Unexpected outcome (positive or negative) including adverse drug reactions

Losartan-induced coronary artery spasm

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Summary

We report a case of coronary artery spasm documented with angiography in a patient with severe chest pain, electrocardiographic ST-segment elevations and highly elevated troponin I. Symptom onset was 15 min after the patient's first-ever intake of losartan. Although parts of the clinical presentation suggested allergy or anaphylaxis, laboratory testing did not support this.

BACKGROUND

Coronary artery spasm is most often a relatively benign condition easily treated with nitrates and calcium antagonists and only rarely is the condition life threatening. The underlying mechanism is typically vasoconstrictor stimuli, postreceptor alterations or a combination. Despite the fact that more than 60 years have lapsed since the first description of coronary artery spasm, surprisingly little is known about the pathophysiology. Some vasoconstrictor drugs such as sumatriptan and cocaine induce coronary spasm while vasodilators normally do not. We present a case of life-threatening coronary artery spasm in a woman 15 min following the intake of her first-ever losartan tablet. There could be different explanations to the patient's clinical presentation:

- ▶ Kounis syndrome, also known as allergic angina syndrome.¹
- ▶ An adverse drug reaction from losartan not related to allergy.
- ▶ Coronary artery spasm induced by the patient's medicine for migraine (triptans).
- ▶ An idiopathic reversible vasospasm.

Coronary artery spasm occurs in both stable and unstable patients with suspected coronary artery disease and because the triggers are many and often ill defined this diagnosis should constantly be part of the diagnostic armamentarium when evaluating patients with ST-segment elevation.

CASE PRESENTATION

A 55-year-old woman with chest pain and ECG ST-segment elevation presented to our cardiac catheterisation laboratory. The symptoms had started 15 min after the patient's first-ever intake of 50 mg of losartan, which had been prescribed for hypertension by her general practitioner. The patient had no family history of coronary artery disease but she suffered from type 2 diabetes mellitus, hypertension and major depression and she had undergone cardiac surgery for congenital ventricular septal defect at the age of 6. She also suffered from the skin disease prurigo nodularis for which she received oral steroids (prednisolone 5 mg once daily) and clemastin (Tavegil) 1 mg three times a day. Periodically, she suffered

from migraine attacks (treated with triptans prn) but her last episode was more than 2 months earlier.

Because of the prehospital ECG-revealed ST-elevations in the lateral leads (figure 1) the patient was admitted directly for primary percutaneous intervention. Coronary angiography demonstrated a severe stenosis of the left main coronary artery while the right and the left anterior descending and the circumflex coronary arteries all appeared normal (figure 2). In additional angiographic projections the left main coronary artery stenosis had disappeared while a new narrowing was seen in the proximal circumflex coronary artery (figure 3), making the diagnosis of coronary artery spasm probable. Following treatment with the calcium channel antagonist diltiazem and intravenous nitrates her symptoms ceased, the coronary artery spasms disappeared and the ECG normalised (figure 4) only to be followed a few minutes later by a new episode of ST-segment elevations and severe chest pain. Histamine receptor blockers, hydrocortisone and later betamethasone were given, but due to persisting symptoms the patient was transferred to the intensive care unit for further treatment. Because of falling systolic blood pressure during continuing ST-elevation, short-term pharmacological inotropic support and later intra-aortic balloon pump were introduced. Symptoms and ECG changes persisted and we suspected that losartan, which is highly bound to plasma proteins, triggered the condition and plasmaferesis was therefore initiated. Symptoms, ECG changes and haemodynamic instability ceased after 12 h and the treatment was confined to routine postmyocardial infarction and heart failure therapy and mobilisation at the coronary care unit. At no time during her hospital stay did the patient experience flushing, excruciating pruritus or have signs of angioneurotic oedema.

The short period of time from losartan ingestion to symptom onset, angiographic findings showing migrating coronary spasms at different locations, severe elevation of markers of cardiac damage (plasma troponin I 237 µg/l), a skin disease (prurigo nodularis) with a higher-than-normal level of mast cells² suggested an allergic myocardial infarction in accordance with Kounis syndrome type 1.

Figure 1 Prehospital electrocardiogram showing ST-elevations in the anterolateral leads V1–V5.

Figure 2 Left main coronary artery spasm.

Figure 3 Left circumflex coronary artery spasm.

Figure 4 Normalised electrocardiogram.

INVESTIGATIONS

Serum tryptase at 12 h following admission was within the normal range, but we cannot exclude that testing on an earlier time point would have shown elevations as is often the case following mast cell activation. Moreover, immunoglobulin E was also not elevated. The concentration of ACE in the plasmaferesis fluid was within the normal range for plasma.

DIFFERENTIAL DIAGNOSIS

Kounis syndrome seems less likely in our patient who had not previously been exposed to angiotensin-II receptor antagonists or ACE inhibitors. However, one cannot exclude the possibility that cross-allergy to other pharmacological or non-pharmacological substances could have played a role.

Concomitant use of selective serotonin reuptake inhibitors and triptans independently increase serotonin levels by different mechanisms and increase the risk of developing coronary artery spasm.³ However, our patient did not experience migraine or use medication for migraine for more than 2 months prior to admission.

The migrating and reversible coronary artery stenoses exclude plaque rupture or coronary artery dissection.

OUTCOME AND FOLLOW-UP

Two weeks after admission, the patient was discharged in good condition but with a left ventricular ejection fraction of 25%. The possibilities to treat her heart failure medically were limited due to the suspected hypersensitivity to angiotensin-II receptor blockers and most likely also ACE inhibitors. Furthermore, her blood pressure was

low at 90 mm Hg systolic. The patient was discharged on a beta adrenoceptor agonist (carvedilol 6.25 mg twice daily), potassium sparing diuretic (spironolactone 25 mg once daily), long-acting nitrates (isosorbide mononitrate 60 mg once daily) and loop diuretics (furosemide 20 mg once daily).

DISCUSSION

In an extensive literature search we did not find other cases describing an angiotensin-II receptor antagonist directly or indirectly provoking coronary artery spasm and only one recent case describing losartan-associated anaphylaxis and angioneurotic oedema⁴, which our patient did not have.

Drug-related allergy or adverse drug reactions rarely cause coronary artery spasms but the diagnosis should be kept in mind and an ECG should be recorded when symptoms or haemodynamics indicate involvement of the heart.

Learning points

- Coronary artery spasm should always be considered when a patient presents with chest pain and ST-segment elevation in the ECG.
- Most drugs can trigger an allergic type 1 reaction that can release histamine and provoke vasoconstriction.
- Coronary artery spasm can also be triggered by a more ill-defined 'adverse drug reaction'.

Competing interest None.

Patient consent Obtained.

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