Misdiagnosis of Behçet's disease presented with intracardiac mass as inflammatory myofibroblastic tumor

Kalp içinde kitle ile başvuran Behçet hastalığının enflamatuvar miyofibroblastik tümör olarak yanlış tanısı

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Summary– Behçet's disease is a chronic multisystem inflammatory disorder. There are limited data about cardiac involvement, but it is seen rarely. Herein, we present a 33-year-old male patient with heart failure secondary to a right ventricular mass. It was first diagnosed as inflammatory myofibroblastic tumor (IMT) histopathologically. During the postoperative follow-up, a thrombus was detected at the interatrial septum, and the patient was reevaluated. The diagnosis was possible Behçet's disease, and the mass, previously reported as IMT, was determined to be an organizing thrombus with a mixture of granulation tissue and thrombotic material.

Özet– Behçet hastalığı, çoklu sistem tutulumu olan kronik enflamatuvar bir hastalıktır. Kalp tutulumu nadir olup konuyla ilgili veriler kısıtlıdır. Bu yazıda, sağ ventrikül kitlesine sekonder kalp yetersizliği olan 33 yaşında bir erkek hasta sunuldu. Kitle ilk önce histopatolojik olarak enflamatuvar miyofibroblastik tümör (IMT) olarak teşhis edildi. Operasyon sonrası takiplerde atriyumlar arası septumda thrombüs saptandı ve hasta yeniden değerlendirildi. Tanı Behçet hastalığı idi ve daha önce IMT olarak rapor edilen kitle granülasyon dokusu ve trombotik materyal karışımından oluşan organize trombüstü.

Behçet disease (BD) is a multisystem, inflammatory, relapsing, chronic disorder that was first described by Hulusi Behçet, a Turkish dermatologist, in 1937.[1] Although oral and genital ulceration and uveitis are the classic triad of manifestations, the disease may include articular, vascular, central nervous system, and gastrointestinal involvement. The disorder typically begins in the third decade, but a juvenile form has also been described. Although the actual cause is unknown, immunologic (including autoimmune) and viral causes and a human leukocyte antigen (HLA)-related immunogenetic predisposition (HLA-B51) have been suggested.

Cardiac involvement has been reported in 1-6% of BD patients[2-5] and may present as different forms.

We report a case of a 33-year-old man with heart failure secondary to a right ventricular mass that was initially misdiagnosed as inflammatory myofibroblastic tumor (IMT).

CASE REPORT

A 33-year-old male patient with a cardiac mass detected on the echocardiographic examination was referred to our heart center for further evaluation and treatment. The patient had experienced shortness of breath, fatigue and weight loss for the past three months.

The patient had tachycardia with normal blood pressure. Arterial oxygen saturation (SpO_2) was 75%. Laboratory data showed a white blood cell count of

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Abbreviations:

BD	*Behçet disease*
CT	*Computed tomography*
HLA	*Human leukocyte antigen*
IMT	*Inflammatory myofibroblastic tumor*
MRI	*Magnetic resonance imaging*
RV	*Right ventricle*
SpO_2	*Oxygen saturation*
TEE	*Transesophageal echocardiography*

9000/mm^3 with a normal differential count. The C-reactive protein level was 25 mg/dl, and the erythrocyte sedimentation rate was 15 m/h. The other laboratory parameters were within normal limits.

Transthoracic echocardiography showed severe dilatation of the right ventricle (RV) and septal paradoxical motion. The left ventricular cavity was smaller than expected, and its filling was deteriorated because of paradoxical septal motion. There was a mass on the RV free wall that had similar echogenicity to the myocardial tissue (Figure 1). This mass appeared to be extending toward the RV outflow tract and severely impairing RV function, but did not cause any RV inflow or outflow obstruction. A pulmonary artery systolic pressure of 35 mmHg was also recorded. Transesophageal echocardiography (TEE) revealed patent foramen ovale and a right-to-left shunt across it, in addition to the mass.

Cardiac magnetic resonance imaging (MRI) revealed septum paradoxical contraction and a tubular lesion with heterogeneous signal intensity extending from the inferior wall of the RV to the superior outflow tract. The lesion had the same intensity as the myocardium in precontrast examinations. With contrast injection, MRI showed dense contrast enhancement because of the fibrotic component, and the MRI report indicated that the lesion did not resemble a thrombus. MRI provided anatomic definition, location and extension, but was nondiagnostic. Right heart

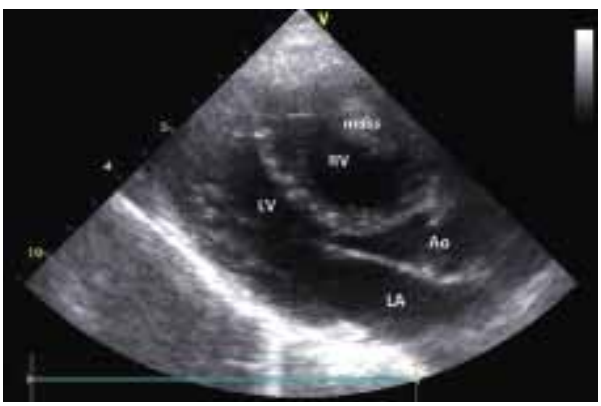

Figure 1. Transthoracic echocardiographic image of the mass.

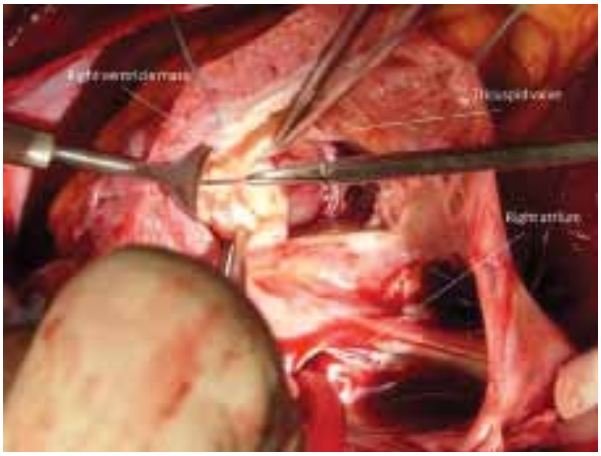

Figure 2. Excision of the right ventricular mass through the tricuspid valve with a right atrial approach.

catheterization and transvenous biopsy were done to aid in the diagnosis. Histopathologic findings of the biopsy specimen disclosed myocardial tissue with lipomatous changes, but did not completely exclude the diagnosis of tumor. Mean pulmonary artery pressure was measured as 10 mmHg during catheterization.

On follow-up, as the patient's clinical status was deteriorating, surgery was planned to resect the RV mass, if it was surgically resectable, and/or to bypass the RV by cavopulmonary anastomosis or to perform a Fontan operation because of severe RV dysfunction and possible recurrence of the mass.

A cardiopulmonary bypass was established, and the right atrium was opened. An RV mass with a fibrotic appearance having the consistency of myocardial muscle was found during surgery. The mass was firmly adhered to the RV endocardium and seen extending from the tricuspid valve to the pulmonary valve. The right atrium was severely enlarged, and the foramen ovale was largely open. The mass was resected with a sharp dissection together with endocardium until normal-appearing myocardial muscle was visible. The mass measured 2.5x2.2 cm and was almost completely excised (Figure 2). The foramen ovale was closed, and cavopulmonary anastomosis was performed to reduce the volume load of the dysfunctional RV and as a prophylactic measure in case of tumor recurrence. The patient was weaned from the cardiopulmonary bypass without difficulty. Pulmonary artery pressure was 11 mmHg and SpO_2 was 100% under 40% fraction of inspired oxygen (FiO_2).

The patient had deep venous thrombosis in the postoperative period and was prescribed oral anticoagulant therapy. He was discharged eight days after his operation.

Macroscopic examination showed a lobular mass measuring 2.5x2.2 cm (Figure 3). Histologic examination revealed dense proliferation of cells of myofibroblast and fibroblast morphology, nonspecific chronic inflammation, plasma cells, and eosinophil infiltration between this proliferation. On immunohistochemical staining, the tumor cells expressed muscle-specific actin but were negative for CD34 and anaplastic large-cell lymphoma kinase protein. Based on these findings, a diagnosis of cardiac IMT was made.

Routine transthoracic echocardiographic examinations and clinical assessments were performed by the same physician at three-month intervals. During the follow-up of the patient, although the tricuspid annular plane systolic excursion had not improved completely, RV dilatation had regressed on echocardiographic examinations, and clinically, there were no symptoms of signs of right heart failure. At the one-year follow-up, a mass was detected on the right side of the interatrial septum, and TEE was performed. There was a mass on the right atrial side of the interatrial septum that was 2.8x1.7 cm in diameter (Figure 4), which was thought to be a thrombus, and oral anticoagulation was prescribed. The patient was reevaluated for a thrombophilic condition, especially for BD. The physical examination was negative for any oral or genital ulcers, but the patient reported having had some oral aphthous lesions in the past. The patient was admitted to the university rheumatology department for further diagnosis and treatment and was diagnosed as possible BD. The pathology specimen of the operation was also reassessed in light of this new information, and the histopathology of the specimen, previously diagnosed as IMT, was diagnosed as an organizing thrombus with a mixture of granulation tissue and thrombotic material. He was prescribed a steroid and colchicine treatment, and both cardiology and rheumatology departments continued follow-up. The interatrial septal mass disappeared in less than three months of the steroid, oral anticoagulant and colchicine treatment.

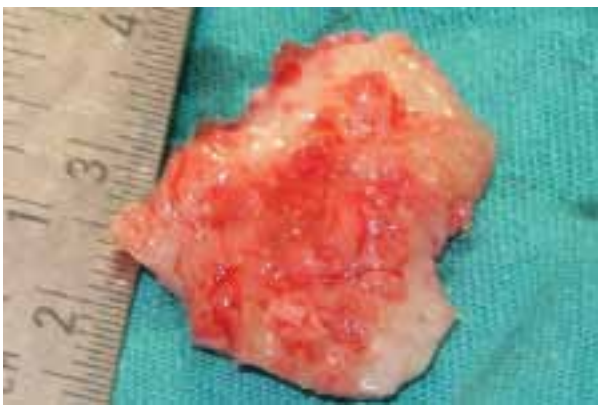

Figure 3. Photograph of the surgically excised lesion.

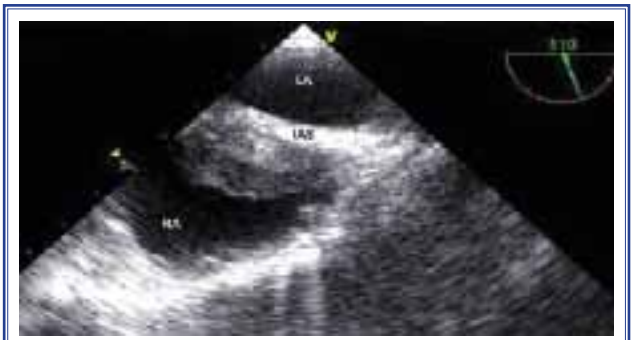

Figure 4. Transesophageal echocardiographic bicaval image of the interatrial septal mass.

DISCUSSION

Primary cardiac tumors are rare; the prevalence reported from autopsy series of patients of all ages varies from 0.0017% to 0.28%.[6] Mass-forming non-neoplastic lesions (reactive and pseudoneoplastic growths) are less common, but distinguishing these lesions from neoplasms is important for appropriate clinical care.

We have reported here a patient with very severe RV dysfunction with a mass on the RV free wall. Mass diagnosis was nonspecific preoperatively with cardiac MRI, computed tomography (CT) and biopsy, so an operation was performed to relieve cardiac failure. We also performed an additional cavopulmonary anastomosis to ensure pulmonary blood flow if the growth of the residual tumor caused future recurrent obstruction. We consider the addition of cavopulmonary anastomosis possible without increasing the risk to patients with suitable mean pulmonary artery pressure, which is usually <15 mmHg for most RV bypass operations. The histopathologic diagnosis was IMT, which was compatible with our findings; the patient had an associated inflammatory syndrome of fever,

malaise and weight loss, and the mass did not have a unique appearance on CT or MRI that would have distinguished it from other tumors. Definitive diagnosis by imaging is unlikely for IMTs without histology, and although various sites of cardiac involvement have been reported, involvement of the right atrium and RV is predominant. However, we detected interatrial septal thrombus during the routine follow-up of the patient, and our diagnosis was reevaluated and changed to possible BD, which also has rare cardiac involvement.

BD is a systemic vasculitis that can involve arteries and veins of all sizes. Diagnosis of the disease is frequently delayed by several years because different symptoms may present over months or years with different clinicians involved at different stages. Additionally, there are no diagnostic laboratory tests for BD, and this delay may contribute to morbidity from the disease. High clinical suspicion is essential in the diagnosis. According to the International Study Group for BD,[7] diagnosis requires recurrent oral ulceration together with two of the following: ocular involvement, genital ulceration, skin lesions, or a positive pathergy test. Pathergy test positivity varies between populations, and approximately 60% of BD patients in Turkey are positive. As our patient's pathergy test was negative, his diagnosis was based on clinical criteria.

Cardiac involvement occurs in 1-6% of BD patients,[2-5] but this may be an underestimation because an autopsy series from Japan indicated 16.5% cardiac involvement in BD.[8] Cardiac involvement may manifest as pancarditis, endomyocardial fibrosis, acute myocardial infarction, conduction system disturbances, intracardiac thrombosis, aneurysms of coronary arteries or sinus Valsalva, and coronary arteritis. Cardiac involvement may be the first manifestation of BD.[2] Intracardiac thrombus formation is uncommon, and young men appear to be most at risk; the most frequent site of involvement is the right side of the heart.[9] More than half of BD patients with intracardiac thrombus have obvious intracardiac thrombus formation upon initial diagnosis of the disease.[9]

Clinical presentation of intracardiac thrombus is nonspecific in patients, and heart failure without valvular involvement is rare. In a review of BD, only two of 25 BD patients with intracardiac thrombus had heart failure without accompanying valvular disease, and both patients died.[9] There are possible explanations for heart failure: the mass is larger than shown on echocardiography, may obstruct the outflow tract or undergo spontaneous fibrinolysis, or the patient may have endocardial fibrosis together with the thrombus. However, we have no evidence to support these hypotheses.

Diagnosis of intracardiac thrombus is sometimes difficult. The most common misdiagnosis on the basis of echocardiography is that of a primary cardiac tumor, as in our patient. Initially, we clinically suspected the mass to be a cardiac tumor. Intracardiac thrombi can occur secondary to several clinical conditions, such as myocardial infarction, hypercoagulable states (e.g., protein C, S deficiencies), some types of cancers (e.g., renal cell carcinoma), and BD. There are also case reports of intracardiac thrombus secondary to some rare conditions, such as hemoglobin sickle cell disease, antiphospholipid syndrome, hypereosinophilic syndrome, and pheochromocytoma.

Yao et al.[10] reported a case of BD with inflammatory pseudotumor in a patient who had a clinical picture similar to our patient's. IMT may be present with BD, or cardiac thrombus may be entrapped in inflammation and fibrosis may be mistakenly reported as IMT, as in our patient. Zou et al.[11] reported the case of a patient with cardiac tumor and BD who was misdiagnosed as infective endocarditis. This report also supports the difficulty in diagnosing cardiac tumor in BD, and the clinical presentation may sometimes mimic other diseases.

No standard treatment modality exists for intracardiac thrombus in BD. Reports in the literature suggest that surgery is performed in approximately half of the patients. Other treatment regimens include anticoagulation, corticosteroids and immunosuppressive drugs.

In conclusion, BD must be considered when evaluating cardiac masses, especially when these masses are on the right side of the heart in young men from epidemic areas.

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Key words: Behçet's disease; heart neoplasms; inflammatory myofibroblastic tumor.

Anahtar sözcükler: Behçet hastalığı; kalp tümörleri; enflamatuvar miyofibroblastik tümör.