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Cardiac arrest secondary to type 2 Kounis syndrome resulting from urticaria and angioedema

Suzy Connor,¹ Nick Child,² David Burdon-Jones,³ Andrew Connor⁴

A 43-year-old man with no cardiac history presented with chest pain followed by cardiac arrest. He was successfully defibrillated and underwent primary percutaneous coronary angioplasty to a culprit coronary artery lesion. He later re-presented with a diffuse urticarial rash and lip swelling, reporting that these symptoms had been present for 4 weeks before his cardiac arrest and voicing concern that a further cardiac arrest may be imminent. A diagnosis of post-viral or idiopathic autoimmune urticaria and angioedema was made. Given the absence of cardiac symptoms before the development of the rash, it was hypothesised that coronary artery spasm precipitated by histamine release due to his dermatological condition contributed to his myocardial infarction and cardiac arrest. The final diagnosis was therefore cardiac arrest secondary to type II Kounis syndrome, resulting from idiopathic autoimmune or post-viral urticaria and angioedema.

An ambulance was called to a 43-year-old man who reported 2 h of central chest pain. He had recently purchased chlorpheniramine over the counter to treat an itchy rash for which he had not sought medical attention. He had no other past medical history and no known allergies. He had no cardiovascular risk factors and had an excellent exercise tolerance.

The patient subsequently had two cardiac arrests; the first en route to hospital and the second in the emergency department. He was intubated, ventilated and defibrillated with eight shocks to treat ventricular fibrillation before the return of spontaneous circulation with a blood pressure of 130/80 mm Hg. Examination revealed normal heart sounds and no wheeze.

A 12-lead electrocardiogram showed ST-segment elevation in leads II, III and aVF. Thrombolysis was not administered due to the prolonged cardiopulmonary resuscitation. He was transferred to the regional centre for primary coronary intervention. A bare metal stent was sited in a culprit proximal occlusion of the right coronary artery (figure 1). The patient made a full recovery. He was discharged on clopidogrel, bisoprolol, aspirin, simvastatin and ramipril.

One week later he re-presented with lip swelling and a rash over his trunk and limbs (figure 2). He reported that these symptoms had initially developed during the weeks before his cardiac arrest and tended to occur in the evening and resolve overnight. Examination revealed angioedema of his lips and an urticarial rash affecting his trunk and limbs. He was admitted to hospital and received hydrocortisone intravenously and chlorpheniramine orally.

Blood tests revealed a mildly elevated serum C1 esterase inhibitor level (0.38 g/l, normal range 0.15–0.35 g/l), normal C1 esterase inhibitor function (109 ku/l, normal range 40–150 ku/l), normal complement levels, and a normal serum IgE level (6 ku/l). Anticytoplasmic and antineutrophil antibodies were negative.

A dermatology consult was requested; post-viral or idiopathic autoimmune aetiologies were considered the most likely explanations of the patient's angioedema and urticaria, which was anticipated to be self-limiting. The patient was discharged and at 3 months has reported no further chest pain or dermatological symptoms since his initial presentation.

DISCUSSION

Given the high individual prevalence of both allergic conditions and acute coronary syndromes, there have been relatively few reported cases of myocardial infarction occurring in the context of an urticarial eruption (although myocardial infarction in the setting of anaphylactic shock, in which hypotension may precipitate myocardial ischaemia, has been reported more frequently).

Gupta *et al*¹ described a 28-year-old woman, with no risk factors for coronary artery disease, who developed urticaria associated with an inferolateral myocardial infarction. The patient recovered uneventfully. Vaswani *et al*² described a 56-year-old man with swelling of his hands and face arising 8 h before a myocardial infarction. He received thrombolysis, and a culprit lesion in the right coronary artery was subsequently

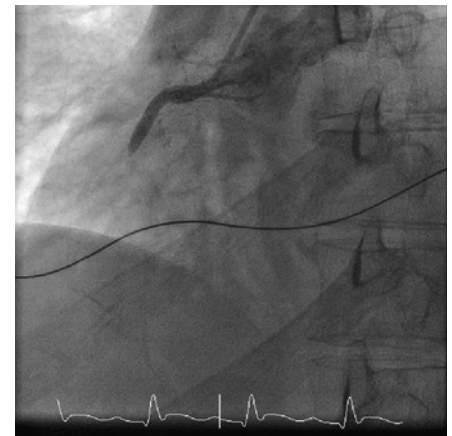


Figure 1 Angiography showing culprit proximal occlusion of the RCA.

stented. Pontillo *et al*³ reported an 81-year-old man who developed diffuse urticaria following exposure to grass, and subsequently had an inferior myocardial infarction. He received medical therapy and corticosteroids.

Histamine is a biogenic amine found in high concentrations in the healthy heart and in very high concentrations in the coronary arteries of patients known to have died from coronary heart disease.^{4 5} It is known to provoke coronary artery spasm.⁶ The concurrence of acute coronary syndromes with conditions associated with mast cell degranulation has been termed Kounis syndrome after his description in 1991,⁷ in which it was noted that histamine receptors are found in the four cardiac chambers and coronary arteries.

Two types of Kounis syndrome are recognised, unified by the occurrence of vasoconstriction of the coronary arteries.⁸ Type I Kounis syndrome describes cases in which angiography subsequently confirms normal coronary vasculature; in these patients, myocardial ischaemia is believed to be precipitated by an abnormal endothelial response to the substances released during an allergic reaction (including histamine) in



Figure 2 The patient's urticarial rash.

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which vasospasm occurs instead of the normal response of vasodilation.

Type II Kounis syndrome describes cases in which concomitant atheromatic lesions are identified at angiography. In these patients, an increased content of histamine and mast cells in the walls of the diseased vessels is believed to precipitate severe constriction and to provoke rupture of the atheromatous plaques. Additional factors predisposing the plaque to rupture are proteolytic enzymes, such as chymase and tryptase, which when released by activated mast cells degrade the collagen cover of the lipid core of the plaque. This hypothesis would explain why our patient had never previously had angina and had excellent exercise tolerance.

The final diagnosis in the case we report was therefore cardiac arrest secondary to type II Kounis syndrome, resulting from idiopathic autoimmune or post-viral urticaria and angioedema.

The role of epinephrine in the treatment of patients presenting in this way remains a particular dilemma for clinicians, as it potentially worsens coronary artery spasm.

¹Department of Emergency Medicine, Dorset County Hospital, Dorchester, Dorset, UK; ²Department of Cardiology, Dorset County Hospital, Dorchester, Dorset, UK; ³Department of Dermatology, Dorset County Hospital, Dorchester, Dorset, UK; ⁴Department of Medicine, Dorset County Hospital, Dorchester, Dorset, UK

Correspondence to Dr Andrew Connor, 3 Hope Terrace, Martinstown, Dorset, DT2 9JN, UK; andrewconnor1974@hotmail.co.uk

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