Clinical and Experimental Rheumatology 2024; 42: 2092-2095

Atrial myxoma as a mimicker of intracardiac thrombus in Behçet's syndrome: a case study with histopathological confirmation

T. Ak[1], B. Bayrakdar[1], S. Batur[2], E.S. Durmaz[3], M. Cimci[4], E. Seyahi[5,6]

[1]Department of Internal Medicine, [2]Department of Pathology, [3]Department of Radiology, [4]Department of Cardiology, [5]Department of Internal Medicine, Division of Rheumatology, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Istanbul; [6]Behçet's Disease Research Centre, Istanbul University-Cerrahpasa, Istanbul, Turkey.

Tumay Ak, MD
Bahar Bayrakdar, MD
Sebnem Batur, MD
Emine Sebnem Durmaz, MD
Murat Cimci, MD
Emire Seyahi, MD

Please address correspondence to:
Emire Seyahi
Department of Internal Medicine, Division of Rheumatology and Behçet's Disease Research Centre, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, 34810 Istanbul, Turkey
E-mail: eseyahi@yahoo.com

Received on January 23, 2024; accepted in revised form on May 17, 2024.

Key words: Behçet's syndrome, myxoma, intracardiac thrombus, acute-phase reaction, inflammation

ORCID iD
T. Ak: 0000-0002-1548-7638
B. Bayrakdar: 0000-0002-1515-7460
S. Batur: 0000-0001-6577-8970
E.S. Durmaz: 0000-0002-1840-2361
M. Cimci: 0000-0002-7848-627X
E. Seyahi: 0000-0003-4965-2918

Competing interests: E. Seyahi has received honoraria or speaker fees from Novartis, Pfizer and AbbVie. The other authors have declared no competing interests.

ABSTRACT

Cardiomyopathies cause most intracardiac thrombosis (ICT), and Behçet's syndrome (BS) is a rare inflammatory disease that can be responsible for a proportion of ICT. Other inflammatory disorders involved in the aetiology of ICT include antiphospholipid syndrome, Henoch-Schönlein purpura, COVID-19, and Loeffler endocarditis. ICT usually occur during the active phase of BS, and they have a close relationship with vascular involvement. Atrial myxomas are benign cardiac tumours arising from the interatrial septum. They can lead to a substantial acute phase response, making them difficult to distinguish from inflammatory diseases. In this case study, we present a 46-year-old female BS patient who presented with constitutional symptoms mimicking BS flare in a routine follow-up visit and was diagnosed with left atrial myxoma after administration of several lines of immunosuppressives. Then, she underwent surgical tumour excision, and a histopathological examination confirmed the diagnosis. In conclusion, atrial myxoma should be kept in mind first of all when suspecting ICT, and advanced imaging methods such as cardiac magnetic resonance imaging (MRI) should be used if necessary.

Introduction

Behçet's syndrome (BS) is a rare, chronic inflammatory disease of unknown aetiology, and recurrent oral and genital aphthous ulcers and uveitis are hallmarks. Vascular involvement occurs in up to 50% of patients, with superficial and deep veins being the most common targets (1, 2). Intracardiac thrombosis (ICT) is an uncommon condition in BS and usually presents along with pulmonary artery involvement. It mainly involves the right chambers, and the right ventricular involvement is more common than the right atrium (3). BS patients with ICT typically present with constitutional symptoms with high acute phase response, necessitating to discriminate it from malignancies, infective endocarditis, and atrial myxoma. Surgical procedures are not generally indicated in the treatment of ICT because an exaggerated inflammatory situation precludes urgent surgical intervention and expose patients to postoperative complications (3, 4). Moreover, post-surgical relapses are frequently observed (5, 6). Hence, aggressive immunosuppression (steroid pulses in combination with cyclophosphamide or azathioprine), with or without anticoagulation is regarded as the preferred treatment option (7-9). Complete resolution of ICT with immunosuppressive agents has been documented, without the administration of anticoagulation (10-12).

Atrial myxomas are benign tumours originating from the endocardium, primarily found in the atria and with a preference for the left atrium, and they are more common in women than men (13). These tumours consist of a blend of stellate or globular cells embedded in a mucinous matrix, endowing them with a distinct histopathological composition. Atrial myxomas have a varied clinical presentation, including obstructive symptoms like dyspnoea and syncope, constitutional symptoms, and even silent cases (14, 15). There are several cases of ICT related to BS mimicking atrial myxoma in the literature (16, 17). In this manuscript, we present a female case who developed left atrial myxoma 20 years after the diagnosis of BS, and thus, we aim to show the co-occurrence of two rare diseases.

Case presentation

A 46-year-old female patient presented for a routine follow-up visit, and she complained of intermittent fever attacks, fatigue and stabbing chest pain for several months. She was diagnosed with BS in 2003 based on recurrent orogenital aphthous ulcers, skin pathergy positivity (5/6), and arthritis. One month after the diagnosis, she developed diplopia and blurry vision, and cranial magnetic resonance imaging (MRI) was compatible with the neurological involvement of BS with contrast-enhancing lesions in the pontomesencephalic area and thalamus. Therefore, she received induction therapy with intravenous (IV) methylprednisolone 1 gr/d for ten days and followed by azathioprine 125 mg/d and oral methylprednisolone 45 mg/d

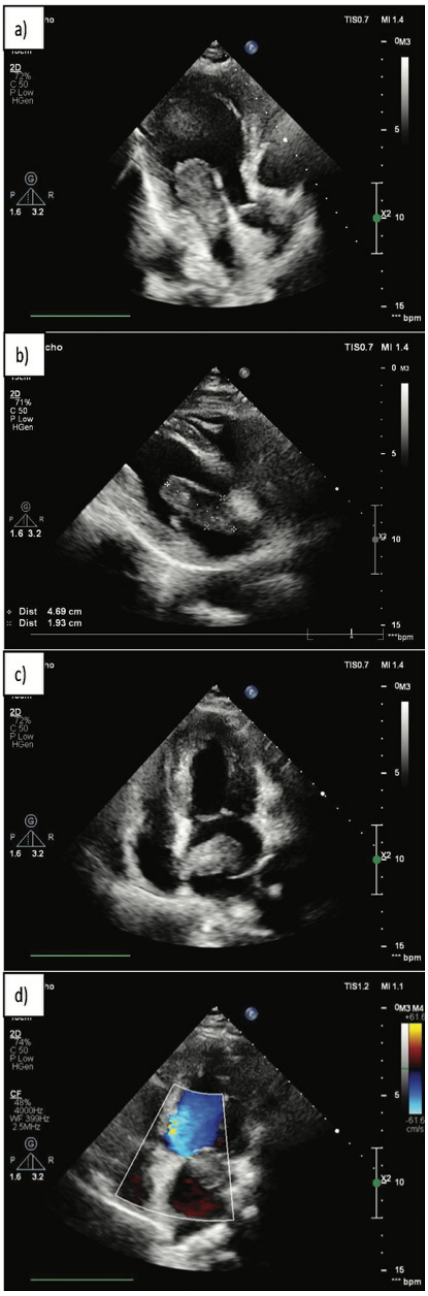

Fig. 1. Transthoracic echocardiography.
a: Colour Doppler shows mild mitral regurgitation with a maximum gradient 3 mmHg.
b-**c**-**d**: A pedicled mass, 5x2 cm in size, connected to the septum within the left atrium and protruding into the left ventricle.

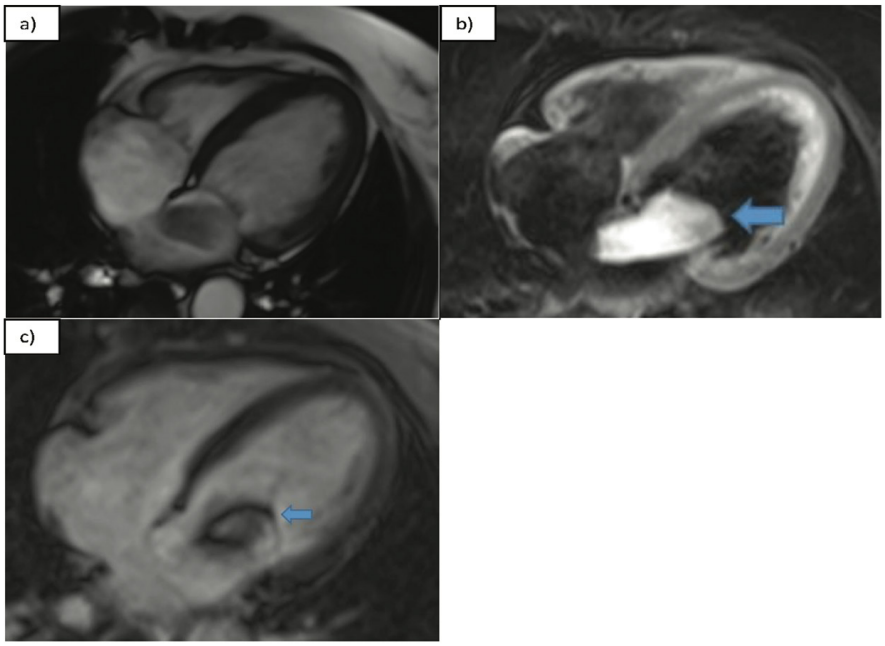

Fig. 2. Cardiac magnetic resonance (CMR) imaging in four chamber view.
Bright blood SSFP shows that the well-circumscribed mass has an intermediate signal (**a**), T2-weighted sequence with fat supression shows high signal throughout the mass due to presence of myxoid component. The arrow shows the component of the mass that protrudes through the mitral valve (**b**).
Late gadolinium enhancement (LGE) sequence is shown similarly (**c**).

for one year. However, azathioprine had to be discontinued due to thrombocytopenia. Although mycophenolate mofetil and methotrexate were tried as alternative immunosuppressive therapies, these agents could not be continued because of gastrointestinal intolerance. Hence, colchicine 1.5 mg/d was started, and glucocorticoids were tapered off in around a year. In 2018, she developed recurrent fever episodes and mild weight loss accompanied by a high acute phase, and her genetic test revealed homozygous M726A positivity. Fever episodes were controlled by increasing the colchicine dosage up to 2 mg/d. Since then, she has used only colchicine treatment without any flares. The physical examination performed for the symptoms described by the patient at her last visit was unrevealing. The laboratory tests were unremarkable except for elevated C-reactive protein (CRP) (63.18 mg/L) and the erythrocyte sedimentation rate (ESR) of 40 mm/hr. Although the patient was in remission for BS manifestations, increased acute phase response prompted us to investigate vascular involvement. Thorax computed tomography (CT) angiography and ventilation/perfusion (V/Q) scintigraphy were ordered primarily to detect pulmonary in situ thombosis or pulmonary artery aneurysms. Thorax CT showed a left atrial mass connected with the interatrial septum and V/Q scintigraphy disclosed no perfusion defect. No deep venous thrombosis was observed on bilateral lower extremity venous Doppler sonography. Transthoracic echocardiography showed a 5x3x1.5 cm mass in the left atrium, which prolapsed into the left ventricle (Fig. 1). Blood cultures taken to investigate infective endocarditis were negative. Since the patient was thought to have ICT secondary to BS, immunosuppressive therapy was administered with IV pulse methylprednisolone (1 gr/d) treatment for three days, followed by oral prednisolone 1 mg/kg/d and IV cyclophosphamide (1 gr/month). After two months of treatment, the size of the mass lesion was stable on control echocardiography, and the patient's initial symptoms persisted. Because of the unusual location of the thrombus, positron emission tomography (PET)-CT was performed, and it showed a hypodense prolapsed mass from the left atrium to the left ventricle without significant fluorodeoxyglucose (FDG)-uptake suggestive of benign tumoral lesion. A cardiac MRI demonstrated a well-defined tumoral lesion of 4x2 cm size in the left atrium extending from the interatrial septum protruding through the mitral valve (Fig. 2). After that, immunosuppressive treatment was discontinued. She underwent cardiovascular surgery consultation, and an open surgical ex-

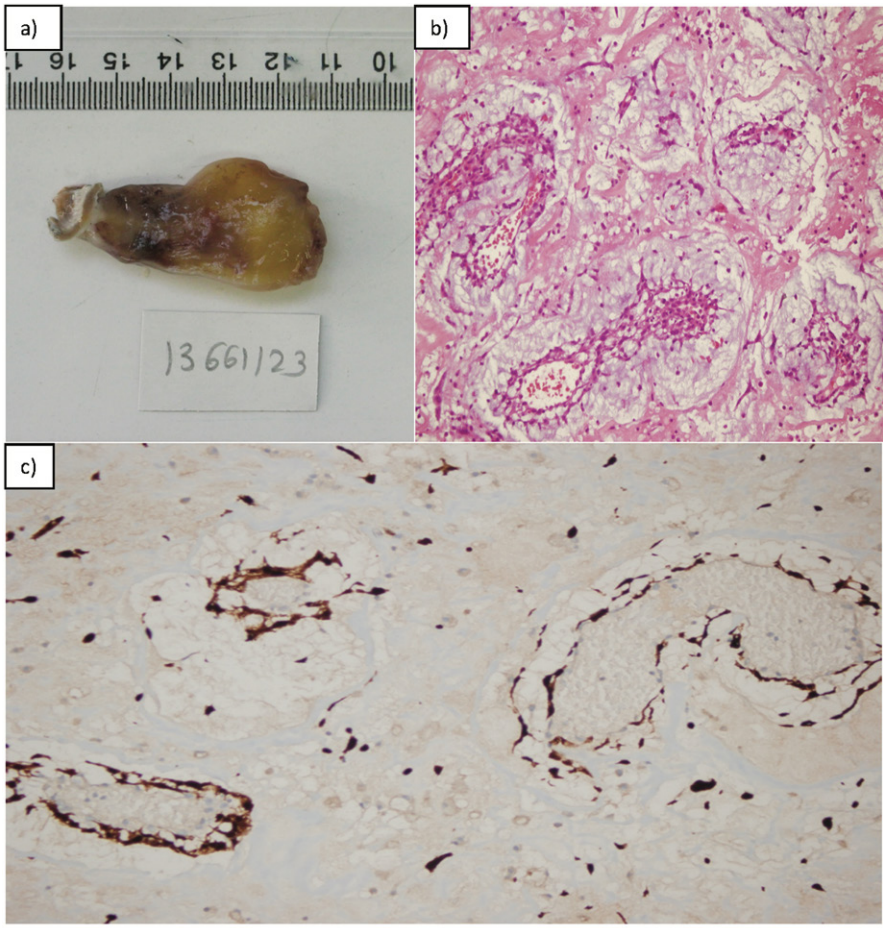

Fig. 3. Histopathological examination of the tumoral lesion recovered from the left atrium.
a: Gross photo of a smooth-surfaced myxoma that was surgically resected from the atrium.
b: Perivascular complex structures resembling cords, nests or rings composed of myxoma cells growing around small intratumoural blood vessels (HEx200).
c: Myxoma cells are typically reactive with antibodies directed against calretinin (x200).

cision of the lesion was performed. The definitive diagnosis of left atrial myxoma was established based on histopathological examination of the specimen (Fig. 3). She is currently doing well and is under follow-up in our outpatient clinic.

Discussion

BS is linked with various vascular complications, such as the formation of ICT (18, 19). ICT, a crucial yet rare manifestation of BS, can precede other presentations of the disorder (20). The complex interplay between the immune system and vascular system is probably operative in developing ICT in BS. Right cardiac chambers, particularly the right ventricle, are most commonly affected, and right-sided endocarditis is thought to be the underlying cause of thrombosis (3, 9, 21). Indeed, the histopathology of ICT in BS is compatible with inflammatory thrombus with adherence to the endocardium and lymphocytic infiltration (21). ICT can cause life-threatening consequences, and it requires prompt and effective treatment with immunosuppression. Surgical intervention might be required if the thrombus persists and results in complications such as endomyocardial fibrosis or valvular insufficiency, ultimately leading to heart failure (6, 21). Thus, a multidisciplinary approach is essential in diagnosing and managing these patients (2, 7).

Atrial myxoma can mimic vasculitis; thus, it should be considered in the differential diagnosis for patients presenting with persistent fever, arthralgia, myalgia, weight loss, malaise, and elevated acute phase reactants. Furthermore, the predominance of women, usually in their fifth or sixth decade, may complicate its differentiation from an inflammatory condition. (13). Constitutional symptoms related to this tumour type probably stem from IL-6 cytokine production (13). Even though these tumours are predominantly benign, they can result in significant levels of morbidity and mortality due to the potential of the atrial myxomas causing mechanical blockages of blood flow, embolisation, and cardiovascular complications (13, 15). Diagnosing atrial myxomas can pose a challenge since they resemble other cardiac masses like thrombi or papillary fibroelastoma (15). Accurate imaging and differential diagnosis are crucial for their identification, and surgical excision of the tumour is the treatment of choice (22). In our experience, we suggest that atrial myxoma should be considered in a BS patient when symptoms such as atypical chest pain, dyspnea, fever, and hemoptysis can not be explained by the most frequent cardiac and pulmonary disturbances (negative laboratory and microbiological tests and negative first-level radiological exams). Diaz Garcia *et al*. reported a case of BS with mucocutaneous, gastrointestinal, and vascular involvement (23). This patient presented with dyspnea, cough, hemoptysis, and fever. Thorax CT angiography revealed bilateral fusiform aneurysms in the lobar and segmental portions of pulmonary arteries, and lower extremity Doppler ultrasonography evidenced bilateral deep venous thrombosis. Echocardiography showed a right atrial pedunculate mass originating from the septum, with a tricuspid protrusion, and cardiac MRI confirmed the diagnosis of atrial myxoma. Similar to our patient, this patient was treated with methylprednisolone (1 gr/d) for three consecutive days and cyclophosphamide (0.75 mg/m^2), followed by oral prednisolone (1 mg/kg). However, unlike our case, this patient did not undergo cardiac surgery and histological confirmation was not available. In addition, the presence of pulmonary artery aneurysms in this patient showed that BS was in its active phase, whereas our patient did not have any signs of activation of BS except for elevated acute phase reactants (23).

Conclusions

ICT is a rare manifestation of BS and is often accompanied by vascular, particularly pulmonary involvement. Unresponsiveness to immunosuppressive treatment, echocardiographic features (location in the interatrial septum and prolapse into the atrioventricular valve), and female gender should be warning signs for myxoma. Cardiac MRI can guide the decision of surgical intervention in this case.

Acknowledgments

The patient gave informed consent for publication of her data.

We thank Professor Deniz Goksedef and Associate Professor Serkan Arıbal for their valuable contributions.

References

1. YAZICI H, SEYAHI E, HATEMI G, YAZICI Y: Behçet syndrome: a contemporary view. *Nat Rev Rheumatol* 2018; 14(2): 107-19. https://doi.org/10.1038/nrrheum.2017.208
2. BETTIOL A, ALIBAZ-ONER F, DIRESKENELI H *et al*.: Vascular Behçet syndrome: from pathogenesis to treatment. *Nat Rev Rheumatol* 2023; 19(2): 111-26. https://doi.org/10.1038/s41584-022-00880-7
3. HATEMİ G, SEYAHI E, FRESKO I, TALARICO R, UCAR D, HAMURYUDAN V: Behçet's syndrome: one year in review 2023. *Clin Exp Rheumatol* 2023; 41(10): 1945-54. https://doi.org/10.55563/clinexprheumatol/7kdo9x
4. HATEMİ G, SEYAHI E, FRESKO I, TALARICO R, UCAR D, HAMURYUDAN V: Behçet's syndrome: one year in review 2022. *Clin Exp Rheumatol* 2022; 40(8): 1461-71. https://doi.org/10.55563/clinexprheumatol/h4dkrs
5. MOGULKOC N, BURGESS MI, BISHOP PW: Intracardiac thrombus in Behçet's disease: a systematic review. *Chest* 2000; 118(2): 479-87. https://doi.org/10.1378/chest.118.2.47
6. GERI G, WECHSLER B, THI HUONG DL *et al*.: Spectrum of cardiac lesions in Behçet disease: a series of 52 patients and review of the literature. *Medicine* (Baltimore) 2012; 91(1): 25-34. https://doi.org/10.1097/MD.0b013e3182428f49
7. SEYAHI E, YAZICI H: Behçet's syndrome: pulmonary vascular disease. *Curr Opin Rheumatol* 2015; 27(1): 18-23. https://doi.org/10.1097/bor.0000000000000131
8. BEN GHORBEL I, BELFEKI N, HOUMAN MH: Intracardiac thrombus in Behçet's disease. *Reumatismo* 2016; 68(3): 148-153. https://doi.org/10.4081/reumatismo.2016.887
9. TOLEDO-SAMANIEGO N, OBLITAS CM, PENALOZA-MARTINEZ E *et al*.: Arterial and venous involvement in Behçet's syndrome: a narrative review. *J Thromb Thrombolysis* 2022; 54(1): 162-171. https://doi.org/10.1007/s11239-022-02637-1
10. DUZGUN N, KUCUKSAHIN O, ATASOY KÇ *et al*.: Behçet's disease and intracardiac thrombosis: a report of three cases. *Case Rep Rheumatol* 2013; 2013: 637015. https://doi.org/10.1155/2013/637015
11. SAMRAH SM, SAADEH SS, ALAWNEH KM: Resolution of intracardiac and pulmonary thrombi without anticoagulation in a patient with Behçet's disease: a case report. *Clin Exp Rheumatol* 2013; 31 (Suppl. 77): S90-2.
12. KANEKO Y, TANAKA K, YOSHIZAWA A *et al*.: Successful treatment of recurrent intracardiac thrombus in Behçet's disease with immunosuppressive therapy. *Clin Exp Rheumatol* 2005; 23(6): 885-7.
13. AIELLO VD, DE CAMPOS FP: Cardiac myxoma. *Autops Case Rep* 2016; 6(2): 5-7. https://doi.org/10.4322/acr.2016.030
14. YOUNES M, AL-DAIRY A, ALBADR A: Right atrial myxoma detected in a child two months after open-heart surgery. *Asian Cardiovasc Thorac Ann* 2019; 27(7): 584-6. https://doi.org/10.1177/0218492319827658
15. LEE SH, PARK JS, PARK JH *et al*.: Comparison of clinical and echocardiographic characteristics between cardiac myxomas and masses mimicking myxoma. *Korean Circ J* 2020; 50(9): 822-32. https://doi.org/10.4070/kcj.2020.0024
16. MADANAT WY, PROKAEVA TB, KOTEL'NİKOVA GP, ALEKBEROVA ZS: Endocarditis with left atrial thrombus formation in Behçet's disease mimicking myxoma. *J Rheumatol* 1993; 20(11): 1982-84
17. 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(1): 15-18. https://doi.org/10.1046/j.1540-8175.2001.00015.x
18. AKSU T, TUFEKCIOGLU O: Intracardiac thrombus in Behçet's disease: four new cases and a comprehensive literature review. *Rheumatol Int* 2015; 35(7): 1269-79. https://doi.org/10.1007/s00296-014-3174-0
19. AMCHICH Y, REGUIG N, BOUCAID A, BELGHOULE R, ZEGMOUT A, BOURKADI JE: Intracardiac thrombus in Behçet's disease: a rare case in Morocco. *Pan Afr Med J* 2020; 36: 92. https://doi.org/10.11604/pamj.2020.36.92.23741
20. HAMMAMI R, ABID L, FRIKHA F *et al*.: Intracardiac thrombus in a young man: don't forget Behçet's disease! *Intern Med* 2012; 51(14): 1865-67. https://doi.org/10.2169/internalmedicine.51.7640
21. ARSLAN C, ARAPI B, SEYAHI E, TEL C, TUZUN KH: Right ventricular thrombus and tricuspid valve dysfunction in a patient with Behçet's syndrome. *Clin Exp Rheumatol* 2014; 32 (Suppl. 84): S109-11.
22. LONE RA, AHANGER AG, SINGH S *et al*.: Atrial myxoma: trends in management. *Int J Health Sci* (Qassim) 2008; 2(2): 141-51.
23. DIAZ GARCIA JD, RODRIGUEZ HENRIQUEZ PJ, BALDERAS JUAREZ J, GONZÁLEZ SÁNCHEZ HR, GONZÁLEZ GALLO O, PALACİOS HERRERA A: Hughes Stovin Syndrome as a variant of Behçet disease associated with a right atrial myxoma. *J Clin Rheumatol* 2021; 27(8S): S434-S436. https://doi.org/10.1097/rhu.0000000000001291