are indistinguishable from infectious endocarditis, which were also observed in our study. Since immunosuppressive therapy required for BD, contrasts with treatment strategy for infectious endocarditis, differential diagnosis is important. Ineffectiveness of blood and/or tissue culture together with an underlying valvular pathology of aortic regurgitation, plus inappropriate response to antibiotics treatment, resolution of the thrombus with immunosuppressive therapy helps to exclude the diagnosis of infectious endocarditis.

The precise pathogenetic mechanism of prothrombotic state in BD is unknown. Similar to the other disorders with increased risk of thrombosis formation, endothelial cell injury and hypercoagulability are thought to be responsible in BD. Endothelial dysfunction due to anti-endothelial cell antibodies and elevated plasma Vascular Endothelial Growth Factor (VEGF) levels lead to microcirculation disturbance and increased blood viscosity and abnormal blood flow (9–11). Furthermore, selectins, a group of adhesion molecules consist of P and E-selectins that mediate leukocyte adhesion to platelets and endothelium and have a role in thrombogenesis. Increased P and E-selectin levels in BD was reported in some studies (12–16). In addition, it seems that thrombophilic factors could contribute to thrombosis in BD (17, 18). However, in the current study, only 6 out of 18 patients had MTHFR mutations and whether it contributes hypercoagulable state is unclear.

But whatever the cause, development of thrombus is still one of major causes of death in patients with BD. Cardiac thrombi in BD, similar to our results, is located mainly in the right ventricle are often associated with pulmonary arteritis (4, 6–8). The reason for predilection to involve RV is unclear. Based on autopsy findings, it looks that endomyocardial fibrosis plays a role in the intracardiac thrombus formation in some

patients (19), but it is not clear whether they are secondary to underlying endocarditis or endomyocardial fibrosis, because of the normal myocardium described in some case reports (20). Due to high specificity of right heart thrombus in BD, in any patient with this finding, diagnosis of BD should be considered (19, 21, 22). A systematic review by Mogulkoc *et al.* revealed that up to one third of BD patients with intra-cardiac thrombi had pulmonary infarction (19). Similarly, our series show that 16 of 22 patients had simultaneously pulmonary thrombus and/or occlusion. As right heart thrombi and pulmonary arteritis are seen together, one may speculate that right heart thrombi predispose to pulmonary embolic events. Differentiation of pulmonary embolism from pulmonary vasculitis leading to in situ thrombosis is a debate issue. However, because of the pulmonary embolism was not observed in any of the patients in the one of the largest postmortem series in BD reported (8) and the thrombus inside the heart is as hard as a rock. We think pulmonary vasculitis and right ventricle endocarditis occur simultaneously resulting in pulmonary infarction and cardiac mass. Moreover, anticoagulation without immunosuppressive treatment is most probably ineffective in preventing relapses in BD, as shown in one study and one review (23, 24). Whatever the cause, this frequent togetherness must be a reason for routine evaluation of patients for pulmonary vascular involvement.

Although there is not controlled trial about cardiac involvement in BD, most of the experts recommend immunosuppressive treatment including steroids with or without CYP. On the other hand, there is no consensus about anticoagulation treatment in BD. At the beginning, it looks like contradiction to not start heparin/warfarin in a patient with thrombosis. However, physicians should keep in mind that most important cause of mortality in patients with BD is pulmonary arterial aneurysm rupture. Besides, intracardiac thrombosis was found simultaneously with pulmonary arterial aneurysm; four patients had pulmonary aneurysm and one patient had abdominal aortic an-

Table I. The clinical features of BD patients with intra-cardiac thrombus.

Age, Sex	Clinical Presentation	Location of Intra-cardiac Thrombus	Other Vascular Involvement	Treatment	Follow-up – Outcome
25, M	Fever, chest pain	Right ventricle	Iliac and popliteal venous thrombus	Azathioprine Steroid Warfarin	3-year follow-up. Right ventricular thrombus disappeared.
32, M	Fever, Dyspnea, Haemoptysis	Right ventricle	Iliac and popliteal venous thrombus and pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	7-year follow-up. Marked decreases the size of the thrombus in the 9 months of therapy. No recurrences.
24, M	Fever, Cough	Right ventricle	Pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	18-month follow-up. Marked decreases the size of the thrombus in the 6 months of therapy.
44, M	Fever, Haemoptysis	Right ventricle	Iliac and popliteal venous thrombus and pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	4-year follow-up. Right ventricular thrombus disappeared. No recurrences.
22, M	Fever, neurologic symptoms	Left ventricle	Iliac, popliteal, vena cava inferior venous thrombus	Cyclophosphamide Steroid	6-year follow-up. Left ventricular thrombus disappeared
30, M	Fever, Dyspnea	Right atrium	Iliac and popliteal venous thrombus, pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	15-months follow-up. Right atrial thrombus disappeared.
25, M	Fever, Dyspnea	Right atrium and ventricle	Hepatic venous, inferior vena cava and pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	15-month follow-up. Marked decreases the size of the thrombus.
32, M	Fever, Cough	Right ventricle	–	Steroid Warfarin	10-year follow-up. Right ventricular thrombus disappeared
27, M	Fever, Chest pain	Right atrium	Pulmonary arterial involvement	Cyclophosphamide Steroid Warfarin	3-year follow-up. Right atrial thrombus disappeared on 6 months of therapy. One year later relaps of the intra-cardiac thrombus, massive pulmonary arteritis and died.
22, M	Fever, Neurologic symptoms	Left ventricle	Pulmonary arterial involvement, carotid arterial	Cyclophosphamide Steroid	1-year follow-up. Left ventricular thrombus disappeared.
26, M	Fever, Cough	Right atrium and ventricle	Pulmonary arterial involvement	Surgery Steroid Azathioprine	7-month follow-up. After the operation thrombus disappeared.
25, M	Fever, Chest pain and Haemoptysis	Right ventricle	Pulmonary arterial involvement and pulmonary arterial aneurysm	Cyclophosphamide Steroid and aneurysm.	6-month follow-up. Marked decreases the size of the thrombus
29, F	Chest pain, Dyspnea	Right ventricle	–	Surgery Steroid IFN- α	6-year follow-up. Despite long-term oral anticoagulation and immunosuppressive treatment, RV thrombus persisted. After the operation thrombus disappeared. No recurrences.
24, F	Dyspnea, Chest pain and Haemoptysis	Right ventricle	Iliac and popliteal venous thrombus Pulmonary arterial involvement Pulmonary arterial aneurysm	Cyclophosphamide Steroid IFN- α	6-month follow-up. Right ventricular thrombus and aneurysm disappeared.
24, M	Chest pain	Right atrium	Hepatic venous, inferior vena cava, renal arterial and Pulmonary arterial involvement	Cyclophosphamide Steroid IFN- α	2-year follow-up. Right atrial thrombus disappeared.
31, M	Chest pain, Dyspnea	Right ventricle	Iliac and popliteal venous thrombus Pulmonary arterial involvement	Cyclophosphamide Steroid IFN- α Warfarin	1-year follow-up. Right ventricular thrombus disappeared.
36, M	Fever, Dyspnea, Chest pain and Haemoptysis	Right ventricle	Inferior vena cava, iliac and popliteal venous thrombus	Cyclophosphamide Steroid Azathioprine	2-year follow-up. Right ventricular thrombus disappeared.
41, M	Fever, Haemoptysis	Right atrium and ventricle	Pulmonary arterial involvement Pulmonary arterial aneurysm	Cyclophosphamide Steroid	1-year follow-up. Thrombus disappeared and Marked decreases the size of the aneurysm.
28, M	Fever, Haemoptysis	Right atrium and ventricle	Pulmonary arterial involvement	Cyclophosphamide Steroid	14-month follow-up. Marked decreases the size of the thrombus
37, M	Fever	Right ventricle	Iliac and popliteal venous thrombus	Cyclophosphamide Steroid Azathioprine	2-year follow-up. Right ventricular thrombus disappeared.
27, M	Fever, Dyspnea	Right ventricle	Pulmonary arterial involvement Pulmonary arterial aneurysm	Cyclophosphamide Steroid and aneurysm.	7-month follow-up. Marked decreases the size of the thrombus
31, M	Fever, Dyspnea, Chest pain	Right atrium	Pulmonary arterial involvement Abdominal aortic aneurysm	Cyclophosphamide Steroid Azathioprine	7-month follow-up. Marked decreases the size of the thrombus

eurysm in our series. Some authors do not recommend anticoagulant therapy combined with immunosuppressive therapy in BD patients, for the high risk of haemorrhage and small benefit (25). However, in our series, anticoagulation was well-tolerated, and there was no haemorrhagic complication.

There are several case reports and case series about BD and cardiac involvement in English literature. Treatment protocols in these published cases were not homogeneous, changing from no treatment to a combination of steroids, cyclophosphamide and anticoagulant therapy. Since our study is retrospective, the data collection and approach to treatment are not homogenous between centres. Most of the patients treated with CYP and high dose steroids as induction treatment, few patients treated by combination treatment (CYP and IFN, CYP and AZA) as preferred by one centre. Rationale for this combination treatments are BD (especially with intra-cardiac thrombus) is a disease with abundant inflammatory burden and some of the patients have old and resistant disease. Although, we could not propose a treatment protocol for such patients, we could say that, intensive immunosuppressive (If necessary combination) treatment should start as soon as possible.

Surgical removal was not preferred because of the high rate of surgical complications and without surgery thrombus may completely disappear with only medical treatment as most of the patients in our study. However, surgery should be considered when the cardiac mass is complicated with heart failure or valvular disease, and resistant cases (19, 26, 27). Most of the patients had good outcome with corticosteroids, immunosuppressive agents, and anticoagulation in our study. Only one patient died because of the recurrences of massive pulmonary thromboembolism. Not only intracardiac thrombus, by also arterial aneurysms respond well to immunosuppressive treatment. However, since BD a remitting and relapsing disease patients should be followed closely.

Although underlining a rare complication of BD our study has some limitations. Retrospective design of the study

and small number of the patients and multicentre study prevents us to make a generalisation.

In conclusion, development of intracardiac thrombus is a rare finding of BD however it is more common among young men and early, intense immunosuppressive therapy results with a better outcome. A routine echocardiographic control to BD patients is not recommended because of the infrequency of the entity. But once intra-cardiac thrombus is diagnosed evaluation for pulmonary arteritis is required because of the good response to the treatment. Intra-cardiac thrombus due to BD should be kept in mind when a young male patient presents with right heart mass or a patient with diagnosis of BD admits with fever.

References

1. LEE YJ, KANG SW, YANG JI *et al.*: Coagulation parameters and plasma total homocysteine levels in Behçet's disease. *Thromb Res* 2002; 106: 19-24.
2. LENK N, OZET G, ALLI N *et al.*: Protein C and protein S activities in Behçet's disease as risk factors of thrombosis. *Int J Dermatol* 1997; 37: 124-5.
3. YURDAKUL S, YAZICI H: Behçet's Syndrome. *Bailliere's Best Pract Res Clin Rheumatol* 2008; 22: 793-809.
4. GERI G, WECHSLER B, THI HUONG DU L *et al.*: Spectrum of cardiac lesions in Behçet disease: a series of 52 patients and review of the literature. *Medicine* 2012; 91: 25-34.
5. WECHSLER B, DAVATCHI F, HAMZA M *et al.*: Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's disease. *Lancet* 1990; 335: 1078-80.
6. WECHSLER B, DU LT, KIEFFER E: Cardiovascular manifestations of Behçet's disease. *Ann Med Interne* 1999; 150: 542-54.
7. IDEGUCHI H, SUDA A, TAKENO M, UEDA A, OHNO S, ISHIGATSUBO Y: Characteristics of vascular involvement in Behçet's disease in Japan: a retrospective cohort study. *Clin Exp Rheumatol* 2011; 29: 47-53.
8. LAKPANHAL S, TANI K, LIE JT, KATOH K, ISHIGATSUBO Y, OHOKUBO T: Pathologic features of Behçet's syndrome: a review of Japanese autopsy registry data. *Hum Pathol* 1985; 16: 790-5.
9. CLAYTON JA, CHALOTHORN D, FABER JE: Vascular endothelial growth factor-A specifies formation of native collaterals and regulates collateral growth in ischemia. *Circulation Research* 2008; 103: 1027-36.
10. BOZOGLU E, DINC A, ERDEM H, PAY S, SIMSEK I, KOCAR IH: Vascular endothelial growth factor and monocyte chemoattractant protein-1 in Behçet's patients with venous thrombosis. *Clin Exp Rheumatol* 2005; 23: 42-8.
11. LEE KW, LIP GY, BLANN AD: Plasma angiopoietin-1, angiopoietin-2, angiopoietin receptor Tie-2, and vascular endothelial growth factor levels in acute coronary syndromes. *Circulation* 2004; 110: 2355-60.
12. TURKOZ Y, EVEREKLIOGLU C, OZKIRIS A *et al.*: Serum levels of soluble P-selectin are increased and associated with disease activity in patients with Behçet's syndrome. *Mediators Inflamm* 2005; 4: 237-41.
13. SARI RA, KIZILTUNC A, TAYSI S, AKDEMIR S, GUNDOGDU M: Levels of soluble E-selectin in patients with active Behçet's disease. *Clin Rheumatol* 2005; 24: 55-9.
14. TUNC SE, AKSU K, KESER G *et al.*: Platelet-activating factor and P-selectin activities in thrombotic and nonthrombotic Behçet's patients. *Rheumatology Int* 2005; 25: 326-31.
15. HAZNEDAROĞLU S, KARAASLAN Y, BÜYÜKAŞIK Y *et al.*: Selectin adhesion molecules in Behçet's disease. *Ann Rheum Dis* 2000; 59: 61-3.
16. TRILO G, ACCARDO-PALUMBO A, TRILO G, CARBONE MC, FERRANTE A, GIARDINA E: Enhancement of endothelial cell E-selectin expression by sera from patients with active Behçet's disease: moderate correlation with anti-endothelial cell antibodies and serum myeloperoxidase levels. *Clin Immunol* 1999; 91: 330-37.
17. OWLIA MB, MEHRPOOR G: Behçet's disease: New concepts in cardiovascular involvement and future direction for treatment. *ISRN Pharmacol* 2012; 2012:760484.
18. YAŞAR NŞ, SALGÜR F, CANSU DÜ, KAŞIFOĞLU T, KORKMAZ C: Combined thrombophilic factors increase the risk of recurrent thrombotic events in Behçet's disease. *Clin Rheumatol* 2010; 29: 1367-72.
19. MOGULKOC N, BURGESS MI, BISHOP PW: Intracardiac thrombus in Behçet's disease: a systematic review. *Chest* 2000; 118: 479-87.
20. ATZENI F, SARZI-PUTTINI P, DORIA A, BOIARDI L, PIPITONE N, SALVARANI C: Behçet's disease and cardiovascular involvement. *Lupus* 2005; 14: 723-6.
21. ELQATNI M, SEKKACH Y, ABOUZHAR A, GHAFIR D: Right atrium thrombus and pulmonary artery aneurysm in a man with behçet's disease. *Intern Med* 2011; 50: 263-4.
22. DINCER I, DANDACHI R, ATMACA Y, EROL C, CAGLAR N, ORAL D: A recurrent right heart thrombus in a patient with Behçet's disease. *Echocardiography* 2001; 18: 15-8.
23. AHN JK, LEE YS, JEON CH, KOH EM, CHA HS: Treatment of venous thrombosis associated with Behçet's disease: immunosuppressive therapy alone versus immunosuppressive therapy plus anticoagulation. *Clin Rheumatol* 2008; 27: 201-5.
24. UZUN O, AKPOLAT T, ERKAN L: Pulmonary vasculitis in Behçet disease: a cumulative analysis. *Chest* 2005; 127: 2243-53.
25. HATEMI G, SILMAN A, BANG D *et al.*: EULAR recommendations for the management of Behçet disease. *Ann Rheum Dis* 2008; 67: 1656-62.
26. HUONG DL, WECHSLER B, PAPO T *et al.*: Endomyocardial fibrosis in Behçet's disease. *Ann Rheum Dis* 1997; 56: 205-8.
27. LEE I, PARK S, HWANG I *et al.*: Cardiac Behçet disease presenting as aortic valvulitis/aortitis or right heart inflammatory mass: a clinicopathologic study of 12 cases. *Am J Surg Pathol* 2008; 32: 390-8.