Pathobiology of Myocardial Necrosis

Bruce F. Waller
Cardiovascular Pathology Registry, St. Vincent Hospital,
Nasser Smith & Pinkerton Cardiology, Inc., Indianapolis,
Indiana, USA

Although there has been a recent decline in the mortality from atherosclerotic coronary heart disease in the United States, this disease continues to be the leading cause of death [1]. Approximately one third of all deaths in the United States are due to atherosclerotic coronary heart disease and of these 50% are attributable to acute myocardial infarction (MI) [3,4]. About 50% of patients with acute MI die within 1 hour of onset of symptoms [2]; most of the remaining patients are admitted to hospitals (738,000 patients in 1986). The mortality rates during hospitalization approximate 15% and are about 10% during the year following acute MI [2,3]. In addition to a high frequency of death within the first year after acute MI, a three- to fourfold excess in the risk of death persists even 10 years postinfarct [5].

Despite the frequency and severity of acute MI, little is known about the events that transform a chronic, stable condition or a totally asymptomatic state into an acute life-threatening illness. It is now recognized that transmural MI is usually preceded by coronary artery thrombosis, which in turn is often associated with disruption of the fibrous cap of the underlying atherosclerotic plaque [6,8].

In view of the continuing importance of this clinical event and recent attempts to reduce infarct size and mortality by restoring blood flow to an acutely occluded artery by various reperfusion therapies, this article reviews the definitions of myocardial necrosis, the currently understood pathogenesis of acute myocardial necrosis (acute MI), and certain aspects of the pathology of acute reperfusion efforts for evolving acute MI.

Definition and Gross and Histologic Changes of Myocardial Necrosis

Necrosis may be defined as an irreversible cellular change or death of all or a group of cells. Myocardial infarction is ischemic coagulative necrosis involving a polymorphonuclear leukocyte response. Gross changes do not appear in the myocardium until about 6 hours after the onset of acute MI. Initially, the involved myocardium is pale, soft, and swollen. At about 18–36 hours after the onset of the infarct, the myocardium appears tan or reddish-purple in color, and the epicardial surface (visceral pericardium) has a fibrinous exudate. (Pericardial involvement implies transmurality of the necrosis.) These changes persist for about 2 days; the infarct becomes gray and yellow lines are seen near the periphery (neutrophilic infiltrate). Eight to 10 days after the onset of acute MI, the wall in the area of the infarct is thinner as necrotic muscle is removed by mononuclear cells. The infarct at this age appears yellow, surrounded by a reddish-purple band (hyperemic zone).

Granulation tissue appears at about 1 week and extends through the necrotic zone by 3–4 weeks. Beginning at about 1 month and continuing over the next 2–3 months, the infarct becomes gray in color and gelatinous in appearance. After several months, the infarct shrinks to a white, thin, firm scar. This healing process begins at the periphery of the infarct and moves centrally. The visceral and parietal pericardial layers become adherent over the infarct, and the endocardium becomes thickened and white below the infarct [2,9–11].

On light microscopy, severe ischemia (potentially reversible) causes cloudy swelling and hydropic degeneration. Cells that are irreversibly damaged (necrotic) exhibit cytoplasmic hypereosinophilia and nuclear pyknosis. Bouchardy and Majno [12] have called attention to a wavy pattern of myocardial cells that presents as early as 1 hour after the onset of acute MI. This pattern is probably the result of stretching of the myocardial fibers during agonial contraction of the myocardial cells. The combination of waviness with cellular hypereosinophilia bordering on a zone of hydropic cell swelling and contraction bands is a diagnostic sign of early infarction. After about 6 hours, interstitial widening (edema) and fatty deposits within the myocyte occur. Also, about 8–10 hours after the onset of acute MI, neutrophile polymorphonuclear leukocytes begin to appear. Focal and mild areas of interstitial erythrocytes appear that extravasate from necrotic interstitial small vessels.

In the absence of acute thrombolytic reperfusion therapy, this interstitial hemorrhage is extremely mild and visible only histologically (i.e., as anemic in-

Address for correspondence: 8333 Naab Road, Suite 400, Indianapolis, IN 46260, USA.
Patterns of Myocardial Necrosis

Three patterns of myocardial necrosis are recognized: coagulation necrosis, contraction band necrosis, and myocytolysis. These patterns have been reviewed by Hutchins [14].

Coagulation necrosis

Coagulation necrosis results from severe, persistent ischemia and is present in the central zone of infarcts. The gross morphologic and light microscopic findings have been described previously.

Contraction band necrosis

Contraction band necrosis (also known as coagulative myocytolysis, reflow necrosis, reperfusion necrosis, and myofibrillar degeneration) results primarily from severe ischemia caused by increased calcium ion influx into dying cells in the contracted state. It may be seen at the edges of large infarcts or may constitute a major portion of the infarct in patients undergoing reperfusion (thrombolytic, surgical) therapy. It is characterized by hypercontracted myofibrils with contraction bands, mitochondrial damage, and marked vascular congestion. Spasm of the coronary arteries may lead to contraction band necrosis [14].

It is now clear that reflow may actually produce further necrosis in addition to simply altering the disposition previously damaged cells [15]. On gross examination, the areas of contraction band necrosis are dark red or hemorrhagic. This appearance is caused by the marked distention of the capillary bed in the injured zone. Since the vascular bed has also been injured, extravasation of red cells frequently occurs (hemorrhagic infarction). The histologic appearance of contraction band necrosis consists of irregular dense transverse masses of contractile elements, with intervening cleared areas of sarcoplasm devoid of cross-striations. The nuclei undergo lysis and disappear after the first day following injury. The inflammatory response and reparative process in contraction band necrosis are presumed to be identical to those described for coagulation necrosis, but no studies are available comparing the final appearance of the healed infarct. This is of particular importance because of the hemorrhagic infarcts seen with current reperfusion therapies for evolving acute MI [15].

Myocytolysis

Myocytolysis (collagative necrosis) results from prolonged moderate ischemia and is seen at the borders or transition zones of an infarct. It also occurs in patchy areas of infarction in patients with chronic ischemic heart disease. Histologically, myocytolysis is characterized by cell swelling, early lysis of myofilaments, late lysis of nuclei, no neutrophilic response, and healing by lysis and phagocytosis of necrotic myocytes [2,9,14].

Location and Classification of Myocardial Infarcts at Necropsy

Anatomically, five items are useful in the description and classification of ventricular myocardial infarcts: (1) transmural/nontransmural (type), (2) anterior/lateral/posterior (location), (3) base/mid/apex (location), (4) left/right/both (location), and (5) acute/healing/healed (stage) [13].

Transmural/nontransmural

Transmural is defined as involvement of greater than the inner half of the ventricular wall. Various definitions of transmural have been proposed varying from one-third, one-half, two-thirds, three-quarters, to “full-thickness” involvement of the ventricular wall. Nontransmural is defined as involvement of less than or equal to the inner half of the ventricular wall or the remaining fraction of ventricular wall in the other definitions of transmural infarction [13].

Anterior/lateral/posterior

Infarcts evaluated in transverse sections (bread-loaf sectioning) localize infarcts to anterior (anteroseptal), lateral (between the anterolateral and posteromedial papillary muscles), or posterior (posteroseptal, true posterior, inferior) positions. At necropsy, all anterior infarcts involve some portion of the ventricular septum and, likewise, all posterior infarcts involved some portion of the septum. Thus, the terms anteroseptal and posteroseptal are somewhat redundant. Crawford [16] reported the frequency of anterior, lateral, or posterior infarcts observed in 100 necropsy specimens with recent acute MI: anterior infarcts occurred in 49%, lateral in 16%, and posterior infarcts in 26%. Ten hearts had circumferential infarcts.