CASE REPORT

Wasp sting induced STEMI with complete coronary artery occlusion: a case of Kounis syndrome

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SUMMARY

A 45-year-old previously healthy man with minimal coronary artery disease on imaging presented with an acute MI after sustaining a wasp sting following previous non-eventful exposures throughout his life. This is the first case of Kounis syndrome with optical coherence tomography imaging and proven IgE wasp venom hypersensitivity. The Hymenoptera venom is composed of allergenic proteins and vasoactive amines which are responsible for venom toxicity. This patient also has a history of atopy giving a predisposition for developing IgE-mediated allergic reactions. Hymenoptera stings can be severe in atopic individuals and anaphylaxis may ensue. However, it is a rare cause of myocardial infarction (MI) (Kounis syndrome). Multiple wasp stings in the past may have contributed to sensitisation. Kounis syndrome is a rare clinical manifestation which should remain in the minds of physicians, especially with younger patients with no history of ischaemic heart disease or few risk factors.

BACKGROUND

Hymenoptera is an insect class including all wasps, bees and ants¹ and has been known to rarely induce hypersensitivity acute coronary syndromes in some susceptible individuals. Kounis and Zavras first described the syndrome of allergic angina in 1991 when they discovered clinical and laboratory findings indicative of angina pectoris in combination with an acute allergic reaction.² Three variants of Kounis syndrome have now been recognised. Type 1 variant occurs in patients with normal coronary arteries without predisposing factors for coronary artery disease. The acute allergic insult can cause a progressive coronary artery spasm resulting in myocardial infarction (MI). Type 2 variant occurs in patients with pre-existing quiescent atheromatous disease in whom allergic insult may induce acute plaque rupture presenting as an MI. Type 3 variant occurs as thrombosis in previous coronary artery stents.^{3–7}

We report in this work the case of a 45-year-old man with no history of coronary artery disease and minimal coronary artery disease displayed on optical coherence tomography (OCT) coronary imaging, who presented soon after sustaining a wasp sting after multiple previous exposures throughout his life. To our knowledge, this is the first case of Kounis syndrome with OCT imaging to support minimal coronary artery disease and proven IgE wasp venom hypersensitivity.

CASE PRESENTATION

A 45-year-old man with a 38 pack-year smoking history with a history of well-controlled asthma, allergic rhinitis and eczema presented to the cardiac unit in Blackpool Victoria Hospital with persistent ST segment elevation following a systemic allergic reaction to a wasp sting.

The patient was stung by a wasp at 14:30 whilst entering his van. Minutes later he began to feel 'light headed' and itchy all over his body. The patient started to notice the eruption of an urticarial rash which he described as 'red and bumpy' which began on his arms and spread within 10 min all over his body accompanied by worsening, recurrent bouts of light-headedness. Around this time, the patient began to develop a 'funny feeling' in his left hand which felt heavy with a dull ache. The pain was rated as 4–5 out of 10 for severity, was not constant and was not accompanied by chest pain or breathlessness.

Around 3 hours after the sting, while at home, the patient began to feel very lethargic and weak accompanied by a cold feeling with shaking and sweating. The hand pain had progressed to involve the patient's left arm and was becoming more frequent. The pain improved with cold but had not worsened in severity.

At 17:52 his partner called an ambulance as he had become drowsy and looked unwell. At this point, the patient became more concerned with his arm pain which had become constant and involved his left shoulder and back. He had no associated breathlessness. In the ambulance, the patient lost consciousness and deteriorated into a ventricular fibrillation arrest. Cardiopulmonary resuscitation and one 200 J shock returned spontaneous circulation in the patient.

INVESTIGATIONS

Initial ECG changes demonstrated ST segment elevation in anterolateral leads V2–6, I, II and aVL accompanied with reciprocal ST depression in leads III, aVF and aVR (figure 1). Observations on admission included a heart rate of 111, blood pressure of 137/99 mmHg, a respiratory rate of 22, oxygen saturations 98% on room air and a temperature of 36.6°C.

Coronary angiography revealed minimal proximal right coronary artery atheroma with no flow-limiting disease, a large circumflex which appeared normal and a proximally occluded left anterior descending (LAD) artery which was

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Figure 1 Above image depicts ambulance ECG showing widespread anterolateral ST elevation (V1-6, I, II and aVL) and reciprocal changes in III, aVR and aVF. Below image depicts post-PCI procedural ECG showing good resolution >50% ST segment and success of the intervention.

culprit (figure 2A). An angioplasty and stent procedure was then undertaken. The vessel was wired with a BMW Universal Wire. Thrombus was then aspirated using an Export catheter, re-establishing flow. This showed an irregular ulcerated plaque with a thrombus in situ (figure 2B). The lesion was then direct stented with a 4.0 mm×2.5 mm drug-eluting stent, with an excellent final result (figure 2C).

In view of the unusual presentation, OCT imaging of the LAD was undertaken after stent deployment to look for underlying atheroma and to assess the vessel fully. This postprocedural imaging showed that the majority of the vessel was free from plaque, with atheroma seen only at the site of the occlusion now covered by the stent (figure 3). This would be in keeping with a plaque rupture event occurring at the site of the minor coronary atheroma in response to a wasp sting, all suggestive of a type 2 variant Kounis syndrome.

Blood marker examination on the day of admission revealed a high-sensitivity troponin level of 284 (normal <59), aspartate

aminotransferase (AST) of 39, cholesterol 5.2, high-density lipoprotein 0.91 and a raised white cell count (WCC) of 27.7×10⁹/L. One day after admission, troponin levels had risen above the assay maximum of >50 000. Serum AST levels had also increased to 666. Serum creatine kinase levels were also notably elevated at 5962 and WCC remained elevated at 22.5. This was all in keeping with a significant MI.

Postprocedural transthoracic echocardiography found evidence of an akinetic septum and anterolateral wall with the remaining cardiac walls contracting well. Overall left ventricular (LV) ejection failure was estimated at approximately 40%, accordant with mild to moderate overall LV impairment.

After discharge, the patient's general practitioner (GP) arranged immunological testing revealing elevated serum IgE levels of 471. Specific IgE testing for honeybee, yellow hornet and yellow jacket wasp was also conducted. Normal IgE response was seen to honeybee venom. A grade 1 radioallergen sorbent test (RAST) score response was observed with yellow

Figure 2 Image (A) depicting preprocedural complete proximal LAD occlusion (anterior-posterior caudal view). Image (B) displays the irregular ulcerated plaque seen in the LAD post-thrombus aspiration during the procedure which is suggestive of a plaque rupture event. Image (C) demonstrates site of stent insertion with resumption of TIMI (thrombolysis in myocardial infarction) 3 grade flow to the LAD (left anterior oblique cranial view). LAD, left anterior descending.

hornet venom and a grade 5 response was seen with yellow jacket wasp venom.

TREATMENT

On arrival, paramedics gave 10mg chlorphenamine intravenously for the hypersensitivity reaction and subsequently gave 500 mcg glyceryl trinitrate sublingually, 300mg aspirin orally

and 10mg morphine intravenously as the cardiac symptoms became increasingly apparent.

On admission to Blackpool Victoria Hospital, the patient went for a primary percutaneous coronary intervention (PCI) procedure in keeping with European Society of Cardiology and NICE (National Institute for Health and Care Excellence) guidelines.^{8–10}

OUTCOME AND FOLLOW-UP

The patient had an uncomplicated follow-up and was discharged after 4 days without any adverse events. After discharge, the patient's community GP arranged follow-up immunological testing and management.

DISCUSSION

The described patient developed a generalised urticarial rash followed by symptoms and signs of an acute MI following a wasp sting. There was evidence of only minimal atheroma on coronary angiography at the site of the acute coronary occlusion, with normal coronary arteries elsewhere along that artery on OCT imaging, with the angiogram suggestive of a plaque rupture event. This would be in keeping with a type 2 variant Kounis syndrome where an acute allergic reaction to a wasp sting leads to coronary plaque rupture and an acute coronary syndrome at the site of previously quiescent atheroma. OCT imagery was conducted in this case due to the unusual nature of the presentation to exclude additional pathology. Unfortunately, due to the emergency nature of the presentation, and due to its short-lived nature, an image of the original urticarial rash was not captured, relying on the patient's history. This is a limitation of the case report.

MI following Hymenoptera stings can be prolonged or severe in atopic individuals and in some cases anaphylaxis may ensue, with urticaria, circulatory collapse and bronchospasm¹¹; however, it remains a rare cause of MI.

Hymenoptera stings can result in MI either by direct action of the venom or by inducing an allergic response. Although the full mechanism is still unclear, mast cell degranulation following an acute allergic insult is thought to play a key role in Kounis syndrome.⁵ Anaphylactic reactions are mediated via IgE which activates mast cells causing degranulation and release of mediators such as histamine, leukotrienes and cytokines causing the allergic response.⁶ Mast cells are particularly

Figure 3 Image (A) is an optical coherence tomography (OCT) image of stented segment showing stent well deployed and minor underlying coronary atheroma. Image (B) displays OCT imaging of the LAD a short distance from the deployed stent; showing virtually normal coronary artery architecture with no significant atheroma. Image (C) demonstrates OCT imaging showing stented segment with virtually normal LAD coronary artery both proximally and distally (longitudinal cut). LAD, left anterior descending.

prominent in coronary arteries both during spasm and during coronary plaque rupture events.^{4 12} Furthermore, mast cells are known to accumulate at the shoulder regions of coronary atheroma, the sites at which erosion or rupture is most likely to occur.¹² In type 2 variant Kounis syndrome, it is postulated that mast cell activation triggers release of neutral proteinases capable of triggering extracellular matrix degradation via activation of matrix metalloproteinases, culminating in plaque rupture.¹² In a postmortem study of 20 patients who had died of acute MI, for example, mast cells accounted for 6% of all nucleated cells at the immediate site of erosion or rupture, 1% in the adjacent atheromatous area, but only 0.1% in the unaffected intimal area.¹² Similarly, the proportion of mast cells that were activated in these three areas was 86%, 63% and 27%, respectively. This all suggests that mast cell activation may be an important process in causing plaque rupture events in general, but also specifically in cases of an IgE-mediated allergic response as appears to have occurred here.

Hymenoptera venom is also composed of peptides, proteins and vasoactive amines including: acetylcholine, norepinephrine, histamine, dopamine, 5-hydroxytryptamine as well as allergenic proteins such as melittin, hyaluronidases, phospholipases and acid phosphatases.¹³ These factors can directly cause coronary vasoconstriction or favour platelet aggregation and thrombosis.¹⁴ It is thus possible that the venom itself plays a direct toxic role in Kounis syndrome. Such effects may be triggers for type 1 variant Kounis syndrome as well as contributing potentially to plaque rupture and thrombosis.

Following his MI, this patient was tested for and then found to have elevated serum IgE levels in accordance with his atopic history which potentially predisposed him to the reaction seen. The delayed time course of the reaction is also indicative of an IgE-mediated allergic reaction¹⁵ with anaphylactic reactions generally the most serious form of allergic reactions to insect stings seen.¹³ The grade 5 RAST score response to yellow jacket wasp venom is a strongly positive result¹⁶ proving both that this patient has now become sensitised to this venom but also that it was almost certainly a yellow jacket wasp that both stung the patient and caused this cascade of events. The severe systemic allergic reaction and positive IgE results for this patient suggest venom immunotherapy for desensitisation is indicated and has been undertaken.¹⁷

This patient has a history of atopy with history of asthma, allergic rhinitis and eczema. Atopy is the most important risk factor for the development of allergic diseases and provides a predisposition for developing IgE-mediated allergic reactions in response to low allergen doses.¹⁸ Atopy often contains a genetic element which may have increased this patient's risk of developing Kounis syndrome.

The reaction to any given sting can be variable and even with multiple intervening stings, sensitisation can persist and result in subsequent hypersensitivity reactions. If there have been intervening stings with no response then the risk of a severe reaction may be reduced. However, with positive diagnostic venom-specific IgE antibodies, future anaphylaxis cannot be excluded.¹³ Multiple wasp stings in this patient's past may have contributed to this patient's hypersensitivity due to sensitisation.

There are no treatment guidelines for managing Kounis syndrome. The literature suggests that patients who develop Kounis syndrome will require early control of their systemic allergic reaction with steroids, antihistamines, fluid resuscitation, oxygen, nitroglycerin and antithrombotics, before definitive treatment in a cardiac catheterisation lab. The use of chlorphenamine in this instance may have

contributed to this patient's cardiac arrest due to the proarrhythmic potential of antihistamines.¹⁹

The use of epinephrine in these patients is controversial due to its vasoconstrictive effects; however, in current guidelines there are no contraindications for the use of epinephrine in an acute anaphylaxis. Beta blockers use in an acute coronary syndrome should commence within the first 24 hours or if the patient cannot tolerate; a non-dihydropyridine calcium channel blocker should be used as an alternative. Beta blockers used in these patients may again be controversial however as their effects may counteract that of epinephrine in the management of anaphylaxis. Morphine should also be used cautiously in this group of patients as opioids can induce mast cell degranulation which may further worsen the clinical presentation.^{7 20} Mast cell degranulation is one of the primary mechanisms in the pathophysiology in Kounis syndrome. Although the efficacy is questionable for mast cell stabilisers such as sodium cromoglycate and ketotifen, their use could be considered in future patients with Kounis syndrome.^{7 19}

Learning points

- ▶ Multiple previous allergen exposures can cause sensitisation and intervening stings can occur with little reaction.
- ▶ Kounis syndrome is a rare but important differential for chest pain particularly in young with few risk factors and an allergic insult.
- ▶ Those with severe venom allergies should be treated with immunotherapy desensitisation.
- ▶ IgE-mediated mast cell degranulation is the most important pathway for the allergic response observed in Kounis syndrome.

Contributors GG was the consultant responsible for the care of the patient, drafted and revised the paper and acts as the guarantor. BC wrote, drafted and revised the paper. TRC and MH drafted and revised the paper.

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