

CASE REPORT

Simultaneous total occlusion of two coronary arteries associated with use of drospirenone-ethinyl estradiol (oral contraceptive)

Drospirenon-etinil estradiol (oral kontraseptif) kullanımına bağlı iki koroner arterin eş zamanlı tam tıkanması

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Summary– Although the use of oral contraceptives is associated with an increased risk of venous thromboembolic disease, the risk of myocardial infarction (MI) is unclear. A new, third-generation contraceptive agent, drospirenone-ethinyl estradiol, which contains less estrogen and a new progestogen, drospirenone, in a different combination, has been considered more reliable in terms of risk of MI. However, there have been some cases of MI associated with the use of drospirenone-ethinyl estradiol, despite the protective effects of this oral contraceptive. In this report, a 33-year-old woman who had used drospirenone-ethinyl estradiol for 6 months was admitted with MI and symptoms of cardiogenic shock. Coronary angiography revealed the total occlusion of 2 coronary arteries and so percutaneous coronary intervention was performed. To the best of our knowledge, this is the first case report of simultaneous total occlusion of 2 coronary arteries associated with the use of drospirenone-ethinyl estradiol in the English-language medical literature.

Özet– Oral kontraseptiflerin kullanımına bağlı olarak venöz tromboemboli riski artmasına rağmen, miyokart enfarktüsü (ME) riski tam belli değildir. Yeni bir üçüncü kuşak oral kontraseptif ajan olan drospirenon-etinil estradiol daha düşük östrojen ve yeni bir progesteron olan drospirenonun farklı kombinasyonundan oluşmakta olup, ME riski açısından daha güvenilir kabul edilmektedir. Bununla birlikte drospirenon-etinil estradiol kullanımına bağlı ME olguları bildirilmiştir. Bu yazıda, altı aydır drospirenon-etinil estradiol kullanan ve ME ve kardiyojenik şok belirtileri ile başvuran 33 yaşında bir kadın hasta sunuldu. Koroner anjiyografide iki koroner arterin aynı anda tam tıkanmış olduğu görüldü, hastaya primer perkütan koroner girişim yapıldı. Bildiğimiz kadarıyla, bu olgu İngilizce tıp literatürü tarihinde drospirenon-etinil estradiol'ün kullanımıyla ilişkili iki koroner arterin eşzamanlı olarak tam tıkanmasıyla sonuçlanan ilk olgudur.

Oral contraceptives (OCs) containing different types and dosages of estrogen and progestin are one of the most used medications to prevent pregnancy. However, their side effects cannot be underestimated. Cigarette smoking, in particular, increases the risk of serious side effects from oral contraceptives, including heart attack, blood clot,

Abbreviations:

BMI	Body mass index
CX	Circumflex
EF	Ejection fraction
LAD	Left anterior descending
LV	Left ventricle
MI	Myocardial infarction
OC	Oral contraceptive
STEMI	ST-elevation myocardial infarction
TIMI	Thrombolysis in myocardial infarction

and stroke. While venous thromboembolism is well known among these side effects, myocardial infarction (MI) is being reported with increasing frequency.

CASE REPORT

A 33-year-old female patient with no known disease was admitted to the hospital with severe chest pain ongoing for 1 hour. She had no coronary risk factors except smoking for 3 years. She reported use of a combined OC pill (drospirenone-ethinyl estradiol) for 8 months. Her body mass index (BMI) was 28 kg/m².

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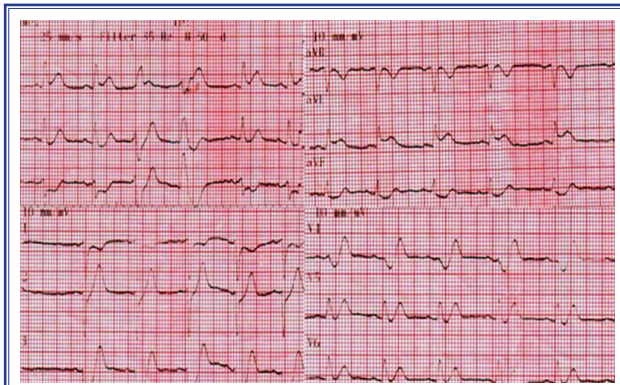


Figure 1. Electrocardiographic features of acute anterolateral myocardial infarction at diagnosis.

On physical examination, she was pale and cold, her pulse was weak, and her heart rate was 130 beats per minute. Her blood pressure was measured at 60/40 mmHg. On auscultation, she had a third heart sound and rales in the lower zones of bilateral lungs. Her electrocardiogram revealed ST-segment elevation and an acute anterolateral MI (Fig. 1). The initial diagnosis was acute MI causing cardiogenic shock, so the patient was immediately transferred to the cardiac catheterization laboratory for coronary angiography and intervention.

Coronary angiography revealed that the left anterior descending (LAD) and circumflex (CX) coronary arteries were totally occluded at the proximal segments. The right coronary artery was normal. Coronary intervention was performed. The total lesions of the LAD and CX coronary arteries were crossed with 2 coronary soft guidewires (Fig. 2). The LAD was predilated with a 2.0x20-mm balloon and

weak antegrade coronary flow was obtained. A long lesion with a high thrombus burden was observed (Fig. 2). A 2.75x32-mm bare-metal stent was implanted into the LAD. The CX lesion was predilated with a 2.0x15-mm balloon and a 2.75x32-mm bare-metal stent was implanted. A Thrombolysis in Myocardial Infarction (TIMI) Score of grade 3 flow was restored in both coronary arteries (Fig. 2). A tirofiban infusion was initiated as adjunctive therapy and was maintained for 48 hours in the intensive care unit, in combination with intravenous heparin infusion. In addition, an intra-aortic balloon pump (IABP) was used to manage cardiogenic shock.

Her vital signs stabilized after 48 hours and the IABP was removed after 72 hours. Echocardiography revealed hypokinesia of the anterior, anteroseptal, and apical segments of the left ventricle (LV) and the LV ejection fraction (EF) was determined to be 30%. Her routine biochemical parameters were within normal limits. In addition, abnormalities related to hypercoagulable status were investigated; protein C, protein S, fibrinogen, and homocysteine levels were examined; and clotting tests and lupus anticoagulant tests were all normal. Factor V Leiden and prothrombin G20210A mutations were also ruled out in genetic analysis. She had no familial tendency to cardiac disease. The patient was discharged home and she was symptom-free after 8 days. LVEF was 35% at second- and fourth-month follow-up visits.

DISCUSSION

Since their introduction in the 1960s, OCs have become a very popular method of birth control. How-

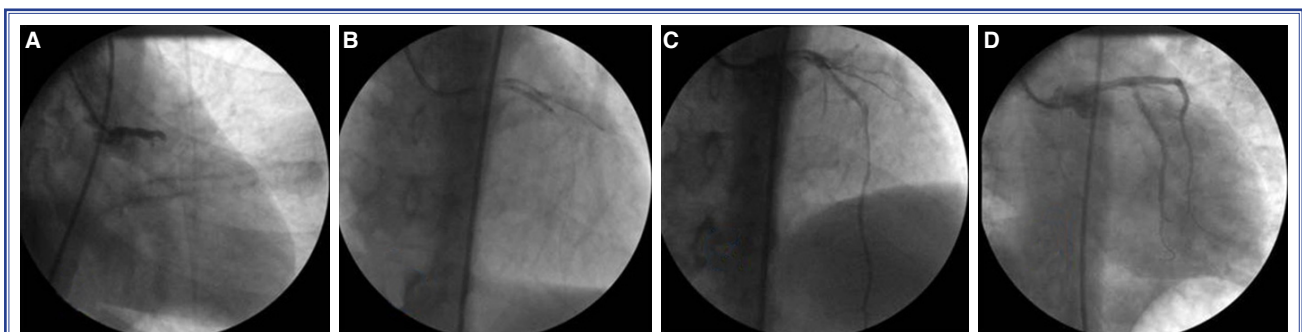


Figure 2. Angiographic views. **(A)** Simultaneous total occlusion of the left anterior descending coronary artery (LAD) and circumflex coronary artery (CX) in right caudal projection; **(B)** Passage of the coronary obstructions with guidewires and balloon angioplasty of the LAD lesion; **(C)** Angiographic imaging of dense thrombotic residual lesion after balloon angioplasty in LAD with cranial projection; **(D)** Angiographic imaging of the LAD and CX coronary arteries after successful percutaneous coronary intervention with right caudal projection.

ever, cardiovascular and cerebrovascular adverse events, such as deep vein thrombosis, stroke, and MI associated with OCs were published as early as the 1990s. While the relationship between OC use and venous thromboembolic diseases and the underlying mechanisms are well-defined, the association between MI and OC use remains controversial.^[11] A prospective study performed in Swedish women demonstrated that use of a combined OC was not associated with an increased risk of MI.^[12] On the other hand, in another clinical study, OC use caused a 2-fold increase in the risk of MI. It was determined in this study that the risk appeared to be amplified by cigarette smoking.^[13]

OCs are classified into generations (first, second, third) and they vary according to the dose of estrogen and the type of progestin used. In the third-generation OCs, the estrogen dose was decreased from 150 mcg to between 20 and 35 mcg, and their androgenic and metabolic side effects were reduced with non-testosterone progestins. The new generation of OC contains drospirenone, which has antiminerlocorticoid and antiandrogenic properties, as a new progestogen. Drospirenone has the potential to reduce body weight, blood pressure, and the low-density lipoprotein level, as well as to enhance the high-density lipoprotein level.^[14] Due to the favorable effects of this newer OC on plasma lipids and cardiovascular events, the risk of MI directly related to drospirenone-ethinyl estradiol use is difficult to define.

There are cases reporting ST-elevation myocardial infarction (STEMI) associated with the use of OCs.^[5,6] The simultaneous total occlusion of 2 coronary arteries in an OC user is a rare clinical entity and we did not find another case report of this occurrence in the English-language medical literature. Kocabay et al.^[5] and Ortí et al.^[6] reported cases of MI associated with use of drospirenone-ethinyl estradiol. However, the culprit lesion was confined to 1 coronary artery in these reports. The pathogenesis of MI is not atherosclerosis in OC users. Acute thrombosis secondary to an increased prothrombin level, platelet reactivity and adhesiveness, and a decreased antithrombin III level are accepted as the possible mechanisms of MI in OC users.^[7] However, in our case, the biochemical parameters were within normal limits. High-sensitivity C-reactive protein levels are reported to be higher in OC users. Chronic inflammatory changes may be a

contributing factor to the development of cardiovascular disease in young women using an OC with no other atherogenic risk factors.^[8] It is well known that the incidence of MI and stroke is greater in smokers.^[9] Smoking seems to increase the risk of clot formation in the coronary arteries of OC users, possibly secondary to an increase of fibrinogen, Factor VII, prothrombin, Factor XI, and Factor X.^[10] In our case, the patient did not have any of the traditional risk factors for atherosclerotic disease other than smoking.

A case control study showed that OC users in the higher BMI category had a significantly increased risk of acute MI compared to normal-weight non-OC users.^[11] The threshold used in this study for high BMI (27.3 kg/m²) was below the threshold of the conventional definition of obesity (BMI \geq 30 kg/m²). Thus, this study might have underestimated the risk of MI in obese OC users. There is no certain therapy for patients who develop MI during OC use. In 2 case reports, a TIMI 3 flow was obtained with thrombolytic therapy before percutaneous coronary intervention.^[5,6] Karabay et al.^[12] demonstrated that women who were using drospirenone-ethinyl estradiol had a higher angiographic thrombus burden and TIMI thrombus grade compared with women who did not. Furthermore, the incidence of a final TIMI 3 flow was lower and the incidence of congestive heart failure and systolic dysfunction was greater in drospirenone-ethinyl estradiol users. Utilization of thrombus aspiration and GP IIb/IIIa receptor antagonists to decrease the thrombus burden before stent implantation is the suggested therapy.^[13] Thrombolytic therapy seems to be a more reasonable choice in patients with STEMI caused by a thrombotic event associated with use of an OC. In our case, the clinical status of the patient called for early recanalization of the arteries, thus we performed predilatation and stent implantation for both coronary arteries. Unfortunately, we could not perform thrombus aspiration, as the catheter was not available at that time.

In conclusion, our case suggests that even if women do not have traditional risk factors for MI, drospirenone-ethinyl estradiol use and smoking may lead to multivessel thrombus formation and multivessel occlusion, leading to MI and a severe clinical condition.

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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Keywords: Cardiogenic shock; drospirenone-ethinyl estradiol; myocardial infarction; oral contraceptives.

Anahtar sözcükler: Kardiyojenik şok; drospirenon-etinil estradiol; miyokart enfarktüsü; oral kontraseptifler.