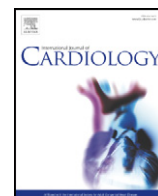




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Letters to the Editor

Allergic reaction to proton pump inhibitor: Pantoprazole induced Kounis syndrome ☆☆☆

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Letter to Editor

A 38-year-old male patient was admitted to our emergency department with the complaints of generalized pruritis, malaise, dyspnea and severe squeezing chest pain just starting 30 min after taking an oral dose of 40 mg pantoprazole for new onset gastroesophageal reflux. His past history was unremarkable for any allergic reaction, hypertension, diabetes mellitus or dyslipidemia. He was a nonsmoker. Physical examination revealed blood pressure of 110/80 mmHg, pulse of 81 beats/min regular, oxygen saturation of 92% and also he had erythematous rash over the whole body without angioedema, he was sweating and pale. Initial electrocardiography (ECG) showed sinus rhythm and ST segment elevation in leads D2, D3, aVF compatible with acute inferior myocardial infarction (Fig. 1A). Medical management was administrated as oxygen 2 lt/min, aspirin 300 mg, clopidogrel 300 mg loading dose, unfractionated heparin 4000 IU bolus, glycerol trinitrate 10 mcg/min and atorvastatin 40 mg. Also parenteral diphenhydramine 2 mg/kg and prednisolone 25 mg were given for his allergic reaction. His chest pain and itching were relieved just after initiation of medical therapy and also control ECG revealed no ST

segment elevation at II, III and aVF derivations (Fig. 1B). Transthoracic echocardiography revealed normal left ventricular systolic functions and no segmentary wall motion abnormality. He was immediately transferred for coronary angiography which revealed hemodynamically nonsignificant plaques in the circumflex and left anterior descending coronary arteries. Angiogram of the right coronary artery (RCA) showed vasospasm at mid segment of the RCA (Fig. 2A) which relieved by intracoronary 100 mcg nitrate administration (Fig. 2B and C). He was hospitalized in the coronary care unit with the diagnosis of coronary vasospasm secondary to pantoprazole ingestion. Calcium channel blockers and intravenous glycerol trinitrate were administered. Laboratory tests showed no elevation of cardiac biomarkers. We performed skin prick tests with pantoprazole (40 mg in 1 mL saline) and omeprazole (20 mg in 1 mL saline) which produced a wheal of 5 mm at 10 min and with lansoprazole (20 mg in 1 mL saline), ranitidine (50 mg in mL saline) and buffered saline which produced no reaction, thus confirming only pantoprazole and omeprazole hypersensitivity. His recovery was uneventful and he was discharged on his 3rd day of hospitalization.

Development of acute coronary syndrome after exposure to an allergic insult is an unexpected and rarely reported phenomenon. This concept of “the coincidental occurrence of chest pain and allergic reactions accompanied by clinical and laboratory findings of angina pectoris” was first described in 1991 and named as the “Kounis syndrome” [1]. Upon the recognition of this clinical entity, many hypotheses have been proposed to explain a causal relationship between allergic reactions and the acute coronary events. Of these, mast cell driven vasospastic and inflammatory response acting on the coronary endothelium has gained acceptance as the main causative mechanism. Mast cells are found in most parts of the human body including the heart and vessels. During an acute allergic reaction, activated mast cells degranulate and release a number of mediators such as histamine, tryptase, platelet activating factor, leukotrienes and thromboxane which were experimentally shown to lead coronary artery spasm or plaque rupture. Two variants of the KS have been described. Type 1 refers to patients with normal coronary arteries who develop coronary vasospasm, a representative of endothelial dysfunction. Type 2 occurs in patients with atheromatous coronary artery disease in whom plaque rupture is incriminated for the ensuing angina episode [1]. Our patient was diagnosed as type I KS because of the coronary vasospasm.

Proton pump inhibitors are most commonly used in clinical practice for the treatment of various gastrointestinal disorders including gastroesophageal reflux and are well tolerated by the patients [2].

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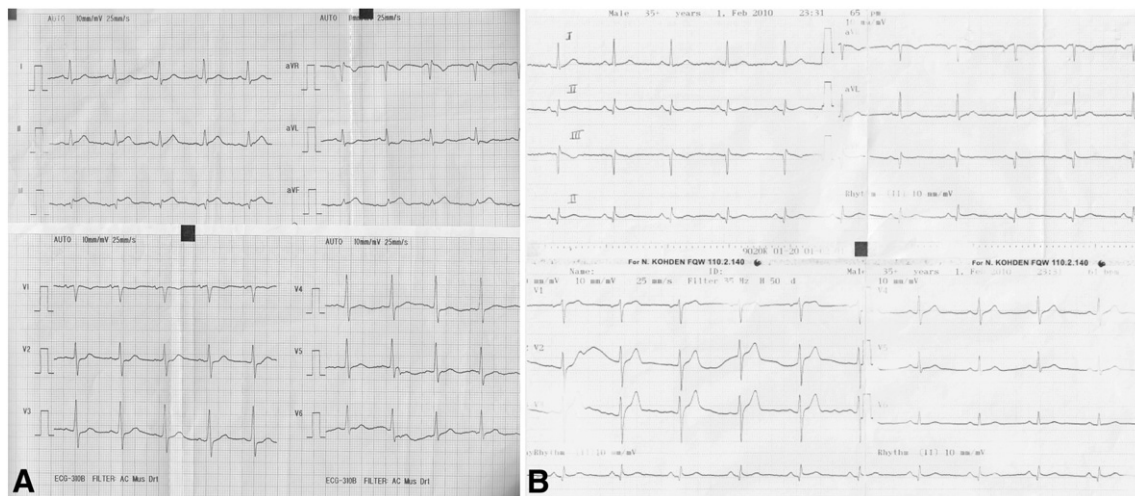


Fig. 1. Initial ECG showing sinus rhythm and ST segment elevation at derivations of II, III and aVF (A). After initiation of medical therapy, ECG changes returned to normal (B).

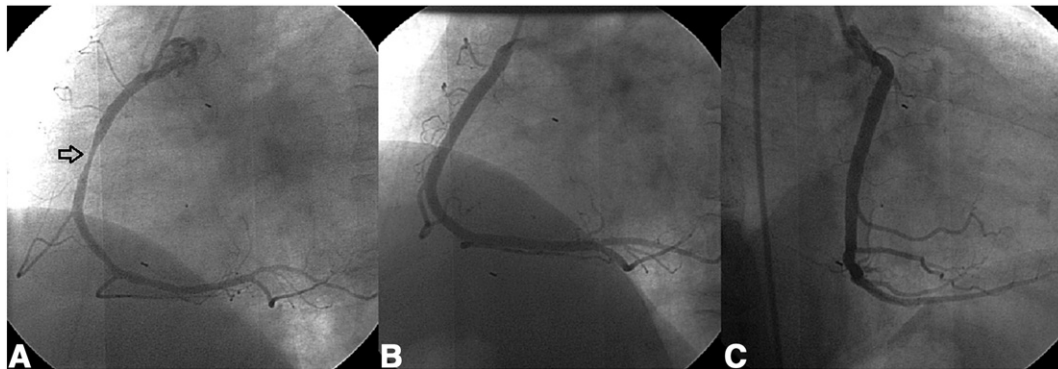


Fig. 2. Initial angiogram of the right coronary artery at right oblique view revealed narrowing at mid segment (A). After administration of intracoronary nitrate, control angiogram at right (B) and left (C) oblique views showed normal RCA.

Their administration is rarely associated with allergic reactions. But there were few cases of hypersensitivity to proton pump inhibitors including pantoprazole in the literature [3,4]. We present a patient who developed Kounis syndrome after taking 40 mg of pantoprazole. This is the first report of Kounis syndrome associated with pantoprazole administration in the world literature.

This report shows that the proton pump inhibitor pantoprazole can induce allergic myocardial infarction and should be added in the list of drugs capable to induce Kounis Syndrome.

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