

Kounis Syndrome Presenting as Very Late Stent Thrombosis in an Everolimus-Eluting Stent Following Wasp Stings

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Kounis syndrome is the concurrence of acute coronary syndromes with conditions associated with mast cell activation following an allergic insult. We report a 56-year-old man who experienced a ST-segment elevation myocardial infarction after wasp stings. The patient presented without signs of anaphylaxis or shock. Coronary angiography showed an everolimus-eluting stent thrombosis (ST) of the left anterior descending artery occluding the vessel completely which was deployed for stable angina 3 years ago. The patient had been compliant with anti-platelet therapy, and no relevant cardiovascular events occurred until the day of admission. We interpreted our patient's condition as a manifestation of Kounis syndrome. To our knowledge, this is the first case of Kounis syndrome showing very late ST in a second-generation drug-eluting stent caused by wasp stings. (**Korean Circ J 2013;43:561-564**)

KEY WORDS: Hypersensitivity; Drug-eluting stent; Thrombosis; Acute coronary syndrome.

Introduction

Kounis syndrome is the concurrence of acute coronary syndromes (ACS) with conditions associated with mast cell activation including allergic or hypersensitivity as well as anaphylactic or anaphylactoid reaction.^{1,2)} There have been a few reports on extraordinary causes other than wasp stings leading to a drug-eluting stent (DES) thrombosis as a manifestation of Kounis syndrome.³⁻⁶⁾ As far as we knew, very late stent thrombosis (ST) in a second-generation DES following wasp stings has not yet been reported.

We describe a case of very late ST in an everolimus-eluting stent as a consequence of wasp stings and present the pathophysiology and clinical implications of this syndrome with a review of the literature.

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Case

A 56-year old man was referred by an emergency physician to our hospital with an impression of ST-segment elevation myocardial infarction (STEMI). The patient was stung on the arm, neck and head several times by wasps while working on his field about 7 hours prior to admission. He had a mild allergic reaction involving local pain and urticarial swelling immediately after the incident without signs of anaphylaxis or shock. Just a few minutes after being stung, he started complaining of chest pain and called the emergency service. His blood pressure was 120/80 mm Hg, pulse rate was 90 beats per minute and electrocardiogram revealed ST-segment elevation with Q wave formation in the anterior leads and reciprocal ST-segment depression in the inferior leads (Fig. 1). His troponin T level was elevated to 1.86 ng/mL. After being given intravenous dexamethasone and antihistamine, he was promptly transferred to our catheterization laboratory. He had undergone an everolimus-eluting 3.5×15 mm stent placement (Promus®, Boston Scientific, MN, USA) in the mid-left anterior descending (LAD) artery for stable angina 3 years prior in our hospital. Clopidogrel (75 mg/d) was withdrawn 24 months after stent implantation, while aspirin (100 mg/d) had been continued until that day. Coronary angiography demonstrated a thrombosis in the previous stent in the LAD artery, completely occluding the vessel (Fig. 2A). The remaining vessels showed insignificant stenosis. The lesion was crossed with a Runthrough® NS guidewire (Terumo) and sequential inflations using Nimbus PICO® (BARD) 1.25×

12 mm, followed by 2.0×12 mm balloons to disperse the thrombus. Next, thrombus aspiration with a thrombus aspiration catheter (Thrombuster II®, Kaneka Corp., Japan) was performed. Abciximab infusion was started, of which half of the initial bolus was given directly into the left coronary system. However, Thrombolysis in Myocardial Infarction flow 3 was not established despite these measures. In the end, an everolimus-eluting 3.5×15 mm stent (Promus Element™, Boston Scientific, MN, USA) was deployed with an excellent angiographic result (Fig. 2B). We did not measure serum tryptase and histamine levels with a half life of 90 minutes and of less

than 30 minutes respectively because 7 hours had passed after the onset of symptoms. He was discharged from the hospital 6 days after the index procedure with dual anti-platelet therapy (DAPT). The patient is currently doing well and is being followed up in the outpatient department.

Discussion

Stent thrombosis is the primary concern regarding long-term safety outcome in the current DES Era, which is a fatal complication

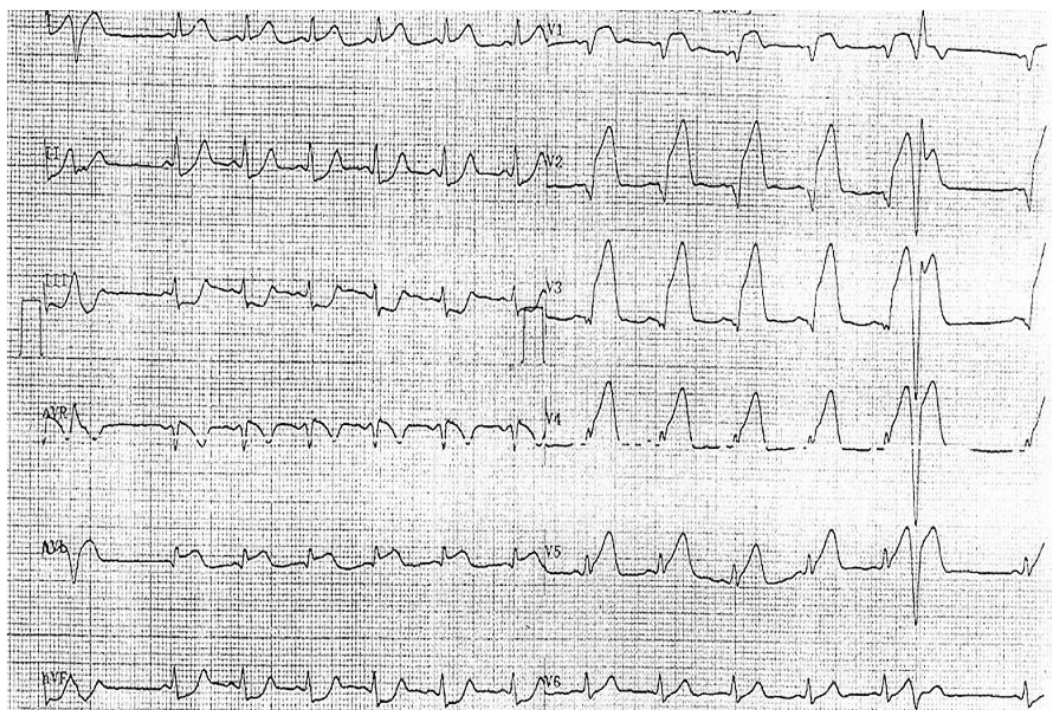


Fig. 1. Electrocardiogram showing ST-segment elevation in the anterior leads and reciprocal ST-segment depression in the inferior leads at presentation.

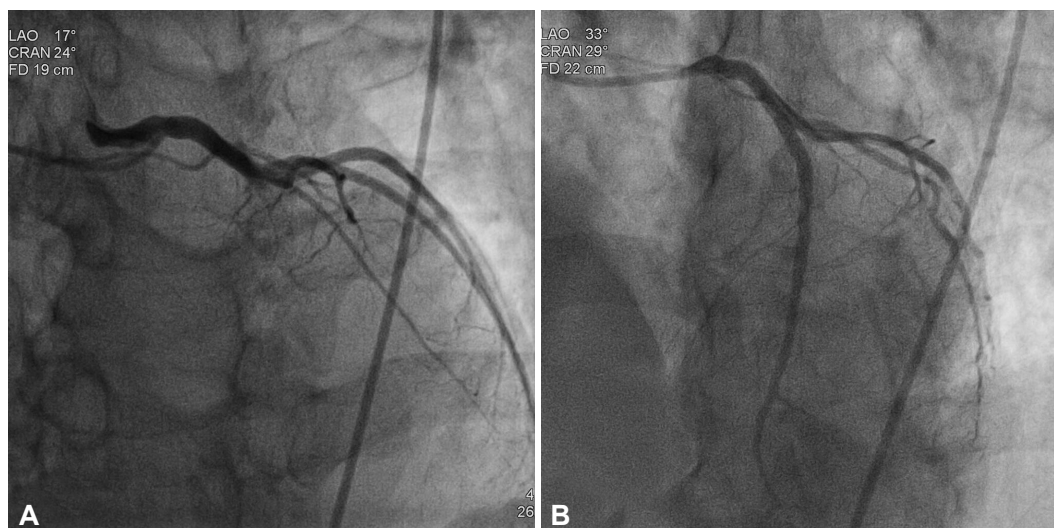


Fig. 2. Coronary angiography of the left coronary artery. A: coronary angiography showing stent thrombosis occluding the left anterior descending artery completely. B: a new drug-eluting stent was deployed with a good angiographic result.

that often leads to myocardial infarction or death. Early ST is likely due to clinical factors such as STEMI, chronic kidney disease or premature discontinuation of clopidogrel and procedural issues such as stent malapposition, plaque protrusion or vessel dissection, while late or very late ST is associated with late-acquired stent malapposition, delayed reendothelialization and neoatherosclerosis with plaque rupture.⁷⁾ The occurrence of ACS during the course of an allergic reaction constitutes Kounis syndrome.¹⁾²⁾⁸⁾ ST in DES due to hypersensitivity reactions to components of DES (metallic strut, impregnated drug and especially polymer) is known as type III Kounis syndrome.⁹⁾¹⁰⁾ Other types include patients with normal coronary arteries (type I) and patients with quiescent, pre-existing atherosclerotic disease (type II). There are several causes that are capable of inducing Kounis syndrome. These include drugs (antibiotics, analgesics, non-steroidal anti-inflammatory drugs), conditions (asthma, food allergy, urticaria) or environmental exposures (hymenoptera and others stings, shellfish consumption, latex contact).¹⁾²⁾⁸⁾ Myocardial infarction following hymenoptera stings (bees, wasps and hornets) is rare with less than twenty documented reports in the literature.¹¹⁻¹⁴⁾ Furthermore, ST in DES leading to myocardial infarction secondary to wasp envenomation is much rarer and existing report was about first-generation DES.¹⁵⁾ To the best of our knowledge, this case is the first description of very late ST in a second-generation DES caused by wasp stings as a manifestation of Kounis syndrome.

Although the exact mechanism of Kounis syndrome is still under discussion, mast cell degranulation following an allergic insult is known to play a key role. Mast cells usually exist within atherosclerotic lesions. Chemical mediators released from mast cells such as histamine, neutral proteases (tryptase and chymase), platelet activating factors, cytokines, chemokines and metabolites of arachidonic acid (leukotrienes and thromboxane) have been incriminated to induce coronary artery spasm, to promote platelets aggregation, and to transform a pre-existing stable atherosclerotic plaque to a vulnerable plaque leading to rupture.²⁾⁶⁾⁹⁾¹¹⁾ Other possible mechanisms involve: 1) the direct action of wasp venom constituents such as histamine and phospholipase A₂,¹³⁾ 2) the anaphylactic reaction itself with severe hypotension, and 3) adrenalin use which can induce coronary spasm and myocardial damage.¹⁶⁾ Our patient had previously undergone short and large-diameter (3.5×15 mm) stent implantation without underexpansion or dissection under non-ACS conditions. The current guideline recommends at least 12 months of DAPT after DES implantation,¹⁷⁾ and he had received DAPT for 2 years and then aspirin until the day of admission. He developed chest pain just a few minutes after being stung by wasps, had no signs of anaphylaxis or shock and did not receive therapeutic adrenaline. Based on these observations, it is reasonable that we can classify our pa-

tient as having Kounis syndrome.

In the present case, the patient was treated with everolimus-eluting stent implantation again this time. Recent studies have shown that second-generation DESs (Everolimus-eluting or Zotarolimus-eluting stent) lead to more favorable healing profiles¹⁸⁾ and are associated with lower rates of ST compared with first-generation DESs.¹⁹⁾²⁰⁾

In conclusion, Kounis syndrome is an uncommon clinical entity, and its diagnosis is difficult to make owing to its variable manifestations. It is important for clinicians to keep this potential fatal scenario in mind while treating an allergic reaction associated with acute chest pain.

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