Neth Heart J (2014) 22:77–79
DOI 10.1007/s12471-013-0440-9

CASE REPORT

ST-segment elevation associated with allergic reaction to echocardiographic contrast agent administration

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Published online: 3 July 2013

Abstract We report a case of an allergic reaction after the administration of an echocardiographic contrast agent which resulted in ST-segment elevation. Hypersensitivity and allergic reactions are known causes of acute cardiovascular events. However, only limited reports are available which suggest the exact mechanism of the occurrence of angina or myocardial infarction during severe allergic reactions. In our case, through invasive imaging (coronary angiography and IVUS) we have shown for the first time a transient coronary spasm in the absence of intra-coronary thrombus and only minimal neointimal hyperplasia.

Keywords Allergic reaction · echocardiographic contrast agent · cardiovascular event

Introduction

Contrast echocardiography for opacification of the left ventricle is widely used to enhance diagnostic accuracy of conventional two-dimensional or three-dimensional stress echocardiography [1, 2]. SonoVue® (BraccoSPA, Milan, Italy) is a second-generation ultrasound contrast agent that is made of stabilised microbubbles containing sulphur-hexafluoride, for which an incidence of allergic reactions of approximately 2 % has been reported, including anaphylactic shock [3]. We describe a rare complication following SonoVue® administration.

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Case

A 60-year-old man was referred for contrast-enhanced dobutamine stress echocardiography (DSE) for detection of ischaemia. Two years before, the patient had an inferolateral myocardial infarction treated with a primary percutaneous coronary intervention and implantation of a drug-eluting stent in the right coronary artery (RCA). A few months before DSE, he complained of recurrence of typical angina pectoris due to a stenosis proximal to the stented segment in the RCA, which was successfully treated with implantation of a second drug-eluting stent (Fig. 1a). However, few weeks later, he developed new atypical thoracic symptoms, for which he was referred for DSE[4].

At the beginning of the procedure, the patient's blood pressure was 135/75 mmHg, his heart rate was 79 beats/min and ECG showed sinus rhythm and right bundle-branch block (Fig. 1a). Before starting the infusion of dobutamine, SonoVue® was administered to optimise visualisation of the left ventricle. One minute after administration of a 1 ml bolus of SonoVue®, the patient started complaining of nausea with profuse sweating and hypotension (100/45 mmHg). These signs were treated as an allergic reaction with clemastine (2 mg), hydrocortisone (100 mg), oxygen and saline infusion. Two minutes later, sudden severe chest pain occurred and the ECG showed ST-segment elevation in leads II, III, aVF and V2-V4, with ST-segment depression in V2-V4, I, and aVL, and total AV-nodal block (Fig. 1b). During this episode, echocardiography showed akinesia of the inferior wall, whereas baseline echocardiography showed only mild mid-inferior hypokinesia. After 8 min (as measured on the monitor), the symptoms started to decrease and the ST segments normalised (Fig. 1b). Immediate coronary angiography was performed showing a good patency of the stents in the RCA. However, a 50 % stenosis was observed proximally to the stented segment, which was interpreted as a possible coronary spasm (Fig. 1b). No significant pathology was observed in the

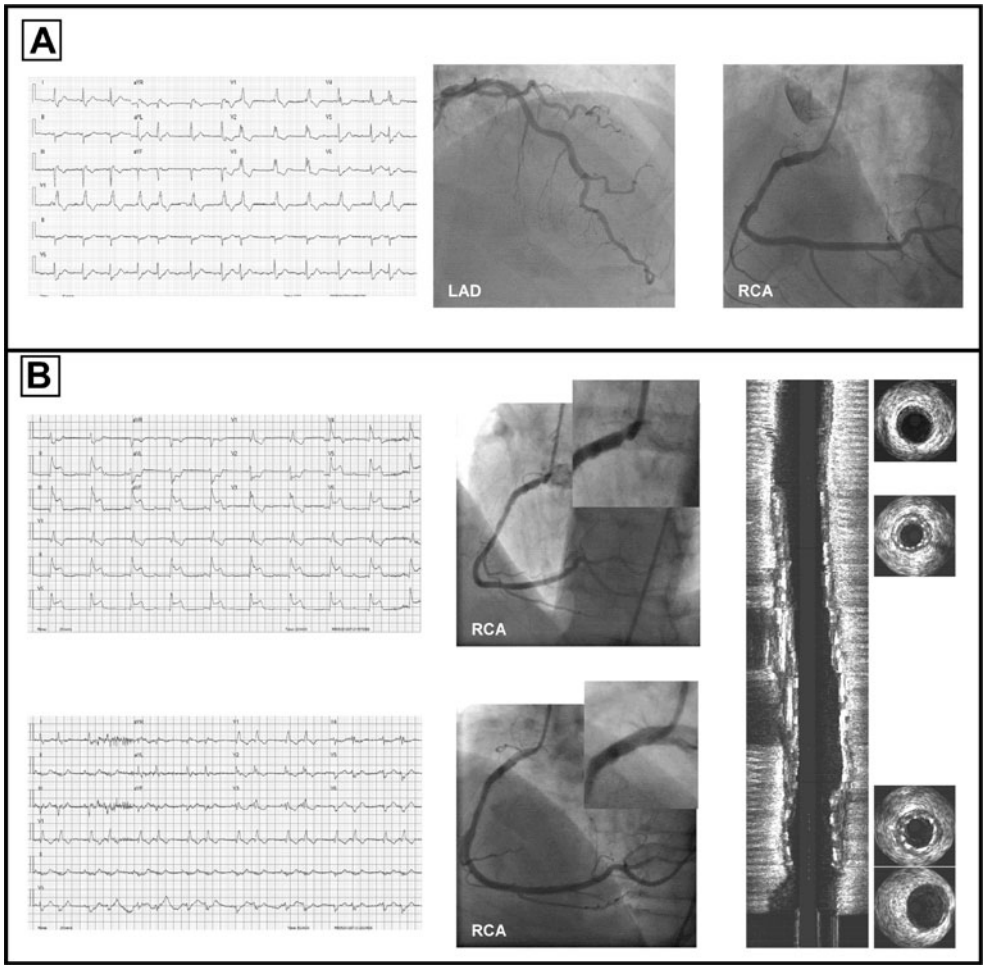

Fig. 1 **Panel a:** ECG (left panel, showing RBBB) and coronary angiography (*right panel*, showing the result of the implantation of two drug-eluting stents in the RCA and normal LAD) of the patient before DSE. **Panel b:** ECG of the patient during the allergic reaction to SonoVue® (*left, upper panel*) and after resolution of the symptoms (*left, lower panel*). Coronary angiography of the RCA shortly after the beginning of the allergic reaction to SonoVue® (*middle, upper panel*, showing 50 % proximal stenosis due to coronary spasm) and few minutes later after resolution of the symptoms (*middle, lower panel*, showing resolution of the coronary spasm). IVUS of the RCA (*right panel*, with *longitudinal* and *cross-sectional* views) showing the presence of two drug-eluting stents with minimal neointimal hyperplasia with no significant lumen reduction. RBBB=right bundle branch block, RCA=right coronary artery, LAD=left anterior descending coronary artery, DSE=dobutamine stress echocardiography, IVUS=intravascular ultrasonography

left coronary artery. Intravascular ultrasonography of the RCA was also performed and showed minimal neo-intimal hyperplasia (Fig.1b) with no significant stenosis. Further angiographic projections confirmed complete resolution of the spasm (Fig.1b). The patient was admitted to the coronary care unit and observed for 12 h. His recovery was uneventful and troponin T remained within normal ranges (0.016 μg/l).

Discussion

Hypersensitivity and allergic reactions are well-known causes of acute cardiovascular events. In 1991 a syndrome including angina pectoris together with the occurrence of an allergic reaction was described and called Kounis syndrome[5]. The Type I variant of this syndrome includes patients with normal coronary arteries. Type II includes patients with significant but quiescent atherosclerotic disease[6]. In both cases, activation of the mast cells leads to the release of several compounds, including histamine, platelet-activating factor and cytokines, which have been shown to induce coronary artery spasm and/or acute myocardial infarction in several clinical and experimental studies [7].

In this case administration of the echo contrast caused the Kounis syndrome.

Endocardial visualisation with contrast echocardiography is widely used to improve the diagnostic accuracy of DSE [1, 2]. In particular, SonoVue® was introduced in 2001 and is currently the only echo contrast agent used in European countries. After its introduction, the European Medicines Agency (EMA) received several alerts of allergic reactions with secondary cardiovascular problems[8]. After these reports, in 2004, the

EMA took precautionary measures to limit the use of SonoVue® in patients with unstable cardiac conditions[9]. A post-marketing analysis of the manufacturer of SonoVue® involving 157,838 patients showed 0.01 % nonfatal severe and 0.02 % fatal complications. In 2006, a safety study of contrast DSE was performed and showed that among 419 patients receiving SonoVue® or Optison®, an overall 4 % experienced side effects, with no deaths or myocardial infarctions[10]. Geleijnse et al. systematically reviewed all adverse events reported in patients receiving SonoVue® during DSE in their centre[11]: 1.1 % had mild allergic reactions and 0.9 % experienced a severe allergic reaction resulting in (nonfatal) shock.

However, a severe anaphylactic reaction with reversible ST-segment elevation was reported by Calco et al. when SonoVue® was administered at a peak dose in DSE[12]. In another case report, reversible ST-segment elevation was reported after administration of Sonovue® but before starting DSE[13]. However, coronary angiography was not performed in either of these patients, while the current case report could demonstrate the absence of intra-coronary thrombus, but the presence of significant coronary spasm as a cause of the ST-segment elevation [14].

In conclusion, SonoVue®, which is often indispensable to improve the diagnostic accuracy of DSE, is a safe pharmacological agent, for which adverse events are rare and usually of minor consequences. However, a few cases of life-threatening allergic reaction have been described, making it essential that its use is restricted to a safe environment, under monitoring of vital signs and with availability of full resuscitation facilities.

Funding The Department of Cardiology has received research grants from Biotronik, Medtronic, Boston Scientific, Lantheus Medical Imaging, Edwards Lifesciences, St. Jude Medical and GE Healthcare.

Conflicts of interest None declared.

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