Does sildenafil contribute to acute coronary thrombosis?

Sildenafil akut koroner tromboza yol açar mı?

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Summary– Sildenafil was the first oral compound to be approved for the treatment of erectile dysfunction. It is a selective inhibitor of isoform 5 of phosphodiesterase, which is the enzyme responsible for the breakdown of 3', 5'-cyclic guanosine mono-phosphate. Sildenafil-associated myocardial infarction (MI) is rarely seen in patients without previous history of coronary artery disease. A 43-year-old man presented with sudden onset of chest pain. It was determined that his chest pain started after sildenafil intake. Findings consistent with acute anterior MI were observed on electrocardiography. Coronary angiography showed total occlusion of left anterior descending artery with thrombosis. Coronary angioplasty and stenting was successfully performed.

Özet– Sildenafil erektil fonksiyon bozukluğunun tedavisinde onaylanan oral yolla kullanılan ilk ajandır. Sildenafil 3'-5' monosiklik guanizin monofosfatın yıkımından sorumlu olan 5-fosfodiesterazın selektif inhibitörüdür. Sildenafil ile ilişkili miyokart enfarktüsü (ME) daha öncesinde koroner arter hastalığı olmayan hastalarda oldukça nadirdir. Kırk üç yaşında erkek hasta ani başlayan göğüs ağrısı ile başvurdu. Göğüs ağrısının sildenafil alımı sonrası başladığı öğrenildi. Elektrokardiyografide akut anteriyor ME bulguları saptandı. Yapılan koroner anjiyografide sol ön inen arterin tam tıkalı ve tromboze olduğu görüldü. Koroner anjiyoplasti ve stent işlemi başarıyla uygulandı.

Sildenafil was the first oral compound to be approved for the treatment of erectile dysfunction. It is a selective inhibitor of isoform 5 of phosphodiesterase (PDE5), the enzyme responsible for the breakdown of 3′, 5′-cyclic guanosine mono-phosphate (cGMP). The subsequent increase of cGMP leads to relaxation of the vascular smooth muscle cells of the corpora cavernosa, as well as the systemic and pulmonary vasculature. Pooled data regarding myocardial infarction (MI) and cardiovascular death from sildenafil have shown that the rate of MI or cardiovascular death is nearly 0.0015.[1] Furthermore, it is notable that sildenafil-associated MI is rarely seen in patients without previous history of coronary artery disease.[2]

We report the case of a 43-year-old man who developed thrombotic occlusion of LAD and presented with acute MI after the use of sildenafil. The coronary angiogram demonstrated total thrombotic occlusion in the left anterior descending (LAD) artery. To the best of our knowledge, our patient is the second case documented in the literature presenting with acute coronary thrombosis after using sildenafil. This case emphasizes the potential for precipitating coronary thrombosis after the use of sildenafil.

Abbreviations:

MI	*Myocardial infarction*
LAD	*Left anterior descending*

CASE REPORT

A 43-year-old man was admitted to our hospital with acute severe left-sided chest pain, nausea, and vomiting for 3 hours that started approximately 30 minutes after taking one 100-mg tablet of sildenafil and before any attempted sexual contact. His medical history revealed no preexisting cardiovascular disease, hyperlipidemia, hypertension, smoking or diabetes mellitus. He was receiving no other medications, including other phosphodiesterase type 5 inhibitors, and was

Received: February 07, 2012 *Accepted:* March 03, 2012

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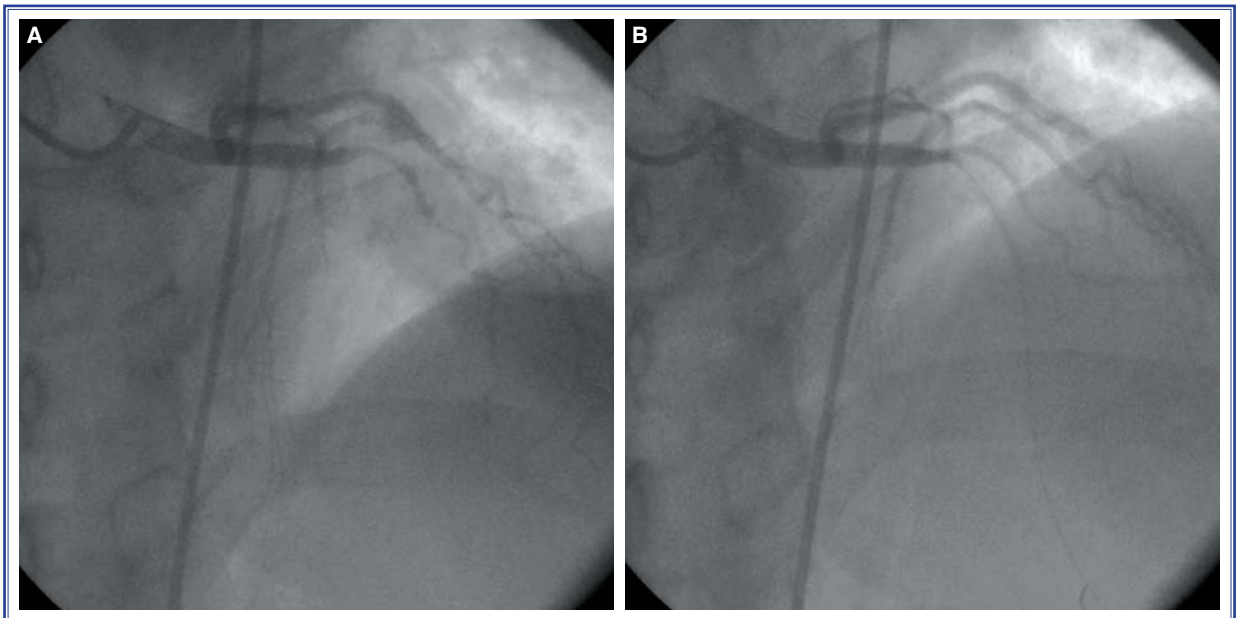

Figure 1. **(A, B)** Right anterior oblique cranial view coronary angiogram demonstrating thrombotic occlusion of the left anterior descending (LAD) artery and the presence of a thrombus in the proximal LAD artery.

taking no dietary or natural product supplements. On physical examination, BP was 130/80 mmHg, heart rate was regular and 105 beats/min. The remainder of the physical examination was also normal. A blood workup on admission revealed cardiac troponin T of 15.20 ng/mL. The electrocardiogram showed ST segment elevation in V1-V6 precordial derivations that was consistent with acute anterior MI. After the patient was diagnosed with an acute anterior MI, therapy with aspirin, metoprolol, and unfractionated heparin was initiated. Early coronary reperfusion treatment with primary percutaneous transluminal coronary angioplasty (PTCA) was performed after initial evaluation that revealed total thrombotic occlusion proximal of the LAD artery and normal circumflex and right coronary arteries (Fig. 1a, b). Balloon angioplasty followed by coronary stenting was successfully performed on the LAD lesion (Fig. 2a, b). The patient was

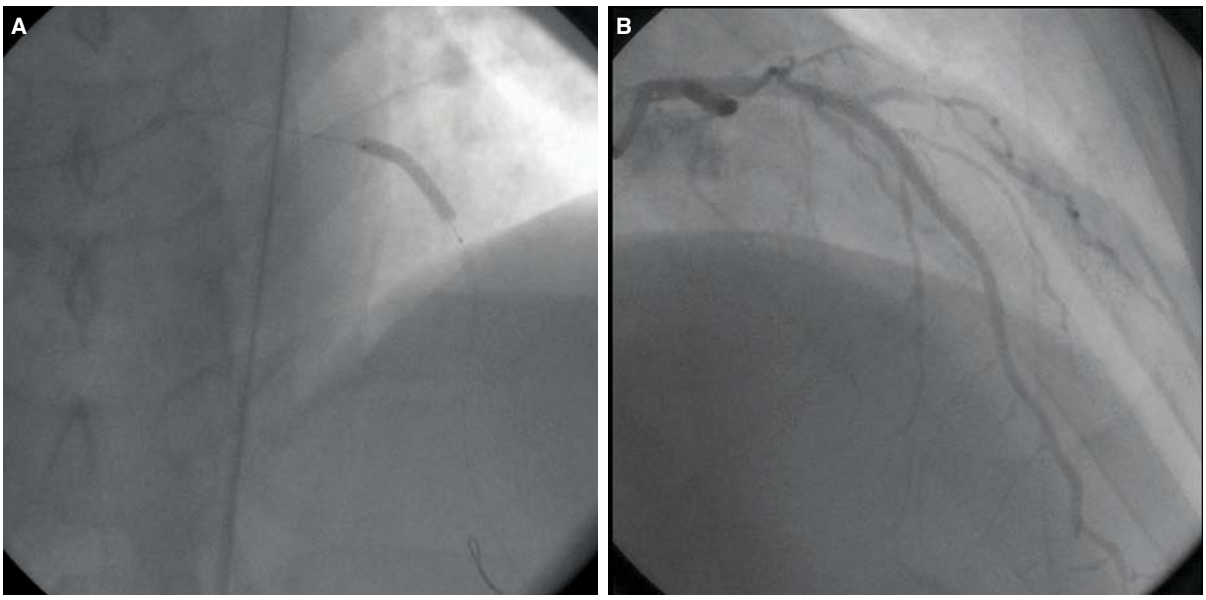

Figure 2. **(A, B)** Final angiogram of the proximal LAD artery after balloon angioplasty and stenting.

transferred to the coronary care unit and subsequently discharged 2 days later with no complications. Factor V Leiden, antithrombin III, protein C and protein S levels were within the normal range.

DISCUSSION

Patients with known coronary artery disease using nitrates are at increaded risk of developing MI after receiving sildenafil, as this could cause prolonged and exaggerated vasodilatation and hypotension. This so-called "coronary steal phenomenon" has not been documented in animal models.[1] On the contrary, sildenafil-associated MI is rarely seen in patients without previous history of coronary artery disease.[2] Feenstra et al.[3] reported the first case of sildenafil associated MI in a patient with no known cardiac history. The authors advocated that redistribution of arterial blood flow may reduce coronary perfusion and lead to MI.[3] However, they did not perform coronary arteriography, and it was uncertain whether preexisting coronary artery disease contributed to MI in their patient.

Recently, a few cases have been published regarding sildenafil-associated MI in the absence of known cardiac history.[4,5] Atherosclerotic critical occlusion was demonstrated by coronary angiography, but coronary thrombosis was not seen in these cases. Only one case has been published presenting acute coronary thrombosis after using sildenafil, by Saha et al.[6] They reported the case of a 66-year-old man who developed thrombotic total occlusion of LAD and presented with acute MI after using of sildenafil. Their patient had presented with chest pain syndrome a week before using sildenafil, and a coronary angiogram had demonstrated normal coronary arteries.[6] We report the case of a 43-year-old man who developed thrombotic occlusion of LAD and presented with acute MI after the use of sildenafil. The coronary angiogram demonstrated thrombotic occlusion in LAD. Lewis et al.[7] conducted a study to determine the effects of sildenafil on platelet-mediated thrombosis in a well-characterized canine model of coronary artery thrombosis after thrombolysis. Their study demonstrated that intravenous sildenafil increased coronary artery patency, reduced *ex vivo* platelet aggregability, and stopped cyclic flow reduction in the majority of animals.

Halcox et al.[8] observed that sildenafil decreased platelet aggregation in patients with coronary artery disease. However, Przyklenk et al.[9] have been reported that sildenafil did not improve coronary patency in a canine model of coronary thrombosis. Li et al.[10] have reported concurrent addition of cGMP analogs and sildenafil potentiated ristocetin- or thrombin-induced platelet aggregation *in vitro* when the proaggregatory stimulus was administered within 10 min of sildenafil exposure. These investigators proposed that the platelet responses to cGMP are biphasic, initially promoting aggregation and subsequently limiting thrombus formation. Based on the case presented here, it should be noted that sildenafil use can lead to acute coronary thrombosis.

This report shows a rare sildenafil-associated acute thrombotic occlusion and myocardial infarction in a patient without previous history of coronary artery disease. Physicians should be aware of this possibility when prescribing sildenafil.

Conflict-of-interest issues regarding the authorship or article: None declared

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Key words: Erectile dysfunction/drug therapy; myocardial infarction; phosphodiesterase inhibitors/adverse effects; sildenafil.

Anahtar sözcükler: Erektil işlev bozukluğu/ilaç tedavisi; miyokart enfarktüsü; fosfodiesteraz inhibitörleri/yan etkileri; sildenafil.