CASE REPORT

Acute inferior myocardial infarction in a young male patient associated with Behcet's disease and sildenafil

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SUMMARY

Behcet's disease (BD) is a multisystemic inflammatory disorder of unknown origin, presenting with mucocutaneous, ocular, articular, vascular, gastrointestinal and central nervous system manifestations. Coronary involvement is very rare in patients with BD. Sildenafil, an oral drug used to treat erectile dysfunction, was shown to cause significant cardiovascular problems including acute myocardial infarction (MI) and sudden cardiac death. Acute MI associated with BD and sildenafil has not been reported previously. We present a case of a 23-year-old male patient with an acute inferior MI associated with BD diagnosed after admission of sildenafil, who was successfully treated with thrombus aspiration and tirofiban administration.

BACKGROUND

Coronary involvement is extremely rare in Behcet's disease (BD), especially in young patients. In addition, acute myocardial infarction (AMI) associated with sildenafil has never been reported in BD.

CASE PRESENTATION

A 23-year-old man was admitted to our emergency department due to persisting angina for an hour. His ECG showed normal sinus rhythm with ST segment elevation in leads II, III and aVF and reciprocal ST segment depression in leads V1–V6. Traditional risk factors for coronary artery disease (CAD) were absent in the patient's medical history. However, the patient described that his chest pain had started 2 h after self-administration of sildenafil 100 mg for sexual intercourse. On physical examination, cardiac sounds were normal on auscultation. His blood pressure was 92/64 mm Hg and heart rate was 93 bpm. Transthoracic echocardiography revealed hypokinesia of the inferior wall with a left ventricular ejection fraction of 50% and there was no intracardiac thrombosis or mass. On admission, the white cell count was $18.5 \times 10^9/L$, the platelets count $380 \times 10^3/mm^3$, low-density lipoprotein cholesterol 123 mg/dL, high-density lipoprotein cholesterol 38 mg/dL, triglyceride 148 mg/dL, serum troponin-I 0.70 ng/mL (normal range (NR) 0–0.2 ng/mL), creatine kinase myocardial band (CK-MB) 54 ng/mL (NR 0–25 ng/mL), erythrocyte sedimentation rate 42 mm/h (NR 0–20 mm/h) and C reactive protein 10.76 mg/dL (NR 0–0.5 mg/dL).

INVESTIGATIONS

After an initial evaluation, coronary angiography (CAG) was immediately performed. The CAG revealed total occlusion with a thrombus in the proximal segment of the right coronary artery (RCA) and diffuse coronary ectasia in the proximal and mid segments of all three coronary arteries (figure 1). A 600 mg loading dose of clopidogrel, 300 mg of acetylsalicylic acid and unfractionated heparin as an initial IV bolus dose (5000 IU) were initiated. After crossing the lesion with a floppy guidewire, TIMI 0 flow had persisted in the RCA. Subsequently, we performed manual thrombus aspiration as an initial strategy using a 6 Fr ASAP aspiration catheter (Merit Medical Systems, South Jordan, Utah, USA) with multiple slow-passages across the lesion, and tirofiban 25 µg/kg was given as an intracoronary (IC) bolus for 3 min. Thereafter, CAG revealed TIMI 3 flow in the RCA with reduced thrombus (figure 2A,B). A quantitative coronary analysis (QCA) showed that the diameter of the occluded segment was about 5.5 mm in diameter. As the RCA was enlarged and the patient described that his angina had relieved, stent implantation was not considered, and the patient was transferred to the coronary care unit. We continued the treatment with acetylsalicylic acid 300 mg/day, clopidogrel 75 mg/day, unfractionated heparin infusion by adjusting activated clotting time to 200–250 s and tirofiban infusion 0.15 µg/kg/min for 48 h. On the third day of hospital admission, we performed control CAG showing no luminal obstruction and thrombus in the mid-RCA (figure 2C).

DIFFERENTIAL DIAGNOSIS

On suspicion of coronary artery vasculitis, the patient was referred to rheumatology, dermatology and ophthalmology departments. Antinuclear antibody, antineutrophil cytoplasmic antibodies, lupus anticoagulant and cardiolipin antibody were negative. The protein C, protein S and antithrombin levels were within normal ranges, and factor V Leiden mutation was not present. As a result of consultations, the patient was diagnosed with BD because of recurring mouth ulcers at least three times a year, recurring genital ulcers and positive pathergy test.

TREATMENT

The patient was discharged with clopidogrel 75 mg/day, acetylsalicylic acid 100 mg/day, oral

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Figure 1 (A) The right coronary angiography showing totally occluded with thrombus in the proximal segment of the right coronary artery. (B) The left coronary angiography showing coronary artery ectasia in the proximal and mid segment of the left anterior descending and circumflex coronary artery.

prednisolone 30 mg/day which gradually tapered to 5 mg/day for 3 months and azathioprine 50 mg three times a day as the treatment for BD.

OUTCOME AND FOLLOW-UP

The patient was symptom-free at 1 year follow-up.

DISCUSSION

In our view, a few points can be emphasised for the present case. (1) The patient was too young to have an AMI; (2) diagnosis of BD was made after acute MI on suspicion of coronary arteritis; (3) coronary artery ectasia appears as the main factor causing acute MI, however, coronary ectasia has been little reported in the literature related to BD^{1 2}; (4) acute MI might be precipitated by sildenafil; (5) treatment of large coronary thrombus has some difficulties especially in patients with BD.

BD is a multisystemic inflammatory process and mainly affects people between the ages 20 and 40. It has the ability to involve blood vessels of nearly all sizes and types. Because no specific test confirms it, the diagnosis of BD depends on clinical criteria. According to the criteria of International Study Group, the presence of oral aphthous ulcerations and two of the following clinical manifestations are required for the diagnosis of BD: recurrent genital ulcerations, skin lesions, papulopustular lesions, ocular involvement and positive pathergy test.³ The pathergy test is a simple test in which the forearm is pricked with a small, sterile needle. Occurrence of a small red bump or pustule at the site of needle insertion 1 to 2 days after the test

constitutes a positive test. In our case, it was learnt that recurring mouth ulcers, genital ulcers and acne-like lesions affecting face, limbs, trunk and buttocks were present in his history regarding BD for 1 year. However, the diagnosis of BD for this case was made after admission on suspicion of vasculitis involving coronary artery.

Arterial lesions in BD include thrombosis, stenosis and aneurysms, and affect mainly pulmonary, iliac, popliteal, femoral and carotid arteries. It is suggested that arterial involvement of BD may result from neutrophilic vasculitis targeting the vasa vasorum.⁴ Coronary involvement in BD including aneurysm formation and AMI are rarely reported.^{5–8} We considered that coronary ectasia might be an early stage of aneurysmal formation and an early sign of BD. The precise pathogenetic mechanisms underlying the prothrombotic state of BD is unknown. Several factors including endothelial cell injury, the presence of antiphospholipid antibodies, the presence of prothrombotic factors, such as deficiencies of protein S, protein C and antithrombin, and homozygosity for the factor V Leiden mutation have been suggested.^{9–12} Hypercoagulable state was not determined in our case, thus vasculitic endothelial injury might be one of the main mechanisms to trigger or enhance the coronary thrombus formation.

Sildenafil may lead to a prolonged and exaggerated vasodilation causing mild-to-severe hypotension in patients with known CAD and in those taking nitrate therapy. Although it has been rarely reported, sildenafil-associated AMI can be seen in patients without a history of CAD and also nitrate-free

Figure 2 (A) Massive thrombus are seen after the first manual thrombus aspiration in the proximal to mid segment of the right coronary artery in the left anterior oblique view. (B) By thrombectomy with several passages across the lesion, a large amount thrombus is removed using the ASAP aspiration catheter (Merit Medical Systems, South Jordan, Utah, USA). Final result after thrombectomy and intracoronary tirofiban bolus are shown; there is still intraluminal filling defects due to thrombus in the mid segment of the right coronary artery. (C) Control coronary angiography performed after tirofiban infusion on the third day of hospitalisation showing a complete disappearance of the intracoronary thrombus.

patient.^{13 14} Because AMI occurred after taking a high dose (100 mg) of sildenafil that had been received for the first time in his life, it may suggest us to trigger impact of this drug. We also thought that sildenafil could have facilitated the thrombus formation by decreasing the blood pressure and slowing down the coronary flow in the present case having coronary artery ectasia.

According to the European Society of Cardiology (ESC) guidelines of 2012 for the management of AMI in patients presenting with ST-segment elevation, reperfusion therapy is indicated in all patients with symptoms of <12 h duration and persistent ST-segment elevation or new left bundle branch block, and primary percutaneous coronary intervention (PCI) is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 min of the first medical contact. Stenting is recommended (over balloon angioplasty alone) for primary PCI. In the setting of ST elevation MI (STEMI), PCI could be challenging in patients with BD for the following reasons: (1) Our patient demonstrated a totally occluded ectatic coronary artery with a huge thrombus which is associated with an increased incidence of distal embolisation, no-reflow phenomena and poor reperfusion, (2) Arishiro *et al*⁸ reported a case of BD with a coronary artery aneurysm developing after PCI with the use of balloon inflation because of pathergy-like effect. (3) Additionally, there is no consensus on how to treat a large coronary thrombus in the guidelines. Recently, Dudek *et al* have recommended that thrombectomy should be used as an initial strategy in case of TIMI 0–1 flow in the infarct-related artery after crossing the culprit lesion with a guidewire in patients with STEMI.¹⁵ In addition, routine thrombus aspiration is recommended by the ESC guidelines of 2012 for STEMI and has a class IIA, level B recommendation. Therefore, we did not plan ballooning in first place and performed thrombus aspiration and intracoronary bolus administration of tirofiban. In our case, due to the inappropriate coronary structure (about 5.5 mm in diameter in the QCA analysis) and the presence of massive thrombus which is associated with an increased risk of distal embolisation and no-reflow phenomena, we did not consider a ballooning or stent implantation. The effects of thrombus aspiration in STEMI have been evaluated in several clinical trials using a variety of devices.^{16 17} Thrombus aspiration is accepted as an effective strategy to further enhance the benefit of myocardial reperfusion in patients with STEMI, and improves the efficacy of primary PCI.^{18 19} Tirofiban, a glycoprotein IIb/IIIa (GP IIb/IIIa) receptor antagonist, is a potent antiplatelet agent inhibiting the final common pathway of platelet aggregation. The contribution of GP IIb/IIIa inhibitor therapy on clot dissolution remains unclear, but it was thought to have a beneficial effect on coronary clot dissolution. GP IIb/IIIa inhibitors can be helpful for dissolving coronary thrombus by assisting spontaneous fibrinolysis.^{20 21}

Consequently, in the present case, exact mechanism leading to acute MI is unclear. However, we thought that all factors including BD and sildenafil might have affected thrombus formation together. In addition, we propose that thrombus aspiration and administration of GP IIb/IIIa inhibitors should be performed first, ballooning and/or stenting should be selected as the second choice on account of a pathergy-like effect, while treating a coronary thrombosis in patients with BD. Based on this case, BD should be considered as an underlying cause in patients with AMI, especially in young patients with ectatic coronary arteries and it should be kept in mind that sildenafil may trigger an AMI in patients with BD.

Learning points

- Coronary involvement is uncommon in patients with Behçet's disease (BD). However, it may occur irrespective of their age.
- Sildenafil may trigger an acute myocardial infarction in patients with BD.
- In the setting of ST elevation MI, percutaneous coronary intervention might be challenging due to a large thrombus burden and pathergy-like effect.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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