

Anaphylaxis-Induced Acute ST-Segment Elevation Myocardial Ischemia Treated with Primary Percutaneous Coronary Intervention: Report of Two Cases

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ABSTRACT: Acute coronary syndromes have been described as potential complications of any type of anaphylactic reaction. The real pathogenic mechanism inducing acute myocardial ischemia in the setting of anaphylaxis is not yet completely understood. Some pathogenic mechanisms, like coronary vasospasm, plaque activation and systemic hypotension, have been suggested. The hypothesis of a central role of mast cell and inflammatory cell activation and release of potent vasoactive mediators, inducing the mechanisms mentioned above, is the mainstay of so-called "cardiac anaphylaxis". Herein we have reported two cases of anaphylaxis-induced acute ST-segment elevation myocardial ischemia which occurred during coronary angiography. The first one was probably related to contrast media contact, the second one to latex glove contact. Both of them were treated with percutaneous coronary intervention that immediately resolved the myocardial ischemia.

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Anaphylaxis is a severe, life-threatening, generalized hypersensitivity reaction that is mostly mediated by IgE antibodies, often starting with erythema, urticaria and/or angioedema, and occasionally involving cardiovascular and respiratory systems. However, non-IgE-mediated reactions, clinically indistinguishable, may occur.¹

Acute coronary syndromes have been described as potential, yet rare, complications of any type of anaphylactic reaction, and have been reported as a consequence of insect sting,^{2,3} shellfish ingestion,⁴ drugs^{5–8} or contrast media administration.^{9–12} However, the mechanisms involved are not yet completely understood.^{13,14}

Case 1. A 61-year-old male was admitted to the emergency department because of chest pain at rest lasting 30 minutes. At admission, the patient was asymptomatic. The electrocardiogram (ECG) showed sinus bradycardia and ST-segment abnormalities with T-wave inversion in leads V1–V5. On echocardiography, hypokinesis of the distal anterior septum was present. The patient was then referred to the coronary care unit. The only risk factor for coronary artery disease was smoking. The patient

denied any previous history of heart disease, chest pain or exertional limitation. Physical examination was normal. Blood tests, including troponin I evaluated at admission and after 6 hours, were normal. Coronary angiography performed 24 hours after admission showed severe obstructive coronary atherosclerosis and subocclusive stenosis of the proximal left anterior descending (LAD) artery with ulcerated plaque and TIMI grade 3 flow (Figure 1). Within a few minutes from the start of coronary angiography the patient showed diffuse erythema and severe systemic arterial hypotension (systolic arterial pressure of 60 mmHg). He also reported sudden onset of chest pain. The ECG showed sinus rhythm (heart rate of 95 beats/minute [bpm]) and 3 mm ST-segment elevation in V1–V5. Left coronary angiography showed complete occlusion of the proximal LAD with TIMI grade 0 flow at the site of the previously documented stenosis and diffuse vasospasm of the circumflex artery (Figure 2). The patient was given intravenous (IV) hydrocortisone, IV hydroxyzine, IV noradrenaline and fluids. His arterial pressure progressively rose to 90 mmHg. Primary percutaneous coronary intervention (PCI) with direct drug-eluting stent implantation of the LAD was immediately performed, resulting in TIMI grade 3 flow restoration (Figure 3). There was an immediate resolution of chest pain and ST-segment elevation disappeared. Blood tests after the procedure were normal, including troponin I at 6 and 12 hours. The patient was discharged 72 hours later. He was referred to the immunology department. An allergy examination did not show any previous history of food and/or drug allergy. Moreover, the patient did not suffer from asthma and/or rhinitis. A skin-prick test performed with a complete panel of commercial reagents was negative. Total IgE serum levels were 247 KU/l (normal value < 85 KU/l), but an in vitro assay for allergen-specific IgE was negative. The patient underwent prick and intradermal tests for lidocaine, with a negative result, to rule out an hypersensitivity to the local anesthetics used just before the injection of contrast medium.

Case 2. A 57-year-old female was referred to our department for coronary angiography due to unstable angina. Risk factors for coronary artery disease included hypercholesterolemia and systemic hypertension. At admission, the patient was asymptomatic, and her blood tests, including troponin I and echocardiography were normal. Coronary angiography, performed the day following her admission, showed subocclusive stenosis (95%) of the mid dominant right coronary artery (RCA) with TIMI grade 3 flow (Figure 4); subcritical stenosis of the mid

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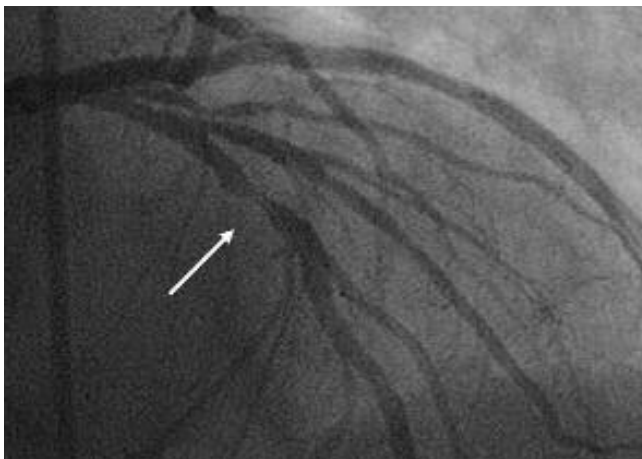


Figure 1. Case 1. Baseline coronary angiogram (30° anteroposterior cranial view) shows severe obstructive coronary atherosclerosis with subocclusive stenosis of the proximal left anterior descending artery with an ulcerated plaque and TIMI grade 3 flow (white arrow).

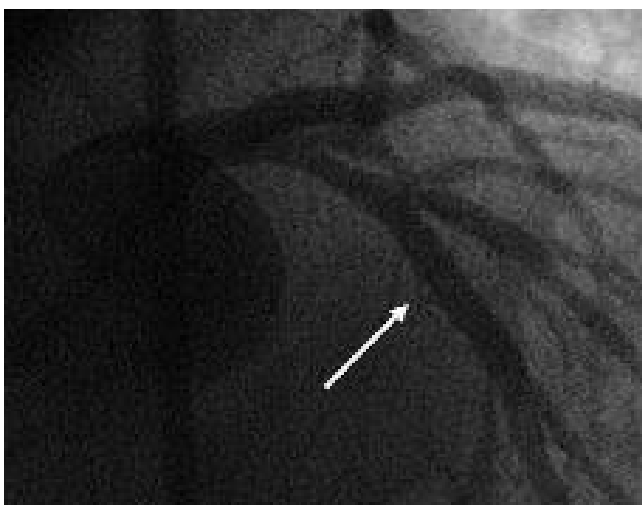


Figure 3. Case 1. Coronary angiography after stent implantation in the left anterior descending artery (30° anteroposterior cranial view) shows a good result with TIMI grade 3 flow restoration (white arrow).

LAD, critical stenosis (75%) of a small second diagonal branch, subcritical stenosis of the distal obtuse marginal branch were also present. At the end of coronary angiography, the patient experienced diffuse erythema, lip and tongue swelling and systemic hypotension (systolic arterial pressure of 80 mmHg). At that point, she remembered having had angioedema in the past after contact with latex gloves. She reported new onset of typical chest pain. The ECG showed complete atrioventricular (AV) block (with a ventricular rhythm rate of 40 bpm) and 3 mm ST-segment elevation in leads II–III–aVF. Her systolic arterial pressure rapidly dropped to 50–60 mmHg. Coronary angiography showed persistent patency of the RCA, but with diffuse spasm and TIMI grade 1–2 flow (the image during the anaphylactic reaction was not acquired due to the critical situation). The patient was given IV hydrocortisone, IV hydroxyzine, IV norepinephrine and fluids. PCI with stent implantation in the RCA was immediately performed with TIMI grade 3 flow restoration

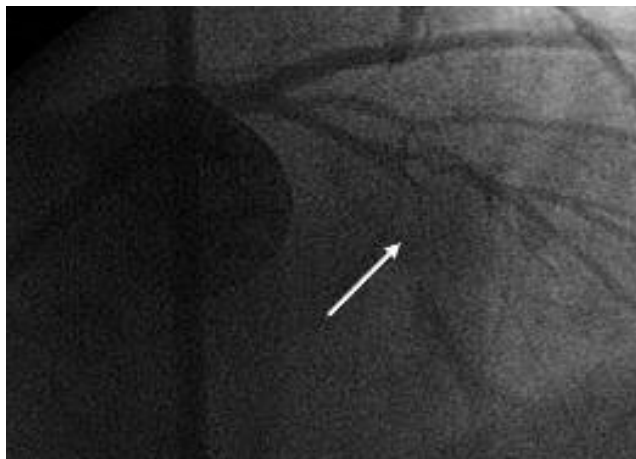


Figure 2. Case 1. Coronary angiography during the anaphylactic reaction (30° anteroposterior cranial view) shows complete occlusion of the proximal left anterior descending artery, with TIMI grade 0 flow at the site of the previously documented stenosis (white arrow) and diffuse vasospasm of the circumflex artery.

(Figure 5). There was rapid resolution of the patient's hypotension and AV block, and the ST-segment elevation disappeared. She showed no postprocedural troponin I elevation. The patient was discharged 3 days later and she was referred to the immunology department of our hospital. During allergy evaluation, the patient reported a history of rhinitis and asthma, as well as previous angioedema episodes after contact with latex gloves at work. In vitro assays confirmed the atopic condition by showing a high level of serum total IgE (955 KU/l) and sensitization to dogs (0.86 kUA/l, normal value < 0.35 kUA/l), dust mites (3.71 kUA/l) and grass pollen (5.24 kUA/l). They also confirmed high-grade sensitization to latex (78.5 kUA/l). Skin-prick tests with latex were not performed due to the severe reaction which had already occurred.

Discussion. Acute coronary syndromes have been described as potential complications of any type of anaphylactic reaction. The hypothesis suggested for the pathogenesis of acute myocardial ischemia refers to the so called “cardiac anaphylaxis”, including the functional and metabolic changes in the heart caused by the anaphylactic release of histamine and vasoactive mediators by mast cells located within the human heart.^{13,14} The mechanisms inducing acute myocardial ischemia are not yet completely understood.

Coronary vasospasm is one of the primary mechanisms proposed, as it is superimposed on a fixed coronary lesion in up to 60% of cases, but may also occur in normal coronary arteries.^{15,16} H1 receptors, expressed on vascular smooth cells, mediate coronary artery vasoconstriction and increase vascular permeability such that massive histamine release from mast cells during anaphylactic reactions may trigger coronary spasm. Coronary spasm can be caused by other mast cell-derived vasoactive mediators such as PGD₂ and LTs.¹⁷ Moreover, mast cells may also induce plaque activation in patients with underlying coronary atherosclerosis. There is evidence that mast cells are an integral component of the inflammatory infiltrate of eroded or ruptured coronary plaques.¹⁸

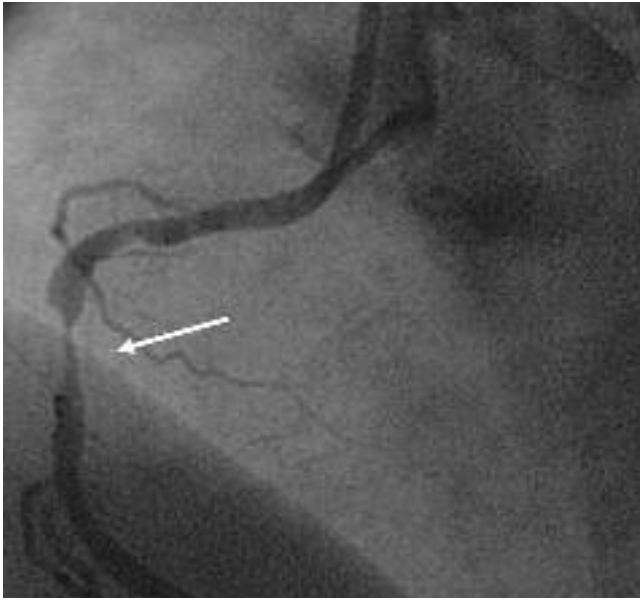


Figure 4. Case 2. Baseline coronary angiography (LAO 30° view) shows subocclusive stenosis of the mid dominant right coronary artery with TIMI grade 3 flow (white arrow). The image during the anaphylactic reaction was not acquired due to the critical situation.

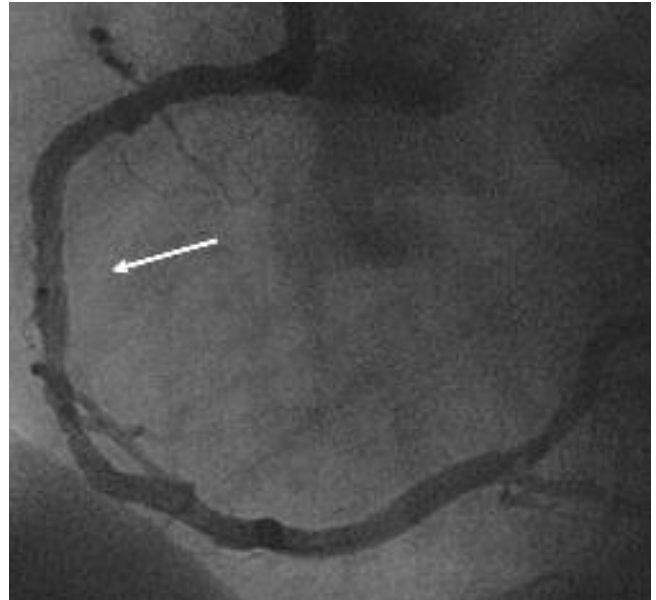


Figure 5. Case 2. Coronary angiography (LAO 30° view) after RCA stent implantation shows good angiographic result with TIMI grade 3 flow restoration (white arrow).

Another mechanism is prolonged systemic hypotension, especially in patients with underlying critical coronary stenoses in whom an abrupt reduction of coronary flow in the territory of the stenotic artery could provoke myocardial ischemia.

Finally, there are cases of acute coronary syndromes caused by the administration of drugs like epinephrine,¹⁹ which is a life-saving drug to treat anaphylaxis, but can aggravate a condition of coronary vasospasm induced by mast cell-derived mediators. Which of these mechanisms is the predominant one remains unclear.

We reported two cases here of anaphylaxis-induced acute ST-segment elevation myocardial ischemia which occurred during coronary angiography and were treated with immediate PCI. The occurrence of the anaphylactic reaction during the diagnostic procedure allowed an accurate evaluation of the mechanisms involved in the pathogenesis of ischemia.

In the first case, an acute thrombotic occlusion at the site of the previously documented coronary stenosis, probably facilitated by diffuse coronary vasospasm induced by mast cell-derived mediators and prolonged hypotension, appeared to be the main pathogenic mechanism. In the second case, acute myocardial ischemia was precipitated by the sudden drop in the transtenotic pressure gradient secondary to significant systemic hypotension, with coronary vasospasm as a probable secondary contributor.

It is our opinion that mast cells and inflammatory cell-derived mediators played a pivotal role in these two cases. Myocardial necrosis did not occur, as PCI was rapidly performed and resulted in immediate resolution of ischemia. In the first case, mechanical intervention rapidly resolved the thrombotic occlusion, while in the second one, it eliminated the flow-limiting stenosis. In both cases, nitrates could not be

used to treat the superimposed vasospasm due to the patients' marked systemic hypotension. However, despite the inability to treat one of the mechanisms involved in the genesis of ischemia, immediate PCI was successful in restoring TIMI grade 3 flow and avoiding myocardial damage. As regards the anaphylactic reaction precipitating myocardial ischemia, contrast media injection and latex contact were identified as trigger factors in both of the patients described here.

It is well known that iodinated contrast media can cause anaphylaxis within minutes after administration. Although the exact pathogenesis of anaphylaxis is unknown, an IgE-independent pathway activated by the histamine-releasing activity of iodinated material appears to be the primary mechanism involved. However, IgE-mediated mast cell activation is suspected in some cases.²⁰ On the other hand, latex allergy-related anaphylaxis represents a classic type I systemic reaction, sustained by IgE-dependent mast cell activation.

In conclusion anaphylaxis-induced myocardial ischemia depends on a variable combination of several mechanisms that contribute to a critical reduction in myocardial flow. The timely application of PCI may prevent the development of myocardial necrosis in such situations.

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