Vasospastic angina induced by prostaglandin F_{2α}

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Abstract

A 56 year old woman underwent cholecystectomy. Postoperative paralytic ileus was treated with an intravenous infusion of prostaglandin F_{2α}. During infusion she complained of oppressive chest pain. This was accompanied by ST segment depression, and was relieved by sublingual glyceryl trinitrate. Coronary arteriography did not show significant stenosis, but subsequent intravenous infusion of prostaglandin F_{2α} provoked multiple segmental spasm of both the right and left coronary arteries.

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The cardiovascular effects of prostaglandin F_{2α} (PGF_{2α}), especially on coronary arterial tone have not been fully established. We report a patient in whom vasospastic angina

was induced by intravenous infusion of PGF_{2α} and in whom coronary arterial spasm was demonstrated angiographically.

Case report

A 56 year old housewife was admitted with cholecystolithiasis. She had had a small cerebral infarction at the age of 48, when hypertension and hypercholesterolaemia were found. She had been treated with enalapril and probucol. She was non-smoker and had no previous history of angina. She was obese (height 156 cm, weight 83 kg) and her blood pressure was 170/90 mm Hg. Concentrations of total serum cholesterol and HDL cholesterol were 220 and 38 mg/dl respectively. The resting electrocardiogram showed no abnormalities (fig 1A) and a Master's single step test was normal. She underwent cholecystectomy under general anaesthesia.

On the fourth day after the operation paralytic ileus developed and she was treated with intravenous drip infusion of PGF_{2α} (8 µg/min). Fifteen minutes after the infusion started she suddenly complained of oppressive chest pain. Her electrocardiogram showed ST segment depression and inverted T wave in leads II, III, aVF, V5, and V6 (not shown in the figure). When the infusion of PGF_{2α} was stopped and sublingual glyceryl trinitrate was given her symptoms were relieved and her electrocardiogram returned to normal.

Cardiac catheterisation was performed a month after the episode. Haemodynamic measurements at rest were normal. Selective coronary arteriography was carried out by the Sones' technique. The right and left basal coronary arteriograms showed no significant coronary stenosis (fig 2 A and B). PGF_{2α} was infused intravenously (0.4 µg/kg/min) with the patient's informed consent. During infusion she complained of crushing chest pain. This was associated with ST segment depression and negative T wave in the same electrocardiographic leads as before (fig 1B). Coronary arteriograms obtained immediately after the onset of chest pain showed multiple segmental spasms of both right and left coronary arteries (fig 2 C and D). The spasms resolved (fig 2 E and F) and her electrocardiogram became normal (fig 1C) after 5 mg of isosorbide dinitrate was injected into the sinus of Valsalva.

Discussion

PGF_{2α}, an arachidonic acid metabolite which causes rhythmic constriction of smooth

Figure 1 Serial standard 12 lead electrocardiograms during coronary arteriography: (A) during an angina attack (B) and after injection of isosorbide dinitrate (C).

Figure 2 Coronary arteriograms before (A and B) and after intravenous prostaglandin $F_{2\alpha}$ infusion (C and D) and after isosorbide dinitrate administration (E and F). Multiple segmental spasms develop after prostaglandin $F_{2\alpha}$ infusion. Note severe narrowing (black arrows) at first diagonal branch, obtuse branch, and posterior descending artery (C), right ventricular branch atrioventricular nodal artery, and posterior descending artery (D). A, C, and E: left coronary artery; B, D, and F: right coronary artery.

muscle of intestine and uterus is used as oxytocic agent and to treat paralytic ileus. However, its cardiovascular effects are not fully understood. Treatment with $\text{PGF}_{2\alpha}$ was reported to have few effects on systemic blood pressure, heart rate, and coronary flow.¹⁻³

In experimental studies on isolated blood vessels $\text{PGF}_{2\alpha}$ constricted the arteries.^{4,5} But in clinical settings intravascular injection of $\text{PGF}_{2\alpha}$ was reported to dilate vessels. It has been used as a vasodilating agent during pharmacological angiography.^{3,6} These contradictory vascular effects have not been explained.

Kawai *et al*⁷ reported that lower concentrations of $\text{PGF}_{2\alpha}$ (10^{-11} – 10^{-7} mol/l) relaxed isolated monkey cerebral arteries with intact endothelium, whereas higher concentrations ($>10^{-6}$ mol/l) induced a dose dependent constriction. On the other hand, in the arteries without endothelium or in arteries in which endothelium-derived relaxing factor (EDRF) release was blocked by L-N^G-monomethyl-arginine (L-NMMA), a selective inhibitor of EDRF synthesis, $\text{PGF}_{2\alpha}$ caused constriction even in lower concentrations. Kawai *et al* suggested that $\text{PGF}_{2\alpha}$ might stimulate the release of EDRF, resulting in vasodilation.

There are few reports of the effects of $\text{PGF}_{2\alpha}$ on the coronary artery in clinical practice. However, in patients with early coronary atherosclerosis less EDRF was released from the coronary arteries.^{8,9} The patient we described here had several coronary risk factors, so she was likely to have had mild coronary atherosclerosis and secondary endothelial dysfunction. Accordingly, the vasoconstrictive effect would predominate when $\text{PGF}_{2\alpha}$ was given.

We know of no other reports of $\text{PGF}_{2\alpha}$ -induced vasospastic angina.

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