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Patients with Behcet's Disease and Cardiovascular Risk Factors are at Risk for Early Cardiovascular and Renal Disease

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Abstract

We present a case of a 39-year-old Turkish female patient with a mild clinical phenotype of Behçet's disease (BD), but experiencing severe cardiac and renal disease, probably enhanced by microvascular atherosclerosis and hypertension. In this case, several cardiovascular risk factors like positive family history, hypertension and smoking were present. Up until recently cardiovascular risk factors were relatively neglected in BD, however recent reports suggest that traditional risk factors are an independent predictor of early coronary artery disease-related morbidity in young BD patients. With this case report we want to stress the fact that severe atherosclerotic complications occur even in young BD patients with longstanding stable, mild disease. This is probably due to chronic inflammation process in chronic diseases like BD, which is a known factor in the initiation and progression of the atherosclerotic process. Therefore, a tight, careful risk factor management should be implied during the follow-up of BD patients.

Keywords: Behçet's disease; Early cardiovascular disease; Renal disease; Risk factors; Case report

Introduction

Behçet's disease (BD) is an idiopathic systemic autoinflammatory vasculitis characterized by recurrent orogenital aphthous ulcers, skin lesions, and ocular inflammation [1]. Arthritis, inflammation of the central nervous system, and involvement of the gastrointestinal tract are less common. Vascular involvement also occurs less often, but has a high mortality rate of 20% [2]. Both arterial and venous involvement have been reported and may involve vasculitis of all types of blood vessels [3]. Complications of vascular origin in BD patients, appearing in 7% to 46% of patients, include aortic and pulmonary artery aneurysms, thrombophlebitis, and venous and arterial occlusions [1,2]. Cardiac complications such as (post) inflammatory occlusion of coronary arteries due to either vasculitis or coagulation disorders [4], and heart failure as a result of either inflammation of the aortic valves or the right ventricle have been observed in BD patients [5]. Despite the fact that no unambiguous relationship between heart failure and BD has been established [2], other cardiovascular complications including pericarditis, conduction disturbances, myocardial lesions, and valvular disease [6,7] have been described in BD patients. However, although inflammatory vascular disorders are related with cardiovascular complications, remarkably little cardiovascular comorbidity is reported in BD.

We present a rare case of a young Turkish BD patient with congestive heart failure and accelerated atherosclerotic renal failure and review the existing literature.

Case Report

A Turkish 39-year-old female BD patient was admitted in 2010 with complaints of dyspnea, painful respiration and palpitations. Her history of BD included orogenital ulcerations, typical skin lesions and intestinal inflammation. These were stable and treated with topical steroids, colchicine and budesonide for more than 1 year. A few weeks before admission she experienced a first episode of nycturia, orthopnoea, dyspnoea and retrosternal pain during effort. Cardiovascular risk factors included pre-existing sub-optimally regulated hypertension, smoking and a family history of cardiovascular diseases.

Physical examination revealed a regular heart rate of 80 per minute, blood pressure of 150/90 mm Hg and elevated central venous pressure. Over the lungs inspiratory crackles were heard. The electrocardiogram showed sinus rhythm, signs of left ventricular hypertrophy, without signs of ischemia. Laboratory evaluations demonstrated microcytic anemia (5.5 mmol/L, mean corpuscular volume of 66 fL), C-reactive protein of 12 mg/mL, acute renal function impairment (creatinine of 120 µm/L, estimated glomerular filtration rate of 40 mL/min, that was previously stable around 74 µmol/L (reference values 55 to 90 µmol/L)) with 0.4 to 0.7 gr/L proteinuria, highly increased NT-pro-brain natriuretic peptide of 1656 pg/L, and negative troponin T. Decreased systolic left ventricle function (estimated ejection fraction of 31%) with diffuse severe hypokinesia was demonstrated by a cardiac ultrasound. Late enhancement cardiac MRI revealed signs of infero-postero-lateral scarring compatible with ischemic cardiac disease. Coronary angiogram showed tortuous coronary arteries, suiting hypertensive heart disease. In addition to this it revealed a small aneurysm in distal right coronary artery (RCA), with probably local plaque rupture (Figures 1 and 2). Extensive viral serology for eventual myocarditis was negative. Also, at endomyocardial biopsy no signs of myocarditis were shown.

A spiral CT-scan excluded pulmonary embolisms or BD-associated pulmonary artery aneurysms. Renal histology revealed severe chronic damage and ischemic changes. No signs of amyloidosis or glomerulonephritis were found.

Treatment for heart failure was commenced with angiotensin-converting enzyme inhibitors, loops diuretics and digoxin, along with acetylsalicylate acid and clopidogrel, given the possible coronary vascular event at the distal RCA. The dosage of prescribed beta-blockers

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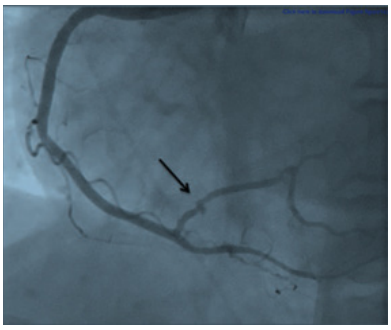

Figure 1: Coronary angiography showing right coronary artery (RCA). Arrow points at small aneurysm of the posterior left ventricular branch.

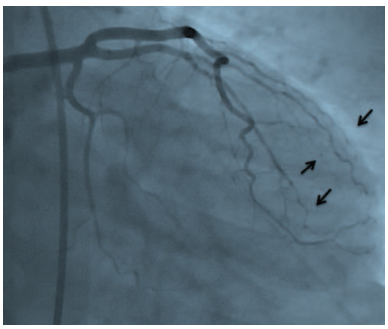

Figure 2: Coronary angiography showing left coronary artery (LCA) showing tortuous coronary arteries and diffuse peripheral small vessel disease (marked by arrows).

was increased. No additional immunosuppressive agents were given. Hereafter the left ventricle ejection fraction of the patient improved in a couple of months, with left ventricular ejection fraction of 63% in 2015.

The renal function however, progressively worsened, leading to pre-terminal end stage renal disease, for which the patient awaits a pre-emptive renal transplantation since March 2015.

Discussion

This case of a young BD patient with cardiovascular disease-induced heart and renal failure demonstrates that patients with mild BD and cardiovascular risk factors are at risk for early onset severe vascular complications.

Traditionally the focus on treating BD patients has been directed towards treating the inflammatory symptoms, even in the case of pulmonary embolisms and pulmonary artery aneurysms [8]. Cardiac inflammation occurs in up to 6% of BD patients, and is a fatal complication of disease [9,10]. Overall vascular involvement is a common complication of BD and affects up to 40% of patients and worsen the prognosis of BD. Vascular manifestations particularly affect young men, in the first years following onset of the disease. Venous complications are the most frequent vascular complications. Superficial and deep lower limb thrombosis are the most frequent venous complications but one third of venous thrombosis concerns large vessels (such as cerebral venous thrombosis, pulmonary embolism, and inferior or superior vena cava). Arterial complications include aneurysms and occlusions/stenosis [3].

Renal involvement in BD is uncommon and mostly due to renal amyloidosis, and occasionally glomerulonephritis or renal artery stenosis/aneurysm [11]. In our patient, renal failure was caused by hypertensive glomerulosclerosis and atherosclerotic ischemic disease. No signs of amyloidosis or glomerulonephritis were found. We regard it unlikely that cardiac symptoms in our patient were an inflammatory complication of BD, because of the relatively mild pre-existing inflammatory complaints and histopathological cardiologic and renal findings. Beside this, intensification of the cardiac medication was beneficial for the heart failure. Additionally, this patient did not develop other BD-related vascular problems such as intrathoracic aneurysms, deep venous or pulmonary thrombosis, or thrombophlebitis. The left ventricular dysfunction is not explained by the small infarction caused by the distal RCA lesion, but the coronary angiogram suggested extensive microvascular disease at the tertiary coronary vessels (Figure 2). Although the gradual improvement in left ventricular function suggests a myocarditis, we believe this is unlikely because of the histologic findings, negative virology and improvement without immunosuppressive medication. In similar inflammatory disorders such as rheumatoid arthritis or systemic lupus erythematosus, higher frequencies of cardiovascular disease are noted [12]. As a result of longstanding inflammation and vascular damage, hypertension and successive cardiovascular disease in BD patientsis expected to be abundant, especially since BD-related symptoms appear to benefit from smoking, adding an extra cardiovascular risk factor [13]. Recently, a prevalence of 12% for coronary artery disease (CAD) in BD patients was reported in a large cohort in the USA. This retrospective study, in which only hospitalized BD patients were included, urged to screen BD patients for CAD risk factors, to prevent cardiovascular disease [14]. However, so far only this report of a subgroup of BD patients and 4 cases with non-BD-related cardiovascular disease have been reported [15-17]. Prevalence of risk factors associated with coronary artery disease are similar as compared to the overall population, however the high incidence of cardiovascular disease at a relatively young age in these BD patients suggest that atherosclerosis might be accelerated in BD patients [14]. In addition to this, in BD patients without risk factors, subclinical atherosclerosis is found [18]. In our patient, the coronary angiogram was more suggestive for microvascular disease, along with local aneurysm, which were to our best knowledge not earlier reported. Further studies with more comprehensive coronary arterial evaluation are needed focussing on microvascular coronary diseases. Until now coronary microvascular dysfunction is found in BD patients with active disease only [19]. In addition to this, myocardial dysperfusion and dysfunctioning due to microvascular disease is found in BD patients by gated single-photon emission computed tomography (SPECT) [20]. Also, in similar inflammatory disease as RA and SLE, chronic inflammatory disease strongly contributes to coronary microvascular dysfunction [21]. As shown in our patient, this early occurrence of atherosclerosis causes significant morbidity, corresponding with the observations that traditional risk factors are an independent predictor of CAD-related morbidity in young BD patients [14]. Therefore, we believe optimal risk stratification is necessary to prevent morbidity in BD patients.

Conclusion

In conclusion, we present a rare case of a BD patient with heart and renal failure due to (microvascular) cardiovascular atherosclerotic disease. We want to stress the need for patients and clinicians to be aware to reduce the presence of these risk factors to prevent early onset or accelerated cardiovascular disease. Therefore, the importance of early risk factor management deserves increased attention in BD patients.

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