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A subset of type I variant Kounis syndrome: Allergic angina syndrome and persistent presence of coronary spasm



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Kounis syndrome is defined as the concurrent development of acute coronary syndrome, with an allergic or hypersensitivity and anaphylactic response to anaphylactoid insults [1]. Clinical manifestations of Kounis syndrome include the spectrum of acute coronary syndromes, including coronary spasm, acute myocardial infarction, or stent thrombosis, which is associated with mast-cell and platelet activation caused by a hypersensitivity reaction [2–4]. Coronary spasm provoked by histamine release during an allergic reaction is a key mechanism leading to acute coronary events; [5] however, it remains unclear whether coronary spasm is an insult-related, transient phenomenon during an allergic reaction or expression of a preexisting condition provoked by hypersensitivity insult. We report a case of Kounis syndrome with cardiovascular collapse that developed after the injection of medications and the persistent presence of coronary spasm documented by an ergonovine stimulation test. We also propose a sub-classification of Kounis syndrome.

We present a case of a 69-year-old man who was resuscitated from cardiac arrest caused by hypersensitivity coronary spasm. He had a history of a hepatic lobectomy due to hepatocellular carcinoma. He was a former smoker and had no previous history of chest pain. He was in relatively good health until he came to the emergency department with right upper quadrant pain lasting for 1 h. On admission, his vital signs were stable and mild direct tenderness in the epigastric area and right upper quadrant of the abdomen were noted. Previous ECG revealed normal sinus rhythm (Fig. 1A). Ranitidine and tramadol were injected intravenously due to suspicion of non-ulcer

dyspepsia. Two minutes after injection, he complained of sudden dyspnea and collapsed; a carotid pulse was not palpable. The ECG monitor showed marked bradycardia with wide QRS complexes, suggesting pulseless electrical activity. Advanced life support was started immediately, and 1 mg of epinephrine was injected intravenously. Spontaneous circulation was restored after 8 min of cardiopulmonary resuscitation (CPR). On ECG after restoration of spontaneous circulation (ROSC), ST segment elevations in leads II, III, and aVF and ST depressions in leads V1 and V2 were present, suggesting an inferoposterior myocardial infarction (Fig. 1B). After transient ROSC, ventricular fibrillation occurred. ROSC was re-obtained after 1 min of CPR and defibrillation. Emergency coronary angiography showed 30% stenosis of the proximal right coronary artery (RCA) with diffuse spasm of the RCA (Fig. 2A and B). Blood tests showed elevation of tryptase, Ig E, and troponin (peak value of tryptase, Ig E, and troponin I, 139.7 µg/L, 2030 IU/ml, and 0.975 ng/ml, respectively). After 3 days of post-cardiac arrest care, including targeted temperature management, he regained consciousness without any neurological impairment. On the 15th day of admission, follow-up coronary angiography revealed the persistent presence of diffuse coronary vasospasm of the RCA on an ergonovine provocation test (Fig. 2C). Intracoronary administration of nitroglycerin (500 µg) resolved the spasm (Fig. 2D). He was discharged with a calcium channel blocker, isosorbide dinitrate, and nicorandil.

Acute coronary syndrome of Kounis syndrome is caused by inflammatory mediators released from mast cells that are present during an allergic reaction due to various etiologies [6]. Histamine is the most important chemical mediator that provokes cardiac manifestations by inducing coronary vasoconstriction and platelet activation, which are associated with the development of coronary spasm, myocardial infarction, and stent thrombosis [7]. In this context, three variants of Kounis syndrome have been described [8,9]. The type I variant (coronary spasm) includes patients with normal or nearly normal coronary arteries without risk factors for coronary artery disease; these patients exhibit coronary spasm provoked by acute release of inflammatory mediators. The type II variant (coronary thrombosis) includes patients with preexisting atheromatous coronary artery disease in whom the acute release of inflammatory mediators can induce either coronary spasm or plaque rupture, leading to acute myocardial infarction. The type III variant (drug-eluting thrombosis) includes patients with stent thrombosis in whom harvested thrombi show the presence of eosinophil and mast cells on pathology review. Our patient had sudden cardiovascular collapse immediately after IV medication administration, with

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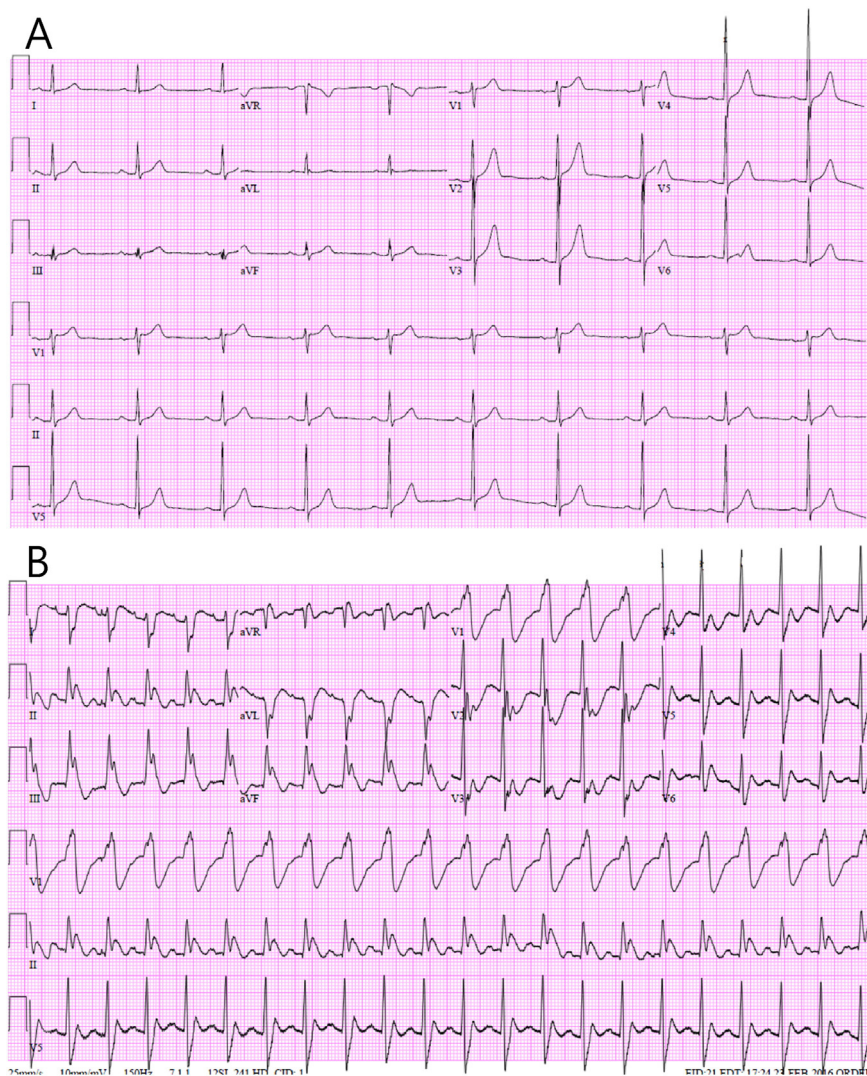


Fig. 1. ECG findings. A. On admission, ECG showed a normal sinus rhythm. B. After restoration of spontaneous circulation following cardiac arrest, ECG showed ST segment elevation in leads II, III, and aVF and ST depressions in leads V1 and V2, suggesting an inferoposterior myocardial infarction. ECG, electrocardiography.

evidence of an anaphylactic reaction on blood tests; he also had angiographically documented episodes of severe coronary spasm. These findings are compatible with the type I variant of Kounis syndrome. However, our case demonstrated a different type of coronary spasm in contrast to other reports of type I [4,10]. Coronary spasm of Kounis syndrome is believed to be a transient episode limited to the period of the allergic reaction accompanying elevated levels of chemical mediators. In our case, coronary spasm was provoked and documented 14 days after the allergic reaction. This finding indicates that, in our case, coronary spasm may be a preexisting condition that is provoked by an allergic reaction. In the presence of preexisting coronary spasm, patients may encounter conditions inducing an allergic reaction. In this regard, we propose two subtypes of the type I variant of Kounis syndrome. One subtype of the type I variant includes patients who have coronary spasm during an allergic reaction and have normal coronary arteries without coronary spasm (subtype A). The other subtype of the type I variant includes patients who have coronary spasm during an allergic reaction and have normal coronary arteries with preexisting or residual coronary spasm (subtype B).

Coronary spasm is not a rare disease. The presence of preexisting or residual coronary spasm can be a potential threat for patients after an allergic reaction. Our experience with this case indicates the necessity of determining the presence of preexisting or residual coronary spasm in patients with Kounis syndrome.

Conflict of interest

All authors have nothing to declare on conflict of interest.

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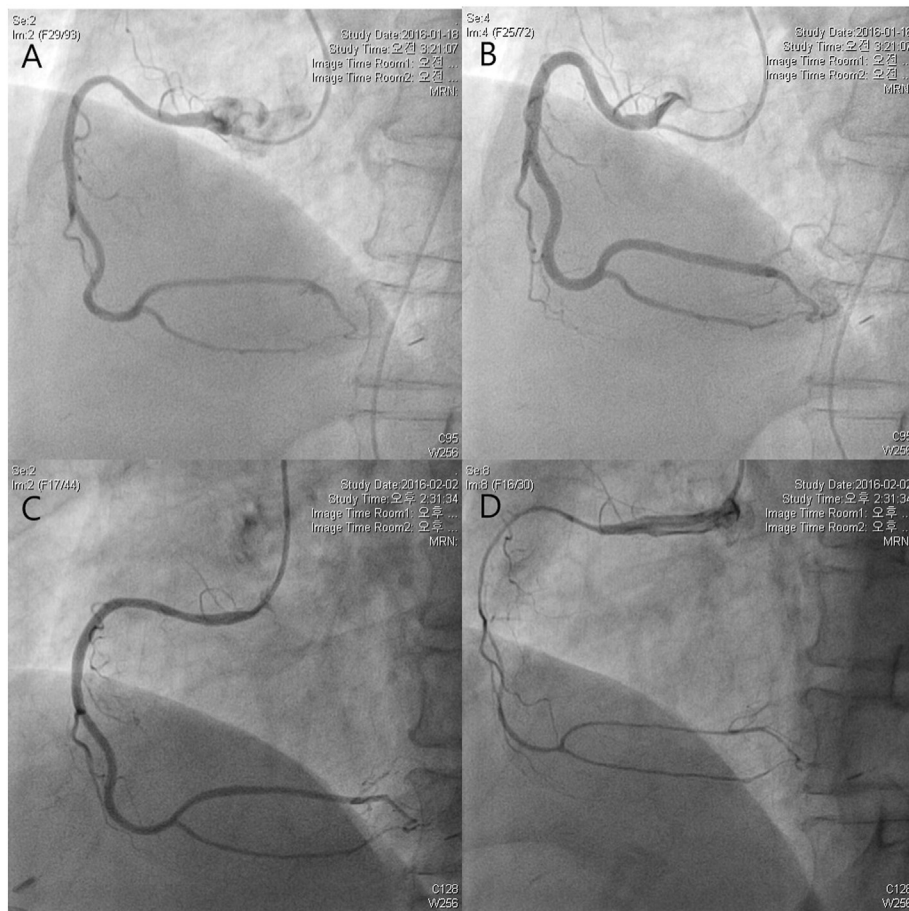


Fig. 2. Coronary angiographic findings. Coronary angiography immediately after resuscitation showed 30% stenosis of the proximal RCA with diffuse spasm of the distal runoff (A). After intracoronary injection of nitroglycerin, coronary spasm was relieved (B). Follow-up coronary angiography on the 15th day of admission showed a normal RCA (C). Severe coronary spasm was provoked by intracoronary injection of ergonovine (D).