Coronary Spastic Angina Induced after Oral Desmopressin (DDAVP) Administration

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Abstract

A 60-year-old man was prescribed oral desmopressin (1-deamino-8-D-arginine vasopressin acetate trihydrate; DDAVP) for nocturnal polyuria. One week after starting to take desmopressin, he frequently felt chest pain while resting. Coronary angiography revealed no organic stenosis; however, an acetylcholine provocation test showed severe coronary spasm with ST elevation. He was diagnosed with coronary spastic angina, and we stopped the oral desmopressin and added diltiazem. While DDAVP should dilate the coronary vessels in healthy subjects, it may provoke coronary vasospasm in patients with endothelial dysfunction. We should be careful to avoid triggering coronary spasm when administering DDAVP to patients that may have potential endothelial dysfunction.

Key words: coronary spastic angina, desmopressin, DDAVP

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Introduction

Arginine vasopressin (AVP) is known to induce both systemic and coronary vasoconstriction mainly via the vasopressin V1 receptor (1-3). A previous study showed that vasopressin causes decreased coronary flow via the constriction of small coronary arteries without large-sized focal spasm (4). Desmopressin (1-deamino-8-D-arginine vasopressin acetate trihydrate; DDAVP) is a synthetic analogue of arginine vasopressin used to treat central diabetes insipidus (5) or nocturnal polyuria (6) as a selective agonist for the vasopressin V2 receptor. Although DDAVP is an agonist for the vasopressin receptor, it has been considered that DDAVP does not induce coronary spasm (vasoconstriction), given its selectivity for the vasopressin V2 receptor. We report a case of coronary spastic angina induced after oral DDAVP administration.

Case Report

A 60-year-old man was admitted to our hospital complaining of chest pain at rest. Ten days prior to this admission, he was prescribed oral desmopressin acetate hydrate (MINIRINMELT OD Tablet® 120 µg/day before sleeping) by a urologist at a nearby hospital for the treatment of nocturnal polyuria. After starting the administration of oral desmopressin, chest pain at rest frequently occurred, especially at night. On the day of hospital admission, he felt chest oppression at rest in succession at 2 AM, 5 AM, 6 AM, and 8 AM, and these episodes were relieved spontaneously or after sublingual administration of nitroglycerin. The patient then visited our hospital and was admitted emergently. An initial electrocardiogram (ECG) showed no significant ST-T changes (Fig. 1), the findings for troponin-T were negative (troponin-I level was 6.5 pg/mL), and transthoracic echocardiography showed no segmental asynergy at rest. His low-density cholesterol level (LDL-C) was 80.8 mg/dL.

The patient was an ex-smoker and had a history of pulmonary adenocarcinoma which was cured by lung lobectomy one year prior to the admission. He also had a history of unstable angina three years prior to this admission and received percutaneous coronary intervention to the left circumflex artery with a drug-eluting stent. He had hypertension, dyslipidemia, and a smoking habit as coronary risk factors. He had been prescribed aspirin, statins, and a cal-
spasm for 10 months. He was followed up without any recurrence of coronary artery disease. After that, he did not complain of angina (CSA), and we stopped the oral DDAVP and added diltiazem (200 mg/day). Despite the continuous administration of an oral calcium channel blocker (amlodipine besilate 2.5 mg/day) before the admission.

On Day 2, we underwent coronary angiography, which revealed no organic stenosis, including in-stent restenosis. We performed the acetylcholine provocation test to investigate whether or not his chest pain was due to coronary spasm. Despite the continuous administration of an oral calcium channel blocker during the test, the administration of only 20 μg of acetylcholine chloride into the left coronary artery induced excessive spasm (Fig. 2) and total occlusion of the left anterior descending artery, with ST segment elevation in leads II, III, and aVF (Fig. 3). The intracoronary administration of nitroglycerin and nicorandil relieved the severe coronary spasm has yet been clearly demonstrated.

The intra-arterial infusion of DDAVP, a selective V2 receptor agonist, was reported to cause a dose-dependent increase in the forearm blood flow (10). Several studies have also suggested the existence of extrarenal V2 receptors that may mediate a vasodilatory effect of AVP (10-13). Another study revealed that AVP caused endothelium-dependent relaxation of the canine basilar and coronary artery, whereas the removal of the endothelium caused basilar artery contraction by AVP (14). Endothelial NO synthase (eNOS) is known to be activated by several agonists, including acetylcholine, via an increase in the intracellular free calcium level and the binding of calmodulin to eNOS (15, 16). Furthermore, cAMP-increasing agents lead to an increase in eNOS activity, and protein kinase A (PKA) induces eNOS phosphorylation in cultured endothelial cells (17-19).

Our report suggests that DDAVP may provoke vasospasm of the coronary arteries via V2 receptors, which can be visu-
Figure 2. Coronary angiography and the acetylcholine provocation test. (a) The left cranial view of the left coronary artery. (b) The right caudal view of the left coronary artery. There was no organic stenosis, including in-stent restenosis. (c) The left cranial view of the left coronary artery after the administration of acetylcholine chloride. (d) The right caudal view of the left coronary artery after the administration of acetylcholine chloride. Excessive coronary spasm was induced only by 20 μg administration of acetylcholine chloride. The drug-eluting stent previously implanted in the left circumflex artery is indicated by arrows.

Figure 3. ECG during acetylcholine provocation test. ST segment elevation was observed in leads I, aVL, and V2-6 accompanied by reciprocal changes in leads II, III, and aVF.
alized by coronary angiography.

We reported a case of CSA induced by oral DDAVP administration. While DDAVP should dilate coronary vessels in healthy subjects, DDAVP may provoke coronary vasoconstriction in patients with endothelial dysfunction. This case suggests that the mechanism of DDAVP in endothelial dysfunction is at least partially responsible for the myocardial ischemia caused by vasopressin. Further, in clinical settings, we should be alert for the emergence of coronary spasm when administering DDAVP to patients that may have endothelial dysfunction.

The authors state that they have no Conflict of Interest (COI).

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