

Ten-year progress of coronary artery lesions prior to Behçet disease diagnosis

A case report and care-compliant article

Wenfang Ma, MD*, Yan Liang, PhD*, Jun Zhu, MD

Abstract

Introduction: Behçet disease is a multisystemic chronic inflammatory disorder characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. However, particularly part of patients would present cardiovascular involvements and vascular lesions could be the presenting sign of Behçet disease preceding classical symptoms. We presented a middle aged male patient, in whom abdominal aorta pseudoaneurysm was as the first leading sign to reveal Behçet disease, and with his coronary artery lesions progress through a 10-year period before Behçet disease was diagnosed.

Conclusions: Coronary artery involvement of Behçet disease warrants more attention and investigation; repeated in-stent stenosis, aggressive progress, and elevated inflammation markers should be regard with more care earlier in clinical practice.

Abbreviations: APOE = apolipoprotein E, ISR = in-stent stenosis, LAD = anterior descending artery, LCX = left circumflex artery, PDA = postdescending artery, RCA = right coronary artery, SVG = saphenous vein grafts.

Keywords: aorta pseudoaneurysm, Behçet disease, coronary artery disease

1. Introduction

A 52-year-old man was admitted to this hospital because of precordial discomfort, sense of pharyngeal congestion, and shortness of breath (January 2017).

2. Presentation of the case

The patient had hypertension, hyperlipidemia, diabetes mellitus, and coronary artery disease with a history of myocardial infarction. Twelve years before the current admission (May 2005), the patient began to report precordial chest pain with shortness of breath; it was associated with exertion, lasting for 3 to 5 minutes each time, and was relieved by rest or sublingual nitroglycerin. He was first seen at this hospital and was diagnosed with exertional angina pectoris. Coronary angiography revealed

triple-vessel lesions involving mid left anterior descending artery (LAD) (100%), distal left circumflex artery (LCX) (90%), and right coronary postdescending artery (RCA-PDA) (95%). Percutaneous balloon angioplasty for LCX and stenting for LAD were performed. After intervention, the patient reported persistent precordial discomfort. Eleven years earlier (December 2006), the patient suffered acute antero-septal myocardial infarction after drinking alcohol. Angiography showed in-stent stenosis (ISR) for 95% in the LAD and another stent was implanted within the original stent. Ten years earlier (April 2007), exertional angina occurred again, lasting for 10 minutes each time and radiated to the left shoulder. Angiography showed severe stenosis at the distal RCA (95%) and a stent was implanted. After discharge, the patient reported precordial discomfort or exertional angina intermittently, and gradually spontaneous angina.

Seven years earlier (June 2010), the patient was admitted again due to sense of pharyngeal congestion. Angiography showed ISR again (twice) for 85% in the LAD and a coronary artery bypass grafting was suggested and performed by using left internal mammary artery (LIMA-LAD). The patient reported insufficient relief of symptoms and had chest pain and tightness when weather change after operation. Six years earlier (January 2011), angiography showed poor imaging of left internal mammary artery and coronary computer tomography angiography presented almost no contrast agent filling in the graft. Adenosine stress and resting nuclide myocardial perfusion image (by single photon emission computed tomography) confirmed infarction without viable myocardium at anterior wall and apex of left ventricular. Thereupon another coronary artery bypass grafting was scheduled and the patient received saphenous vein grafts to LAD and PDA (SVG-LAD; SVG-PDA). However, the patient reported that symptoms remained after surgery and spontaneous chest pain and tightness could last for several hours sometimes, also accompanied by dizziness. Later that same year (December 2011), angiography showed severe discrete stenosis at the distal

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State Key Laboratory of Cardiovascular Disease, Emergency and Critical Care Center, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China.

* Correspondence: Yan Liang, State Key Laboratory of Cardiovascular Disease, Emergency and Critical Care Center, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China (e-mail: fwliangyan@sina.cn); Wenfang Ma, (e-mail mawenfang0525@163.com).

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anastomosis of SVG-LAD (95%) and a stent was implanted. Five years earlier (June 2012), the patient reported worsen symptoms with more frequency and resting onset. Angiography showed that the distal LCX (90%) became severely stenotic again and a stent was implanted. Thereafter the patient reported milder symptoms.

Four years earlier (May 2013), the patient was diagnosed as cholelithiasis with acute cholecystitis after onset of upper abdominal pain accompanied with anorexia at local hospital. Repeated angiography was suggested before surgical operation and the result presented obstructing lesions involving proximal, mid, and distal RCA (70%, 90%, and 90%), and 3 stents were implanted at this hospital. Three years earlier (May 2014), angina recurred; angiography showed severe stenosis at the mid-LCX (80%) and a stent was implanted. After that, the patient reported intermittent precordial discomfort without chest pain and tightness, behaved normally when there was no symptom, and repeated electrocardiography at local hospital showed ST-segment elevation of 1 mm in leads V₄ and V₅. Later that same year (December 2014), resting chest pain recurred lasting for 1 minute and relieved itself. Angiography revealed no significant lesions progress and continued medical therapy was recommend.

Two years earlier (July 2015), the patient was diagnosed as abdominal aorta pseudoaneurysm after backache at another hospital and an aortic stent was implanted. Later that same year (December 2015), backache recurred. Computed tomography angiography revealed abdominal aortic stent deformation. After comprehensive examination, the patient was diagnosed as active systematic vasculitis in the setting of Behçet disease (Fig. 1). Thus, immunosuppressive treatment with prednisolone and cyclophosphamide was initiated and 2 months later (Feb 2016) the patient received another aortic stent implantation. About half a year before this admission (June 2016), the patient reported again about exertion-related precordial discomfort, sense of pharyngeal congestion, and shortness of breath, lasting for 10 minutes, without chest tightness or pain, abdominal or back pain, sweating, fever, fatigue, anorexia, dizziness, and palpitation. He came back to this hospital for repeated angiography. However, the procedure was not performed due to hemorrhoid hemorrhage, and a strengthen medication was given. After the bleeding was corrected, the patient readmitted. Angiography showed plaque at the left main, 100% ISR at the proximal LAD, 70% ISR at the distal RCA, and in-stent hyperplasia at the distal anastomosis of SVG to LAD. No ISRs were observed at the mid-LCX, proximal, and mid-RCA; the bridge of SVG to LAD was unblocked. Intervention was not needed.

After admitting this patient, we reviewed his medical records over the 12 years period at this hospital (Supplementary Tables 1–5, <http://links.lww.com/MD/C9>). This male patient was diagnosed with coronary artery triple-vessel lesions at his 40 years old, with major cardiovascular risk factors including smoking, drinking, obesity, hypertension, and hyperlipidemia at first (before 2005), then diabetes mellitus later (2010) (Supplementary Table 1, <http://links.lww.com/MD/C9>). The patient had good compliance and received standard target vessel revascularization and medication treatment (Supplementary Table 4, <http://links.lww.com/MD/C9>). He gradually quit smoking and drinking, ate lightly, and was still at work. His body mass index went down; blood pressure and heart rate were mainly kept in normal range; blood glucose and glycosylated hemoglobin were in target levels; and blood lipid especially the low-density lipoprotein cholesterol was always in good control (Supplementary Tables 2–3, <http://links.lww.com/MD/C9>). However, we noticed that before the discovery of Behçet disease, several inflammation markers including erythrocyte sedimentation rate, C-reactive protein, high sensitivity C-reative protein, and big endothelin were in different degree of elevation at almost each hospitalization (Supplementary Table 3, <http://links.lww.com/MD/C9>). These markers went down remarkably after receiving immunosuppressive treatment, which followed by both relief of symptoms and importantly slower progress of coronary artery as well as abdominal aorta lesions.

Considering the particularity of this patient, metabolic genes referring to clopidogrel and statin were detected during hospitalization (Supplementary Table 5, <http://links.lww.com/MD/C9>). This patient carries wild cytochrome P450 (CYP) 2C19 genotype (CYP2C19*1/*1), an advantageous one which would not influence clopidogrel responsiveness, platelet aggregation, and cardiovascular events.^[1] Statin metabolism-related genotypes were TT for solute carrier organic anion transporter 1B1 c. 521T>C, a good one since there were studies shown that possession of at least one C-allele (CT/CC) is a significant risk factor for statin-induced myopathy and this gene has a larger effect on atorvastatin than rosuvastatin^[2,3]; E3/E3 for apolipoprotein E (APOE) represents normal responsive to statin therapy in view of the associations between the APOE E4 and the APOE E2 alleles with increased and decreased low-density lipoprotein cholesterol concentrations have been reported in many studies.^[4–6] Based on these results, antiplatelet treatment was only focused on clopidogrel to avoid bleeding events on the premise of steroid therapy; atorvastatin was replaced by rosuvastatin to lower lipid intensively and stabilize plaques.

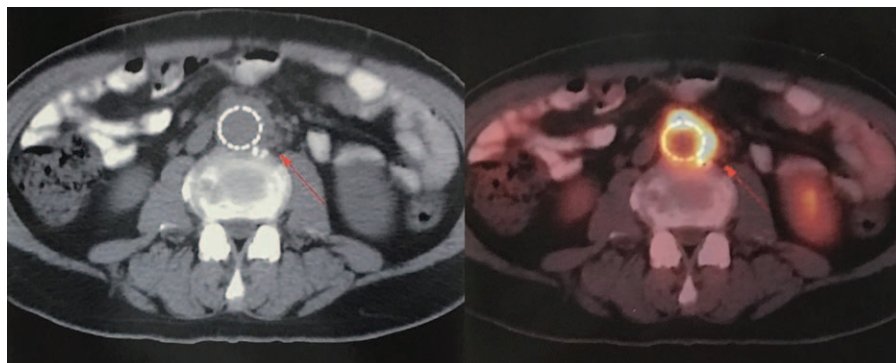


Figure 1. Fluorodeoxyglucose (FDG)-positron emission magnet resonance imaging revealed abnormal FDG uptake within the intra-aortic wall in abdominal aorta.

Table 1
Coronary artery revascularization treatments during each hospitalization.

Admission	CAG/graft date	Diagnosis	LM	LAD	LCX	LCX-OM1	RCA	RCA-PDA	LIMA/SVG	Stenting or grafts	Stent/graft type	Stent size, mm × mm
2005-05	~05-17	Triple-vessel lesion		Mid 100%* CMB	Distal 90%	80%	Proximal 50%	95%		LAD-PCI LCX-PTCA	CypherSelect Sprinter	3.0 × 23 2.5 × 20
2006-12	~12-05	Triple-vessel lesion		Mid ISR 95%		90%		80%		LAD-PCI	Excel	3.0 × 24
2007-04	~04-23	Double-vessel disease		Proximal no ISR		90%	Distal 95%			RCA-PCI	Excel	2.5 × 18
2007-12	~12-28	Single-vessel disease		Proximal 50% Mid no ISR			Distal no ISR			No	No	No
2010-06	~06-18 ~06-24	Triple-vessel lesion		Mid ISR 85%	Ostial 50%			Ostial 70%		No CABG	No LIMA-LAD	No
2011-01	~01-11	Single-vessel disease		Proximal ISR 99%				80%	LIMA Poor imaging	No	No	No
2011-01	~01-25									CABG	AAD-SVG-LAD AAD-SVG-PDA	
2011-12	~12-13	Triple-vessel lesion		Proximal ISR 100%		80%		90%	SVG-LAD Distal anastomosis 95%	SVG-LAD-PCI	Xience V	2.75 × 15
2012-06	~06-05	Triple-vessel lesion		Mid ISR 100%*	Distal 90%	60%	Mid 60% Distal 90%	90%	LIMA Mid 100%	LCX-PCI	Xience V	2.5 × 18
2013-05	~05-21	Double-vessel disease		Proximal ISR 100%†			Proximal 70% Mid 90% Distal 90%	Proximal 100%‡	SVG-LAD SVG- PDA Patency	RCA-PCI proximal/ mid /distal	Firebird	2.5 × 29 2.75 × 23 2.75 × 33
2014-05	~05-13	Double-vessel disease		Proximal ISR 100%	Mid 80% Distal no ISR	70%	Proximal no ISR Mid no ISR			LCX-PCI	Xience Xpedition	2.5 × 12
2014-12	~12-12	Left main and triple- vessel lesion	50%	Proximal ISR 100%	Proximal 50%		Proximal no ISR Mid no ISR Distal no ISR	90%	LIMA Mid 100%	No	No	No
2016-07	No									No	No	No
2017-01	~01-11	Single-vessel disease	plaque	Proximal ISR 100%	Mid no ISR		Proximal no ISR Mid no ISR Distal 70%		SVG-LAD patency distal anastomosis in-stent hyperplasia	No	No	No

AAO=ascending aorta, CABG=coronary artery bypass grafting, CAG=coronary angiography, CMB=cardiac muscle bridge, ISR=in-stent restenosis, LAD=left anterior descending, LCX=left circumflex coronary artery, LIMA=left internal mammary artery, LM=left main, OM1=obtuse marginal 1, PCI=percutaneous coronary intervention, PDA=posterior descending artery, RCA=right coronary artery, SVG= Saphenous vein grafts.
 * Collateral circulation by LCX.
 † Collateral circulation by RCA.
 ‡ Collateral circulation by LAD.

3. Comment

We presented a middle aged male patient with his coronary artery lesions progress through a 10-year period before Behçet disease was diagnosed (Table 1). We believe that the major contributors to the coronary artery disease at first in this patient were traditional risk factors such as smoking, hypertension, and hyperlipidemia. However, triple-vessel lesions at a younger age (40 years), rapid and aggressive disease progress, repeated in-stent and bypass graft restenosis involving anastomosis in spite of good control of risk factors and intensive medical treatment, and ignored elevated inflammation markers (also elevated in the setting of acute coronary event); all those facts have indicated inflammation involvement during the process. Unfortunately, when the vasculitis initiated for sure and started to involve coronary artery and what the extent of influence on each stage were unknown for this patient.

Behçet disease is a multisystemic chronic inflammatory disorder characterized by intervals of relapse and remission. The International Study Group Criteria for Behçet disease is based on mucocutaneous impairments including recurrent oral ulceration, recurrent genital ulceration, eye lesions, skin lesions, and a positive pathergy test,^[7] which were not exist or obvious enough to attract attention as in the patient we presented. However, several large sample studies revealed about 4.4% to 16.8% patients would present vascular involvements, among which venous involvements were more common and arterial lesions were rare.^[8-10] Vascular lesions can be the presenting sign (2.1%) of Behçet disease preceding classical symptoms.^[9] Although remains relatively rare, there were also various forms of cardiac involvement described in the literature including pericarditis, myocarditis, endocarditis with valve insufficiency, intracardiac thrombosis, endomyocardial fibrosis, coronary

arteritis with or without myocardial infarction, and aneurysms of the coronary arteries or sinus of Valsalva.^[11]

For the patient we presented, abdominal aorta pseudoaneurysm was as the first leading sign to reveal Behçet disease, which aggravated the progress of coronary atherosclerosis. Coronary artery involvement of Behçet disease warrants attention and investigation because it affects young subjects, presents various lesions include stenosis, occlusion, ISR, and pseudoaneurysm, with or without myocardial infarction. Repeated ISR, aggressive progress, and elevated inflammation markers should be regard with more care earlier in clinical practice.

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