



Case Report

Kounis Syndrome: A Case of Vancomycin-Associated Coronary Artery Vasospasm Resulting in Myocardial Infarction

Luke R. Gagnon, MD,^{a,b} Yiming Huang, MD,^{a,b} Robert Kay, MD,^{a,b} and Bibiana Cujec, MD^{a,b}

^aDepartment of Medicine, University of Alberta, Edmonton, Alberta, Canada

^bMazankowski Alberta Heart Institute, University of Alberta, Edmonton, Alberta, Canada

ABSTRACT

We describe a case of Kounis syndrome, an allergic reaction causing coronary artery vasospasm, triggered by a vancomycin infusion, in a healthy 32-year-old man. The patient initially presented with an inguinal abscess requiring intravenous vancomycin. During his third infusion, he developed typical chest pain that resolved with cessation of the infusion. Troponin was elevated, and electrocardiogram showed ST elevation, prompting emergent cardiac catheterization that demonstrated normal coronary arteries. The cause of the myocardial infarction was consistent with Kounis syndrome. Diagnosis of Kounis syndrome is important, as prompt cessation of the offending agent is a priority to reduce further cardiac injury.

RÉSUMÉ

Nous décrivons un cas de syndrome de Kounis, une réaction allergique causant un angiospasme coronarien, déclenchée par une perfusion de vancomycine, chez un homme en bonne santé de 32 ans. Le patient a d'abord présenté un abcès inguinal nécessitant l'administration intraveineuse de vancomycine. Au cours de sa troisième perfusion, il a ressenti une douleur type à la poitrine, qui s'est résorbée après l'interruption de la perfusion. Le taux de troponine était élevé, et l'électrocardiogramme montrait une élévation du segment ST, ce qui a mené à un cathétérisme cardiaque d'urgence qui a révélé des artères coronaires normales. La cause de l'infarctus du myocarde cadrait avec le syndrome de Kounis. Le diagnostic de ce syndrome est important, car l'interruption rapide de l'administration de l'agent concerné est prioritaire pour limiter les lésions cardiaques.

Case

A 32-year-old man presented with an inguinal abscess and overlying cellulitis, requiring incision and drainage. The patient was started on intravenous ceftriaxone with oral trimethoprim-sulfamethoxazole and metronidazole. The patient had a history of occasional migraines and attention deficit hyperactive disorder, for which he was taking rizatriptan 10 mg as needed and methylphenidate 30 mg twice daily. He smoked less than 1 pack of cigarettes per month and had no other cardiac risk factors. The cellulitis showed no signs of improvement over 24 hours, so a loading dose of vancomycin was given (2 g intravenously), then 1.5 g intravenously every 8 hours, and piperacillin-tazobactam was started.

During the first 2 infusions of vancomycin, the patient reported self-limiting chest pain, which he attributed to anxiety secondary to his current illness. However, on his third infusion, the patient developed chest pressure, nausea, and right-arm paresthesia. The vancomycin infusion was stopped. An electrocardiogram (ECG) demonstrated 1 mm of ST-segment elevation in the inferior leads without reciprocal changes (Fig. 1A). High-sensitivity troponin I (hsTnI) was elevated at 12,230 ng/L (99th percentile cutoff < 20 ng/L), and the cardiology service was consulted. Creatinine and electrolytes were normal (creatinine: 95 µmol/L, sodium 141 mmol/L, potassium 3.8 mmol/L, calcium 2.23 mmol/L and magnesium 0.95 mmol/L). Point-of-care echocardiogram demonstrated basal and mid-inferior hypokinesis, with preserved left ventricular function.

Given the persistent ST-segment elevation, echocardiogram findings, and elevated hsTnI the patient was taken emergently for coronary angiogram, which demonstrated no evidence of atherosclerotic coronary artery disease (Fig. 1C, D). Because of the temporal relationship between the initiation of vancomycin infusion, onset of chest pain, and ECG changes, vancomycin-induced Kounis syndrome, an allergic coronary artery vasospasm causing myocardial infarction, was diagnosed.¹ Vancomycin was promptly discontinued and

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Corresponding author: Dr Bibiana Cujec, 2C2.50 Walter Mackenzie Health Sciences Center, 8440-112 Street, Edmonton, Alberta T6G 2B7, Canada. Tel.: +1-780-407-3601; fax: 1-780-407-6452.

E-mail: bibiana.cujec@ualberta.ca

See page 339 for disclosure information.

Novel Teaching Points

- Kounis syndrome is allergic coronary vasospasm and may result in myocardial infarction.
- Triggers for Kounis syndrome include environmental exposures, food, and medications.
- Diagnosis of Kounis syndrome is important as prompt cessation of the offending agent is a priority to reduce further cardiac injury

daptomycin initiated. Abscess cultures returned with methicillin-resistant staphylococcus aureus growth; therefore, piperacillin-tazobactam was discontinued.

Less than 24 hours after the last vancomycin infusion, the patient had another anginal episode, which resolved promptly with nitroglycerine. The patient's ECG showed 3 mm inferolateral ST-segment elevation, and 4 hours later, hsTnI was further elevated at 15,420 ng/L (Fig. 1B). The patient was started on amlodipine 5 mg daily and had no further chest pain while in hospital. HsTnI trended toward normal over the next 48 hours. Twenty-four hours after the initial event, echocardiogram demonstrated normal biventricular size and systolic function.

We recommended that the patient discontinue triptans and methylphenidate in the future, as these medications can precipitate coronary artery vasospasm.²

Discussion

We report a novel case of vancomycin-induced coronary artery spasm in a 32-year-old man with no evidence of

atherosclerotic coronary artery disease on coronary artery angiography, in keeping with Kounis syndrome. To our knowledge, this is the first described case of Kounis syndrome in a young and otherwise healthy patient without any cardiac risk factors. Only 2 cases of vancomycin-induced Kounis syndrome have been reported to date. Martinez et al. described a case of vancomycin induced Kounis syndrome in an 83-year-old woman with known hyperlipidemia and a previous aortic valve replacement.³ Coronary angiogram was not performed to assess for coronary artery disease because of patient preference.³ More recently, Leibe et al. reported the case of a 57-year-old man with peripheral artery disease, diabetes, hypertension, and smoking history and a documented history of vancomycin hypersensitivity.⁴ Subsequent coronary angiogram identified no coronary artery disease.⁴ In both cases, ECG changes were consistent with coronary artery spasm; however, cardiac enzymes were within normal limits.^{3,4}

The clinical presentation of Kounis syndrome is cardiac symptomatology associated with subclinical, clinical, acute or chronic allergic reactions.¹ In this case, the patient had recurrent cardiac chest pain and nausea. Subclinical markers (ie, serum histamine and tryptase) were not tested. In addition, the patient was on medications that can precipitate coronary artery vasospasm, causing him likely to manifest cardiac symptoms primarily.

Intravenously administered vancomycin is characterized by 3 phases for drug elimination. The half-life of the initial phase is approximately 30 minutes, making this a reasonable explanation as to why the pain ceased soon after stopping the infusion.⁵ Less than 24 hours later, the patient had another chest-pain episode with ST-segment elevation that resolved with nitroglycerine. Terminal half-life elimination of

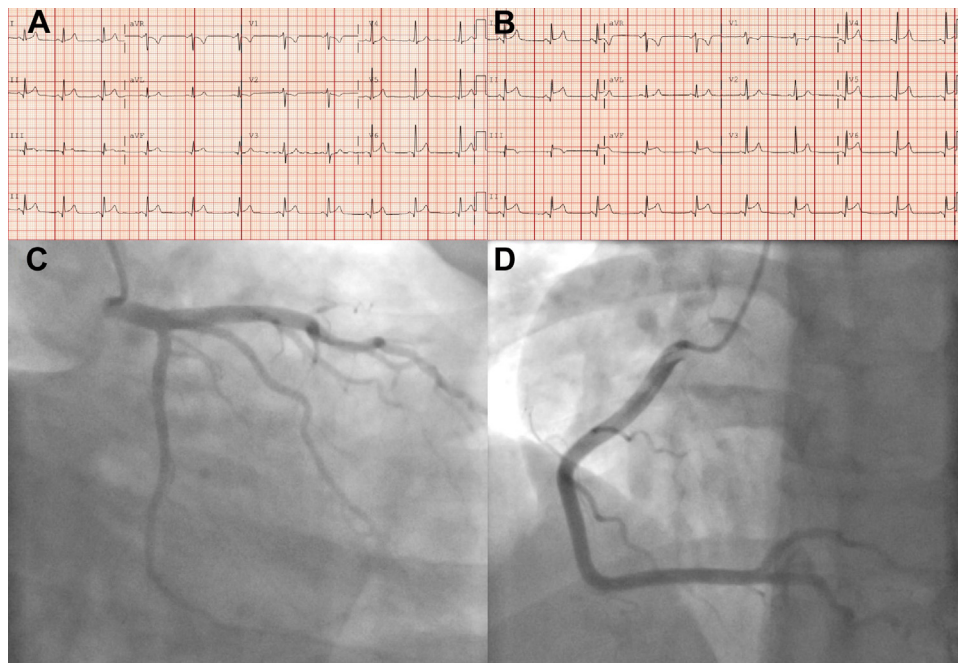


Figure 1. (A) Initial electrocardiogram (ECG) demonstrated 1 mm ST elevation in leads II, III, aVF without reciprocal changes. (B) ECG during repeat chest pain demonstrated 3 mm inferolateral ST elevation. (C) Left coronary artery angiogram. (D) Right coronary artery angiogram.

vancomycin can be up to 12 hours in patients with normal renal function, meaning that vancomycin would still have been present at this time.⁵

For confirmation of vasospastic angina during invasive coronary angiography, intra-coronary acetylcholine, ergonovine, or methylexgonovine could be injected as the provocative stimulus to assess and evaluate the vasoconstriction.² However, because of the novelty of this diagnosis, significantly elevated troponin and ST-segment elevation, a more conservative approach was used with no provocative testing.

Allergic coronary vasospasm (Kounis syndrome) may be mediated through inflammatory mediators or histamine.¹ Triggers for Kounis syndrome include environmental exposures, food and medications.¹ The mechanism of ischemic injury can be further classified as three types of Kounis syndrome. In Type I Kounis syndrome, myocardial ischemia is induced through coronary vasospasm without evidence of preexisting coronary artery disease, as in this case.^{1,5} Type II Kounis syndrome occurs when the hypersensitivity response triggers plaque rupture in keeping with atherosclerotic acute coronary syndrome.¹ Type III Kounis syndrome is specific to patients with previous coronary stenting, whereby chronic allergen exposure and inflammation results in the thrombosis of drug-eluting stents.¹ No consensus guidelines exist on treatment of Kounis syndrome, but all sources emphasize immediate cessation of the offending agent to reduce further cardiac injury.^{1,3,4}

Conclusions

Although not a well-defined entity, as this is only the third case report of vancomycin-induced Kounis syndrome, clinicians should be aware of potential allergic triggers of coronary vasospasm, as prompt removal of the offending agent is necessary to avoid prolonged myocardial ischemia. Diagnosis

should be suspected clinically with history of a trigger and a presentation of acute coronary syndrome or coronary vasospasm.^{1,3,4} Uniquely, in this case, coronary vasospasm from vancomycin can result in cardiomyocyte necrosis. It should be noted that with this patient's history of methylphenidate use, there was a possible predisposition to developing Kounis syndrome.² It is important for clinicians to be aware of Kounis syndrome, as prompt cessation of the causative agent is a priority to reduce cardiac injury.

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Disclosures

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