CASE REPORT

DOI: 10.4274/ijca.2023.43534
Int J Cardiovasc Acad 2023;9(2):48-51

Causation or Coincidence? A Case of Coexisting Spontaneous Coronary Artery Dissection and Coronary Thrombosis in a Patient with Kounis Syndrome

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Abstract

Kounis syndrome (KS) is a hypersensitive coronary disorder leading to acute coronary syndrome triggered by drugs, food, and environmental factors. Herein, we report a 39-year-old patient who was admitted to our clinic due to type 2 KS after oral diclofenac use. Interestingly, spontaneous coronary artery dissection was detected simultaneously on coronary angiography. Up to now, no case has been defined including the combination of these two different conditions.

Keywords: Allergic myocardial infarction, Kounis syndrome, diclofenac potassium, spontaneous coronary artery dissection

INTRODUCTION

Kounis syndrome (KS) is defined as the appearance of acute coronary syndrome symptoms because of activation of mast cells and other inflammatory cells in cases of allergy, hypersensitivity, anaphylaxis or anaphylactic reactions.[1] Various mediators released from mast cells after contact with an allergen may start thrombotic processes by causing spasm in coronary arteries and erosion or rupture of atherosclerotic plaques. KS can be induced by drugs, food, environmental exposures, and other conditions.

The spontaneous coronary artery dissection (SCAD) is also a rare condition with an incidence of 1-4%.[2,3] It may also result in acute coronary syndrome because of disturbance in coronary flow. SCAD has been described commonly in women aged between 47 and 53 years. In this report, we present the case of a patient who had simultaneous type 2 KS and SCAD.

CASE REPORT

A 39-years old male patient who had a history of widespread itching and rashes after oral diclofenac potassium intake for headache came to the emergency department with chest pain. He did not have any known disease and said that he had rashes on his body after taking a medicine 5 years ago. He could not remember his name. On his examination, he had a red-looking face, urticaria-like rashes, and his respiratory rate was increased. Blood pressure was 105/70 mmHg, oxygen saturation 96%, and fever measured 37.2 °C. Electrocardiography revealed sinus rhythm and minimal ST-segment depressions in V1-V3 derivations. Considering an allergic reaction, methylprednisolone and pheniramine were administered intravenously. Considering that KS was possible due to the persistence of severe chest pain, coronary angiography was performed. Coronary angiography showed normal LMCA and LAD artery, total occluded osteal Cx with

To cite this article: Boyacı F, Arslan U. Causation or Coincidence? A Case of Coexisting Spontaneous Coronary Artery Dissection and Coronary Thrombosis in a Patient with Kounis Syndrome. Int J Cardiovasc Acad 2023;9(2):48-51

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Received: 05.03.2023
Revised: 21.05.2023
Accepted: 31.05.2023
Published Online: 07.07.2023

thrombosis, and type 1 SCAD was observed in the mid region of right coronary artery (RCA) (Figure 1A). Three hundred mg acetylsalicylic acid and 600 mg clopidogrel were administered and intravenous 7500 IU heparin was administered to the patient. When the Cx lesion was crossed with a floppy wire, TIMI-3 flow was obtained (Figure 1B). Then, a heavy thrombus burden extending from the Cx osteal to the LMCA was observed and the patient's pain was significantly decreased after coronary flow was established. Considering the high no-reflow risk due to severe thrombus burden, thrombolytic therapy (tPA) was planned to be applied to the patient who was hemodynamically stable. Low dose (25 mg tPA), slow infusion (24 h) tPA were given. Control angiography was performed after 24 h. It was observed that the thrombus in the Cx osteal region completely disappeared (Figure 1C). Since the RCA mid-region SCAD remained unchanged angiographically thrombolysis in myocardial infarction (TIMI) with TIMI-3 flow and the patient was clinically stable, it was decided that he should be followed up medically. The patient was discharged with acetylsalicylic acid, clopidogrel, metoprolol, perindopril, and atorvastatin therapy. After 2 months of follow-up, myocardial perfusion scintigraphy was performed and no ischemia was observed in the RCA area. When the patient was seen at the 6th month of follow-up, he had no complaints. Written consent was obtained from the patient for this case report.

DISCUSSION

KS is defined as the appearance of the acute coronary syndrome symptoms because of activation of mast cells and other inflammatory cells in cases of allergy, hypersensitivity, anaphylaxis or anaphylactic reactions.[1] KS may occur due to various environmental exposures and medications.[4] After contact with the allergen, mast cells are activated and from these cells local and systemic release of biogenic amines such as histamine; neutral proteases such as chimase, tryptase, cathepsin-D; arachidonic acid derivatives and platelet activating factor such as leukotrienes, thromboxane. Histamine causes coronary vasoconstriction, increases tissue factor synthesis, and activates platelets. Proteases, on the other hand, cause plaque wear and tear activating matrix metalloproteinases. Angiotensin-II increase causes vasoconstriction. Thromboxane and thrombocyte activating factor both cause vasoconstriction and activate thrombocytes.[5,6]

Three types of KS have been identified. Type 1; Patients with normal or near-normal coronary arteries without risk factors for coronary artery disease have coronary vasospasm caused by allergic mediators. Type 2; It is the group with an undiagnosed disease, even if there is no history of acute coronary syndrome, with a lesion that causes obstruction in the vein after erosion or rupture of the coronary plaque. Type 3 is the group defined by the presence of eosinophils and mast cells in the extracted thrombus material in some cases who developed stent thrombosis after drug-eluting stent implantation.[5,6]

Previously, KS due to diclofenac have been published in the literature.[7] We wanted to share the treatment management of SCAD occurring in a different coronary artery associated with type 2 KS that developed following allergic findings after oral diclofenac potassium intake without previously known coronary artery disease and risk factors.

SCAD is defined as the separation of coronary artery layers from each other, regardless of trauma, iatrogenic cause, or

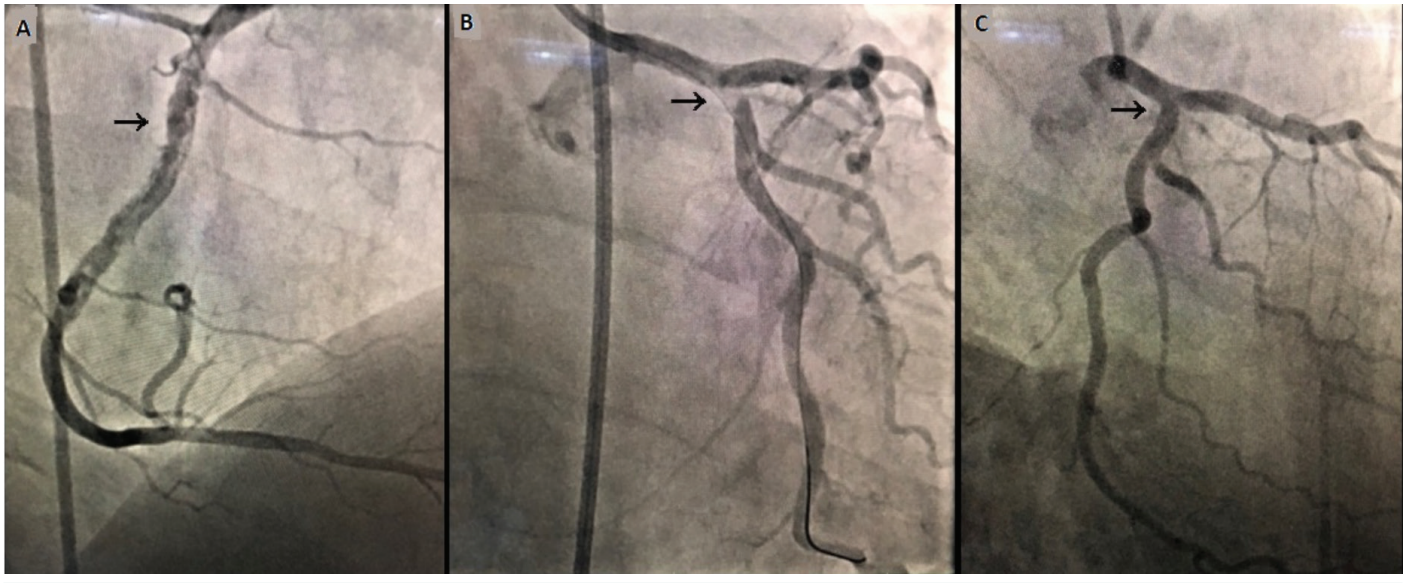

Figure 1. A) Simultaneous coronary dissection in the RCA, **B)** After wire crossing, a heavy thrombus burden was observed in the LAD and Cx osteal region, **C)** Resolution of the thrombus after t-PA infusion

atheromatous plaque rupture. The resulting false lumen can expand and spread, can block the flow within the true lumen, which may cause symptoms of myocardial ischemia. There can be many factors that increase hemodynamic stress and/or increase vessel wall fragility leading SCAD such as pregnancy or heavy sports like wrestling and heavy lifting.[8] On the other hand, the main pathophysiology in KS is coronary vasospasm. Coronary vasospasm increases shear stress on the coronary artery and may lead to dissection. Variant angina has been shown to be associated with SCAD.[9] SCAD cases caused by coronary artery spasm and vasoconstriction related to sympathomimetic drugs (cocaine, amphetamines) use have also been reported.[10] We found our case worth reporting because up to now, no cases have been reported including a combination of these two disorders. Whether it was a cause or co-incidence is not known in our case, but increased shear stress in the coronary artery due to vasospasm in KS might have led to SCAD.

In our patient, when the Cx lesion was crossed with a floppy guidewire, TIMI-3 flow was achieved in Cx. In the Cx osteal, a heavy thrombus burden extending to the LMCA was observed. The patient was hemodynamically stable and pain-free. Because of the high risk of no reflow and stent thrombosis after PCI for a lesion with a heavy thrombus burden in the Cx osteal region, we decided to apply tPA to the patient. Successfully treated cases with low dose, slow infusion thrombolytics have been reported in the literature.[11] The slow and ultraslow infusion of low-dose tPA was first described in the literature for the treatment of prosthetic valve thrombosis in the TROIA and PROMETEE Trials.[12,13] Following these papers, others have successfully used this regime for different clinical scenarios including coronary embolism. Moreover, Karakoyun et al.[14] and Yesin et al.[15] have reported the success of the low-dose t-PA regime in their large series. In fact, the general approach is to avoid thrombolytics specifically in patients with SCAD. However, the risk of propagation of intramural hematoma/complete obstruction of true lumen/vessel rupture is based on previous anecdotal reports where rapidly infused full dose thrombolytics were used. The novel regimen of ultraslow infusion of low-dose t-PA may be less risky in patients with SCAD, but this argument requires confirmation with robust data in the future. In this study, 25 mg tPA was administered to the patient as a slow infusion for 24 h. After 24 h, when we performed control angiography, it was observed that the thrombus in the Cx osteal region and LMCA completely disappeared. There was no progression in RCA dissection, and the appearance was the same as in the first angiography.

In SCAD treatment, conservative treatment is sufficient for most patients who are hemodynamically stable and do not have ongoing ischemia. The majority of conservatively managed SCADs have been found to regain normal coronary architecture, usually within 30 days. To prevent ongoing ischemia, stent implantation can be performed to cover the entire dissection in patients with unstable clinics.[3,16,17] We discharged our patient with dual antiaggregant and beta blocker therapies. In myocardial perfusion scintigraphy after 2 months, no ischemia was observed. The patient did not have any complaints. We decided that SCAD should be followed up medically, and the patient was examined again at the 6th month controls and did not have any complaints.

Negative results regarding the use of thrombolytics in SCAD have been reported due to the prolongation of the dissection or hematoma; therefore, it is generally not recommended. Thrombolytic therapies are not recommended in SCADs because they may cause progress in dissections.[3,16] However, in our case, we applied low-dose slow t-PA infusion successfully because the LMCA and Cx osteal thrombus burden was high, which might have caused no-reflow and cardiogenic shock after PCI. Although there was no negative result in our case, it should be kept in mind that thrombolytic treatments may cause worsening of the dissections.

CONCLUSION

In conclusion, KS is not a rare condition but it can often be overlooked due to cases that cannot be correctly identified. A complete and correct history should be taken before the physical examination. It should also be kept in mind that KS may develop in patients applying with-allergic symptoms, and coronary dissections may also accompany KS.

Ethics

Informed Consent: Written consent was obtained from the patient for this case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.B., U.A., Concept: F.B., U.A., Design: F.B., U.A., Data Collection or Processing: F.B., U.A., Analysis or Interpretation: F.B., U.A., Literature Search: F.B., U.A., Writing: F.B., U.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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