Cardiology in the Young

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A case of Kounis syndrome associated with branched-chain amino acid supplementation in a 17-year-old boy

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Brief Report

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Abstract

Kounis Syndrome is characterised by the concurrence of acute coronary syndrome with mast cell activation induced by inflammatory mediators released during an allergic reaction. Although several factors and diseases were reported to be associated with Kounis Syndrome, branched-chain amino acid supplements have not been previously reported as a cause of Kounis Syndrome. We present a 17-year-old boy admitted to our hospital with thoracic pain after the ingestion of a branched-chain amino acid supplement.

Inflammatory mediators, monocytes, and neutrophil adhesion molecules have been shown to be increased in the plasma of patients presenting with acute coronary syndromes.[1] Anaphylaxis is a systemic, immediate hypersensitivity reaction caused by rapid, immunoglobulin E-mediated release of mediators from mast cells and basophils.[1] Kounis Syndrome is the coincidental occurrence of these two distinct conditions accompanied by clinical and laboratory findings of angina pectoris caused by inflammatory mediators released during an allergic insult.[1] Allergic angina can progress to acute myocardial infarction, which is named "allergic myocardial infarction". There are several causes that have been reported as capable of inducing Kounis Syndrome.[1] These include hymenoptera – e.g. bee – and viper venom; food allergens, e.g. shellfish; drugs; stings by ants and jellyfishes; various conditions such as angio-oedema, bronchial asthma, urticaria, exercise-induced allergy, mastocytosis, and serum sickness; and a variety of environmental exposures such as grass cutting, poison ivy, latex contact, limpet ingestion, and millet allergy.[1]

Branched-chain amino acid supplements have become attractive to young people as an energy source during endurance exercise and related potential to improve athletic performance, as well as the potential to reduce perceived muscle soreness.[2] Despite these metabolic effects, the exact effect of branched-chain amino acid supplementation on coronary artery and myocardial function is unknown. Herein, we present a 17-year-old boy with allergic myocardial infarction after the ingestion of a branched-chain amino acid supplement.

Case report

A 17-year-old boy with no cardiovascular risk factors or a history of any disease presented to our emergency department with chest pain, pruritus, facial rash, and palpitations 30 minutes after taking branched-chain amino acid supplement for muscle growth. On admission, his physical examination was normal and his electrocardiogram showed ST segment elevations in leads II, III, aVF, V4, V5, and V6 (Fig 1). He had no family history of coronary artery disease. Transthoracic echocardiography performed in the emergency department revealed inferior wall hypokinesia. Troponin-I measured on arrival was **3.3** ng/ml (reference: 0.01 ng/ml) and creatine kinase-MB fraction was **45 U/L** (reference: 0–25 U/L). Coronary angiography was performed to exclude coronary artery disease, which revealed normal coronary arteries. Complete blood count, D-dimer, antithrombin III, homocysteine, lipoprotein (a), brain natriuretic peptide, and serum cholesterol levels were normal. Antistreptolysin-O titre, third and fourth complement component levels, and anti-nuclear antibody, anti-DNA, Salmonella, and Brucella agglutination tests were within normal limits. The serologic tests for viral aetiology were negative for hepatitis A, B, C viruses, human immunodeficiency virus, Coxsackievirus B, adenovirus, and parvovirus B19. Cytomegalovirus immunoglobulin M and immunoglobulin G, Epstein–Barr virus viral capsid antigen immunoglobulin M and immunoglobulin G, and Epstein–Barr virus nuclear antigen immunoglobulin M and immunoglobulin G tests were also negative. Anti-cardiolipin immunoglobulin G and immunoglobulin M and lupus anticoagulants were negative. Factor VIII and fibrinogen levels were within normal limits. There was no protein C or protein S

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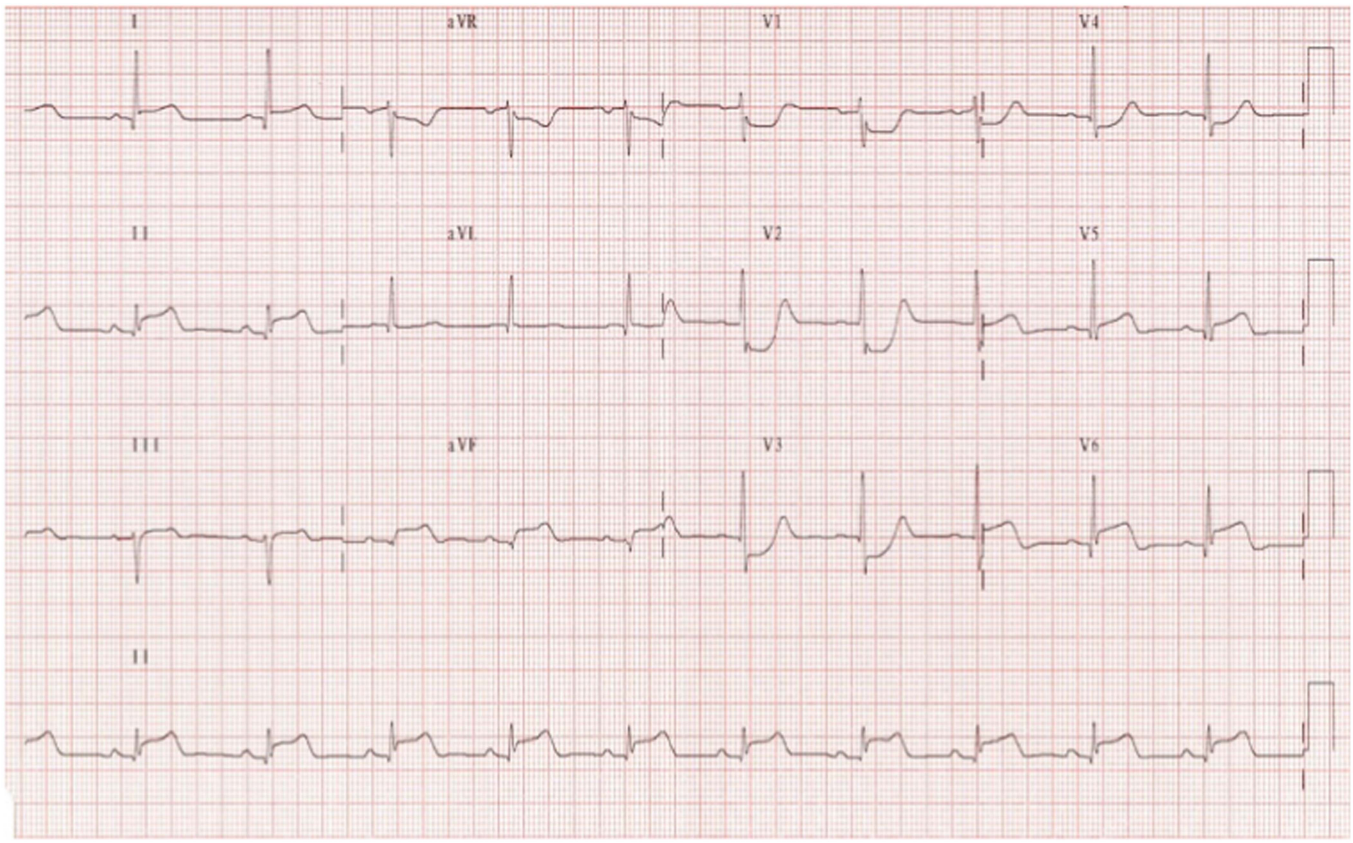

Figure 1. Electrocardiogram showing ST segment elevations in leads II, III, aVF, V4, V5, and V6.

deficiency. Among the thrombogenic gene panel studied – Factor V Leiden, factor V H1299R, prothrombin G20210A, factor XIII V34L, ß- fibrinogen-455 G-A, MTHFR A 1298C, MTHFR C677T, PAI-1 4G-5G, GPIIIa L33P, ACE, ApoB R3500Q, and ApoE – only MTHFR C677T homozygote mutation was disclosed. Total immunoglobulin E was **156 IU/ml** (reference: 0–100) and serum tryptase was **51 µg/L** (reference: 56–135 µg/L). He was diagnosed to have Kounis Syndrome type I variant, secondary to branched-chain amino acid supplement ingestion. The patient was treated with oral anti-histamines – desloratadine at a dose of 20 mg once daily for 2 weeks – and 8 mg prednisolone every 6 hours for 5 days. Although not prescribed for our patient, mast cell membrane stabilisers such as sodium cromoglycate and ketitifen may be considered in patients who develop acute coronary syndrome associated with an allergic reaction. A period of 4 days later, the repeated cardiac markers were within normal limits with resolution of electrocardiographic abnormalities and regression of inferior wall motion abnormality on echocardiographic changes. The patient was discharged from hospital in an excellent condition and after 2 weeks, in a follow-up visit, he was doing well.

Discussion

To the best of our knowledge, this is the first case of Kounis Syndrome following the branched-chain amino acid supplement consumption. Shah et al[3] found a direct cross-sectional association between a principal component-derived factor with branched-chain amino acids and related catabolites and prevalent myocardial infarction. They also showed an association between this branched-chain amino acid-related factor and coronary artery disease, an association that was also replicated in a nested case–control study.[4] Another case–control study observed a positive association between a score of 3 amino acids at baseline – tyrosine, phenylalanine, and isoleucine – and the risk of CVD.[5]

However, allergic myocardial infarction due to branched-chain amino acid ingestion has never been reported. Kounis Syndrome has three variants: type 1, coronary spasm; type 2, coronary thrombosis; and Type IIIa, stent thrombosis due to allergy, and Type IIIb, stent restonosis due to allergy.[6] On the basis of the clinical, laboratory, and electrocardiographic findings, type 1 Kounis Syndrome was diagnosed in our patient. In addition to the routine work-up of patients with acute coronary syndromes (electrocardiogram, cardiac enzymes and troponin, complete blood count, D-dimer, brain natriuretic peptide, and serum cholesterol levels), serum histamine, tryptase, specific immunoglobulin E antibody, and eosinophil levels can help in the identification of Kounis syndrome.[7] Mast cell tryptase plays a key role in allergic diseases by amplifying the responses of mast cells to allergens. Serum tryptase levels are elevated in most patients with systemic anaphylaxis.[7] Histamine levels peak at 5 minutes and decline to baseline within 15–30 minutes, whereas tryptase levels peak 1–1.5 hours after the onset of anaphylaxis and can persist for as long as 5 hours after the onset of symptoms. The best time to measure serum tryptase levels is between 1 and 2 hours but no longer than 6 hours after the onset of symptoms, whereas the best time to measure plasma histamine levels is between 10 minutes and 1 hour after the onset of symptoms.[7] Although elevated serum histamine and tryptase level strongly support the possibility of an ongoing

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allergic reaction, their short half lives make them relatively inconvenient for routine use, and a negative tryptase or histamine test does not exclude this possibility.

Energy drinks are more commonly used by the young population as a source of dietary supplement. Caffeine is one of the main stimulants in energy drinks.[8] The concentration varies in different products. Other components such as guarana, taurine, theophylline, ginkgo biloba, ginseng, vitamins, L-carnitine, and so on are also present in variable amounts. These ingredients also increase one's energy and stimulate mental performance. Previous studies suggest the association between energy drinks and cardiovascular changes including cardiac arrhythmias, prolonged QT interval, ventricular arrhythmias, cardiac arrest, cardiomyopathy, myocardial ischaemia, infarction, aortic dissection, and death.[9] Further studies are needed to reveal whether a hypersensitivity-induced coronary vasospasm triggered by branched-chain amino acids could be responsible for cases of sudden cardiac arrest following consumption of energy drinks.

This case highlights the fact that physicians should be aware of allergic aetiologies for acute coronary syndromes. The diagnosis of this unique disease should be entertained when allergic symptoms, electrocardiographic changes, and high cardiac enzymes accompany acute-onset chest pain. All patients admitted to the emergency department with chest pain and ST elevation on electrocardiography should be asked about allergic insults.

Conclusion

To the best of our knowledge, this is the first case of Kounis Syndrome following the branched-chain amino acid supplement consumption.

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Conflicts of Interest. The author have no financial or any other kind of personal conflicts with this letter.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees.

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