"Infective" Myocardial Infarction

Arnon Blum, M.D.; Samuel Sclarovsky, M.D.; and Eldad Rechavia, M.D.

Four patients who developed acute myocardial infarction (AMI) in the setting of systemic febrile illness are described. They were all treated with anticoagulants or lytic agents (or both), demonstrating patent coronary arteries following infarction. We discuss the pathogenesis and therapeutic implications of AMI occurring in this setting.

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AMI = acute myocardial infarction

Patients undergoing clinically typical acute myocardial infarction (AMI) may, in fact, be victims of another process, namely myocarditis. This implies either direct myocardial infection by viral or other pathogens, an immunopathologic process, or both, producing clinical and laboratory findings related to tissue necrosis and contraction abnormalities as in acute infarction. On the other hand, there is more than anecdotal evidence suggesting an association between prodromal febrile illness and AMI, however, despite widespread clinical concern, the mechanism whereby systemic infection, either viral or bacterial, may enhance susceptibility to AMI is unknown. In this context, the potential thrombogenesis of certain infectious diseases has not yet been systematically addressed.

We and others have noted that in young individuals presenting with clinical, electrocardiographic, and enzymatic findings of AMI, we must be alert to the possibility of viral or bacterial infection as a predisposing cause of AMI, as in the following illustrative cases. We discuss the relationship and interactions between infection, viruses, bacteria, platelet activation, and thrombosis in this clinical setting.

CASE REPORTS

CASE 1

A 26-year-old man presented to the emergency room with intermittent chest pain lasting for a few hours. Three days before, he had begun to experience a flu-like illness consisting of fever and sore throat. A review of the patient’s past medical records indicated that at the age of 7 years, he had been mechanically ventilated for 1 month due to respiratory muscle paralysis, attributed to Guillain-Barre syndrome. On admission, the patient’s blood pressure was 110/80 mm Hg. A loud S4 sound was audible. The ECG revealed sinus tachycardia of 100 beats per minute and ST-segment elevation in leads 1, aVL, and V5 to V6, suggesting lateral wall ischemia. Heparin (5,000 units) was administered intravenously as a bolus, followed by continuous infusion (1,000 units/h). The patient was placed on oral therapy with aspirin, 250 mg/day. Serial ECGs showed gradual resolution of the ST-segment displacement, and T-wave inversions were subsequently noted over the inferolateral leads. Cardiac enzyme assays, including CK-MB fractions, were compatible with AMI. Cross-sectional echocardiography showed global left ventricular hypokinesis. Five days later, the patient had coronary angiography, which showed patent normal coronary arteries. The patient was discharged after a week of uneventful recovery. Two weeks after AMI, his echocardiogram was completely normal.

CASE 2

A 48-year-old man was admitted because of high fever (40°C) of 2 days' duration which had been treated with antibiotics. On his left leg, there was a red discoloration of erysipelas eruption. His history was unremarkable with respect to cardiac disease. On the second day of hospitalization, the patient developed intractable chest pain. The initial ECG showed ST-segment elevation in leads 1, 2, 3, aVF, and V4 to V6, and reciprocal ST depression in the precordial leads (V1 to V3). A continuous infusion of nitrates was promptly started, and the patient was transferred to the coronary unit. As chest pain and ischemic changes persisted, the decision was made to treat him for AMI. Heparin (5,000 units) was given as a bolus, followed by streptokinase (constant intravenous drip infusion of 1.5 million units over 30 min) and subsequently by a maintenance dosage of heparin (1,000 units/h), which kept the partial thromboplastin time at therapeutic levels. Oral therapy with aspirin was simultaneously instituted. Pertinent physical findings included tachycardia of 95 beats per minute and a temperature of 38.2°C. Bedside ECG was constantly recorded. Within 30 min after the patient was placed on the infusion of streptokinase, the pain was relieved, and the ST shift gradually returned to baseline. The final tracing showed T-wave inversion in the inferolateral leads. Laboratory results showed elevated serum cardiac muscle isoenzyme concentrations; the maximal CK-MB fraction was 958 units/L, five times the upper normal limit. Wall motion abnormalities persisted for 10 days and were confined to the diaphragmatic segment. Five days after the MI, cardiac catheterization revealed patent coronary arteries.

CASE 3

A healthy 30-year-old man with no previous cardiac history or risk factors was admitted with severe retrosternal chest pain lasting for an hour. Three days prior to admission, he had started to experience watery diarrhea, vomiting, and fever. The pain was radiating to the left arm and was not relieved by sublingual nitrates. The ECG disclosed ST-segment upward displacement in leads 1, aVL, and V5 to V6. The patient promptly received treatment similar to that of patient 2. Physical examination elicited no abnormal findings. Echocardiography showed inferolateral wall motion abnormality. Findings from a second examination on the fifth day after the MI were normal. Serial determinations of serum enzyme levels were compatible with AMI (CK-MB levels, 790 units/L). Cardiac catheterization performed within a week showed good left ventricular function and normal coronary arteries.

*From the Coronary Care Unit and the Cardiovascular Division, Beilinson Medical Center, Petah Tiqva, Israel. Manuscript received August 10; accepted September 14.

Reprint requests: Dr. Rechavia, Cardiovascular Division, Beilinson Hospital Center, Petach Tiqva 49100, Israel.
CASE 4

A 42-year-old man was hospitalized because of lobar pneumonia. On admission the patient was febrile (39°C). Examination of the cardiovascular system revealed no abnormality other than tachycardia. A chest x-ray film showed a normal heart size and left lower lobar pneumonia. On admission the 12-lead ECG was normal. Treatment was initiated with erythromycin. On the second day of hospitalization, the patient complained of a sharp precordial pain radiating to the left upper limb, accompanied by sweating. The ST segment was markedly elevated in the inferolateral leads, and downward ST displacement was evident in the precordial leads. By the time the patient had reached the coronary unit, he had no pain, although the ischemic findings still persisted. Monitoring revealed short bursts of ventricular tachycardia and a localized area of systolic hypokinesis was detectable in the inferolateral segments. A bolus injection of lidocaine was given, and a continuous infusion was started, together with continuous intravenous administration of heparin. Electrocardiographically, the patient developed inferolateral T-wave inversions and decreased R-wave amplitude which persisted on all ECGs. Serial cardiac isoenzyme assays, including CK-MB fractions, were indicative of AMI. Cardiac catheterization on the third day after the MI showed patent coronary arteries.

DISCUSSION

We present four young patients who had systemic signs of infection preceding AMI. They all had patent coronary arteries even though the clinical history, ECG changes, and laboratory findings fulfilled all of the conventional criteria of AMI. Using anatomic evidence of infarction as reflected by electrocardiographic criteria, contraction abnormality in the distribution territory of the infarct-related artery, and cardiac muscle enzyme release is likely to lead to a diagnosis of MI. The question arises why AMI is far more common in the setting of febrile illness and whether this propensity may be related to an enhanced thrombogenetic state. Regardless of the pathogenesis, infectious myocarditis can simulate AMI, and the development of "localized" ST-segment elevations may be exceedingly difficult to interpret when decisions regarding the use of thrombolytic agents in an individual patient must be taken emergently. In this confounding setting, it is not surprising that patients with pure myocarditis may be incorrectly given a diagnosis of AMI and treated routinely by thrombolytic therapy.

Myocarditis can appear as a focal or multifocal lesion associated with regional wall motion abnormalities and diffuse electrocardiographic changes not in regional lead groups. Given the similarities between AMI and myocarditis, our patients demonstrated localized ischemic changes typical of AMI in leads subtending the distribution territory of either the right or left circumflex coronary artery. Two of them have also shown reciprocal ST-segment changes. Although from the clinical standpoint, diagnosis of myopericarditis could not be noninvasively excluded, neither the non-Q-wave MI pattern nor the angiographically detected patent coronary arteries or the gradual reversibility of contraction abnormalities strongly indicate that diagnosis of AMI in our patients was inappropriate. The non-Q-wave pattern is not rarely seen following thrombolysis, and AMI may occur in the presence of normal coronary arteries. It is also not inconceivable that functional recovery may be attributed to the relatively early thrombolytic intervention. Although we have no angiographic findings of the acute phase, nonocclusive coronary vaso- spasm that culminates in a non-Q-wave MI is also a possible pathogenetic mechanism in our patients.

Previous studies provide no information as to the naturally occurring trigger responsible for the higher propensity towards MI among patients with systemic febrile illness. Spodick et al described 150 patients with an upper respiratory viral infection preceding AMI. Collecting sera on the day of infarction, evidence of a recent Coxsackie B virus infection has been reported to be as high as 26 percent and 9 percent in patients with AMI. Burch and Shewey proved the ability of Coxsackie B, the most cardiotoxic virus, to cause coronary arteritis in animals. Another prototype, the hepatitis B virus, has been claimed to be responsible for coronary arteritis in Kawasaki disease. Terada et al, investigating the interaction between the influenza virus and platelets, found that during the process of virus absorption, a prominent platelet clumping occurs. Movat et al proved that aggregation of human and porcine platelets is induced by release of adenosine diphosphate (ADP) during in vitro phagocytosis of antigen-antibody complexes. This aggregation is associated with the release of coronary vasoactive substances, namely, histamine, serotonin, and ADP. Similarly, interactions between platelets and bacteria are likely to occur in septicemia. Platelets may be activated by damaged endothelium, immune complexes, C-reactive protein, endotoxin, and products released by neutrophils. Bacteria-induced irreversible platelet aggregation has been shown to proceed through several mechanisms, including activation of the complement system, direct lytic destruction of the platelet membrane by hemolysis, and the binding to Fc receptors on the platelet membrane. Viral transformation of vascular smooth muscle cells and endothelial injury might be of critical etiologic significance in atherosclerosis and vascular thrombosis, respectively. It has been demonstrated how human endothelial cells lose their thromboreistance following interaction with the hemangioma-inducing retrovirus. An a-glycoprotein is responsible for this effect, which appears soon after infection without viral replication or cell transformation. In addition, induction of thrombogenicity was associated with a reduction in prostacyclin release and increased expression of tissue factor activity. These observations and interactions may explain the occurrence of thrombosis in associa-
tion with the hemangiosarcomas induced by retrovirus and a possible pathogenesis of various vascular diseases, either acute or chronic. Confirmation of these observations would have a significant therapeutic impact and a favorable influence on prognosis in patients with "infective MI."

In conclusion, four young patients who had an AMI preceded by infection are presented. All were treated with anticoagulants or fibrinolytic agents (or both), and they all had patent coronary arteries. Although a major limitation of this report stems largely from the lack of angiographic findings at real time, and hence the recommendations for the administration of heparin and lytic agents cannot be made with certainty, we believe that this therapeutic approach may offer benefit in certain cases of "infective MI," justifying its clinical and empiric application on an individual basis. Understanding the pathogenesis of "infective MI" may ultimately provide the next generation's means for new therapies, most probably consisting of monoclonal antibodies, efficient antiviral medications, and cell-type-specific antiantigenic blockade or destruction.

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