Acute myocardial infarction associated with hypersensitivity to wasp sting

Akutni miokardni infarkt in preobčutljivostna reakcija po piku ose

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Ključne besede:
preobčutljivostna reakcija, akutni miokardni infarkt

Key words:
hypersensitivity reaction, acute myocardial infarction

Citirajte kot/Cite as:
Zdrav Vestn 2012; 81: 500–4

Prispelo: 9. maj 2011,
Sprejeto: 12. dec. 2011

Izvleček

Izhodišča: Akutni koronarni sindrom, ki ga sproži sistemska alergična reakcija, imenujemo Kounisov sindrom.

Prikaz primera: V prispevku prikazujemo primer 27-letne dotlej zdrave ženske, ki je utrpela akutni miokardni infarkt po anafilaktični reakciji po piku ose. Razpravljamo o patofiziološkem mehanizmu, klinični sliki in zdravljenju bolnikov s Kounisovim sindromom.

Zaključek: Ob pojavu prsne bolečine med alergično reakcijo moramo vselej pomisliti na možnost sočasnega ishemičnega srčnega dogodka in izpeljati ustrezne diagnostične postopke in zdravljenje.

Abstract

Background: Kounis syndrome is the concurrence of acute coronary syndromes with systemic allergic reactions.

Case report: We report the case of a 27-year-old healthy woman who experienced acute myocardial infarction after anaphylactic reaction to Hymenoptera sting. The pathophysiology, clinical implications and therapeutic issues of this unique syndrome are briefly discussed.

Conclusion: Acute onset of chest pain during allergic reaction should always raise suspicion of a concurrent ischemic cardiac event and thus lead to appropriate diagnostic evaluation and treatment.

Introduction

Hypersensitivity reactions from Hymenoptera stings may range from urticaria and angioedema to severe anaphylaxis and anaphylactic shock.[1] In 1991, Kounis described the syndrome of allergic angina as the coincidental occurrence of chest pain and allergic reaction.[2] Symptoms of angina can progress to a frank myocardial infarction, and all spectra of myocardial ischemia accompanying hypersensitivity reactions are now known as Kounis syndrome (KS).[3] We report a case of acute myocardial infarction associated with hypersensitivity to wasp sting.

Case report

A 27-year-old previously healthy woman was stung on her forearm by a wasp. Few minutes later she developed dizziness, shortness of breath, periorbital edema, pruritus, and skin rash. Emergency medical service arrived 7 minutes later and she was given oxygen by face mask, clemastine 2 mg, methylprednisolone 40 mg, and saline intravenously. There was no improvement after

initial therapy, she was still in respiratory distress and started to complain of retrosternal pain. Her blood pressure was 124/87 mmHg and heart rate 126/min. She was given another bolus of methylprednisolone 40 mg and epinephrine 1:10.000 0.1 mg slowly intravenously, and was transferred to the regional hospital. On arrival her blood pressure was 88/43 mmHg, the pulse 60 beats/min regular, respiratory rate 33 breaths/min, and pulse oxymetry 100 %. The 12-lead ECG taken 35 minutes after the sting revealed sinus rhythm with 0.1 mV depression of ST segment and negative T waves in leads II, III, aVF, V5 and V6. The initial serum cardiac troponin-I level was 0.04 µg/L (reference: < 0.06 µg/L). Upon admission to coronary care unit 40 minutes after the initial event, the patient was circulatory stable, and had no respiratory distress or chest pain. She was treated with colloids, clemastine, and methylprednisolone. Skin rash and periorbital edema resolved in the ensuing hours. Electrocardiographic changes returned to normal. Since a repeat troponin-I measurement 8 hours later was 4.96 µg/L, creatin kinase-MB 13.2 µg/L (reference: 0.6–3.5 µg/L), and pro-BNP 1050 ng/L (reference: < 100 ng/L) she was given acetylsalicylic acid and enoxaparine. Transthoracic echocardiography revealed hypokinetic basal segments of inferior and posterior left ventricular wall. On the next day, coronary computed tomographic (CT) angiography showed normal coronary arteries. The therapy for acute coronary syndrome was discontinued and the patient was discharged with an emergency kit containing methylprednisolone, loratadine, and epinephrine auto-injector. A submaximal exercise test performed one week after admission was normal. A repeat echocardiogram revealed normalization of wall motion abnormalities. Hypersensitivity to wasp venom was confirmed by high specific IgE titer (0.88 kU/L). The patient was advised to start specific immunotherapy one month later.

Discussion

KS is the concurrence of acute coronary syndromes with allergic or hypersensitivity reactions secondary to mast cell activation.[2,4] Although the syndrome has been encountered increasingly in clinical practice, its true frequency is difficult to determine due to inadequate reporting.[4] However, in a recent study two of 21 healthy volunteers developed chest pain with ischemic electrocardiographic changes during a diagnostic insect sting challenge.[5] Of note, occurrence of Kounis syndrome has recently also been reported in children.[6] Beside symptoms and signs typical of anaphylactic reaction (pruritus, urticaria, angioedema), patients may present with chest pain, with/or without elevated troponins and cardiac enzymes, dyspnea, faintness, nausea, vomiting, syncope, diaphoresis, pallor, palpitations, hypotension and bradycardia.[3] Two variants of syndrome have been described.[3] Type I variant occurs in patients with angiographically normal coronary arteries without predisposing atherosclerotic risk factors and may represent a manifestation of microvascular angina or endothelial dysfunction leading to coronary vasospasm. On the other hand, type II variant includes patients with preexisting quiescent atheromatous disease of the coronary arteries. In these patients, besides coronary artery spasm, mast cell mediators released during allergic reaction may facilitate plaque erosion or rupture with subsequent thrombosis manifesting as an acute myocardial infarction. Several causes have been reported as capable of inducing KS.[7] These include drugs (antibiotics, analgesics, antineoplastics, contrast media, corticosteroids, proton pump inhibitors), environmental exposures (bee, wasp, ant, and jellyfish stings, viper venom), and various medical conditions (angioneurotic edema, bronchial asthma, exercise induced anaphylaxis, food allergy, mastocytosis, serum sickness).

Hymenoptera venoms contain vasoactive, inflammatory and thrombogenic peptide and amine constituents, including histamine, serotonin, dopamine and epinephrine, able to create vasospasm and/or coronary thrombosis.[8] In addition, the venoms contain allergenic proteins such as mellitin, hyaluronidases, phospholipases and acid phosphatases capable of inducing anaphylactic reactions.[9] When these occur, several vasoconstricting and collagen-degrading

compounds are released locally and in the peripheral circulation from activated mast cells. Inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet-activating factor, and various cytokines and chemokines are supposed to induce coronary artery vasospasm, which can eventually progress to acute myocardial infarction.[4] Neutral proteases (tryptase and chymase) are metalloproteinase activators that can trigger degradation of collagen and induce atheromatous plaque erosion or rupture.[4]

Our patient was a young, healthy woman with no atherosclerotic risk factors who suffered an acute myocardial infarction of type I variant of KS. Coronary CT angiography demonstrated normal coronary arteries with no evidence of variant anatomy and thus obviated the need for invasive cardiac catheterization.[10] However, the causal relationship between Hymenoptera sting and myocardial ischemia may not be so unambiguous. The patient received epinephrine which itself, though considered the treatment of choice for severe anaphylaxis,[11] has thrombogenic effects and is able to induce coronary vasospasm.[12] Several cases of epinephrine-induced coronary vasospasm, chest pain and arrhythmias have been reported.[13] Major adverse effects usually occur when epinephrine has been given intravenously, too rapidly, inadequately diluted, or in excessive dose.[14] In a recent paper, Shaver et al. reviewed articles published over the past 25 years and found only 4 cases, including their own, of myocardial infarction associated with therapeutic doses of epinephrine used for the treatment of anaphylaxis.[13] In our case the dosage of epinephrine was consistent with the current guidelines, but the timing and route of administration were suboptimal.[15-17] In addition to vasoconstrictive and bronchodilatory effects, epinephrine inhibits the release of mediators from mast cells and basophils and should be given as a first drug in respiratory- or cardiovascular--compromised patients. As our patient experienced retrosternal pain before the application of epinephrine, it seems rather unlikely that the acute coronary event was caused by the administration of the drug. However, the use of epinephrine, as well as hypotension due to anaphylactic reaction, may have contributed to aggravation of myocardial ischemia induced by allergic reaction. On the other side, the development of myocardial ischemia might have been precipitated by omitting epinephrine at the beginning of treatment.

KS is a complex and challenging clinical condition since the evaluation and effective treatment need to encompass both the cardiac and allergic syndromes simultaneously.[18] The therapy of anaphylactic reaction is not questionable and in case of respiratory or cardiovascular compromise epinephrine has absolute priority, followed by volume replacement, oxygen and thereafter antihistamines, and glucocorticoids.[15-17] There is also no doubt that the treatment protocol in type 2 variant of KS associated with atheromatous coronary disease should follow the current guidelines on acute coronary syndrome.[19] On the contrary, the treatment guidelines for young and previously healthy individuals with type 1 variant of KS have not been established and most of the information about the management of this syndrome comes from individual case reports or case series.[18] In these patients it is probably also prudent to add acetylsalicylic acid and heparin to the therapy of anaphylactic reaction. Besides, Cevik et al. recommend nitrates and calcium blockers, unless the patient is hypotensive, as first-line therapy since vasospasm is the primary mechanism.[18] If further diagnostic evaluation reveals no atherosclerotic disease of coronary arteries, acetylsalicylic acid and heparin can probably be safely withdrawn as has been done in our case. No clear recommendations on the continuation of antithrombotic and anticoagulant therapy can be found in the literature.

There is also no data from controlled trials concerning the role of specific immunotherapy in allergic myocardial infarction survivors.[20] We believe that immunotherapy is absolutely indicated in anaphylaxis prone patients with concomitant coronary artery disease. Despite the fear of adverse events related to specific immunotherapy in such patients, the prevailing opinion is that desensitization is the only form of treatment

that significantly decreases the risk of a life--threatening allergic reaction and the need for epinephrin self-injector therapy in the case of another sting.[21] There are no reports on KS during immunotherapy even though hundred thousands of patients worldwide received this form of treatment. However, the build up phase of immunotherapy should be performed cautiously, particularly in patients at high risk of side effects, and monitored by an allergologist trained in venom immunotherapy, as systemic side effects may occur at any time during the procedure.[22,23]

KS is not a rare but rather a seldom recognized clinical entity. The acute onset of chest pain during any grade of allergic reaction should always raise suspicion of a concurrent ischemic cardiac event and thus lead to appropriate diagnostic evaluation and treatment. We believe that fewer cases of KS would be missed if ECG and cardiac enzymes have been done routinely in every patient with allergic reaction.

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