Multivessel Coronary Artery Spasm

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SUMMARY A 60-year-old patient with variant angina was shown to have myocardial ischemia in two different regions supplied by separate major coronary arteries. Neither artery had significant coronary atherosclerotic obstruction. Ventricular fibrillation was noted during ST-segment elevation in anteroseptal leads. The attacks of pain and arrhythmias disappeared during nifedipine therapy.

VARIANT ANGINA PECTORIS in patients without coronary artery disease is the result of reduced myocardial perfusion due to coronary artery spasm. The degree and site of spasm may vary, but in any one patient it usually involves the same vessel. This report is the first documented example of a patient who had coronary spasm in separate arteries at different times. The ischemic areas of the myocardium were demonstrated by myocardial perfusion scans during pain.

Case Report

A 60-year-old truckdriver and smoker was admitted in April 1978. For 2 years he had experienced retrosternal chest tightness that occurred at rest and during the night, waking him from sleep. The pain recurred several times each week but resolved within minutes, either spontaneously or after sublingual nitroglycerin. Propranolol was ineffective. Syncope with chest pain occurred on two occasions. The last was the reason for his admission. Mild hypertension was noted 2 years before and a duodenal ulcer had been medically treated over 30 years. Physical examination was normal. The resting ECG showed voltage evidence of left ventricular hypertrophy (fig. 1A).

The patient performed a graded exercise test on a bicycle ergometer and reached 73% predicted maximum heart rate. Effort was stopped by fatigue, not chest pain. The ECG showed 2-mm upsloping ST depression in the lateral chest leads not consistent with ischemia (fig. 1B). Frequent ventricular premature depolarizations were seen during exercise. An exercise thallium-201 myocardial perfusion scan was normal.

At cardiac catheterization the left ventricle contracted normally, with an ejection fraction of 62%. The left anterior descending coronary artery showed a proximal 50% obstruction and the first diagonal branch was obstructed 85% at its origin. The right coronary artery was dominant, and both the right and circumflex coronary arteries had minor lesions only. Because of the normal myocardial perfusion scan and normal stress test these lesions were not thought to explain the patient's nocturnal and rest angina. After cardiac catheterization an ECG recorded during an episode of spontaneous nocturnal pain showed 5-mm ST-segment elevation in the inferior leads with ST-segment depression in the anterior leads (fig. 1C).

To confirm that coronary artery spasm was present, an ergonovine provocation test with ECG monitoring and thallium-201 myocardial perfusion scanning was performed on May 9, 1978. A total of 0.25 mg ergonovine maleate i.v. was given in divided doses. This reproduced his usual chest pain, and the ECG showed 3-mm ST-segment elevation in the inferolateral leads (fig. 1D). Frequent ventricular premature depolarizations occurred with short runs of ventricular tachycardia. A concurrent thallium-201 myocardial perfusion scan showed a reversible defect involving the inferoposterior segment of the left ventricle (figs. 2 and 3). These findings were consistent with spasm of the right coronary artery. The patient was discharged on oral isosorbide dinitrate and intermittent sublingual nitroglycerin.

Over the next 7 weeks his angina occurred infrequently at rest during the day and was quickly relieved by sublingual nitroglycerin. On July 4, 1978 he was admitted to the local hospital with frequent attacks of rest angina. He had noticed malena for 3 days and his hemoglobin was 8.7 mg%. He was transfused and started on propranolol. The chest pain, which was easily relieved by sublingual nitroglycerin, continued up to six times daily, and was associated with ST-segment elevation and short runs of ventricular tachycardia. A 12-lead ECG during chest pain was not recorded. Three days later, after chest pain complicated by ventricular fibrillation, he was transferred.

Over the next week numerous episodes of rest angina with ST-segment elevation on monitor lead V1 and associated ventricular tachycardia (fig. 4) relieved by sublingual nitroglycerin were observed. During one short episode of chest pain, 2 mCi of thallium-201 were injected. The myocardial perfusion scan (figs. 2 and 3) showed irreversible ischemia in the anteroseptal segment, suggesting spasm of the left anterior descending coronary artery.

Various vasodilator medications were given (fig. 5). Neither verapamil or phenoxybenzamine, an α-blocker reduced the frequency or severity of the angina. When nifedipine (10 mg every 6 hours) was

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given, the frequency of attacks decreased, but after a further episode of chest pain with ventricular tachycardia, nifedipine was increased to 20 mg every 6 hours, with complete relief of chest pain and ventricular arrhythmias. The patient's reliance on nifedipine was shown when on one occasion the drug was delayed for 1 1/2 hours: Spontaneous ST-segment elevation without chest pain was seen on the monitor; this improved after sublingual nitroglycerin.

He was discharged 5 weeks after admission, taking oral isosorbide dinitrate, nitroglycerin ointment, quinidine sulphate and nifedipine. At follow-up 5 months after admission he was well, with no further angina. The nitroglycerin ointment was being gradually reduced and the nifedipine continued unchanged.

**Discussion**

Variant angina in patients who have insufficient coronary artery disease to explain symptoms is due to
**FIGURE 3.** Electrocardiographic strips of monitor V1 during second admission: A) at rest; B) during chest pain, showing ST-segment elevation; C) during chest pain, showing ST-segment elevation and the onset of ventricular tachycardia; D) during chest pain, showing rapid ventricular tachycardia returning to sinus rhythm after sublingual nitroglycerin.

**FIGURE 4.** A) During spontaneous chest pain there is ST-segment elevation in V1 and a perfusion defect in the anteroseptal (ANT SEPT) segment of the heart, represented as the shaded area on the diagram on the left. B) On the redistribution scan 4 hours later, both the ECG and the scan are normal. LAO = left anterior oblique; POST = posterior; INF = inferior.
coronary artery spasm. Although spontaneous spasm has been documented during selective angiography, variant angina is usually diagnosed when ECG changes during rest pain suggest transient myocardial ischemia. The ECG localization of the myocardial ischemia may be difficult, because coronary artery spasm may cause both ST-segment elevation with reciprocal ST-segment depression, or ST-segment depression alone. Serial myocardial perfusion scanning, with thallium-201 injected during chest pain, accurately localizes the site of reduced myocardial perfusion secondary to coronary artery spasm. When episodes of variant angina do not occur during patient investigation, provocation with ergonovine may be used to induce coronary artery spasm, which is then documented either directly by selective angiography or indirectly from the ECG or serial thallium-201 myocardial perfusion scan changes. The site and extent of coronary artery spasm do not differ between spontaneous and ergonovine-provoked attacks.

During the initial investigation of our patient, an exercise test and the exercise perfusion scan were normal. Ergonovine provocation reproduced the chest pain and inferior ECG changes similar to those of the spontaneous attack. Thallium-201 myocardial scanning with ergonovine confirmed the presence of a reversible perfusion defect consistent with transient myocardial ischemia and localized it to the inferoposterior wall. Spasm was presumed to have occurred in the right coronary artery, which had only minor disease. Later, thallium-201 scanning during recurrence of severe chest pain showed a transient perfusion defect in the anterior wall. Twelve-lead ECG documentation was not possible because of the rapid onset of life-threatening ventricular arrhythmias with each episode of chest pain.

Although the degree and site of coronary artery spasm may vary in any one patient, it usually involves one vessel. Several investigators have documented simultaneous spasm in more than one coronary artery. Variant angina due to spasm in one vessel and then in another was suggested but not documented in a case reported by Johnson and Detwiler. In our patient, the changes on the ECG and thallium-201 myocardial perfusion scan suggested reversible ischemia in one vascular area and later in a second area. Variant angina on the two occasions was secondary to spasm in two different coronary arteries.

Recent reports suggest that both vasodilators and the calcium antagonist, verapamil, may be effective in variant angina. The combination of isosorbide dinitrate, verapamil and cutaneous nitroglycerin ointment was ineffective in our patient. Only after the introduction of the calcium antagonist, nifedipine, was the frequency of symptoms reduced. The dose had to be increased to 20 mg every 6 hours to eliminate the attacks completely. The effectiveness of nifedipine in preventing coronary artery spasm was further illustrated when a 1½ hour delay in a dose of this drug was associated with ST-segment elevation on the monitor. Beta-blockers were ineffective in this patient and may cause deterioration in variant angina.

Finally, this case illustrates the cyclic nature of coronary artery spasm and its relation to stress. After a relatively stable period on isosorbide dinitrate, there was a recurrence of variant angina after an episode of gastrointestinal bleeding. The spasm involved a different coronary artery, was associated with life-threatening arrhythmias and was difficult to treat.
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