Combined Intracoronary Streptokinase and Percutaneous Coronary Angioplasty for Reperfusion of Chronic Total Coronary Occlusion

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In a 40 year old man with a 1 month total occlusion of a dominant right coronary artery, persistent angina despite medical management indicated inadequate coronary collateral supply to the posterolateral myocardium originally supplied by the totally occluded vessel. Initial attempts at reperfusion of the chronically occluded vessel with an angioplasty guide wire and balloon were unsuccessful. However, administration of intracoronary streptokinase resulted in partial reperfusion, after which successful wire-guided balloon angioplasty was accomplished. This case illustrates the potential utility of combining a thrombolytic agent with angioplasty in attempting reperfusion for management of selected cases of chronic total coronary artery occlusion.

Case Report

A 40 year old white man in previously good health had the onset of prolonged exertional angina on November 25, 1983 after vigorous physical activity. Physical examination by his local physician was unremarkable and a baseline electrocardiogram was normal. Recurrent episodes of angina prompted a repeat electrocardiogram on December 1, which showed new deep symmetric T wave inversions in leads III and aVF. A treadmill exercise test was positive and the patient was referred to our hospital for cardiac catheterization. The patient denied any prolonged episodes of angina other than his initial episode in November. Cardiac risk factors included only a 20 pack-year history of smoking.

Physical examination on admission, (December 7, 1983) was remarkable only for a soft systolic flow murmur along the left sternal border. Admission laboratory data included normal complete blood count, serum chemistry values, electrolytes and coagulation profile. Measurements of all serum enzymes were normal. Fasting triglyceride was normal at 75 mg/dl, as was serum cholesterol at 224 mg/dl. Chest X-ray examination was entirely normal. The electrocardiogram showed normal sinus rhythm with symmetric deep T wave inversions in leads III and aVF that were new since the electrocardiogram of November 25 and that had persisted unchanged since the tracing obtained on December 1. The precordial leads suggested posterior myocardial infarction.

Cardiac catheterization. This was performed on December 9. The initial left ventricular end-diastolic pressure was 24 mm Hg before angiography. Left ventriculography in the 45° right and left anterior oblique projections revealed

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mild inferobasal hypokinesia and normal posterolateral wall motion with a global ejection fraction of 53%. Coronary arteriography revealed a normal left main trunk, minimal (<30%) proximal lesions in the left anterior descending coronary artery and first diagonal branches and a nondominant circumflex system with 30% lesions in the proximal circumflex and obtuse marginal branches. Large collateral vessels from the circumflex system to the posterolateral branch of the right coronary artery were seen in the posterior wall, as well as large septal collateral vessels from the left anterior descending artery to the posterior descending branch of the right coronary artery. The dominant right coronary was seen to fill retrogradely to the midportion (Fig. 2A).

Clinical course. The patient was given maximally tolerated doses of topical nitrates, aspirin and dipyridamole and he was allowed to get out of bed. However, a graded treadmill exercise stress test performed on December 12 remained positive. The patient developed his typical chest and arm discomfort at 10.5 minutes of exercise testing according to a modified Bruce protocol (stage II) with 1 mm horizontal ST segment depression in leads $V_4$ to $V_6$ at a rate-pressure product of 18,400 with a maximum of 2.5 mm ST segment depression at 13 minutes (stage III). The chest discomfort and ST segment changes resolved at 3 minutes of rest. Radionuclide angiography was performed at rest in three projections and showed a global left ventricular ejection fraction of 74% without segmental wall motion abnormalities. Because of objective evidence of persistent ischemic jeopardized myocardium despite medical management, it was elected to attempt angioplasty reconstruction of the totally occluded right coronary artery.

Coronary angioplasty. This procedure was attempted on December 13. The preangioplasty protocol consisted of aspirin, 325 mg orally every 8 hours; dipyridamole, 75 mg orally every 8 hours, nifedipine, 10 mg orally every 8 hours, and nitroglycerin (Transderm-Nitro), 10 mg topically every 24 hours, for 2 days before the procedure. On arrival in the catheterization laboratory, 8 French sheaths were inserted percutaneously in the right femoral artery and vein; the patient was started on an intravenous infusion of nitroglycerin at 25 μg/min and low molecular weight dextran at 200 ml/h. He also received an intravenous dose of 10,000 units of heparin. Repeat coronary arteriograms confirmed the persistent coronary lesions just described.

Using an 8 French Amplatz right no. 1 guiding catheter system (USCI), the ostium of the right coronary artery was cannulated. A 2.0 mm diameter, 25 mm long USCI balloon dilation catheter and a 0.41 mm "J" tip Teflon-coated steerable guide wire (USCI) were then advanced into the proximal right coronary artery. Repeated attempts to pass the guide wire through the total occlusion of the proximal right coronary artery were unsuccessful over a 25 minute period. At this point, the patient was first noted to have a junctional rhythm with atrial arrest and a ventricular rate of 42 beats/min (Fig. 3). Arterial pressure remained normal. Repeat right coronary angiography showed persistent total occlusion of the proximal right coronary artery; however, the sinus node branch appeared occluded 1 cm from its origin from the right coronary artery. The bradycardia failed to respond to a total intravenous dose of 1.2 mg of atropine sulfate, and the occlusion of the sinus node branch persisted after 400 μg of intracoronary nitroglycerin.

Combined streptokinase infusion and angioplasty. Because of persistent atrial arrest and junctional rhythm, it was decided to attempt reperfusion of the sinus node artery with intracoronary streptokinase for presumed thrombotic
occlusion. A total of 200,000 units of streptokinase (Streptase, Hoechst-Roussel) was administered in 20,000 unit bolus injections and an infusion rate of 4,000 units/min for 45 minutes. Atrial activity was first noted at 25 minutes of intracoronary streptokinase infusion, and resumption of sinus rhythm occurred at 30 minutes of infusion or 44 minutes after onset of the junctional rhythm (Fig. 3). Repeat coronary angiography after streptokinase infusion showed partial reperfusion of the sinus node artery and unexpectedly, the right coronary artery demonstrated a small degree of antegrade flow across the previous site of total occlusion with visualization to the distal zone of the vessel (Fig. 4A). A repeat attempt at passage of the guide wire was successful and allowed passage of the 3.0/25 mm angioplasty balloon across the region of prior total occlusion. Successful balloon dilation was performed three times at 6 atm for 40 to 60 second inflation times. This resulted in a reduction in the translesion mean pressure gradient from 57 to 23 mm Hg. Repeat angiography revealed brisk antegrade flow down the entire right coronary system with residual 40% lesions at the site of prior total occlusion and a 40% distal coronary lesion at the origin of the posterior descending branch (Fig. 4B). The patient tolerated the procedure well and was trans-

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**Figure 2.** A, Selective left coronary arteriogram in the 45° right anterior oblique projection. Retrograde filling of the posterior descending branch and distal portion of right coronary artery through collateral vessels from circumflex and left anterior descending coronary systems is demonstrated. B, Selective right coronary arteriogram in the 45° right anterior oblique projection. Total occlusion of the proximal right coronary artery at the level of the sinus node artery branch is demonstrated.

**Figure 3.** Serial six lead electrograms during attempted angioplasty. Control sinus rhythm before catheterization (Pre-Cath) is replaced by atrial arrest and junctional rhythm after angioplasty wire probe of the proximal right coronary artery. These events were associated with occlusion of the sinus node branch. During intracoronary streptokinase (STK) infusion, sinus activity resumes. This was associated with partial reperfusion of the sinus node artery (not shown). Normal sinus rhythm resumed 44 minutes after the onset of atrial arrest.
Figure 4. Selective right coronary arteriograms in the 45° right anterior oblique projection. A. Obtained immediately after completion of streptokinase infusion. Partial reperfusion of the right coronary artery including the distal right vessel and a large acute marginal branch is now visualized. B. After successful wire-guided angioplasty of the proximal vessel. Residual 40% stenosis at the site of prior total occlusion persists with rapid anterograde filling of the entire dominant right coronary system.

Recovery course. This was uncomplicated and the patient was maintained on a regimen of aspirin, dipyridamole, nifedipine and topical nitrates. Repeat exercise treadmill testing performed on December 15 showed significant improvement with the patient achieving 16 minutes of the modified Bruce protocol (stage IV), a rate-pressure product of 26.100 with no chest or arm discomfort and only 1 mm of ST depression in leads V4 to V6. The patient was discharged the same day.

Discussion

To our knowledge, this case represents the first description of the combined use of intracoronary streptokinase and angioplasty for the management of chronic total coronary occlusion. This patient had historical evidence suggesting total coronary occlusion for a minimal period of 2 weeks before initial angiographic study. Definite angiographic evidence of total coronary occlusion was obtained 4 days before attempted angioplasty reconstruction of the occluded vessel. Initial attempts at guide wire-directed reperfusion according to the methods of Dervan et al. (7) were unsuccessful. However, the fortuitous administration of intracoronary streptokinase resulted in partial reperfusion, after which the guide wire and balloon dilation catheter could be passed and successful angioplasty performed.

Previous reports. Recent reports (5–7) have presented initial limited experience with angioplasty in the setting of chronic totally obstructed coronary arteries with primary success rates of 54 to 67%. These rates are significantly below the primary success rates for angioplasty in patients with subtotal occlusive lesions studied in the same institution (7). The most common cause for failure in Dervan’s group (7) was inability to pass the guide wire or balloon, or both, through the total obstruction. In the preliminary reports available, most patients in whom this approach has been attempted have had large collateral vessels supplying the vessels downstream from the total occlusion. This may be the reason that in the rare patient reported to have initial successful reperfusion and then abrupt reclosure, there was no evidence of adverse sequelae.

Rationale for combined therapy. The use of thrombolytic agents in patients in whom initial guide wire passage through the total obstruction fails may improve the primary success rate of angioplasty reconstruction. The mechanism of action of streptokinase in our patient was presumably thrombolysis because the appearance of the lesion immediately after reperfusion was similar to that observed during thrombolysis for acute myocardial infarction. The effectiveness of streptokinase for intracoronary thrombolysis has only been evaluated in large groups of patients up to 18 hours after coronary thrombosis (3). However, studies (8) of thrombolytic agents in pulmonary embolic disease have shown efficacy for as long as weeks after the acute event. Thus, this approach might be considered in selected patients with total coronary occlusion in whom angioplasty is being considered. However, a prospective trial of such an ap-
approach is needed to effectively assess the usefulness of these combined techniques.

References