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Kounis syndrome, a coronary hypersensitivity disorder: A rare case of amiodarone-induced coronary vasospasm and simultaneous peripheral vasodilation intraoperatively

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A 79 year old female with a history of hypertension, cerebrovascular accident, well-controlled hypothyroidism, pulmonary hypertension and severe mitral regurgitation underwent mitral ring annuloplasty. Transesophageal echocardiogram (TEE) pre-procedure showed normal ventricles, with ejection fraction of 55–60%. Cardiac catheterization showed no significant stenosis of arteries. (Fig. 1).

Intra-operatively, the surgical team placed a #34 Colvin–Galloway annuloplasty band. She was then weaned from cardiopulmonary bypass (CPB), and was hemodynamically stable. TEE after CPB showed normal left ventricular function, the mitral valve was functioning normally, and there was only at worst mild mitral valve regurgitation.

Despite the initial hemodynamic stability, within an hour of coming off CPB, intra-operatively she had an episode of atrial fibrillation. She maintained systolic blood pressure greater than 100. IV amiodarone 150 mg was administered for pharmacological cardioversion. She then developed severe hypotension, which dropped to 65/45, and was not responsive to phenylephrine, vasopressin or calcium chloride. She was then given boluses of epinephrine which improved her blood pressure, and an epinephrine infusion was started to maintain adequate cardiac output. At this point, TEE showed left ventricular systolic dysfunction due to new inferolateral wall motion abnormality (hypokinesis), which occurred after administration of amiodarone.

The surgeon elected to have the patient transferred immediately from the operating room to the cardiac catheterization lab to rule out an arterial injury. Coronary angiography demonstrated significant

coronary vasospasm of the distal branches of all three major coronary vessels (Fig. 2).

The patient continued to receive inotropic support on epinephrine infusion and was then taken to the intensive care unit where she received continued support on epinephrine and dobutamine infusions. She was subsequently weaned off all vasopressors prior to discharge. Since this was a post-hoc diagnosis and the patient had been discharged to a distant location, she did not receive a confirmatory skin prick test.

Amiodarone is an iodine-containing highly lipophilic benzofuran derivative and is capable of blocking both α and β adrenoceptors. Amiodarone can induce allergic reactions and anaphylactic shock due to cross-sensitivities [1]. Few reports in the literature discuss allergic reactions to acute administration of IV amiodarone. Several reports discuss more typical anaphylactic shock reactions, such as severe itching, redness, dyspnea, bronchoconstriction [2], hypotension and cyanosis [3]. There is a reported case of toxic epidermal necrolysis after administration of amiodarone [4].

However, there are few reports of cardiogenic manifestations of hypersensitivity reactions to amiodarone. There is a reported case of anaphylactic cardiogenic shock resulting in myocardial ischemia after amiodarone infusion, requiring temporary left ventricular assist device in a 15-year-old boy [5]. In addition, an interesting case was reported of a patient who had tolerance to oral amiodarone. However, when intravenous amiodarone was administered, he developed flushing, dyspnea, wheezing and chest pain, and immediately developed cardiovascular collapse and cardiac arrest necessitating cardiopulmonary resuscitation [6].

Kounis syndrome, first described in 1991 by cardiologist Dr. Kounis, describes anaphylactic cardiac shock resulting in cardiac manifestations [7]. It can be triggered by a wide variety of medications, environmental agents and items such as metals used in bare-metal stents. Kounis syndrome manifests with three variants: coronary artery spasm, myocardial infarction, and stent thrombosis [8].

Coronary artery vasospasm is a rarely reported side-effect of acute administration of amiodarone, and it is unusual to have simultaneous peripheral vasodilation. This case is a rare manifestation of Kounis syndrome, a coronary hypersensitivity disorder.

During a hypersensitivity reaction, inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet-activating factor (PAF), and a variety of cytokines and chemokines are

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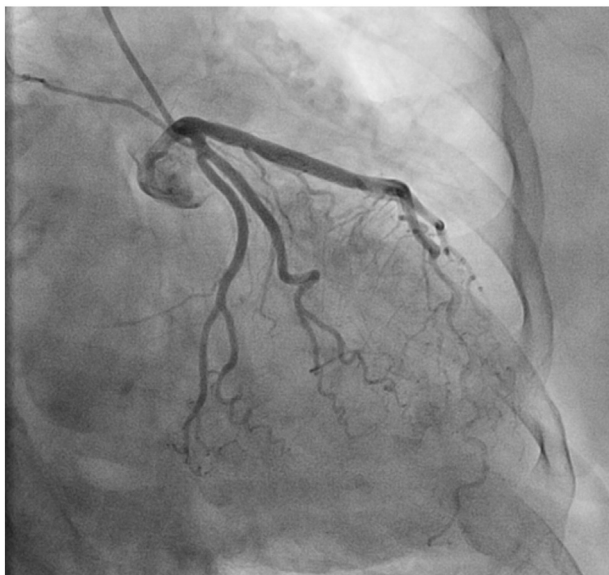


Fig. 1. Normal coronary arteries prior to surgery.

released when mast cell degranulation occurs. This results in constrictive action on vessels, and causes reduced blood flow in splanchnic, cerebral and myocardial vessels. This process constitutes the pathophysiologic basis of Kounis hypersensitivity-associated coronary artery vasospasm and acute coronary syndrome [7].

While multiple inflammatory mediators are involved in hypersensitivity reactions, histamine plays a central role in hypersensitivity reactions, and is the main amine released during allergic reactions. It is likely in this case, to be responsible for the rare dual effect of coronary artery vasospasm via H1 histamine receptors, and simultaneous inhibition of endogenous norepinephrine release and enhanced degree of shock during anaphylaxis via H3 receptors. Histamine has been shown to induce coronary vasospasm via H1 receptors and plays a significant role in cardiac anaphylaxis [9,10,11]. Histamine H3 receptors are mainly located presynaptically on the postganglionic sympathetic nerve fibers. When they are activated, norepinephrine release is

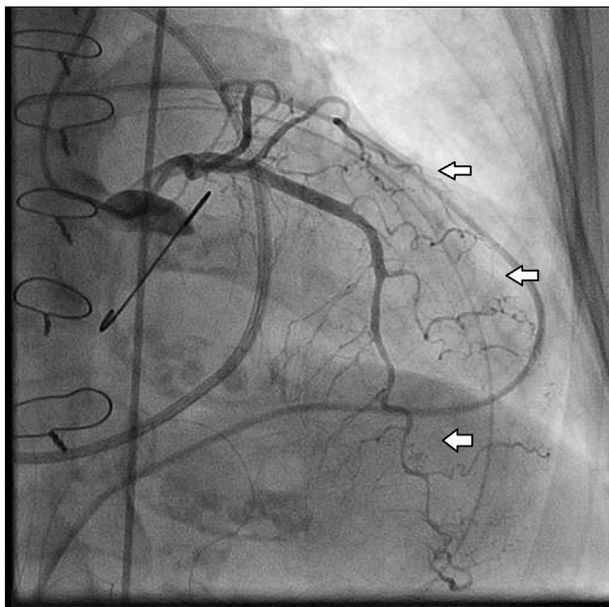


Fig. 2. Coronary vasospasm after IV amiodarone.

inhibited, with subsequent reduction of neurogenic vasopressor and cardiostimulatory responses [12]. Histamine has also demonstrated endothelium-dependent peripheral vasodilation via H3 receptors [13].

Etiologies such as coronary vasospasm or cardiac conditions such as acute myocardial infarction, or plaque erosion, should be considered when patients develop refractory hypotension in response to acute administration of amiodarone or other drugs intra-operatively. Although more common allergic symptoms from mast cell release such as urticaria, bronchospasm, and angioedema can occur, isolated allergic manifestations such as cardiovascular or skin conditions may also occur.

This case highlights a rarely-reported adverse effect of amiodarone, and contributes to the small number of reports in the literature of cardiovascular anaphylactic shock associated with amiodarone.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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