Recurrent myocardial infarction in a patient with Prinzmetal’s angina and normal coronary arteries

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A 55-year-old man was referred for the evaluation of frequent chest pain and syncope. While in the hospital, he experienced severe chest pain accompanied by transient ST segment elevation and a slight elevation of cardiac enzyme levels. Multiple coronary arteriograms were recorded at various times during an interval of 2 months. On one occasion, the results were normal; on another occasion, they showed total occlusion of the left anterior descending, diagonal, and circumflex coronary arteries. The occlusion was completely relieved with sublingual nitroglycerin. Because the patient’s clinical condition deteriorated rapidly, double aortocoronary saphenous vein bypass was performed to the left anterior descending and circumflex coronary arteries. During the induction of anesthesia, ventricular fibrillation occurred, and the patient died from refractory recurrent fibrillation 4 hours after surgery. Postmortem examination revealed normal coronary arteries, patent vein grafts, and multiple focal areas of recent and old myocardial fibrosis. Thus, it appears that coronary spasm, in the presence of otherwise normal coronary arteries, can produce myocardial infarction with necrosis, and that medical management may provide a more successful method of treating such patients.
Prinzmetal and coworkers\(^1\) described a variant form of angina in which recurring attacks of chest pain occurred almost exclusively at rest, were associated with transient ST segment elevation, and frequently were accompanied by ventricular arrhythmia. Previous reports have emphasized the association between coronary spasm and Prinzmetal's variant angina with normal coronary arteries.\(^1\)-\(^7\) Others have suggested that the spasm may cause acute myocardial infarction.\(^8\)-\(^12\) Evidence of the associated coronary spasm and myocardial infarction has also been supported by reports of patients who were withdrawn from chronic exposure to industrial nitroglycerin.\(^13\) These patients subsequently experienced chest pain and acute myocardial infarction. Hellstrom\(^14\) suggested that vasospasm was the immediate cause of infarction in such cases.

This report presents a patient with Prinzmetal's angina whose unusual clinical course was complicated by multiple myocardial infarctions. It also provides new observations concerning the prognosis of patients with Prinzmetal's angina.

**Case Report**

A 55-year-old man was admitted to our hospital with a history of nocturnal chest pain of several months' duration, sometimes followed by episodes of syncope. He had undergone cardiac catheterization and selective coronary angiography at another hospital. Because the results showed complete occlusion of the proximal right coronary artery, he was referred for possible coronary artery bypass. The patient smoked one package of cigarettes a day.

Physical examination showed a blood pressure of 180/103 mm Hg, normal cardiac size, and a Grade 2/6 systolic ejection murmur over the third intercostal space at the sternum. Results of a 12-lead electrocardiogram at rest were normal (Fig. 1A). On exercise, the patient achieved 100% of the maximal predicted heart rate after 100 minutes, and there was no evidence of ST segmental changes. A review of the initial arteriogram suggested that the occlusion had been caused by the catheter-induced spasm. Coronary angiography was repeated, and the results showed all coronary branches to be normal. A cholecystogram revealed multiple stones. Because the coronary arteries appeared normal, the chest pains, which were atypical of angina pectoris, were attributed to cholelithiasis, and an elective cholecystectomy was performed.

Several days after operation, the chest pain recurred, and there was transient elevation of the ST segments in leads II, III, AVF, and V\(_2\)-V\(_5\) (Fig. 1B). Serum enzyme levels were mildly elevated. Symmetrical T wave inversion persisted (Fig. 1C). Two days later, the patient spontaneously developed ventricular fibrillation from which cardioversion successfully restored the sinus rhythm. Because he continued to experi-
Fig. 1 A series of electrocardiographic recordings shows (A) normal tracing on admission, (B) typical elevated ST segment during chest pain, and (C) symmetrical T wave inversion after cardiac arrest, caused by ventricular fibrillation.

ence frequent chest pain, coronary arteriography was performed for the third time in 3 weeks. On this occasion, the findings were entirely different. The right coronary artery appeared normal. In the resting state, first one and then the other branches of the left coronary, circumflex, diagonal, and left anterior descending coronary arteries were obliterated proximally (Fig. 2), with severe coronary artery spasm. These obstructions disappeared partially after sublingual administration of nitroglycerin (Fig. 3). Despite medical treatment with nitrates and reserpine, the patient continued to have pain, and surgical treatment was elected.

During the induction of anesthesia, ventricular fibrillation occurred. Aortocoronary bypass was performed with vein grafts to the extreme distal portions of the left anterior descending and circumflex coronary arteries. The patient’s condition remained poor throughout the operation, and hypotension caused difficulty in weaning him from extracorporeal circulation. He died 4 hours later because of ventricular fibrillation that could not be converted to a satisfactory rhythm.

Results of postmortem study showed that the enlarged heart weighed 475 grams. Before the heart was dissected, postmortem angiograms were performed by indirect aortic root injection at physiologic pressures. The left coronary artery system filled via two aortocoronary bypass grafts extending from the aortic root to the anterior descending and obtuse marginal branch of the circumflex. Satisfactory retrograde filling of the entire left coronary artery system was observed, along with minimal irregularity of the anterior descending branch (Fig. 4A). Additional injections into the ostia of the coronary arteries revealed an adequate filling of the entire coronary artery system (Fig. 4B).
Fig. 2 Arteriogram of left coronary artery in right anterior oblique projection shows total obstruction (arrow) of the left anterior descending (LAD) and circumflex (CIRC) coronary arteries.

Fig. 3 Minimal irregularities are shown on the arteriogram of the left coronary artery in the right anterior oblique projection after administration of nitroglycerin.
Fig. 4 Postmortem angiogram of the coronary arteries: (A) First-step injection shows filling of the aortic root and aortocoronary bypass grafts extending from the aorta to the anterior descending and obtuse marginal branch of the left coronary artery. A retrograde filling of the left coronary artery system was obtained. (B) Second-step injection to the ostia of the coronary arteries shows additional filling of the right coronary artery system. Slight irregularity of the main branches of both the right and left coronary arteries can be seen, which corresponds to the areas of minimal atherosclerosis.

Upon dissection of the heart, the findings included left ventricular hypertrophy with multifocal myocardial fibrosis. Both the coronary artery system and the aortocoronary artery bypasses were patent. A few areas within the main coronary artery branches showed minimal narrowing that did not exceed 10% of the luminal diameter. Microscopically, these changes consisted of fibrous intimal thickening, and no calcifications were present.

The myocardial findings, microscopically, showed foci of cellular fibrosis with granulation tissue in which histiocytes with phagocytized hemosiderin were present (Fig. 5). Circumscribed areas of fibrosis were also present (Fig. 6). These myocardial changes were interpreted to be a consequence of intermittent ischemia. There was no evidence of an acute myocardial infarction.
Fig. 5 A focus of cellular fibrosis within the myocardium of the left ventricle with moderately hypertrophied myocardial fibers (Hematoxylin-eosin, X 208)
Fig. 6 Fibrosis of the left ventricular myocardium (Hematoxylin-eosin, X 165).
Discussion

This case clearly indicates the association of variant angina with coronary artery spasm and recurrent myocardial infarctions. We believe that repeated severe coronary spasms caused the subsequent multiple small myocardial infarctions that were evident at postmortem examination as multifocal fibrosis. Of 15 cases of acute myocardial infarction studied by means of coronary angiography, Oliva\textsuperscript{2,10} demonstrated coronary artery spasm to be associated with coronary artery disease in six (40%). Although pathologists have objected to the idea that sclerotic arteries may constrict,\textsuperscript{15} these reports suggest that spasm, superimposed on an atherosclerotic stenosis, may cause the primary event or may be an insignificant secondary occurrence.

In our patient, spontaneous spasm, relieved by nitroglycerin, was documented during coronary arteriography. The patient developed life-threatening ventricular arrhythmias and ischemia, with muscle damage occurring at the time of spasm. This was documented by mild serum enzyme elevations and postmortem evidence of multiple areas of old myocardial infarctions that had occurred at different times. At autopsy, the coronary arteries were essentially normal.

These findings support our postulation that recurrent and prolonged spasm of the major coronary arteries in patients with Prinzmetal's angina can cause myocardial infarctions. Several previous studies\textsuperscript{16,17} have documented the disappointing results of coronary artery bypass for treatment of angina caused by coronary artery spasm. Because spasm can occur in different areas of the coronary arteries, surgical therapy may not be successful.

As a consequence of this case, we now pursue more aggressive medical treatment of patients with Prinzmetal's angina. Nitrates with sustained action and alpha sympathetic blocking drugs which, theoretically, may chemically denervate the epicardial coronary arteries, provide the basis of our current medical management. Recently, the calcium antagonist, Verapamil, was reported to be effective in relieving chest pain in these patients,\textsuperscript{18} and has appeared to be effective in two patients whom we have treated (unpublished observation). In general, we believe that medical management can provide an acceptable method of control.

References