



Case Report

Allergic myocardial infarction (type III Kounis syndrome) secondary to mushroom ingestion: An unusual cause of very late stent thrombosis of saphenous venous graft and refractory no-reflow phenomenon



Pankaj Jariwala (MD, DNB, DNB, MNAMS, FACC, FSCAI) *, Kartik Jadhav (MD, DM), Saket Khetan (MD, DNB)

Department of Cardiology, Yashoda Hospitals, Somajiguda, Hyderabad, Telangana, India

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ABSTRACT

The clinical presentation of myocardial injury associated with allergy responses is known in the cardiology literature as Kounis syndrome or allergic angina/myocardial infarction. An allergic acute coronary syndrome (ACS) may be caused by systemic increase of allergy mediators, or by local stimulation activating heart tissue mast cells (precipitating coronary spasm or generating plaque rupture and coronary or stent thrombosis). Acute allergic/anaphylactic reactions may cause ACS by directly affecting the heart and atherosclerotic plaque, or by exacerbating underlying illness. We present a case of a 67-year-old, Indian male, who had coronary artery bypass surgery and percutaneous coronary intervention and developed very late stent thrombosis of the saphenous venous graft as a result of an allergic response to mushrooms.

Learning objectives:

- A prototypical patient with Kounis syndrome who experienced allergy symptoms and myocardial ischemia after being exposed to a probable allergenic stimulus.
- A link between Type III Kounis syndrome and drug-eluting stent thrombosis has recently been hypothesized.
- Mast cells are plentiful in cardiac tissue and may lead to coronary artery/stent thrombosis.

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Introduction

Very late stent thrombosis (ST) is a serious complication of coronary stenting that often manifests after 12 months of implantation as an acute myocardial infarction or possibly sudden death. Late stent thrombosis and very late stent thrombosis are caused by several factors, including inadequate endothelialization, inflammation, delayed healing, neoatherosclerosis, and local hypersensitivity response [1].

Kounis syndrome is one example of where the underlying coronary artery disease interacts with 'allergy pathophysiological pathways', potentially leading to an acute coronary syndrome (ACS) [2]. ST may occur simultaneously in patients who have had coronary stents inserted and have developed an allergic reaction elsewhere in the human body. Magnet-like properties of stented vessels attract and activate mast cells and platelets. Under specified circumstances, cytokine release

may cause coronary spasm, plaque rupture, or stent thrombosis. We present a case of very late ST of a saphenous venous graft of a previously placed second-generation drug-eluting stent (DES) as a result of an allergic reaction to mushrooms.

Case report

A 67-years-old man with type 2 diabetes and a history of coronary artery bypass surgery in 2001 presented to the emergency room complaining of chest pain for the previous 2 h. Electrocardiography demonstrated significant ST-segment depression of the lateral leads. Echocardiography revealed regional wall motion abnormality in the form of hypokinesia of lateral wall and apical anterior segments with ejection fraction of 48%. His vital parameters were unremarkable.

A thorough analysis of the events revealed a history of intake of mushrooms contained in a pizza, 24 h before the commencement of his chest discomfort. The patient had a widespread skin rash which disappeared quickly without experiencing anaphylactic shock. The

* Corresponding author at: Department of Cardiology, Yashoda Hospitals, Somajiguda, Raj Bhavan Road, Hyderabad, Telangana 500082, India.

E-mail address: pankajjariwala@yashomail.com (P. Jariwala).

emergency services documented elevated biomarkers (high-sensitivity troponin I – 6.5 ng/ml; normal value <0.12 ng/ml). After being diagnosed with ACS with non-ST-segment elevation myocardial infarction (NSTEMI), the patient was transferred to a catheterization laboratory for coronary angiography as part of an early invasive approach.

He previously experienced NSTEMI in 2008, which was treated with percutaneous coronary intervention with 3.5×28 mm sirolimus-eluting Cypher Select stent (Cordis Corporation, Bridgewater, NJ, USA) implanted to the mid-segment of the saphenous vein graft (SVG) to the first diagonal (D1) branch. Clopidogrel was discontinued 30 months after the first repeat revascularization, although aspirin (75 mg/day) and other guideline-directed medical therapy such as extended-release metoprolol succinate 25 mg once daily, perindopril 8 mg once daily, atorvastatin 40 mg once daily were maintained. His lipid profile was within normal ranges two months prior to the current hospitalization (total cholesterol – 188 mg/dl; low-density lipoprotein cholesterol – 67 mg/dl; high-density lipoprotein cholesterol – 45 mg/dl; very low-density lipoprotein cholesterol – 26 mg/dl; triglycerides – 123 mg/dl).

During present hospitalization, coronary angiography of native coronary arteries revealed a chronic total occlusion of the left anterior descending (LAD), right coronary arteries (RCA), and non-obstructive lesions of the left circumflex artery (Fig. 1A–D). Graft angiography revealed a patent left internal mammary artery graft to the LAD, SVG to the RCA, and proximal in-stent thrombotic occlusion of the SVG to D1. Before starting the percutaneous coronary intervention, a loading dose of ticagrelor (180 mg), aspirin (325 mg), and atorvastatin (80 mg) was given.

Extra back-up Judkins-right guide-catheter (7 Fr.) was utilized to reach the SVG to D1 via a transfemoral route. The obstructed graft

could be crossed with the help of Fielder FC guidewire. We opted to undertake manual thrombo-aspiration because of the suspected significant thrombotic burden in this unusual clinical situation. Even though the thrombo-aspiration (6 Fr. Export catheter) failed to extract the thrombotic material, after successive predilatation with 2.0 mm and 2.5 mm balloons also, the flow could not be restored. As a result, vasodilators (sodium nitroprusside, nicorandil) were injected into the distal bed using thrombo-aspiration catheter and subsequently, the contrast injection through it demonstrated thrombolysis in myocardial infarction (TIMI) grade III flow. Two overlapping everolimus-eluting Xience Xpedition stents (Abbott Vascular, Santa Clara, CA, USA) were implanted across the prior stent from the ostio-proximal segment (3.5×38 mm) to the mid-segment (3.5×33 mm) of the SVG (Fig. 2A–F). At the end of the procedure, we could establish TIMI III flow with residual thrombus or dissection. Tirofiban infusion, a glycoprotein IIb/IIIa inhibitor, was continued for 24 h due to the substantial thrombotic load.

On the second day of the procedure, the patient was discharged without complications. The patient has completed two years of dual antiplatelet therapy (DAPT) (ticagrelor 60 mg twice daily and aspirin 75 mg once daily), and as per the PEGASUS study protocol it could be administered for a total of 30 months of therapy [3].

Discussion

Although ST is thought to be a complex consequence, procedural, clinical, and angiographic factors have all been implicated. Some of the primary reasons for ST seem to be hypersensitivity to stent components and medicines that patients take after stent implantation, as well as any

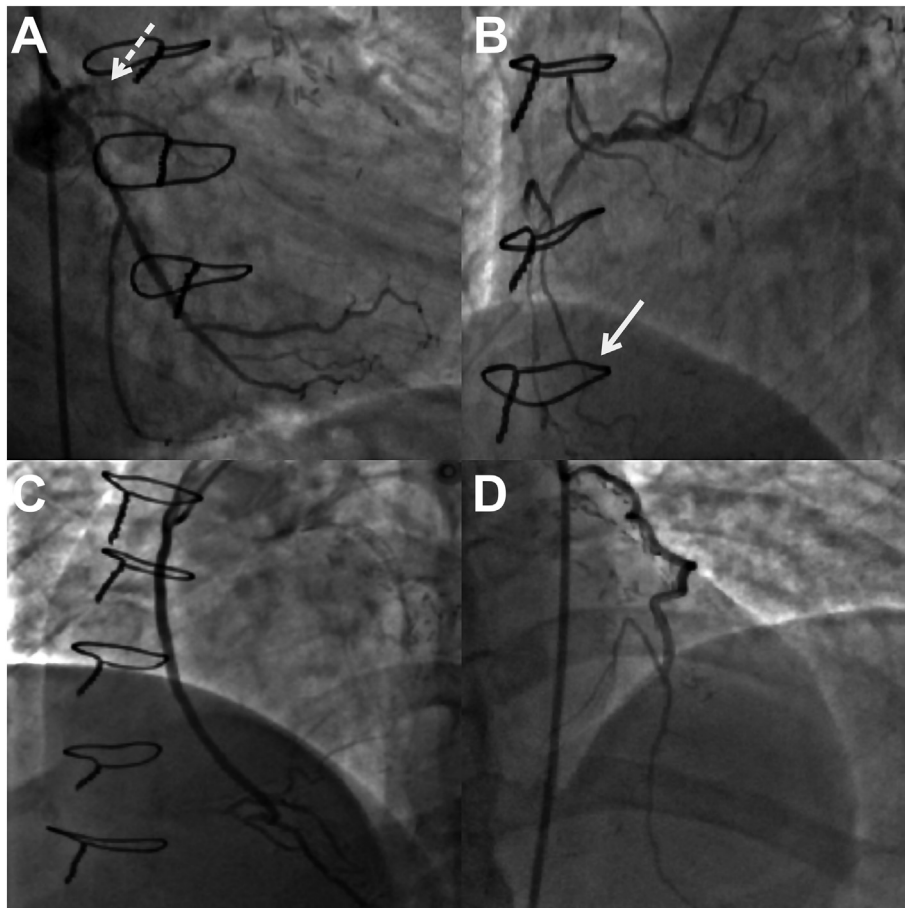
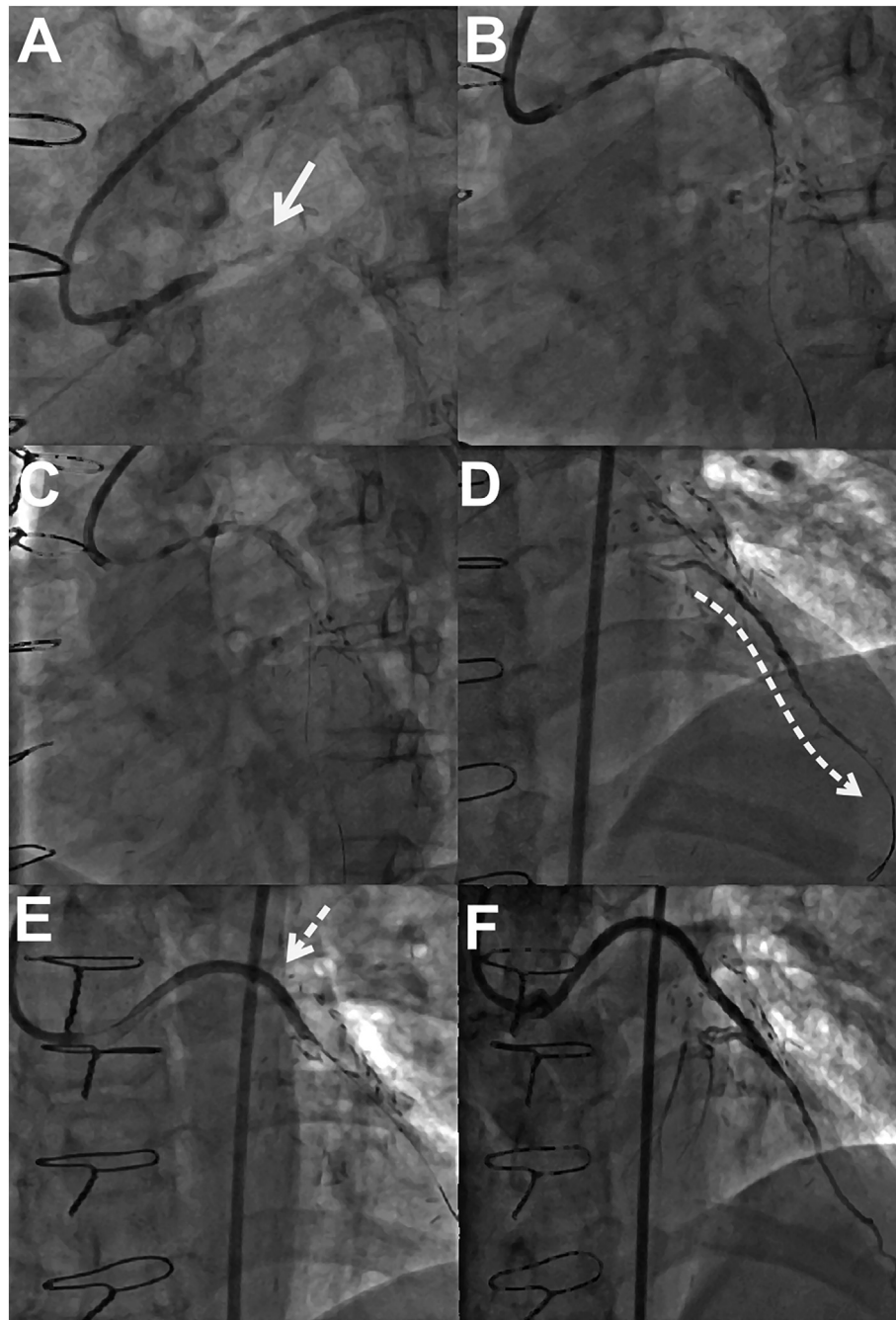


Fig. 1. Coronary angiography of native coronary arteries revealed chronic total occlusions of the left anterior descending artery (LAD) (A), right coronary artery (RCA) (B), and non-obstructive lesions of the left circumflex artery (A). Graft angiography demonstrated patent saphenous vein graft to RCA (C) and left internal mammary artery to LAD (D).

**Fig. 2.**

Graft angiography revealed stent thrombosis in the proximal segment of the saphenous vein graft (SVG) to the first diagonal branch (A). The crossing of an occluded graft with a Fielder FC guidewire (B) and repeated balloon dilatation resulted in the no-reflow phenomena (C). Thrombo-aspiration using an export catheter did not improve flow, thus vasodilators were injected into the distal bed with the same catheter (D). Two overlapping everolimus-eluting stents were inserted over the previously deployed stent from the ostioproximal to mid-segments of the SVG (E). The final angiography showed thrombolysis in myocardial infarction grade III flow (F).

environmental exposure. Any allergic response, atopic diathesis, and medications are examples of such exposures [2,4].

Kounis syndrome, also called allergic myocardial infarction, is characterized by the coexistence of ACSs and mast cell activation-related disorders such as allergy or hypersensitivity, and also anaphylactic or anaphylactoid reaction [5,6]. Type III Kounis syndrome refers to ST in DES caused by hypersensitivity responses to DES components (metallic strut, impregnated medication, and notably polymer). Similar to our case, there have been a few reports of allergic responses to food, such as mushrooms or rice pudding, resulting in DES thrombosis as a symptom of allergic myocardial infarction [7,8]. Although the exact mechanism of Kounis syndrome is uncertain, allergic mast cell degranulation

is known to have a role as shown in Fig. 3. Mast cells are commonly present in the atherosclerotic plaques. Mast cell-produced histamine, neutral proteases (tryptase and chymase), platelet activation factors, cytokines, chemokines, and arachidonic acid metabolites (leukotrienes and thromboxane) have all been linked to coronary artery spasm, platelet aggregation, and rupture in various studies [1,4].

Under ACS circumstances, our patient had previously had a large-diameter (3.5 × 28 mm) sirolimus-eluting first-generation stent placement with no under expansion or dissection. The current guidelines prescribe at least 12 months of DAPT following DES implantation, and he had received DAPT for two years before being admitted [9]. He had chest discomfort after 24 h of mushroom ingestion, showed no

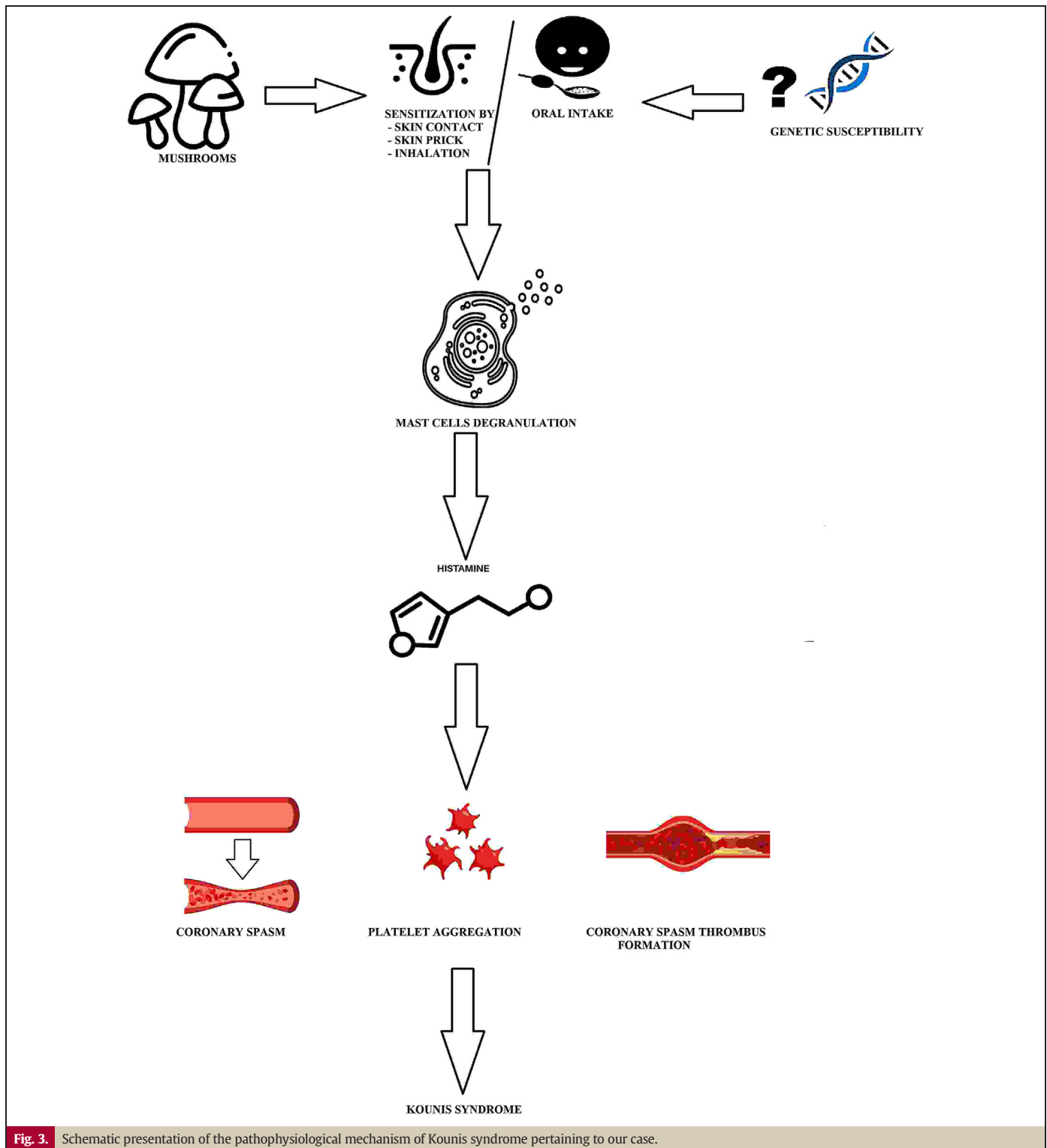


Fig. 3. Schematic presentation of the pathophysiological mechanism of Kounis syndrome pertaining to our case.

indications of anaphylactic shock, and received no therapeutic adrenaline. Based on these findings, we believe we can describe our patient as having Kounis syndrome. In this example, the patient had everolimus-eluting stent implantation for the second time. Recent research has revealed that second-generation DESs (everolimus-eluting or zotarolimus-eluting stents) had better healing profiles and reduced rates of ST when compared to first-generation DESs [10].

Our example demonstrates that an allergic reaction can result in very late ST leading to myocardial infarction in the presence of stable coronary disease. It also implies that type III Kounis syndrome should

be considered in cases of seemingly unexplainable very late ST. Furthermore, ST in DES resulting in myocardial infarction due to mushroom ingestion is extremely infrequent. To our knowledge, this is the first account of very late ST in a second-generation DES-induced by mushroom eating as a manifestation of Kounis syndrome.

Conclusion

Because Kounis syndrome has a wide range of symptoms, diagnosing it may be difficult. Physicians must be aware of this possibly

fatal condition when managing an allergic reaction and severe chest pain. Patients with saphenous vein graft lesions are still difficult to treat. The acute and long-term outcomes for patients with recurrent ACS, regardless of underlying pathophysiology, were previously less favourable, but newer DES and longer duration of DAPT agents with differentiated dosages have brought new hope for these patients.

Consent from patient/patient's attender

As a corresponding author, I declare that there is no financial or non-financial conflict/competing of interests. This manuscript was not submitted to any journal before for publication as a part or complete version. I give complete consent and rights to the journal for its publication. Informed consent was obtained from the participant included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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