Intractable vasospastic angina

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A 48 year old woman with drug refractory vasospastic angina had been in our hospital for nine months. Electrocardiograms recorded during angina attacks showed marked elevation of ST segments in the precordial, inferior, and/or lateral leads, often with ventricular arrhythmia or atrioventricular block (fig 1). Coronary angiography revealed no atherosclerotic stenosis, and intracoronary injection of acetylcholine induced total occlusion of the left anterior descending and right coronary arteries despite continuation of high dose calcium antagonists (fig 2).

Calcium antagonists (nifedipine, nisoldipine, amlodipine, bendipine, diltiazem, and verapamil), nitrates (isosorbide dinitrate, isosorbide mononitrate, and nitroglycerin), nicorandil or various combinations of drugs could not prevent her attacks. Blood concentrations of drugs such as diltiazem and nicorandil were much higher than normal therapeutic values. She did not have signs of a generalised vasospastic disorder such as Raynaud's phenomenon nor a family history of coronary artery disease or sudden death. The patient had stopped smoking after admission. Her attacks occurred not only between midnight and early morning but also in the daytime. The trigger of attacks such as emotional distress, exercise, cold, alcohol, or coffee could not be specified. Her regular menstrual cycle with normal variation of blood oestrogen concentrations was not related to the incidence of attacks.
In general, calcium antagonists are extremely effective in preventing coronary artery spasm, and simultaneous administration of two or three antagonists is rarely required. In this patient, however, even an extremely high dose of calcium antagonists (diltiazem 1400 mg/day) could not prevent attacks, and further increase in the dosage could not be tolerated because of marked hypotension.

Medications other than conventional antianginal drugs were tried over the nine months in hospital: magnesium, α-adrenergic blockers (prazosin and doxazosin), β-adrenergic agonist (denopamine), serotonin 2 receptor antagonist (sarpograpate), prostaglandin I
d, thromboxane A,
synthetase inhibitor (rozagrel), aspirin, heparin, angiotensin converting enzyme inhibitors (captopril and alacepril), prednisolone, biotin, and tranquilizers. These drugs also failed to control her attacks. For prevention of nitrate tolerance she was given N-ethylcysteine after discontinuation of nitrate and nicorandil.

The patient had experienced more than 800 attacks over nine months. Coronary angiography was performed twice, nine months apart, and revealed no fixed stenosis. At least six patterns of ST elevation during attacks suggested that coronary spasm in various sites of arteries might be involved in her anginal attacks; therefore, we did not consider coronary bypass surgery or coronary stenting to be indicated.

Antianginal drugs were stopped because of lack of efficacy, the patient suffered frequent severe chest pain lasting more than 30 minutes; however, serum concentrations of creatine kinase did not exceed the normal upper limit. At present she is taking diltiazem (1200 mg/day), benidipine (16 mg/day), amlodipine (5 mg/day), isosorbide mononitrate (60 mg/day), nicorandil (20 mg/day), and N-ethylcysteine (800 mg/day), and still suffers several attacks per day. We invite new strategies against these attacks from around the world.